From extension to mid flexion, the medial tibial contact area had a more ovoid shape and moved posteriorly (Figs. 5 and 6). This relative internal rotation of the contact locations was offset by relative external femoral rotation, resulting in less rotation measured at the contact locations than was measured from the bone-embedded coordinate systems over this range. From 20° to 80° flexion the contact locations moved posterior, inclined 15° to 20° with respect to the tibia, maintaining the femur approximately in line with the foot as previously reported.[11] However, unlike previous reports, contact-derived rotation continued from 80° to full flexion in squat and kneel. From 80° to maximum flexion, the contact-derived and rigid body bone rotations showed similar curves, which is reasonable considering the circular geometry of the posterior femoral condyles.[11]

Banks et al.[12] showed kinematics varied with implant design and activity in total knee arthroplasty patients. In this study, kinematics varied with activity in healthy knees, particularly with squat and kneel. The greatest total rotation and the most posterior lateral contact was observed with squatting, but the maximum flexion angle and the rate of tibial rotation from 100° to maximum flexion was greater with kneeling. Medial contact was in the same area for both activities. The lateral femoral condyle translated to the posterior edge of the tibial surface during squat, although there was no subluxation. Subjects were encouraged to achieve comfortable maximum flexion, thus results may have differed if the squat was forced to greater knee flexion.

Comparison of stair climb and squat activities revealed small kinematic differences in the middle range of flexion, which were not statistically significant. The femur showed greater external rotation for all flexion angles during squatting. Results from cadaver studies,[11] MRIs of living knees,[13] and living knees with RSA[14] have shown that a posture with tibial external rotation can suppress tibial internal rotation over the flexion arc. The wider stance width used during the squat activity probably biased the knee toward greater femoral external rotation in the mid range of flexion. Standard deviations for the squat and stair activities were 20% greater than for the kneel activity, suggesting kneeling is more geometrically constrained or stereotypic.

Surface distance calculations revealed only two cases showing evidence of condylar separation, both occurring at terminal flexion in kneeling beyond 150°. In the static MRI study of maximally flexed knees, Nakagawa et al.[15] reported the medial condyle remained positioned over the tibial articular surface but lifted away from it, mechanistically similar to the present finding. Two differences may account for infrequent observation of condylar separation in this study. First, a conservative threshold (95% confidence interval) was used for declaring separation, acknowledging uncertainty accrued from measurement uncertainty, surface modeling errors, and possible cartilage deformation. Second, Nakagawa et al.[15] studied a different activity. In this study, subjects knelt to maximum passive flexion with partial body weight and an upright trunk posture (hip angle approximately 90°). The subjects reported in Nakagawa et al.[15] were supine, with the hip extended in the MRI scanner, similar to an athlete's quadriceps stretching posture. Hip extension might have caused greater quadriceps tension and resulted in a more exaggerated joint posture.

Nakagawa et al.[15] also concluded that the lateral femoral condyle subluxed posteriorly from the tibia at full passive flexion, a phenomenon not seen in the present study. Nakagawa et al.[15] tracked a cylindrical axis embedded in the posterior condyles and determined that subluxation occurred when the lateral axis moved posterior to the tibial surface at 162° flexion. However, subluxation is an articular phenomenon where the surfaces of a joint no longer face each other exactly but remain partially aligned. MR and cryosection pictures in the report of Nakagawa et al.[15] show the lateral femoral condyle has adequate contact with the edge of the tibial articular surface even when the cylindrical axis has exceeded the tibial periphery. These pictures are consistent with the observations of this study.

Findings of articular separation and subluxation in healthy joints sometimes can result from methodological issues and sometimes from articular reality. In the latter case, it these phenomena might be better appreciated as the boundaries of the passive characteristics of the normal healthy joint than negative attributes. For example, the healthy knee has been observed to have articular gaps in 90° of flexion in the medial compartment and in the lateral compartment depending on the posture.[16] The knee joint has long been known to possess an envelope of possible motions that only now are being explored by advanced measurement techniques.

The combination of dynamic imaging with flat-panel detectors and CT/MR bone models provide some novel measurement opportunities. However, refinements and enhancements to the method will expand the range of possible studies. First, the flat-panel detector used for this study provided high spatial resolution but only three images/s. Solid-state detectors now commercially available with 30 images/s capabilities will permit study of highly dynamic activities. Second, single-plane imaging provides tremendous experimental flexibility and relatively large viewing volumes, but suffers from the main limitation of monocular vision—poor sensitivity for motions perpendicular to the image plane, which was approximately 2 mm in our preliminary study using a lower resolution image source.[5] Bi-plane imaging techniques can provide measurements with enhanced precision and more uniform uncertainties when required, but restrict the viewing volume, increase X-ray exposure and at least double the cost. Third, geometric and coordinate alignment errors in the CT and MR models affect the measurement accuracy, and it is well known that MR images/models suffer from geometric distortion.[5] For this reason, CT-derived models were used for 3D-to-2D model-to-image registration, only using the MR-derived models for articular surface analysis once the 3D pose of the bones was determined. In addition, the MR scans were performed nonweight bearing, so the compliant cartilage surfaces presumably were unloaded. Additional measurement uncertainty results when interrogating these cartilage surfaces based on weight-bearing conditions,[17] and the contact locations must be defined conservatively. Fourth, the current approach to analyzing joint contact ignores the menisci, which are invisible on X-ray but obviously affect joint contact and load distribution. There is not currently an X-ray-based technique that will overcome this limitation, but dynamic MR studies can provide this capability.[18] Finally, simple experimental issues limited the range of the current observations. Subjects were instructed to perform the three activities in a natural and comfortable manner, and some subjects extended and/or flexed their knees more than others. The data reported here are limited to the common flexion ranges for the subjects. In summary, the study provides observations of healthy knee kinematics in three different activities over the flexion range from extension to 150° using dynamic imaging with CT/MR-derived models. Future experimental and technical improvements might further expand the range and quality of measurements that can be obtained.

REFERENCES

1. Asano T, Akagi M, Tanaka K, et al. 2001. In vivo three-dimensional knee kinematics using a biplanar image-matching technique. Clin Orthop Relat Res 388:157–166.
2. Komistek RD, Dennis DA, Mahfouz M. 2003. In vivo fluoroscopic analysis of the normal human knee. Clin Orthop Relat Res 410:69–81.
3. Li G, DeFrate LE, Park SE, et al. 2005. In vivo articular cartilage contact kinematics of the knee: an investigation using dual-orthogonal fluoroscopy and magnetic resonance image based computer models. Am J Sports Med 33:102–107.
4. Fregly BJ, Rahman HA, Banks SA. 2005. Theoretical accuracy of model-based shape matching for measuring natural knee kinematics with single-plane fluoroscopy. J Biomech Eng 127:692–699.
5. Moro-oka T, Hamai S, Miura H, et al. 2007. Can MR derived bone models be used for accurate motion measurement with single-plane 3D shape registration? J Orthop Res 7:867–872.
6. Banks SA, Hodge WA. 1996. Accurate measurement of three-dimensional knee replacement kinematics using single-plane fluoroscopy. IEEE Trans Biomed Eng 43:638–649.
7. Tupling SJ, Pierrynowski MR. 1987. Use of cardan angles to locate rigid bodies in three-dimensional space. Med Biol Eng Comput 25:527–532.
8. Adam C, Eckstein F, Milz S, et al. 1998. The distribution of cartilage thickness in the knee-joints of old-aged individuals—measurement by A-mode ultrasound. Clin Biomech (Bristol, Avon) 13:1–10.
9. Koo S, Gold GE, Andriacchi TP. 2005. Considerations in measuring cartilage thickness using MRI: factors influencing reproducibility and accuracy. Osteoarthritis Cartilage 13:782–789.
10. Moglo KE, Shirazi-Adl A. 2005. Cruciate coupling and screw-home mechanism in passive knee joint during extension–flexion. J Biomech 38:1075–1083.
11. Iwaki H, Pinskerova V, Freeman MA. 2000. Tibiofemoral movement 1: the shapes and relative movements of the femur and tibia in the unloaded cadaver knee. J Bone Joint Surg Br 82:1189–1195.
12. Banks SA, Hodge WA. 2004. 2003 Hap Paul Award Paper of the International Society for Technology in Arthroplasty. Design and activity dependence of kinematics in fixed and mobile-bearing knee arthroplasties. J Arthroplasty 19:809–816.
13. Hill PF, Vedi V, Williams A, Iwaki H, et al. 2000. Tibiofemoral movement 2: the loaded and unloaded living knee studied by MRI. J Bone Joint Surg Br 82:1196–1198.
14. Karrholm J, Brandsson S, Freeman MA. 2000. Tibiofemoral movement 4: changes of axial tibial rotation caused by forced rotation at the weight-bearing knee studied by RSA. J Bone Joint Surg Br 82:1201–1203.
15. Nakagawa S, Kadoya Y, Todo S, et al. 2000. Tibiofemoral movement 3: full flexion in the living knee studied by MRI. J Bone Joint Surg Br 82:1199–1200.
16. Tokuhara Y, Kadoya Y, Nakagawa S, et al. 2004. The flexion gap in normal knees. An MRI study. J Bone Joint Surg Br 86:1133–1136.
17. Forster H, Fisher J. 1996. The influence of loading time and lubricant on the friction of articular cartilage. Proc Inst Mech Eng [H] 210:109–119.
18. Sheehan FT, Zajac FE, Drace JE. 1999. In vivo tracking of the human patella using cine phase contrast magnetic resonance imaging. J Biomech Eng 121:650–656.

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ORIGINAL ARTICLE

Evaluation of Skills in Arthroscopic Training Based on Trajectory and Force Data

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Abstract Objective evaluation of surgical skills is essential for an arthroscopic training system. We asked whether a quantitative assessment of arthroscopic skills using scores, time to completion, instrument tip trajectory data, and force data was valid. We presumed more experienced surgeons would perform better on a simulated arthroscopic procedure than novices, therefore validating the quantitative assessment. Surgical trainees (n = 12), orthopaedic residents (n = 12), and experienced arthroscopic surgeons (n = 6) were tested on a Sawbones® knee simulator. Subjects performed a joint inspection and probing task and a partial meniscectomy task. The trajectory data were measured using an electromagnetic motion tracking system and the force data were measured using a force sensor. The experienced group performed both tasks with higher scores and more quickly than the less experienced groups. The path length of the probe and the scissors was substantially shorter and the probe velocity was considerably faster in the experienced group. The trainee group applied substantially stronger forces to the joint during the joint inspection and probing task. Our data suggest a performance assessment using an electromagnetic motion tracking system and a force sensor provides an objective means of evaluating surgical skills in an arthroscopic training system.

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Introduction

Arthroscopic surgery has become more common among patients and orthopaedic surgeons in recent years. This surgical technique offers benefits of less trauma, reduced pain, and quick recovery for patients. Diagnostic accuracy and therapeutic efficacy are major characteristics of this technique. However, arthroscopic procedures demand highly developed psychomotor skills, because observation of the field is limited and the ability to manipulate instruments is less than in traditional open surgery. Surgeons must be able to perceive a three-dimensional environment from a two-dimensional camera image and handle the equipment skillfully. Therefore, it is important for arthroscopic trainees to improve their surgical skills and understand their skill levels objectively to safely and effectively perform arthroscopic surgery.

Arthroscopic training and skill assessment with cadavers, animals, or direct observation are limited because of ethical restrictions and low availability [3, 10, 16]. Therefore, numerous investigators have developed virtual reality simulators for arthroscopy [1, 2, 4, 6, 8, 9, 12, 15]. A knee arthroscopy instructional course has been available at the Kyushu University Training Center for Minimally Invasive Surgery since 2005. A critical challenge for surgical education is to objectively evaluate the skill levels of surgical trainees [2, 8, 9, 12, 15]. Assessing the instrument tip trajectory reportedly is useful in training for laparoscopic surgery [5, 11]. Measurement with a force and torque sensor is similarly useful to evaluate skills in endoscopic sinus surgery and laparoscopic surgery training [13, 14, 19].

We asked whether quantitative evaluation using these scores (ie, the score representing the number of figures touched in the time limit in a joint inspection and probing task, and the scores from a partial meniscectomy task), time to completion, instrument tip trajectory data, and force data would be useful to distinguish levels of skill in arthroscopic surgery. We hypothesized more experienced surgeons would have better motor performance in a simulated arthroscopic procedure than individuals with less experience with the technique.

Materials and Methods

We identified three groups of volunteers with different stages of arthroscopic skills. Group 1 consisted of surgical trainees who had observed but had not performed any arthroscopies (n = 12), Group 2 consisted of orthopaedic residents with 10 to 20 cases of actual arthroscopic operations (n = 12), and Group 3 were experienced arthroscopic surgeons (n = 6). All performed two kinds of simulated arthroscopic tasks. Quantitative data of scores, time to completion, instrument tip trajectory, and surgical force were obtained and differences among the three groups were examined. The parameters with a difference in accordance with the surgical skills were regarded to be valid in distinguishing levels of arthroscopic surgical skills. A power analysis was performed based on the path length data of the arthroscope in our preliminary research (a difference in the mean = 2200 mm, the standard deviation = 1500 mm, significant level = 0.05, and power = 0.80) to indicate a sample size of 9.7 in each group could address the questions.

We used an electromagnetic motion tracking system to measure the path length and velocity of the arthroscope and probe and scissors. The Aurora measurement system (Northern Digital Inc, Waterloo, Canada) is designed to calculate the position and orientation of sensor coils (Fig. 1). The field generator creates an electromagnetic field with a characterized volume of 500 mm × 500 mm × 500 mm. Sensor coils react to the electromagnetic field and produce signals. The sensor interface unit transmits the signals to the system control unit. The system control unit calculates the position and orientation of the sensor coils based on these data and communicates the results to the host computer. The system can determine five degrees of freedom for each sensor coil tool except the rotation around the sensor coil's z-axis. It has a maximum measurement rate of 45 Hz if measured with five or less sensor coils. In this experiment, we attached the sensor coils to the shaft of the operative instrument.

Fig. 1 An electromagnetic measurement system is shown. The field generator creates a measurement volume of 500 mm × 500 mm × 500 mm. Sensor coils are attached to the surgical instrument.

We used a force analysis system to estimate the degree of surgical forces administered during operative procedures. The six degrees of freedom force sensor (Nitta Co, Osaka, Japan) provides three force measurements along three orthogonal axes and three torque measurements along the same axes. It is connected to an interface unit, which consists of an analog-to-digital converter and an amplifier. This interface unit is connected to the host computer. The sensor detects values (forces F_x, F_y, F_z; torques M_x, M_y, M_z) concurrently with a sampling frequency of 8 kHz and outputs the data set every 125 μs. We fixed the force sensor beneath the knee model in the training center (Fig. 2). Zero point adjustment can be completed in approximately 5 seconds before the measurement. Once surgical forces are loaded on the joint model, the output of the force sensor is digitized and recorded by the host computer and then shown in real time on a computer display. We used only the data sets of three forces in this study because the load center of surgical force, which was located in front of the origin of coordinates, varied according to each procedure.

After orientation and 5 minutes of practice, subjects performed two kinds of tasks designed to assess the core psychomotor skills needed in arthroscopy. The tasks were

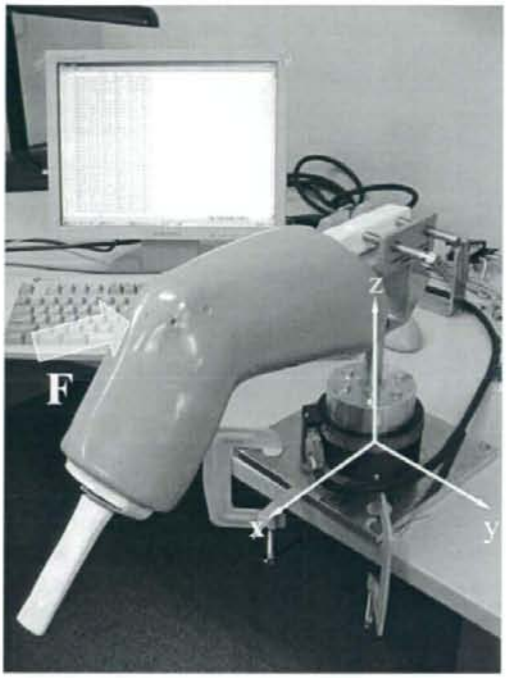


Fig. 2 A six degrees of freedom force sensor is fixed beneath the knee model. This sensor detects surgical forces loaded on the joint, providing the data set of forces F_x, F_y, and F_z and torques M_x, M_y, and M_z.

performed using the Sawbones® knee simulator (Pacific Research Laboratories Inc, Vashon, WA). Task 1 was a joint inspection and probing task. Subjects handled the scope and probe to touch the figures located variously in the joint. A total of 10 figures were placed. This task was limited to 5 minutes. Task 2 was a partial meniscectomy task. The amount of meniscus to be removed was indicated with a line in advance and subjects performed the resection along the line. An excessive resection was indicated with a red line. Task 2 had a limit of 6 minutes. The score in Task 1 was the number of figures touched within the time limit. Scores in Task 2 were graded as excellent, good, fair, or poor for each skill regarding the adequacy of the amount and smoothness of the margin in resection. The computer calculated the following parameters: time to complete each task, trajectory data of the tip of the surgical instruments, and force data. We assessed three indices of force exerted: (1) peak value; (2) average value; and (3) integration of the absolute values.

To determine the differences in the continuous variables (such as scores in Task 1, time to completion, instrument tip trajectory data, and force data) among the three groups, we used a one-way factorial ANOVA with Fisher's protected least significant difference post hoc test. Differences in the discrete variables (scores in Task 2) among the three groups were determined by the Kruskal-Wallis test, Mann-Whitney U test, and Bonferroni correction. Differences in the motor performance on a simulated arthroscopic procedure, in accordance with subjects' surgical skills, was regarded as validation of the quantitative evaluation method.

Results

The expert group obtained better scores ($p = 0.014$) than the resident group, and the resident group obtained better scores ($p = 0.003$) than the trainee group in Task 1 (Table 1). In Task 2, the expert and the resident groups

Table 1. Results of Task 1

Parameter	Group 1 12	Group 2 12	p Value	Group 3 6	p Value
Score	2.5 ± 2.6	6.3 ± 3.6	$0.003^{*,\ddagger}$	10 ± 0	$0.000^{**,\ddagger}$; $0.014^{\dagger,\ddagger}$
Time (seconds)	300 ± 0	287.8 ± 22.9	0.292^{*}	198.8 ± 54.8	$0.000^{**,\ddagger}$; $0.000^{\dagger\ddagger}$
Path length of the scope (mm)	7978 ± 2604	6348 ± 1239	$0.043^{*,\ddagger}$	3815 ± 912	$0.000^{**,\ddagger}$; $0.012^{\dagger,\ddagger}$
Velocity of the scope (mm/second)	26.6 ± 8.7	22.2 ± 4.7	0.111^{*}	21.5 ± 4.7	0.130^{**}; $0.828^{\dagger}$
Path length of the probe (mm)	1262 ± 442	996 ± 420	0.109^{*}	485 ± 134	$0.001^{**,\ddagger}$; $0.015^{\dagger,\ddagger}$
Velocity of the probe (mm/second)	13.6 ± 9.5	18.1 ± 8.5	0.201^{*}	27.1 ± 4.1	$0.003^{**,\ddagger}$; $0.040^{\dagger,\ddagger}$
Peak force (N)	15.6 ± 6.2	18.2 ± 8.7	0.366^{*}	11.7 ± 4.3	0.279^{**}; $0.074^{\dagger}$
Average force (N)	3.4 ± 1.0	3.3 ± 1.1	0.652^{*}	2.4 ± 0.5	$0.049^{**,\ddagger}$; $0.102^{\dagger}$
Integration of force (N second)	1030 ± 310	924.2 ± 285.9	0.357^{*}	455 ± 139	$0.000^{**,\ddagger}$; $0.002^{\dagger,\ddagger}$

Group 1 = surgical trainees; Group 2 = orthopaedic residents; Group 3 = experienced arthroscopic surgeons; mean ± standard deviation; *p value for the comparison of Groups 1 and 2; **p value for the comparison of Groups 1 and 3; †p value for the comparison of Groups 2 and 3; ‡Significant difference.

Table 2. Results of Task 2

Parameter	Group 1 12	Group 2 12	p Value	Group 3 6	p Value
Time (seconds)	360 ± 0	339.6 ± 34.0	0.212*	298.5 ± 75.7	0.004**,‡; 0.045†,‡
Path length of the scope (mm)	2257 ± 1066	4727 ± 1028	0.014*,‡	4894 ± 1717	0.021**,‡; 0.785†
Velocity of the scope (mm/second)	9.3 ± 3.0	14.1 ± 3.7	0.006*,‡	16.7 ± 4.7	0.001**,‡; 0.174†
Path length of the scissors (mm)	12845 ± 3032	10829 ± 1522	0.042*,‡	9661 ± 1848	0.010**,‡; 0.321†
Velocity of the scissors (mm/second)	35.7 ± 8.4	32.0 ± 4.1	0.175*	33.4 ± 6.1	0.496**; 0.658†
Peak force (N)	17.9 ± 6.6	26.3 ± 6.8	0.004*,‡	22.7 ± 6.0	0.154**; 0.285†
Average force (N)	4.0 ± 1.4	4.4 ± 1.0	0.394*	4.4 ± 1.0	0.427**; 0.921†
Integration of force (N·second)	1433 ± 493	1497 ± 395	0.741*	1372 ± 571	0.798**; 0.600†

Group 1 = surgical trainees; Group 2 = orthopaedic residents; Group 3 = experienced arthroscopic surgeons; mean ± standard deviation; *p value for the comparison of Groups 1 and 2; **p value for the comparison of Groups 1 and 3; †p value for the comparison of Groups 2 and 3; ‡Significant difference.

obtained better scores than the trainee group in adequacy of the resection (p = 0.003 for Group 1 vs 3; p = 0.029 for Group 1 vs 2) and smoothness of the margin (p = 0.011 for Group 1 vs 3; p = 0.004 for Group 1 vs 2), but we observed no difference in scores between the expert and resident groups (Fig. 3).

The expert group completed the procedures more quickly than the two less experienced groups in Task 1 (p = 0.000 for Group 1 vs 3; p = 0.000 for Group 2 vs 3) (Table 1) and Task 2 (p = 0.004 for Group 1 vs 3; p = 0.045 for Group 2 vs 3) (Table 2). We observed no difference in the mean time needed for each task between the resident and trainee groups.

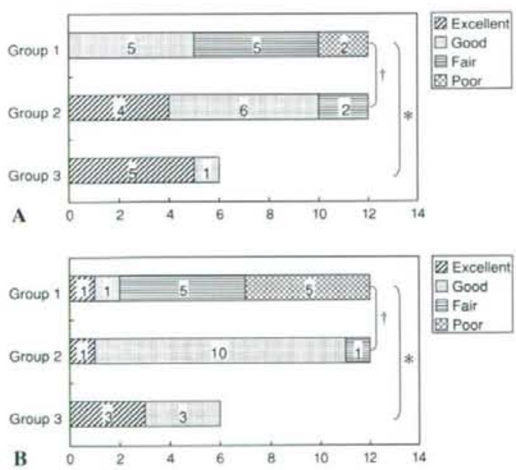


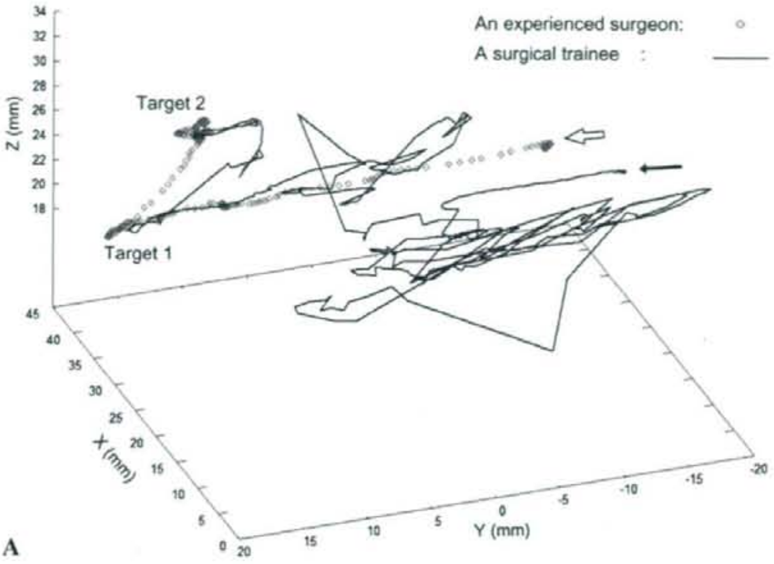
Fig. 3A–B (**A**) Scores for adequacy of the resection in Task 2, the meniscectomy task, are shown. The experienced surgeons (Group 3) and the orthopaedic residents (Group 2) showed better (*: p = 0.003; †: p = 0.029) performance than the surgical trainees (Group 1). (**B**) Scores for smoothness of the margin in Task 2 show Groups 2 and 3 obtained better (*: p = 0.011; †: p = 0.004) scores than Group 1.

In Task 1, the path length of the scope was shorter (p = 0.012) in the expert group than in the resident group and shorter (p = 0.043) in the resident group than in the trainee group, whereas the velocity of the scope was similar (p = 0.180) among the three groups. The path length of the probe was shorter (p = 0.001 for Group 1 vs 3; p = 0.015 for Group 2 vs 3) (Fig. 4A) and the velocity of the probe was faster (p = 0.003 for Group 1 vs 3; p = 0.040 for Group 2 vs 3) in the expert group than in the two less experienced groups (Table 1). In Task 2, the path lengths of the scope were longer (p = 0.021 for Group 1 vs 3; p = 0.014 for Group 1 vs 2) and the velocities of the scope were faster (p = 0.001 for Group 1 vs 3; p = 0.006 for Group 1 vs 2) in the expert and resident groups than in the trainee group (Fig. 4B) The path lengths of the scissors in the expert and resident groups were shorter (p = 0.010 for Group 1 vs 3; p = 0.042 for Group 1 vs 2) than that of the trainee group. The velocities of the scissors were similar (p = 0.389) among the three groups (Table 2).

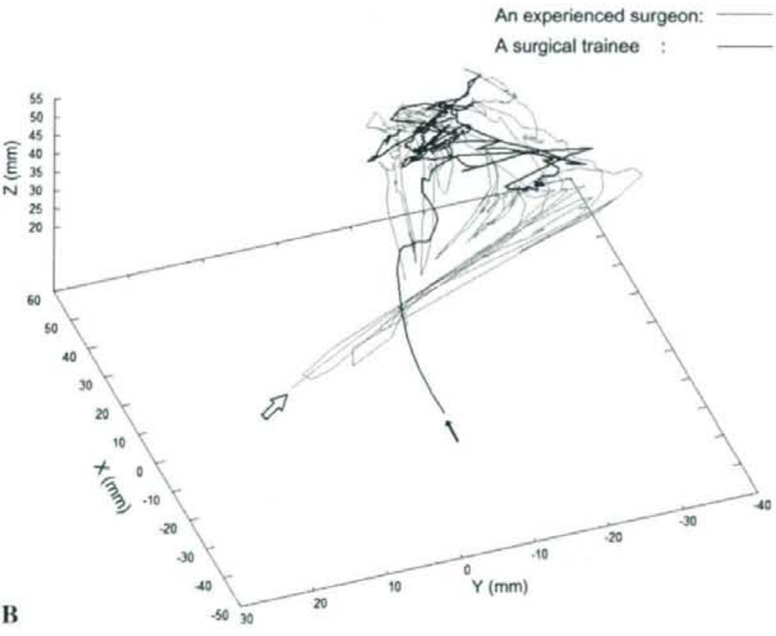
The integrated force values applied by the expert group were lower (p = 0.000 for Group 1 vs 3; p = 0.002 for Group 2 vs 3) in Task 1 than those applied by the two less experienced groups (Table 1; Fig. 5). In Task 2, the peak force applied by the resident group was higher (p = 0.004) than that of the trainee group (Table 2). However, the average (p = 0.613) and integration (p = 0.862) of the force values were similar among the three groups (Table 2).

Discussion

Advances in arthroscopic surgical technique have revolutionized the diagnostic accuracy and therapeutic efficacy



A



B

Fig. 4A–B (**A**) The probe tip trajectories of an experienced surgeon (dotted line) and a surgical trainee (full line) for Task 1 are shown. The probe path length of the experienced surgeon is considerably shorter and smoother than that of the trainee. (**B**) The scope tip trajectories of an experienced surgeon (thin line) and a surgical trainee (thick line) in Task 2 are shown. The experienced surgeon manipulated the scope more for better observation.

for intraarticular disorders [12, 17]. Although arthroscopic procedures demand highly developed psychomotor skills, the opportunity for orthopaedic trainees to learn those skills is limited and a means of objectively evaluating the skill levels of surgical trainees has not been established. This study was designed to clarify whether quantitative evaluation of arthroscopic surgical skills using scores, time to completion, instrument tip trajectory data, and force data was valid. We hypothesized more experienced surgeons therefore would obtain higher scores, complete tasks more

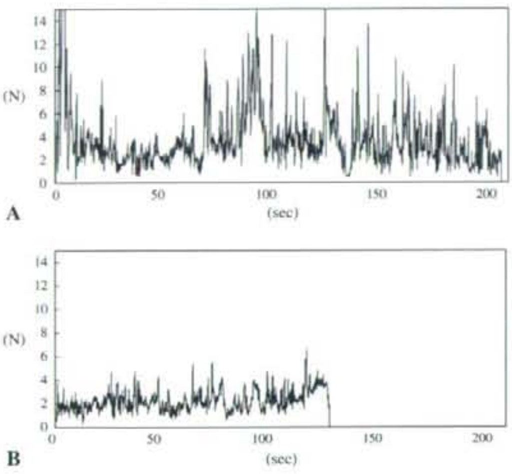


Fig. 5A–B (A) The time-series data of the output of a force sensor for a trainee are shown. Many large spikes are seen. (B) The force data of an experienced surgeon show time to completion is shorter and the forces are lower than those for the trainee.

quickly, and manipulate surgical devices more smoothly without loading any excessive forces on tissues in a simulated arthroscopic procedure than individuals with less experience, and this difference thus would validate the objective evaluation method.

One of the limitations of this study was simulated arthroscopic procedures were performed with Sawbones® physical knee models. Fresh cadavers would be more desirable to train and assess surgical skills of trainees outside the operating room, however, ethical restrictions and limited availability make use of cadavers difficult. To assess improvement of actual surgical skills of a person, a skill evaluation would be needed after he or she had gained a certain amount of real surgical experiences. However, the differences in motor performance depending on the real surgical experience suggest the evaluation method is valid and reliable. We had subjects perform only two kinds of tasks to assess their arthroscopic skills, although there are various situations and numerous techniques in arthroscopic surgery. We believe a simplified method would be more suitable for skill evaluation in surgical training than a complex and time-consuming one. A convenient means of discriminating surgical skills is needed in surgical education.

The score on Task 1 increased according to the surgical experience of the subjects. The score on Task 2 discriminated the more experienced two groups from the less experienced group. Previous studies suggest scoring surgical performance on simulated tasks is useful to assess surgical skills [7, 11, 15].

The experienced group performed both tasks more quickly than the two less experienced groups. Time to completion has been a popular parameter to evaluate surgical skills in arthroscopic and endoscopic training [2, 8, 12, 15, 18], although it cannot clarify the details of psychomotor skills in which the trainee lacks. These results of score and time data support the hypothesis that individuals with more experience in performing actual arthroscopic procedures also will perform better in simulated tasks.

An analysis of the trajectory data suggests experts manipulate the probe more smoothly and quickly than less experienced surgeons. Compared with experienced surgeons, the trainees had more unnecessary movements of the scissors. Similar results were reported in an evaluation study with a virtual reality simulator for shoulder arthroscopy. In that study, the probe path length of specialists was less than half as long as that of novices with no prior experience, and also shorter than that of residents with some experience [2]. Gomoll et al. also reported the probe velocity of specialists was almost double that of novices [2]. Another study with a shoulder arthroscopy simulator reported probe path lengths of experienced surgeons were shorter than those of trainees and residents [12]. A shorter path of the scope during a joint inspection and probing task, depending on surgical experience, suggests smoothness in handling the scope by more skillful surgeons. A validation study for a knee simulator suggested more experienced surgeons had substantially shorter scope path lengths during a loose body searching task, which required similar techniques as our joint inspection and probing task [9]. In Task 2, however, the positional data of the scope did not match this tendency. This suggests an increased trajectory of the scope does not mean more unnecessary movement in a task such as a meniscectomy, which demands different procedures from the joint inspection task. In fact, with Task 2, experienced surgeons tended to change their vantage points with freedom to make the meniscectomy work easier (Fig. 4B).

Force analysis is reportedly valuable to assess interference between surgical tools and tissues [13, 14, 19]. A previous study using a force sensor for an endoscopic sinus surgery training system proposed the peak as the instantaneous strong force, the average as the average force on the tissue, and the integration as the total force on the tissue during the tasks [19]. We found the integration of force by the two less experienced groups to be higher than values of experienced surgeons in the joint inspection and probing task. These forces were believed unnecessary, because the experienced surgeons used no such excessive forces. The use of excessive force might cause damage to the articular cartilage and soft tissues. However, force indices for Task 2 showed no differences between experienced surgeons and the two less experienced groups. The difficulty in distinguishing harmful from harmless contact would be the reason for this result. In one study, high force magnitudes were applied by novice surgeons in comparison to expert surgeons while performing tissue manipulation and vice versa in tasks involving tissue dissection [14]. Even useful manipulation of tools, such as repetitively cutting the meniscus, was detected as a harmful contact with the tissue, because the force sensor fixed beneath the joint model sensed the entire power loaded to the joint. A study evaluating a virtual reality simulator for shoulder arthroscopy also reported some of the useful probe contacts were potentially harmful collisions [15]. A force analysis system is required to improve the discrimination to resolve this problem.

It is important to assess the skill levels of surgical trainees. An objective evaluation system helps surgeons understand their degree of improvement and which technique they need to improve. We found score and time to task completion clearly discriminated the performance of the operators depending on their surgical experience. The path lengths of the probe and scissors by the experienced surgeons were shorter than those of the less experienced. The force analysis system detected excessive interference between the surgical tools and tissues for the joint inspection and probing task. Our data suggest this quantitative method of evaluating arthroscopic surgical skills using scores, time to completion, an electromagnetic motion tracking system, and a force sensor distinguish the level of surgical skill in an arthroscopic training system.

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References

1. Cannon WD, Eckhoff DG, Garrett WE Jr, Hunter RE, Sweeney HJ. Report of a group developing a virtual reality simulator for arthroscopic surgery of the knee joint. *Clin Orthop Relat Res* 2006;442:21–29.
2. Gomoll AH, O'Toole RV, Czarnecki J, Warner JJ. Surgical experience correlates with performance on a virtual reality simulator for shoulder arthroscopy. *Am J Sports Med.* 2007;35:883–888.
3. Grechenig W, Fellinger M, Fankhauser F, Weiglein AH. The Graz learning and training model for arthroscopic surgery. *Surg Radiol Anat.* 1999;21:347–350.
4. Heng PA, Cheng CY, Wong TT, Wu W, Xu Y, Xie Y, Chui YP, Chan KM, Leung KS. Virtual reality techniques: application to anatomic visualization and orthopaedics training. *Clin Orthop Relat Res.* 2006;442:5–12.
5. Leong JJ, Nicolaou M, Atallah L, Mylonas GP, Darzi AW, Yang GZ. HMM assessment of quality of movement trajectory in laparoscopic surgery. *Comput Aided Surg.* 2007;12:335–346.
6. Mabrey JD, Gillogly SD, Kasser JR, Sweeney HJ, Zarins B, Mevis H, Garrett WE Jr, Poss R, Cannon WD. Virtual reality simulation of arthroscopy of the knee. *Arthroscopy.* 2002;18:E28.
7. Martin JA, Regehr G, Reznick R, MacRae H, Murnaghan J, Hutchison C, Brown M. Objective structured assessment of technical skill (OSATS) for surgical residents. *Br J Surg.* 1997;84:273–278.
8. McCarthy A, Harley P, Smallwood R. Virtual arthroscopy training: do the "virtual skills" developed match the real skills required? *Stud Health Technol Inform.* 1999;62:221–227.
9. McCarthy AD, Moody L, Waterworth AR, Bickerstaff DR. Passive haptics in a knee arthroscopy simulator: is it valid for core skills training? *Clin Orthop Relat Res.* 2006;442:13–20.
10. Morris AH, Jennings JE, Stone RG, Katz JA, Garroway RY, Hendler RC. Guidelines for privileges in arthroscopic surgery. *Arthroscopy.* 1993;9:125–127.
11. Munz Y, Kumar BD, Moorthy K, Bann S, Darzi A. Laparoscopic virtual reality and box trainers: is one superior to the other? *Surg Endosc.* 2004;18:485–494.
12. Pedowitz RA, Esch J, Snyder S. Evaluation of a virtual reality simulator for arthroscopy skills development. *Arthroscopy.* 2002;18:E29.
13. Rosen J, Hannaford B, MacFarlane MP, Sinanan MN. Force controlled and teleoperated endoscopic grasper for minimally invasive surgery: experimental performance evaluation. *IEEE Trans Biomed Eng.* 1999;46:1212–1221.
14. Rosen J, Hannaford B, Richards CG, Sinanan MN. Markov modeling of minimally invasive surgery based on tool/tissue interaction and force/torque signatures for evaluating surgical skills. *IEEE Trans Biomed Eng.* 2001;48:579–591.
15. Srivastava S, Youngblood PL, Rawn C, Hariri S, Heinrichs WL, Ladd AL. Initial evaluation of a shoulder arthroscopy simulator: establishing construct validity. *J Shoulder Elbow Surg.* 2004;13:196–205.
16. Voto SJ, Clark RN, Zuelzer WA. Arthroscopic training using pig knee joints. *Clin Orthop Relat Res.* 1988;226:134–137.
17. Yamaguchi K, Ball CM, Galatz LM. Arthroscopic rotator cuff repair: transition from mini-open to all-arthroscopic. *Clin Orthop Relat Res.* 2001;390:83–94.
18. Yamaguchi S, Konishi K, Yasunaga T, Yoshida D, Kinjo N, Kobayashi K, Ieiri S, Okazaki K, Nakashima H, Tanoue K, Maehara Y, Hashizume M. Construct validity for eye-hand coordination skill on a virtual reality laparoscopic surgical simulator. *Surg Endosc.* 2007;21:2253–2257.
19. Yamauchi Y, Yamashita J, Morikawa O, Hashimoto R, Yokoyama K. An endoscopic sinus surgery training system for assessment of surgical skill. *Stud Health Technol Inform.* 2004;98:416–418.

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The Knee

Varus–valgus laxity correlates with pain in osteoarthritis of the knee

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ABSTRACT

Pain during osteoarthritis (OA) of the knee does not necessarily correlate with the severity of the radiographic grade, and the mechanism of pain has not been completely clarified. The purpose of this study was to evaluate risk factors for pain in the knee OA using epidemiologic analyses.
We evaluated 518 out of 4183 people over the age of 40 (156 males and 362 females) from Shinyoshitomi village, Japan. Mean ages were 63.8 years for men and 60.7 years for women. Screening included a physical examination of the knee and a standing AP roentgenogram of the bilateral knee. Radiographic OA was defined as a Kellgren–Lawrence grade 2 or higher. All data were coded and pain risk factors were evaluated using a multiple logistic regression model.
Radiographic OA was observed in 18.4% of men and 26% of women. Of these subjects with OA, 10.9% of men and 32.5% of women complained of knee pain. Seven factors—age, gender, BMI, radiographic grade, varus–valgus laxity, torque of quadriceps muscles, and varus–valgus alignment—were evaluated as potential risk factors for pain. A significant increase in the odds ratio was observed with varus–valgus laxity ($p = 0.005$; odds ratio, 3.04). Our results suggest that varus–valgus laxity is a risk factor for pain during knee OA.

1. Introduction

It is well recognized that pain during knee osteoarthritis (OA) does not necessarily correlate with the severity of the radiographic grade of OA [1]. In spite of severe radiographic OA, some patients, more often men than women, show no pain or mild pain [2,3]. A direct relationship between measures of severity of radiographic knee OA and pain or functional disability has been described by some [4], but not all authors[5,6].

There are various conjectures concerning the etiology of knee pain during OA, but the mechanism of pain has not been completely clarified. Intraosseous hypertension is one factor that has been associated with a deep aching bone pain, particularly at rest [7]. Tissues in the knee that possess nociceptors include the joint capsule, ligaments, synovium, bone, and the outer edge of the menisci [8].

As pain in knee OA occurs predominantly during gait and stair climbing, dynamic factors such as instability or thrust may contribute to pain. A relationship between varus–valgus laxity and progression of OA has been shown [9,10]. However, only a few attempts have been made at characterizing the relationship between laxity and pain. Gibson et al. described that no relationship could be demonstrated between knee pain and joint laxity from their population study in Pakistan [11].

The purpose of this study, therefore, was to evaluate risk factors for pain during knee OA. Towards this end, we investigated the relevance of laxity on pain during knee OA using epidemiologic analyses. The null hypothesis is that the presence of varus–valgus laxity does not influence pain in knee osteoarthritis.

2. Materials and methods

In October 2000 and March 2001, the Survey of Bone and Joint Diseases, which focused on disorders such as knee OA, degenerative spinal disorders, and osteoporosis, was conducted in a rural community. The population of this community was estimated at 4240. A total of 518 subjects (156 men and 362 women), ranging in age between 24 and 87 years, voluntarily participated in this survey which was performed in concert with cancer screening to prevent a self-selection bias of the participants. The mean age was 63.8 years old [standard deviation (SD): 9.9] for men and 60.7 years old (SD: 10.9) for women.

A physical examination of the knee including knee laxity, and varus–valgus deformity was conducted for each subject. Knee laxity was manually evaluated by the one examiner who had more than 20 years of experience in knee surgery. The examiner was blinded to the radiographic data. For assessment of varus–valgus laxity, varus and valgus stress was applied manually with the knee flexed at 20 degrees while subjects were in supine position, and for evaluation of

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Table 1
Incidence of pain and laxity

	Knees	Pain +	V–v laxity +	A–p laxity +
Men				
OA +	46	5 (10.9%)	6 (13.0%) *	1 (2.2%)
OA −	204	25 (12.3%)	18 (8.8%)	0 (0.0%)
Subtotal	250	30 (12.0%)	24 (9.6%)	1 (0.4%)
Women				
OA +	169	55 (32.5%)	82 (48.5%) *	2 (1.2%)
OA −	481	36 (7.5%)	69 (14.3%)	0 (0.0%)
Subtotal	650	91 (14.0%)	151 (23.2%)	2 (0.03%)
Total	900	121 (13.4%)	175 (19.4%) 3	(0.03%)

V–v: varus–valgus, a–p: antero–posterior, *$p<0.0001$.

antero–posterior laxity, the Lachman test and posterior drawer test were performed. The joint laxity in one knee was compared with that of the opposite side. An AP standing radiogram of both knees was taken. A physical test of isometric quadriceps strength measured by a hand-held dynamometer was performed on each subject.

Of these parameters, the AP standing radiogram of the knees, manual joint test for varus–valgus and antero–posterior laxity, varus–valgus deformity, measurement of quadriceps torque, and assessment of current gait pain in the knees were used for this study. Two orthopaedic surgeons with more than 10 years of experience, who were blinded to the data of the physical examination, did the grading of the X-rays using the Kellgren–Lawrence radiographic classification. Knee OA was defined as a Kellgren–Lawrence score greater than grade 2 [12]. Knee laxity was graded manually as −, ±, +, ++. Laxity more than + was defined as "loose" and laxity less than ± was defined as "normal". The varus–valgus deformity was graded as −, +.

Chi-square test and a multiple logistic regression model were used for statistical analysis. The level of absolute statistical significance was set at $p<0.05$. We examined the association between pain and various factors using bivariate regression analyses. A statistical significance level of $p<0.10$ was used as a screening cutoff.

3. Results

A total of 900 knees from 450 subjects (125 men and 325 women) with valid knee X-ray data were analyzed. Radiographic knee OA was observed in 46 knees (18.4%) of men and in 169 knees (26%) of women. In men, knee pain was reported in 25 knees (12.3%) out of the 204 knees without radiographic OA as well as in five knees (10.9%) out of the 46 knees with radiographic OA. In women, knee pain was reported in 36 knees (7.5%) out of the 481 knees without radiographic OA and in 55 knees (32.5%) out of the 169 knees with radiographic OA. The incidence of reported knee pain associated with radiographic OA was significantly greater in women than in men ($p<0.01$).

Varus–valgus laxity was observed in 24 knees (9.6%) of men and 151 knees (23.2%) of women in total. Of these, varus–valgus laxity was observed in six knees (13%) of men and 82 knees (48.5%) of women with actual radiographic OA. The incidence of varus–valgus laxity associated with radiographic OA was significantly greater in women than in men ($p<0.0001$). Antero–posterior laxity was observed only in one knee of men and two knees of women. No significant gender difference in antero–posterior laxity was found (Table 1).

Seven factors—age, gender, body mass index (BMI), radiographic grade, varus–valgus laxity, torque of quadriceps muscles, and varus–valgus alignment—were evaluated by a multiple logistic regression model as possible risk factors for knee pain. A significant increase in the odds ratio of knee pain was only observed with varus–valgus laxity [$p=0.005$; odds ratio, 3.04 (95% CL: 1.41–6.54)] (Table 2).

Table 2
Risk factors for pain in knee OA

	p value	Odds ratio (95% CI)	
Age	0.682	1.01	(0.96–1.06)
Gender	0.246	0.48	(0.14–1.65)
BMI	0.228	1.08	(0.95–1.23)
Radiographic grade	0.267	1.34	(0.80–2.25)
Varus–valgus laxity	0.005	3.04	(1.41–6.54)
Torque of quadriceps	0.316	1.00	(0.99–1.00)
Varus–valgus alignment	0.058	2.00	(0.98–4.10)

Table 3
Risk factors for varus–valgus laxity

	p value	Odds ratio (95% CI)	
Age	0.066	1.05	(1.00–1.10)
Gender	0.007	0.18	(0.05–0.61)
BMI	0.414	1.06	(0.93–1.21)
Radiographic grade	0.006	2.14	(1.24–3.70)
Torque of quadriceps	0.190	1.00	(0.99–1.00)
Varus–valgus alignment	<0.0001	6.10	(3.12–11.93)

Six factors—age, gender, BMI, radiographic grade, torque of quadriceps muscles and varus–valgus alignment—were evaluated as possible risk factors for varus–valgus laxity. A significant increase in the odds ratio of such laxity was observed with female gender, radiographic grade, and varus–valgus alignment (Table 3).

4. Discussion

Static factors such as knee alignment affect progression and functional decline in knee OA [13,14]. However, several authors suggest that varus–valgus laxity is related to the development and progression of knee OA. Wada et al. reported that varus–valgus laxity tends to increase with the severity of disease [9], and Sharma et al. demonstrated that a portion of increasing laxity of the knee precedes disease development and may in fact predispose individuals to disease [10]. Moreover, dynamic factors such as varus thrust are important in the progression of OA. In fact, Chen et al. have asserted that knees with a thrust are a subset of varus-aligned knees that are at particularly high risk for progression of OA [15]. This study shows a relationship between varus–valgus malalignment and varus–valgus laxity. Repetitive stretching of the collateral ligament due to malalignment increases capsulo–ligamentous laxity.

On the other hand, the relationship between OA and pain has not been clearly defined. It is clinically well recognized that even severe OA of the knee is not necessarily associated with severe knee pain [1]. Cicuttini et al. [5] reported that the presence of osteophytes predicts pain more accurately than a radiographic grade of severity, while the presence or absence of joint space narrowing in antero–posterior, lateral and skyline radiological views of the knee does not correlate with knee pain. Bruyere et al. [6], on the other hand, have suggested that radiographic and clinical progression of disease is significantly associated with knee pain. The clinical relevance of this association, however, is questionable.

Because varus–valgus laxity is thought to be intimately related to the onset and progression of knee OA [9,10,15], we hypothesized that pain in knee OA occurs when varus–valgus laxity is present. In this study, we demonstrate that varus–valgus laxity is a risk factor for knee pain in OA and that female gender, the grade of OA and varus–valgus alignment are risk factors for varus–valgus laxity. To our knowledge, this is the first report on the relationship between varus–valgus laxity and pain in knee OA.

Knee varus–valgus laxity in individuals with knee OA is most likely a multi-factorial problem that can result from such factors as increased capsulo–ligamentous laxity, structural damage to the knee, and altered lower extremity muscular strength and neuromuscular control [16]. Varus–valgus laxity increases with age and is greater in women than men [10]. This may well be the reason why men do not report knee pain as frequently as women, even in the setting of severe OA. Notably, antero–posterior laxity is not affected by age, and there is no difference in antero–posterior laxity between the OA and control group [10]. In agreement with our own results, Wada et al. report that antero–posterior laxity with OA steadily declines along with the Kellgren–Lawrence grade [9].

Various conservative treatments are effective in relieving the pain of knee OA. Interestingly, these treatments are all aimed at decreasing varus–valgus laxity. Thus, their effectiveness would seem to support our finding that varus–valgus laxity is fundamentally related to the presence of pain in knee OA. Valgus bracing, for example, is effective in reducing external adduction movement and appears to subsequently provide pain relief [17–20]. The lateral-wedge insole has also been proven effective for the conservative treatment of medial compartment knee OA via a reduction in external varus movement and medial compartment load [21,22]. In addition, several reports describe the effectiveness of quadriceps exercise in pain relief. In our study, we did not find a direct association between quadriceps torque and the presence of pain. Quadriceps exercise may nonetheless effect pain relief through an improvement in instability. High tibial osteotomy is also considered effective for pain relief and functions by reducing peak adduction movement of the knee [23].

There are some limitations to our study. First, varus–valgus laxity of the knee was not quantitatively evaluated. Cushnaghan et al. demonstrate the poor reliability of physical examination in the assessment of laxity even with a single examiner (within-observer agreement: 0.55) [24]. However, computerized systems to measure knee laxity in the frontal plane (such as the Genucom) are no longer available. Even with the use of such a system, it is difficult to evaluate laxity using any special device on a large population of subjects in a short period of time. Yet another limitation of this study is posed by the fact that we measured passive knee laxity, not dynamic instability, i.e., varus thrust. Passive knee laxity and functional knee instability are not synonymous. Passive laxity is a clinical sign that indicates either lack of tension in capsuloligamentous structures of a joint, or the degree of joint looseness on the passive motion testing of the joint [25]. However, in a knee with varus–valgus laxity, thrust is likely to occur, especially in the knee with static malalignment.

In conclusion, our study presents the novel finding that varus–valgus laxity is a risk factor for pain in the knee OA in a Japanese population. As such, it is entirely conceivable that Japanese patients with severe radiographic OA may have mild or no pain if their varus–valgus laxity is well controlled. This raises the potential for the development of new treatments for knee OA in Japanese patients that focus on improving varus–valgus stability.

5. Conflict of interest statement

No author had an association or financial involvement with any organization or commercial entity having a financial interest in or financial conflict with the subject matter or research presented in the manuscript.

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References

[1] Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 2000;27:1513–7.
[2] Keefe FJ, Lefebvre JC, Egert JR, Affleck G, Sullivan MJ, Caldwell DS. The relationship of gender to pain, pain behavior, and disability in osteoarthritis patients: the role of catastrophizing. Pain 2000;87:325–34.
[3] Tsai YF. Gender differences in pain and depressive tendency among Chinese elders with knee osteoarthritis. Pain 2007;130:188–94.
[4] Lethbridge-Cejku M, Scott Jr WW, Reichle R, Ettinger WH, Zonderman A, Costa P, et al. Association of radiographic features of osteoarthritis of the knee with knee pain: data from the Baltimore Longitudinal Study of Aging. Arthritis Care Res 1995;8:182–8.
[5] Cicuttini FM, Baker J, Hart DJ, Spector TD. Association of pain with radiological changes in different compartments and views of the knee joint. Osteoarthr Cartil 1996;4:143–7.
[6] Bruyere O, Honore A, Rovati LC, Giacovelli G, Henrotin YE, Seidel L, et al. Radiologic features poorly predict clinical outcomes in knee osteoarthritis. Scand J Rheumatol 2002;31:13–6.
[7] Simkin PA. Bone pain and pressure in osteoarthritic joints. Novartis Foundation Symposium 260. East Hanover (NJ): Novartis; 2004. p. 179–90.
[8] Felson DT. The sources of pain in knee osteoarthritis. Curr Opin Rheumatol 2005;17:624–8.
[9] Wada M, Imura S, Baba H, Shimada S. Knee laxity in patients with osteoarthritis and rheumatoid arthritis. Br J Rheumatol 1996;35:560–3.
[10] Sharma L, Lou C, Felson DT, Dunlop DD, Kirwan-Mellis G, Hayes KW, et al. Laxity in healthy and osteoarthritic knees. Arthritis Rheum 1999;42:861–70.
[11] Gibson T, Hameed K, Kadir M, Sultana S, Fatima Z, Syed A. Knee pain amongst the poor and affluent in Pakistan. Br J Rheumatol 1996;35:146–9.
[12] Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957;16:494–502.
[13] Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. JAMA 2001;286:188–95.
[14] Brouwer GM, van Tol AW, Bergink AP, Belo JN, Bernsen RM, Reijman M, et al. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. Arthritis Rheum 2007;56:1204–11.
[15] Chang A, Hayes K, Dunlop D, Hurwitz D, Song J, Cahue S, et al. Thrust during ambulation and the progression of knee osteoarthritis. Arthritis Rheum 2004;50:3897–903.
[16] Fitzgerald GK, Piva SR, Irrgang JJ. Reports of joint instability in knee osteoarthritis: its prevalence and relationship to physical function. Arthritis Rheum 2004;51:941–6.
[17] Draganich L, Reider B, Rimington T, Piotrowski G, Mallik K, Nasson S. The effectiveness of self-adjustable custom and off-the-shelf bracing in the treatment of varus gonarthrosis. J Bone Jt Surg [Am] 2006;88:2645–52.
[18] Pollo FE, Otis JC, Backus SI, Warren RF, Wickiewicz TL. Reduction of medial compartment loads with valgus bracing of the osteoarthritic knee. Am J Sports Med 2002;30:414–21.
[19] Lindenfeld TN, Hewett TE, Andriacchi TP. Joint loading with valgus bracing in patients with varus gonarthrosis. Clin Orthop 1997;344:290–7.
[20] Self BP, Greenwald RM, Pflaster DS. A biomechanical analysis of a medial unloading brace for osteoarthritis in the knee. Arthritis Care Res 2000;13:191–7.
[21] Crenshaw SJ, Pollo FE, Calton EF. Effects of lateral-wedged insoles on kinetics at the knee. Clin Orthop 2000;375:185–92.
[22] Yasuda K, Sasaki T. The mechanics of treatment of the osteoarthritic knee with a wedged insole. Clin Orthop 1987;215:162–72.
[23] Wada M, Imura S, Nagatani K, Baba H, Shimada S, Sasaki S. Relationship between gait and clinical results after high tibial osteotomy. Clin Orthop 1998;354:180–8.
[24] Cushnaghan J, Cooper C, Dieppe P, Kirwan J, McAlindon T, McCrae F. Clinical assessment of osteoarthritis of the knee. Ann Rheum Dis 1990;49:768–70.
[25] Noyes FR, Grood ES, Torzilli PA. Current concepts review. The definitions of terms for motion and position of the knee and injuries of the ligaments. J Bone Jt Surg [Am] 1989;71:465–72.

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Mechanical, setting, and biological properties of bone cements containing micron-sized titania particles

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Abstract In this study, polymethylmethacrylate-based composite cements containing 40–55.6 wt% micron-sized titania (titanium oxide) particles were developed, and their mechanical, setting, and biological properties evaluated. Three types of composite cement containing 40, 50, and 55.6 wt% silanized titania were designated ST2-40c, ST2-50c, and ST2-56c, respectively. In animal experiments, ST2-50c and ST2-56c were implanted into rat tibiae and solidified in situ. An affinity index was used to evaluate osteoconductivity. Compressive and bending strength of ST2-56c was 147.7 ± 3.2 and 69.3 ± 7.4; those of the other cements exceeded 100 MPa and 50 MPa, respectively. The affinity indices of ST2-56c were 42.1 ± 12.9 at six weeks and 53.4 ± 16.6 at 12 weeks, and were significantly higher than for ST2-50c and a commercial PMMA bone cement within 12 weeks. Our data indicate that bone cement containing micron-sized titania particles can be applied to prosthesis fixation as well as vertebroplasty, and ST2-56c is a good candidate cement.

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Introduction

Since the 1990s, many types of bioactive bone cement have been developed to overcome the disadvantages of polymethylmethacrylate (PMMA) bone cement [1], especially its lack of bone-bonding ability, which occasionally leads to aseptic loosening of prostheses used for arthroplasty [2, 3]. However, the acceptable long-term clinical results of PMMA bone cement [4, 5], and concerns about the long-term stability of bioactive fillers in the cements have so far prevented bioactive bone cements being used for the fixation of prostheses in arthroplasty. Recently, anatase and rutile, crystal phases of titania, have been shown to have excellent in vitro apatite-forming ability and in vivo bioactivity [6–9]. Titania is stable in the body and does not degrade, so that bone cements containing bioactive titania filler can be stable in the body environment. Then a composite bone cement containing nanosized anatase-type titania particles was developed, and it was reported that certain compositions of the cement had good osteoconductivity [10]. However, some of the nanosized titania particles tended to aggregate in the cement. As a result, the cements containing nanosized titania particles did not reach the minimum bending strength required by the ISO 5833 standard (50 MPa), which is applied to acrylic resin cements used for prosthesis fixation, and could be applied clinically for vertebroplasty, but not for prosthesis fixation. One possible resolution of this problem was to increase the titania particle size. In this study, composite cements that contained micron-sized titania particles were developed. Preliminary PMMA cement candidates with different amounts of titania particles were examined for their mechanical properties and apatite forming ability in vitro [11], and two promising composites were used in an implantation study.

The purpose of the study was to evaluate the mechanical and setting properties, and osteoconductivity of cements containing micron-sized titania.

Materials and methods

Preparation of powders

Titania powder

Plate-like titania powder (Ishihara Sangyo Kaisha, Osaka, Japan) with an average particle size of 1.55 μm was used as supplied. The particle size distribution of the titania powder, which was determined using a laser diffraction analyzer (LA-910; Horiba, Kyoto, Japan), is shown in Fig. 1a. Powder X-ray diffraction of the particles revealed that the titania particles were composed of anatase and rutile phases (Fig. 1b). The weight ratio of anatase:rutile in the 1.55 μm titania powder was about one, based on the peak intensities of each diffraction pattern. The titania powder was mixed into three types of TiO_2-dispersed cements with 40, 50, and 55.6 wt% TiO_2, designated ST2-40c, ST2-50c, and ST2-56c, respectively.

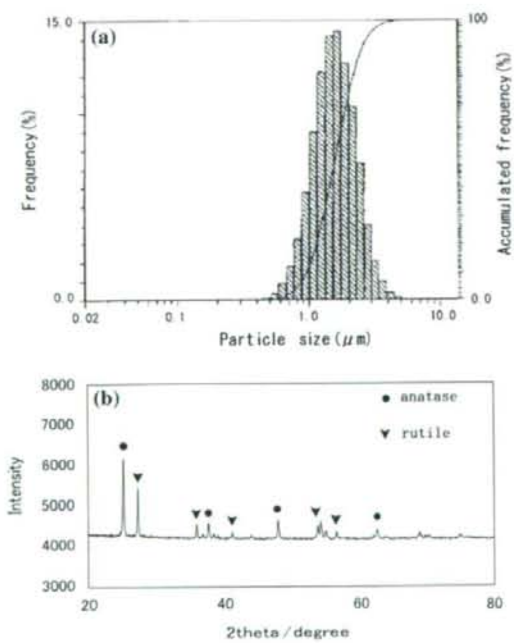


Fig. 1 (**a**) Titania powder particle size distribution. (**b**) Powder X-ray diffraction data for titania powder

Titania powders were treated with a silane-coupling agent as follows: 1.1 g of 3-methacryloxypropyltrimethoxysilane (Shin-Etsu Chemical Co., Tokyo), 1.6 g of ethanol and 0.2 g of deionized water were mixed on a magnetic stirrer for 10 min. The solution containing the silane-coupling agent was added to 110 g of the TiO_2 powder and mixed in a shaker mixer (TURBULA T2F, W. A. Bachofen AG Co., Basel, Switzerland) at 25 °C for 1 h. The rotation speed was 96 rpm. After mixing, the mixtures were dried and heated at 130 °C for 5 min.

Polymethylmethacrylate powder

Spherical PMMA powder, synthesized by suspension polymerization [12], with an average molecular weight of 270,000 Da and an average particle size of 5 μm (standard deviation: 2 μm) [13] was used.

Preparation of the liquid

Liquid methacrylate (MMA) monomer (Wako Pure Chemical Industries, Osaka, Japan) was used.

Cement preparation

Four types of cement, designated ST2-40c, ST2-50c, ST2-56c, and PMMAc, were prepared. PMMAc was a commercially available PMMA-based bone cement (Osteobond; Zimmer, Warsaw, IN, USA) and was used as a control material. The composition of each TiO_2-containing cement is shown in Table 1. As an initiator, benzoyl peroxide (Nacalai Tesque, Kyoto, Japan) was added to the powder at 4.0 wt% of the monomer, and as an accelerator, *N,N*-dimethyl-*p*-toluidine (Kanto Chemical Co. Inc., Tokyo, Japan) was dissolved in the liquid to 2.0 wt% of the monomer. Each cement was prepared by mixing the powder with the liquid for 1 min.

Mechanical testing

The compressive strength, bending strength, and bending modulus of ST2-40c, ST2-50c, and ST2-56c were mea-

Table 1 Composition of PMMA-based cements containing titania powders

Cement	Powders[a] (wt%)		Liquid[b] (wt%)
	Titania	PMMA	MMA
ST2-40c	40	20	40
ST2-50c	50	16.7	33.3
ST2-56c	55.6	14.6	29.6

[a] Benzoyl peroxide was added at 4 wt% of the MMA

[b] *N,N*-Dimethyl-*p*-toluidine was added at 2 wt% of the MMA

sured using five prehardened cement specimens for each mechanical test. For mechanical bending analysis, four-point bending testing was performed with rectangular specimens sized to 70 mm × 20 mm × 5 mm. For compressive mechanical analysis, prehardened cylindrical cement specimens, 6 mm in diameter and 12 mm in length, were prepared. The tests were carried out according to ISO 5833, with a Model 5582 testing machine (Instron Corporation, Canton, MA, USA); the test conditions were previously described in detail [10].

Some of the bending specimens were prepared for observation with a scanning electron microscope (SEM, S-4700; Hitachi, Tokyo, Japan), and the fracture surfaces were analyzed to determine the microstructure of the cements.

Setting of the cements

The cement pastes were mixed for 1 min and cast in a cylindrical mold made of polytetrafluoroethylene (inner diameter 60 mm, inner depth 20 mm). The temperature change during the setting reaction was measured using an infrared thermometer under ambient conditions of 23 °C and 54–65% humidity. By plotting the time and temperature, the setting time of each cement was determined according to ISO 5833.

Animal experiments

Eight-week-old male Wistar rats weighing 180–230 g were used for the implantation study. The animals were reared and the experiments carried out at the Institute of Laboratory Animals, Faculty of Medicine, Kyoto University, under the institutional guidelines for use of experimental animals set by Kyoto University.

The rats were operated on under general anesthesia induced by intraperitoneal injection of sodium 5-ethyl-5-(1-methylbutyl) barbiturate (Nembutal [pentobarbital]; Dainippon Pharmaceutical Company, Osaka, Japan) at 40 mg/kg of body weight. Cortical bone defects measuring 2 mm × 7 mm were created in the medial aspect of the proximal metaphyses of both tibiae, and the bone marrow was curetted. The intramedullary canals of both bone defects were irrigated with physiological saline, and paste-form cement was inserted manually and allowed to cure in situ for evaluation of osteoconductivity [10, 14, 15]. Twelve rats (24 legs) were used for the evaluation of osteoconductivity, with ST2-50c and ST2-56c each being used in 12 legs. Half the rats in each subgroup were killed at six and 12 weeks after the operation.

To confirm the high radiopacity of ST2-56c, another operation was performed using an additional rat. After a hole had been made in the intercondylar space of the distal femur, and the intramedullary canal of the total femur was curetted and irrigated with physiological saline, ST2-56c and PMMAc in liquid phase were inserted into each of the bilateral canals using a syringe fitted with an 18-gauge needle, and this was allowed to cure in situ. One day after the operation, the rat was killed and an X-ray radiograph of the femurs was taken.

Micrographic examination

Specimens were dehydrated through a graded series of ethanol (70, 80, 90, 99, and 100 vol%) and embedded in epoxy resin (Epofix, Struers Co., Copenhagen, Denmark). Thin sections (100 or 500 μm thick) were cut with a band saw (BS-3000; Exakt, Norderstedt, Germany) perpendicular to the axis of the tibias containing the cement. Four sections could be typically made from each leg. The third section (100 μm thick) from the most distal portion of each leg was ground to a thickness of 60–80 μm using a grinding–sliding machine (Microgrinding MG-4000; Exakt) for Giemsa surface staining. The second section (100 μm thick) from each leg was prepared for contact microradiography. The first and fourth sections (500 μm thick) from each leg were polished with diamond paper and coated with a thin layer of carbon for observation by SEM (S-4700, Hitachi, Tokyo, Japan). Some of those specimens were analyzed using an energy-dispersive X-ray microanalyzer (EMAX-7000; Horiba, Kyoto, Japan) attached to the SEM (SEM–EDX). To evaluate osteoconductivity, affinity indices (%) for each subgroup were calculated as previously described [10, 14, 15].

Statistical analysis

Values were expressed as means and standard deviations (SD). Values of mechanical properties for each cement and the affinity indices for each cement at each time interval were compared using one-way analysis of variance. Subsequently, possible differences were investigated using Fisher's PLSD post hoc statistical test using StatView (version 5.0) for Windows. A P value less than 0.01 was considered statistically significant.

Results

Mechanical properties

The results of the mechanical property measurement and their statistical analyses are shown in Table 2. The ultimate compressive strength, flexural strength, and flexural modulus increased as the titania content of the cement increased. SEM revealed that titania particles were

Table 2 Mechanical properties of ST2-40c, ST2-50c, ST2-56c, and PMMAc (means ± SD, $n = 5$)

	Compressive strength (MPa)	Bending strength (MPa)	Bending modulus (GPa)
ST2-40c	106.1 ± 5.5*	54.3 ± 6.6	3.10 ± 0.47
ST2-50c	127.9 ± 6.4*	57.8 ± 4.1	3.88 ± 0.46
ST2-56c	147.7 ± 3.2*	69.3 ± 7.4**	4.07 ± 0.83
PMMAc	87.9 ± 2.7*	59.4 ± 7.8	1.56 ± 0.28***

The values for PMMAc were derived from our previous study[10]

* All pairs were significantly different

** Significantly different to ST2-40c

*** Significantly different to all the other cements

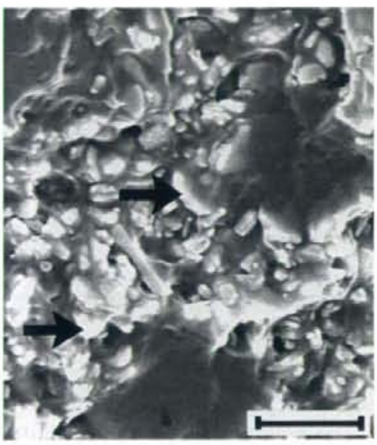


Fig. 2 Scanning electron micrograph of the fracture surface of ST2-56c. Arrows indicate titania particles. Bar = 3 μm

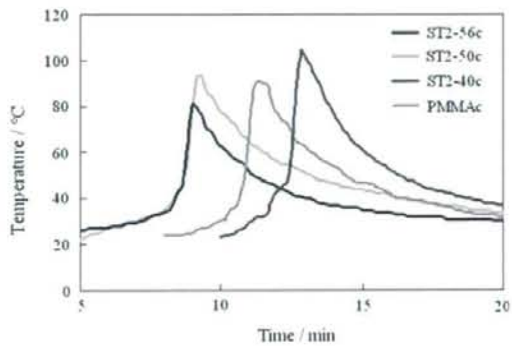


Fig. 3 Heat evolution curves for the setting reactions of ST2-50c, ST2-56c, PMMAc, and ST2-40c

uniformly dispersed and interacted well with the PMMA, and aggregates of titania particles could not be seen in the fracture surfaces of each cement (Fig. 2).

Setting time and peak temperature

The results of the temperature plotting of the cements are shown in Fig. 3. The setting times were 12 min 40 s for ST2-40c, 9 min 0 s for ST2-50c, 8 min 50 s for ST2-56c, and 11 min 0 s for PMMAc. The peak temperatures were 104 °C for ST2-40c, 93 °C for ST2-50c, 81 °C for ST2-56c, and 91 °C for PMMAc. The setting time of the cements containing titania particles reduced and the peak temperature decreased as the titania filler content increased.

Radiopacity

The ST2-56c in the femur was much more radiopaque than the PMMAc (Fig. 4). Both the ST2-56c and PMMAc were injected through an 18-gauge needle without problems, although ST2-56c was more easily injected.

Evaluation of the bone–cement interface

Giemsa surface staining indicated that there was typically no inflammatory reaction around ST2-50c and ST2-56c (Fig. 5a, b). The intervening soft tissue layer between cement and bone was more often seen around ST2-50c than ST2-56c at each time interval. For ST2-56c, no significant change in appearance could be seen with Giemsa surface staining between the 6- and 12-week specimens. On the other hand, for ST2-50c, there appeared to be less intervening soft tissue layer between the cement and bone in the 12-week specimens than in the 6-week specimens.

Low magnification SEM revealed that ST2-56c was in direct contact with bone over large areas within six weeks, whereas ST2-50c was in contact with bone in only small areas (Fig. 6a, b). In the 12-week specimens, both ST2-56c and ST2-50c were in direct contact with bone over large areas (Fig. 6c, d). Both ST2-50c and ST2-56c showed a marginal white line 30–60 μm wide at each time interval,

Fig. 4 X-ray radiograph of bilateral femurs of a rat one day after the operation

regardless of whether they were in contact with bone. These findings were also revealed by contact microradiography, in which each cement appeared to be in direct contact with bone over larger areas than in the SEM observation (Fig. 7a, b).

Backscattered SEM at high magnification revealed that both ST2-56c and ST2-50c were in direct contact with bone within six weeks, but a thin intervening soft tissue layer less than 10 μm thick was often observed between ST2-50c and the bone (Fig. 8a, b). It also showed that ST2-50c and ST2-56c were in contact with bone via a white line, which was demonstrated by SEM–EDX analyses to be a Ti-rich layer (Fig. 8c). An increase in the intensity of calcium was also detected along the outer margin of this white line (Fig. 8c).

Evaluation of osteoconductivity

The affinity indices for all of the cements at six and 12 weeks, and the statistical comparisons, are shown in Fig. 9.

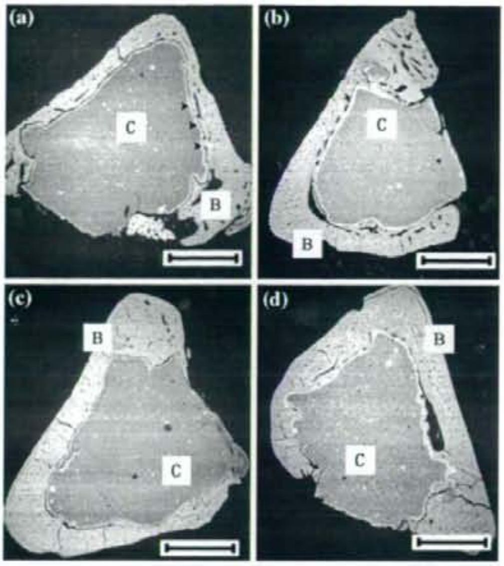


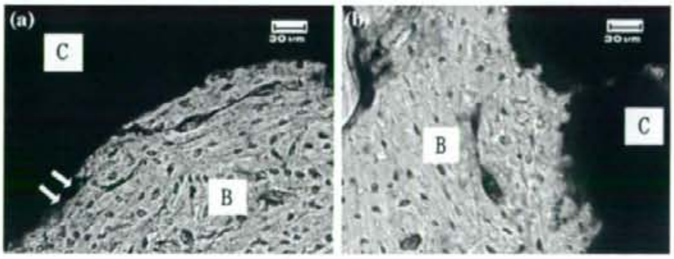
Fig. 6 Low magnification scanning electron micrographs of (a) ST2-50c and (b) ST2-56c in rat tibiae six weeks after implantation; (c) ST2-50c and (d) ST2-56c in rat tibiae 12 weeks after implantation. C, cement; B, bone; Arrowheads indicate the white line. Bar = 30 μm

Discussion

In preliminarily trials, it was attempted to prepare cements containing over 60 wt% micron-sized titania particles, but it was often difficult to effectively mix the powder and the liquid. Preliminary in vitro studies revealed that the apatite-forming ability of the composite cements increased with the content of titania particles. Because ST2-50c and ST2-56c were consistently made in a well-mixed form and were expected to have better osteoconductivity than ST2-40c, as judged from the in vitro studies, they were chosen for the animal study.

With the previously reported composite bone cement containing nanosized anatase-type titania particles, it was difficult to disperse the titania particles uniformly in the

Fig. 5 Giemsa surface staining of (a) ST2-50c and (b) ST2-56c in rat tibiae 12 weeks after implantation. C, cement; B, bone; Arrows indicate intervening soft tissue. Bar = 30 μm



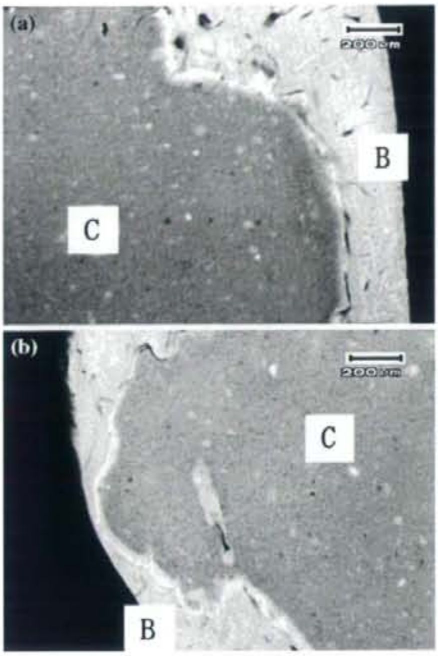


Fig. 7 Contact microradiography of (**a**) ST2-50c and (**b**) ST2-56c in rat tibiae 12 weeks after implantation. C, cement; B, bone. Bar = 200 µm

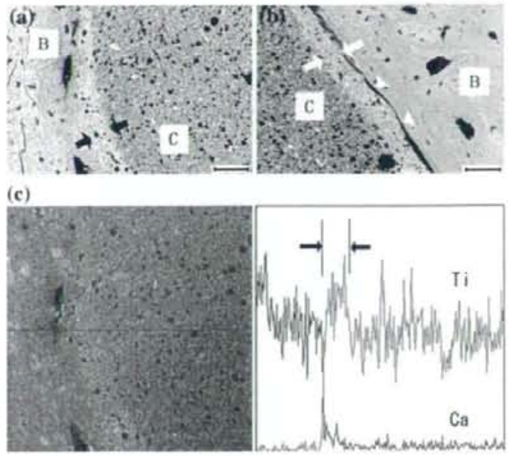


Fig. 8 Back-scattered scanning electron micrographs (SEM) of (**a**) ST2-56c and (**b**) ST2-50c in rat tibiae six weeks after implantation, and (**c**) SEM energy-dispersive X-ray (EDX) analysis of ST2-56c in the same site of (**a**). The white line is clearly visible in (**a**) and (**b**), and SEM-EDX analysis indicated that the white line is a Ti-rich layer. An increase of the intensity of the calcium peak was also detected along the outer margin of the white line. Arrowheads indicate thin intervening soft tissue. Between arrows = white line. C, cement; B, bone. Bar = 40 µm

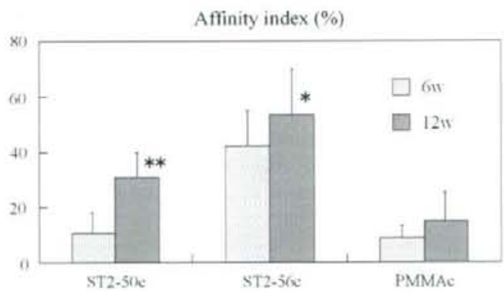


Fig. 9 Affinity indices (%) for ST2-50c, ST2-56c, and PMMAc in rat tibiae at six and 12 weeks after implantation (mean ± SD, $n = 12$). At six weeks, the value for ST2-50c was 10.6 ± 7.8 and 42.1 ± 12.9 for ST2-56c; and at 12 weeks, 30.8 ± 9.0 and 53.4 ± 16.6 respectively. The comparative affinity indices for PMMAc were 8.9 ± 4.4 and 14.9 ± 10.4 at six and 12 weeks, respectively [16]. *Significant compared with ST2-50c and PMMAc at six and 12 weeks. **Significant compared with PMMAc at 12 weeks

cement [10]. In contrast, micron-sized particles of mixed-phase anatase–rutile titania dispersed well in the cements, as was shown in this study. Indeed, it is difficult to simply compare the results of the experiments because there was little difference in the experimental conditions including the PMMA/MMA ratio and silanization of the powders. However, the difference in the particle size presumably influenced the degree of the particle dispersion.

The compressive and bending strengths of ST2-50c were much higher than those previously reported for PMMA-based composite cements containing nanosized spherical titania particles at 50 wt%, the compressive and bending strengths of which were 91.8 ± 7.7 and 25.5 ± 9.5 MPa, respectively [10]. Shinzato et al. developed PMMA-based composite cements containing glass beads and reported that a decreasing trend in the bending strength was observed as the glass bead size increased [16]. Their results suggest that cements containing smaller-sized titania could have higher strength. However, our findings were not consistent with theirs, and were presumably influenced mainly by the difference in filler dispersion in our studies, where the micron-sized titania dispersed well, whereas the nanosized titania used in the previous study formed some aggregates in the cement [10]. In this study, there was an increasing trend in compressive strength, bending strength, and bending modulus with increasing titania filler content. Juhasz et al. investigated the effect of filler content on the mechanical properties of AW-glass ceramic–polyethylene composites, and noted that a stiffening effect was observed as the AW-glass ceramic filler content increased from 10 to 50 vol% [17]. Their results were consistent with ours. In this study, the mechanical strengths of the cements containing micron-sized titania particles met the criteria required by the ISO 5833 standard.

The setting times of the cements containing titania particles in this study were reduced, and the peak temperature decreased, as titania filler content increased. Only ST2-56c exhibited a lower peak temperature than PMMAc, and that of ST2-50c was almost the same as that of PMMAc. This was probably because the weight ratio of PMMA/MMA was 1/2 in ST2-50c, whereas the weight ratio of powder/liquid monomer was about 2/1 in PMMAc, and the content of MMA that polymerizes with an exothermic reaction was almost the same in ST2-50c and PMMAc. As less exothermic setting reactions for bone cement are desirable, both ST2-50c and ST2-56c would be acceptable, but ST2-56c appeared to have lower peak-setting temperature properties and is therefore recommended.

Animal experiments revealed that both ST2-50c and ST2-56c were more osteoconductive than cements containing nanosized titania particles. According to a previous study, the affinity indices of cements containing nanosized titania particles were $20.9 \pm 7.3\%$ for cement containing 50 wt% titania particles and $31.3 \pm 8.7\%$ for cement containing 60 wt% titania particles at 12 weeks [10]. In the previous study [10] and in this study, high molecular weight PMMA powder was used because it showed low solubility in the MMA monomer during the polymerizing reaction [14]. As a result, bioactive fillers could be exposed at the cement surface without being covered by a layer of polymerized MMA [14]. Therefore, the amount of bioactive particles exposed on the cement surface, which must be proportional to cement bioactivity, was greatly influenced by the particle size of bioactive fillers. In this study, the micron size of the titania particles presumably had a beneficial effect on the osteoconductivity of ST2-50c and ST2-56c. However, ST2-56c was in direct contact with bone over larger areas than ST2-50c, at both six and 12 weeks after implantation into rat tibiae. As well as the larger amount of titania filler, presumably the decrease in toxic monomer content contributed to the higher affinity indices of ST2-56c compared with those of ST2-50c. Further research on bone-bonding strength is necessary to demonstrate the bioactivity of ST2-50c and ST2-56c.

The marginal white line seen on SEM was a Ti-rich layer, as revealed by SEM–EDX analyses (Fig. 8c) and has been similarly observed in cements containing nanosized titania particles [10]. In contrast, it has been reported that PMMA-based composite cement containing glass beads, AW-GC, or hydroxyapatite fillers developed by Shinzato et al. exhibited no such marginal line, although they used a similar PMMA/MMA system and bioactive fillers silanized with γ-methacryloxypropyltrimethoxy silane [14]. Therefore, the properties of the titania filler itself are suggested to contribute to the formation of the white line. Because a Ti-rich layer indicated bioactive titania gathered at the cement surface, it presumably contributes to the osteoconductivity of cements containing titania particles. SEM–EDX analyses also revealed an increase in the concentration of calcium along the outer margin of the white line, which suggests calcium ion transfer or bony tissue invasion into the cement margin. Although a small amount of unpolymerized MMA might leak out of the cement surface, SEM observations revealed no such cement degradation and that leakage was minimal. No toxic effects of the monomer were detected by Giemsa surface staining, and excellent osteointegration of ST2-56c and ST2-50c was seen.

The overall results of this study indicate that PMMA bone cement containing micron-sized titania particles is a promising bone cement for prosthesis fixation as well as for vertebroplasty, but further research on long-term osteointegration and bone-bonding strength should be performed before clinical application.

Conclusions

Three types of PMMA-based composite cements containing 40–56 wt% micron-sized bioactive titania powder were prepared, and their mechanical, setting, and biological properties were evaluated. Compressive strength, bending strength, and bending modulus increased with increasing content of titania filler. The mechanical strengths met the criteria required in the ISO 5833 standard. The peak temperature during the setting reaction decreased as the amount of filler increased, and ST2-56c exhibited a lower peak temperature than commercial PMMA cement. Cements ST2-50c and ST2-56c were revealed to be biocompatible and osteoconductive. This was especially the case with ST2-56c, as it was in direct contact with bone over large areas within six weeks after implantation into rat tibiae, and showed significantly higher affinity indices than those of ST2-50c within 12 weeks. Overall, the data indicate that bone cement containing micron-sized titania particles can be applied to prosthesis fixation as well as vertebroplasty, and ST2-56c is a good candidate cement.

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References

1. S. M. KENNY and M. BUGGY, *J. Mater. Sci. Mater. Med.* **14** (2003) 923
2. M. A. FREEMAN, G. W. BRADLEY and P. A. REVEL, *J. Bone Joint Surg. Br.* **64** (1982) 489

3. S. R. GOLDRING, A. L. SCHILLER, M. ROELKE, C. M. ROURKE, D. A. O'NEIL and W. H. HARRIS, *J. Bone Joint Surg. Am.* **65** (1983) 575
4. F. M. KHAW, L. M. KIRK, R. W. MORRIS and P. J. GREGG, *J. Bone Joint Surg. Br.* **84** (2002) 658
5. J. J. CALLAGHAN, J. E. TEMPLETON, S. S. LIU, D. R. PEDERSEN, D. D. GOETZ, P. M. SULLIVAN and R. C. JOHNSTON, *J. Bone Joint Surg. Am.* **86-A** (2004) 690
6. M. UCHIDA, H. M. KIM, T. KOKUBO, S. FUJIBAYASHI and T. NAKAMURA, *J. Biomed. Mater. Res.* **64A** (2003) 164
7. M. UCHIDA, H. M. KIM, T. KOKUBO, S. FUJIBAYASHI and T. NAKAMURA, *J. Biomed. Mater. Res.* **63** (2002) 522
8. W. Q. YAN, T. NAKAMURA, M. KOBAYASHI, H. M. KIM, J. MIYAJI and T. KOKUBO, *J. Biomed. Mater. Res.* **37** (1997) 267
9. Y. T. SUL, *Biomaterials* **24** (2003) 3893
10. K. GOTO, J. TAMURA, S. SHINZATO, S. FUJIBAYASHI, M. HASHIMOTO, M. KAWASHITA, T. KOKUBO and T. NAKAMURA, *Biomaterials* **26** (2005) 6496
11. T. KOKUBO, S. ITO, Z. T. HUANG, T. HAYASHI, S. SAKKA, T. KITSUGI and T. YAMAMURO, *J. Biomed. Mater. Res.* **24** (1990) 331
12. S. SHINZATO, T. NAKAMURA, T. KOKUBO and Y. KITAMURA, *J. Biomed. Mater. Res.* **54** (2001) 491
13. T. NAKAMURA, H. KATO, Y. OKADA, S. SHINZATO, K. KAWANABE, J. TAMURA and T. KOKUBO, In *Bioceramics*, edited by S. Gianniniand A. Moroni (Bologna: Trans Tech, 2000), p. 661
14. S. SHINZATO, M. KOBAYASHI, W. F. MOUSA, M. KAMIMURA, M. NEO, Y. KITAMURA, T. KOKUBO and T. NAKAMURA, *J. Biomed. Mater. Res.* **51** (2000) 258
15. J. TAMURA, K. KAWANABE, T. YAMAMURO, T. NAKAMURA, T. KOKUBO, S. YOSHIHARA and T. SHIBUYA, *J. Biomed. Mater. Res.* **29** (1995) 551
16. S. SHINZATO, T. NAKAMURA, T. KOKUBO and Y. KITAMURA, *J. Biomed. Mater. Res.* **56** (2001) 452
17. J. A. JUHASZ, S. M. BEST, R. BROOKS, M. KAWASHITA, N. MIYATA, T. KOKUBO, T. NAKAMURA and W. BONFIELD, *Biomaterials* **25** (2004) 949