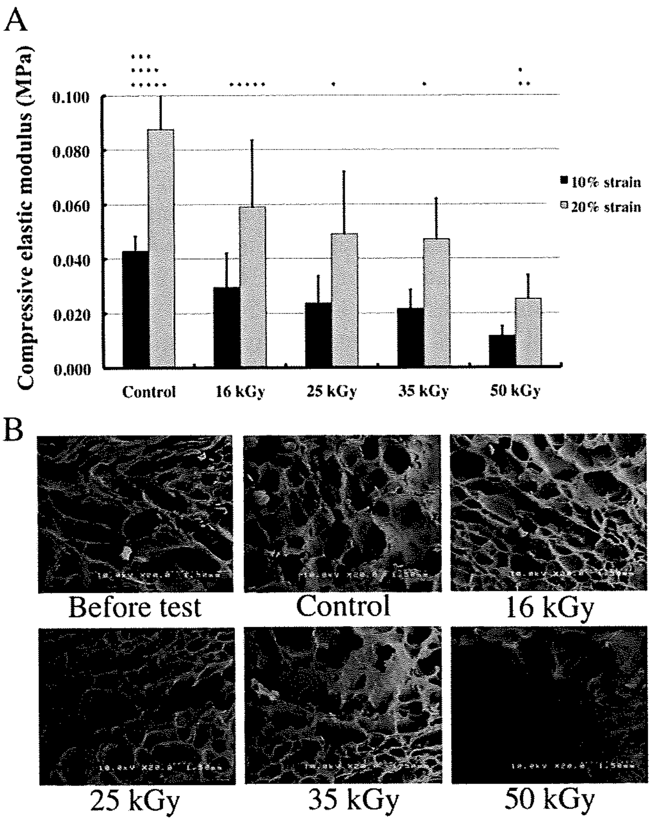

Figure 1. (A) Elastic moduli of porous HAp/Col after gamma-ray irradiation at 10 and 20% strain (N = 5). *$p < 0.05$ versus control, **$p < 0.05$ versus 16 kGy, ***$p < 0.05$ versus 25 kGy, ****$p < 0.05$ versus 35 kGy, *****$p < 0.05$ versus 50 kGy. (B) SEM images of the porous structure of HAp/Col before and after compression testing.

kGy implant was advanced when compared with the 16-kGy and control groups. Some control implants even maintained their original porous structure at 8 weeks.

Porous HAp/Col at the Skeletal Site. At 2 weeks after implantation, absorption of the irradiated implants was

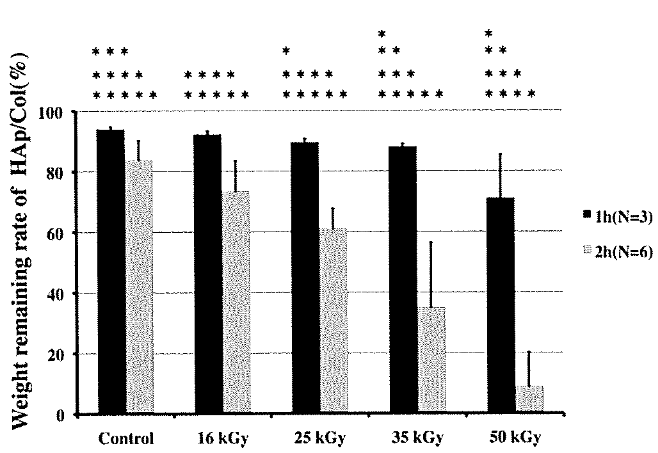

Figure 2. Weight of porous HAp/Col remaining after collagenase digestion. Incubation time of 1 (N = 3) or 2 h (N = 6). *$p < 0.05$ versus control, **$p < 0.05$ versus 16 kGy, ***$p < 0.05$ versus 25 kGy, ****$p < 0.05$ versus 35 kGy, *****$p < 0.05$ versus 50 kGy.

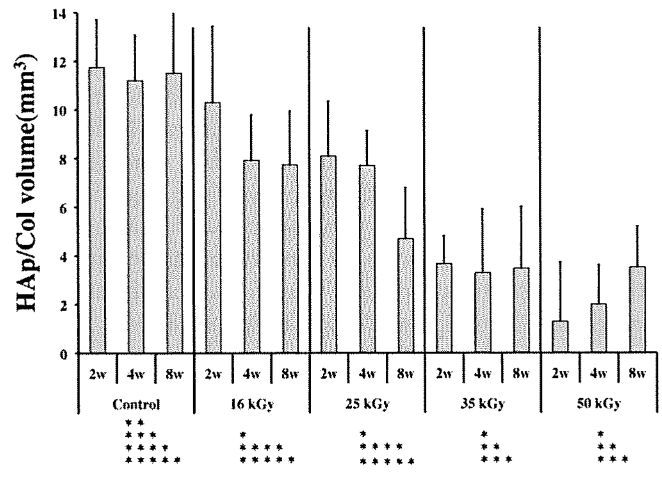

Figure 3. Residual volume of porous HAp/Col in back muscle quantified by micro-CT analysis. *$p < 0.05$ versus control, **$p < 0.05$ versus 16 kGy, ***$p < 0.05$ versus 25 kGy, ****$p < 0.05$ versus 35 kGy, *****$p < 0.05$ versus 50 kGy.

dose-dependent, with bioabsorption, fragmentation, and soft tissue invasion from the extraskeletal site observed for 50-kGy implants. Bone formation in the marrow cavity also showed irradiation dose-dependent increases (Figure 5).

At 4 weeks postoperatively, the bone defects of each group were almost completely closed, with no significant differences in the amount of residual implant or bone tissue in the marrow cavity. At 8 weeks, normal bone marrow cavities were restored; implants and surplus bone in the cavities were almost completely absorbed, and small remnants of the implants surrounded by the bone tissue were observed in all groups.

In 2-week implants, TRAP-positive multinucleated cells were attached to both the cavity and extraskeletal sides, and the number of TRAP-positive cells increased as the irradiation dose increased (Figure 6).

The 4-week implants also exhibited a large number of TRAP-positive cells in every group. The cells were mainly attached to newly formed bone in the 50-kGy gamma-irradiated implants, whereas in the control group, cells mainly adhered to the implant remnant. The number of TRAP-positive cells was markedly decreased at 8 weeks when compared with 2 and 4 weeks postimplantation.

DISCUSSION

In this study, gamma-ray irradiation resulted in dose-dependent reduction of elastic modulus and resistance to biological digestion for porous HAp/Col, although bone conductivity at skeletal implantation sites was not impaired.

Gamma-ray irradiation from Cobalt 60 sources is a popular sterilization method for medical devices, including implant materials. However, gamma-ray irradiation has also been reported to degrade collagen by splitting the peptide chains, thus adversely affecting the mechanical and biological properties of collagen-containing materials.[13,17] Porous

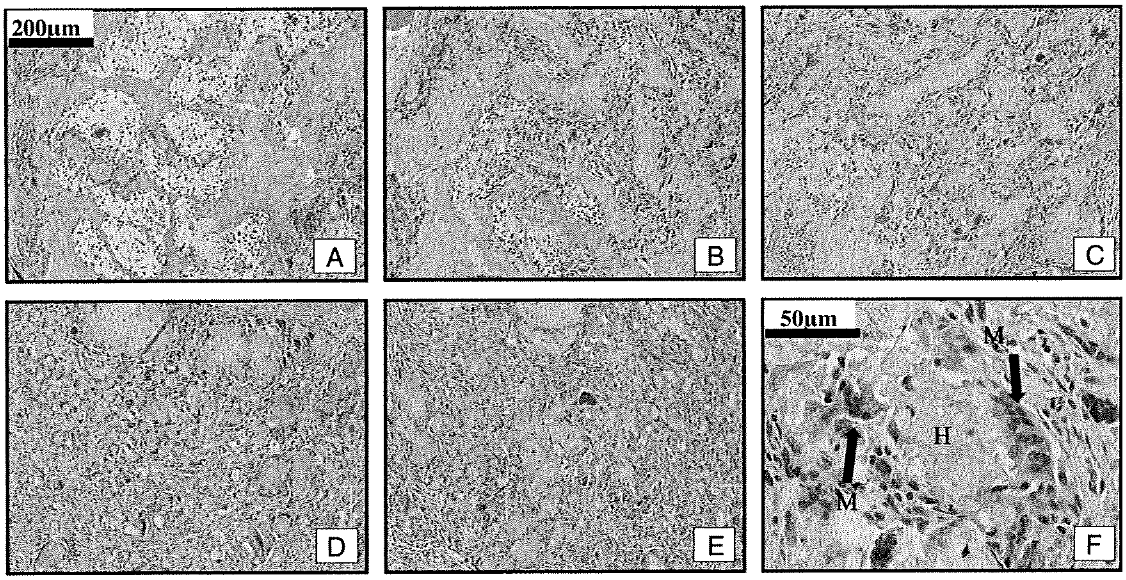

Figure 4. Sections of the HAp/Col implant harvested from back muscle at 2 weeks after implantation (HE staining). (A) Control group (70% ethanol), (B) 16-kGy-irradiated group, (C) 25-kGy-irradiated group, (D) 35-kGy-irradiated group, (E) 50-kGy-irradiated group, (F) high-magnification views of 25-kGy-irradiated group. H, HAp/Col. M, multinucleated macrophage. Implant fragmentation in the 35- and 50-kGy groups was severe. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

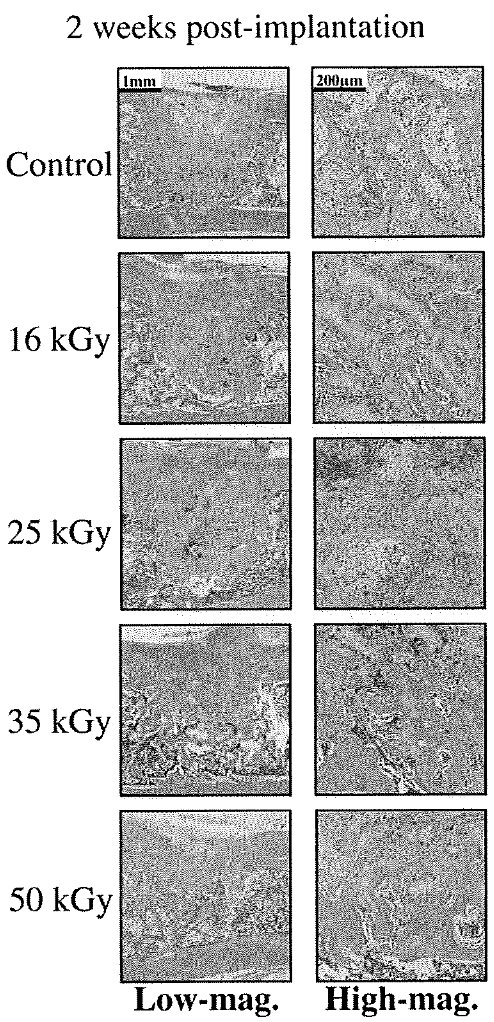

Figure 5. Coronal sections of femurs crossing the center of the implant 2 weeks postoperatively (HE staining). Left column shows lower magnification (×1.25), right column shows higher magnification (×10). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

HAp/Col is a bioabsorbable bone substitute with high osteoconductivity and unique mechanical properties including elasticity; these properties permit facile handling during surgery.[9,18,19] Thus, the fragmentation of collagen fibers in HAp/Col by gamma-ray irradiation may significantly affect the ease of use of porous HAp/Col implants.

Porous HAp/Col is elastic and sponge-like and does not have weight-bearing mechanical strength. As a result, its mechanical properties do not contribute directly to its clinical usefulness and, for orthopedic applications, fixation devices must also be used at weight-bearing sites. However, the elasticity of HAp/Col is important for ease of handling and implantation, and therefore, we evaluated the effects of gamma-ray irradiation on elasticity. The elastic moduli of all HAp/Col implants showed irradiation dose-dependent decrease, with the most noticeable decrease observed for the 50-kGy group. Additionally, the 50-kGy-irradiated implants were noticeably fragile during *in vivo* transplantation experiments, although SEM images and the recovery rate after uniaxial compression did not reveal much degradation.

Bone prosthetic materials are commonly used to fill bone defects and accelerate natural bone ingrowth. Ideally, these materials should be absorbed and completely replaced

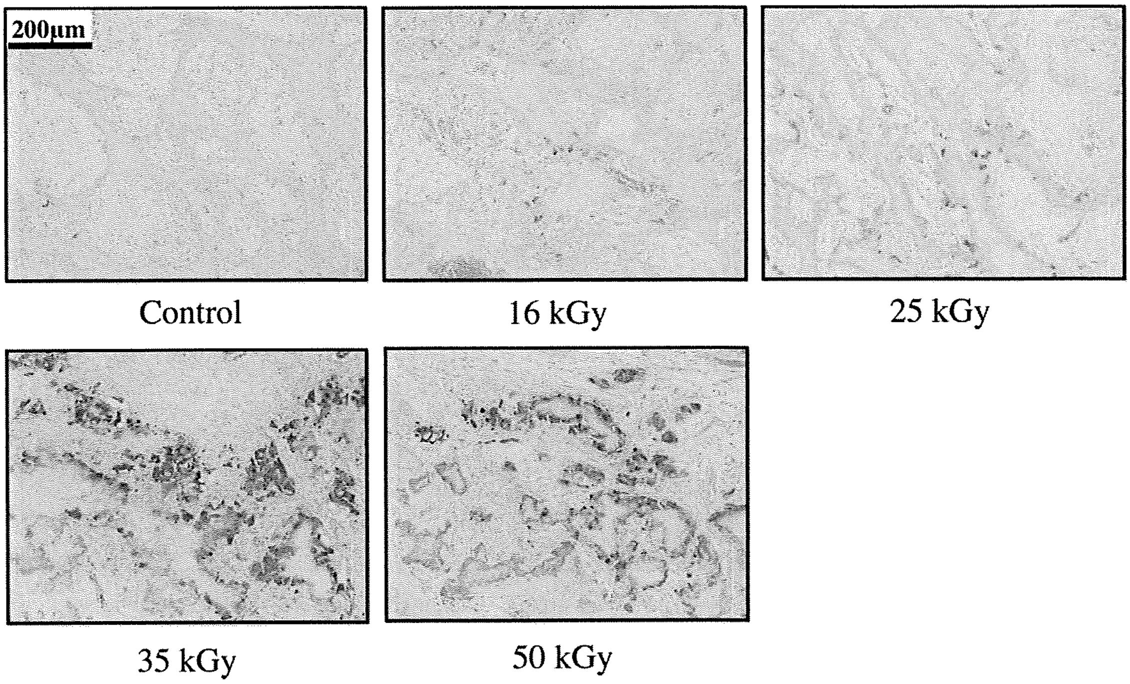

Figure 6. TRAP staining of femur sections 2 weeks postoperatively. The number of TRAP-positive cells was irradiation dose-dependent. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

by natural bone in the long term. However, in the clinic, bone defects are not always surrounded by cortical bone or periosteum, and healing may be disrupted by soft tissue invasion of the defect.[20] Bone substitutes implanted in bone defects promote healing by accelerating bone ingrowth due to osteoconductivity and prevention of soft tissue invasion.[21,22] Hence, bone substitutes should resist bioabsorption by macrophages with subsequent soft tissue invasion. Therefore, the effects of gamma-ray irradiation on the bioabsorbability of porous HAp/Col were tested using *in vitro* enzymatic digestion test and *in vivo* implantation models.

In vitro tests were performed using collagenase, which is responsible for collagen degradation *in vivo*.[16] *In vitro* digestion of the HAp/Col implant by collagenase was irradiation dose-dependent, with particularly notable degradation after gamma-ray irradiation at 35 or 50 kGy.

In muscular tissue, the porous HAp/Col nonirradiated implant maintained its volume and porous structure until 8 weeks after implantation, whereas in skeletal implantation sites, implants were almost completely absorbed and replaced by bone tissue. Control implants resisted bioabsorption from the extraskeletal site and soft tissue invasion. Intramuscular absorption of irradiated HAp/Col progressed faster than that of the control, especially for 35-and 50-kGy implants, whose volume decreased markedly at early time points. Absorption of the irradiated implants in the marrow cavities also progressed faster than that of the control, although this absorption was followed by the ingrowth of new bone. Notably, implant absorption and bone ingrowth were synchronized; thus, bone ingrowth of the 50-kGy group was most vigorous at early time points after transplantation. These findings indicate that osteoclast–osteoblast coupling mechanisms might be involved in the osteoconductivity of porous HAp/Col. Although all bone defects treated with irradiated implants eventually healed in the *in vivo* model, concavity and soft tissue invasion were observed on the extraskeletal side of 50-kGy implants due to macrophage adhesion. Thus, if the bone defects had been larger and a porous HAp/Col implant sterilized with 50 kGy or more gamma-ray irradiation had been transplanted, the implant may have been absorbed and the defect may not have healed completely.

In this study, porous HAp/Col was treated with gamma-ray irradiation at 16, 25, 35, and 50 kGy. Irradiation of porous HAp/Col at 16 kGy is the minimum dose for which we could validate sterility (ISO11137-2006, data not shown). Gamma-ray irradiation of porous HAp/Col has few beneficial effects and should thus be applied sparingly. Our results suggest that the proper gamma-ray irradiation dose for sterilization of porous HAp/Col is 16 or 25 kGy.

Porous HAp/Col was jointly developed by the Tokyo Medical and Dental University, the HOYA Corporation, and the National Institute for Materials Science (NIMS). The authors thank Dr. Masanori Kikuchi at NIMS for excellent technical support and advice.

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Original Article

The effect of preoperative lateral flexibility of the lumbar spine on perceived leg length discrepancy after total hip arthroplasty.

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Background: Leg length discrepancy (LLD) after total hip arthroplasty (THA) is a significant factor of patient dissatisfaction. Patients with dissociation between preoperative radiographic LLD and perceived LLD sometimes feel LLD postoperatively even if bilateral leg lengths are equal. There is no publication describing how to decide the amount of leg lengthening in such cases.
Purpose: By examining the influence of preoperative lumbar lateral flexibility on postoperative perceived LLD, this study aims at creating a guideline for the optimal planning of leg lengthening in THA.
Methods: In 59 cases undergoing primary unilateral THA, radiographic LLD, perceived LLD, pelvic tilting and lumbar lateral flexibility were measured preoperatively. The amount of leg lengthening and the sequential change of the perceived LLD were measured postoperatively.
Results: Twelve cases (20%) felt the perceived LLD at two years after surgery. All these cases felt the operative side longer than the non-operative side. In 32 cases with preoperative pelvic inclination to the affected side, postoperative perceived LLD was significantly greater if lumbar spine was rigid. In eight cases with pelvic tilting and rigid lumber spine, the amount of leg lengthening that exceeded preoperative perceived LLD affected the postoperative perceived LLD.
Conclusions: In cases with preoperative pelvic inclination downward to the affected side and with rigid lumbar spine, amount of leg lengthening should not be excessively greater than preoperative perceived LLD. In other cases, lengthening the leg to the same length as the contralateral side rarely results in postoperative perceived LLD.

Key word: Total hip arthroplasty,Perceived leg length discrepancy,Lateral flexibility of lumbar spine

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Introduction

Leg length discrepancy (LLD) after total hip arthroplasty (THA) is a significant factor of patient dissatisfaction. In fact, perceived LLD after THA is one of the largest causes of litigation [1]. In most of cases, LLD is presented as the feeling that the affected side is too long [2]. Avoiding perceived postoperative LLD requires both appropriate preoperative planning and the accurate surgical technique for lengthening the leg during surgery. While there have been several publications describing intraoperative techniques [2-7], there are none, to our knowledge, that address the adequate amount of leg lengthening in planning of THA in order to avoid patient-perceived LLD postoperatively.

In patients with hip diseases where the morbidity period is short, such as rapidly destructive coxarthrosis, lengthening the leg to the same length as the contralateral side rarely results in patient-perceived LLD problems. However, in cases with chronic hip disease (e.g. unilateral secondary osteoarthritis due to developmental dysplasia of the hip), the patient-perceived LLD may be more or less compared to the true LLD, which can be clinically confirmed by the radiograph, due to the pelvic inclination. In such cases, it is not easy to determine the optimal amount of lengthening. If the amount of leg lengthening is as the same length as the preoperative patient-perceived LLD, it is unlikely that the patient feel LLD postoperatively. However, the true LLD and the inclination of the pelvis remain postoperatively. Such a situation is not ideal since the inclination of the pelvis has been suggested to be the cause of the lumbar disease [8]. On the other hand, if we lengthen the affected leg to the extent of the true LLD, patients may perceive the LLD when the pelvic inclination remains postoperatively. While the optimal leg lengthening amount may lie between the perceived and actual leg-length discrepancy values, the determination procedure remains unclear.

We hypothesized that the degree of preoperative lumbar spine mobility plays a role in determining perceived postoperative LLD: If the patient who has a flexible lumbar spine receives leg lengthening equal to the true LLD, it is less likely that they will perceive a discrepancy postoperatively. On the other hand, if the patient who has a rigid lumbar spine receives leg lengthening equal to the true LLD, the chances for perceived LLD are increased. By examining the influence of preoperative lumbar lateral flexibility on postoperative perceived LLD, this study aims at creating a guideline for the optimal lengthening of the leg during the operation in order to avoid patient-perceived LLD problems.

Materials and Methods

Sixty two consecutive cases (53 female, nine male) undergoing primary unilateral THA due to hip disease between January 2004 and March 2005 were investigated prospectively. Three patients whose postoperative radiographic LLD were 10 mm or more (the operative side was longer than the contralateral side radiographically) were excluded from this study. The average age at the time of the operation was 63.9 years old (47 to 86). Of the 59 cases, 53 were diagnosed as osteoarthritis (secondary osteoarthritis due to developmental dysplasia of the hip: 50, traumatic osteoarthritis: one, primary osteoarthritis: two), three as rapidly destructive coxarthrosis, and three as idiopathic osteonecrosis of the femoral head. All the operations were carried out in the lateral decubitus position using the posterolateral approach. Care was taken not to lengthen the leg over the preoperative radiographic LLD. Verification of the leg length via radiography or navigation system was not employed intraoperatively.

All 59 cases were followed up for two years. With all the cases, the following items were measured at one or two weeks preoperatively: The teardrop tilting angle, radiographic LLD, bending range of the lumbar spine, and perceived LLD. All the items except perceived LLD were measured using plain radiographs. We defined the terms and methods of measurement of these values as below.

- Perceived LLD: In order to measure the patient' s perceived LLD, we placed blocks beneath the leg perceived to be shorter. We defined "perceived LLD" as the thickness of the block at the point at which the patient did not perceive LLD. It was measured repeatedly until the value was confirmed. It was recorded in 2.5 mm unit intervals (Figure 1). A positive value indicates that the patient feels the affected side longer than the contralateral side.
- Radiographic LLD: Radiographic LLD was measured on standard anteroposterior views of the pelvis with the hips extended and internally rotated. Radiographic LLD was defined as the difference between the distances from teardrop line (a line that connects bilateral inferior margin of the acetabular teardrop) to the center of the lesser trochanter for each femur as in previous studies [4, 9]. The value was corrected with magnifying power of the radiograph which was calculated using the known diameter of the metal head of the femoral component in each case. A positive value indicates that an affected side is longer than the contralateral side.
- Teardrop tilting angle: An angle between the teardrop line and the horizontal line in the standing position. A positive value indicates that the pelvis tilts toward the affected side. Cases were classified into three groups according to tear drop tilting angle: tilt-affected-side group (tear drop tilting angle$\geq$2 degrees), horizontal group (-2 degrees < tear drop tilting angle<2 degrees), and tilt-unoperated-side group (tear drop tilting angle $\leq$ -2 degrees) (Figure 2).
- Lumbar bending range: An angle between the upper surface of the first lumbar vertebra and the Jacoby line was measured using the anteroposterior radiographs of the lumbar spine taken in standing position. A positive value indicates that the lumbar spine bends to the operative side. We defined "lumbar bending range" of the lumbar spine as the difference of the angles between the natural standing position and the maximum lateroflexion to the affected side (Figure 3).

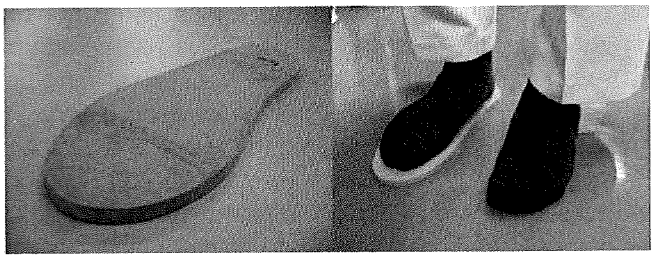


Figure 1. Measurement of "perceived LLD".
Perceived LLD was defined as the thickness of the block at the point at which the patient did not perceive LLD.

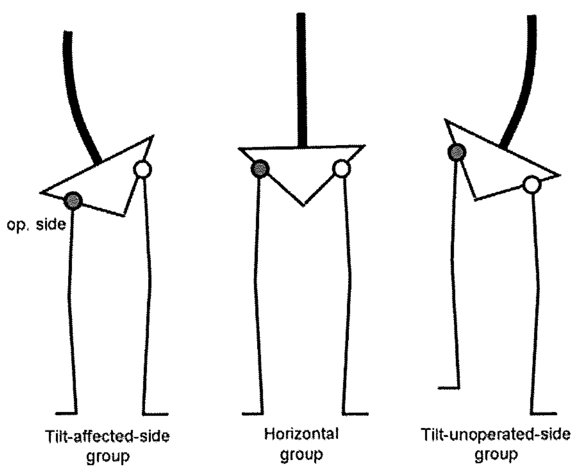
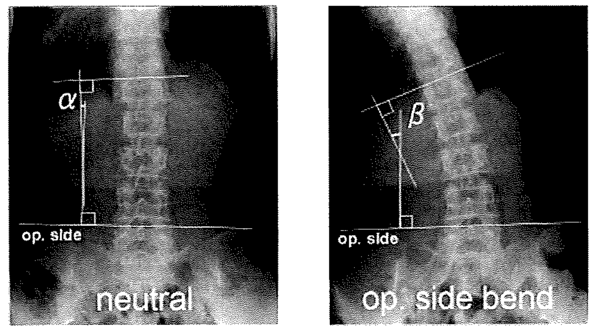


Figure 2. Classification according to the preoperative pelvic tilting.
Tilt-affected-side group: tear drop tilting angle ≥ 2 degrees
Horizontal group: -2 degrees < tear drop tilting angle < 2 degrees
Tilt-unoperated-side group: tear drop tilting angle ≤ -2 degrees



β - α = lumbar bending range

Figure 3. Definition of the "lumbar bending range".
Lumbar bending range was measured using the anteroposterior radiographs of the lumbar spine taken in the natural standing position and the maximum lateroflexion to the affected side. A positive value of both α and β indicates that the lumbar spine bends to the operative side.

Cases were classified into three groups according to lumbar lateral flexibility: flexible group (lumbar bending range > 15 degrees), mid group (5 degrees < lumbar bending range ≤15 degrees), and rigid group (lumbar bending range ≤ 5 degrees).
Additionally, radiographic leg lengthening and lengthening beyond perceived LLD were measured postoperatively. We defined the terms as below.

- Radiographic leg lengthening: Radiographic LLD measured at three months postoperatively minus preoperative radiographic LLD. A positive value indicates that the operated side was lengthened. Radiographic LLD was also measured at six months, one year, and two years postoperatively.
- Lengthening beyond perceived LLD: Preoperative perceived (not radiographic) LLD plus amount of leg lengthening. This value means the amount of leg lengthening beyond the preoperative perceived LLD.

We investigated the following: 1) the relation between the preoperative radiographic LLD and the perceived LLD; the preoperative perceived LLD was compared with the preoperative radiographic LLD in each group classified according to the pelvic tilting, and in each group classified according to the lumbar bending range. 2) The sequential change of the perceived LLD and the radiographic LLD; measurement of the perceived LLD was carried out the day before the surgery, at the hospital discharge (one to two weeks postoperatively), and at three months, six months, one year, and two years postoperatively, and the postoperative sequential change of the perceived LLD was investigated. The postoperative sequential change of the radiographic LLD was also investigated. 3) The relation between the postoperative perceived LLD and the preoperative lumbar bending range; in each group classified according to the pelvic tilting, the average perceived LLD at two years postoperatively were compared among the groups classified according to the lumbar bending range. 4) Factors affecting the postoperative perceived LLD; each subgroup classified according to the pelvic tilting and the lumbar bending range was divided into two groups: cases with the perceived LLD and the cases without the perceived LLD. The postoperative radiographic LLD, the radiographic leg lengthening, and the lengthening beyond perceived LLD were compared between the two groups to investigate the significant factor affecting the postoperative perceived LLD.

Table 1. Relation between preoperative radiographic LLD and preoperative perceived LLD in each group according to pelvic tilting.

	n	preop. radiographic LLD (mm)	preop. perceived LLD (mm)	
tilt-affected-side group	32	-14.4 ± 9.3	-7.0 ± 6.0	p < 0.0001
horizontal group	24	-6.0 ± 6.5	-4.3 ± 6.4	p = 0.03
tilt-unoperated -side group	3	-9.2 ± 10.7	-16.7 ± 15.3	p = 0.52
		(average ± SD)		(paired t-test)

We obtained informed consent about this study from all the patients.

Statistical analysis: The preoperative radiographic LLD and the perceived LLD were compared by a paired t-test. The sequential change of the perceived LLD was analyzed by a repeated measure one way ANOVA. The average of postoperative perceived LLD in each group classified according to the lumbar bending range was compared by a one way ANOVA followed by a Scheffe test. The postoperative radiographic LLD, the radiographic leg lengthening and the lengthening beyond perceived LLD were compared between the cases with the perceived LLD and the cases without the perceived LLD by a Mann-Whitney test. All the analyses were performed using StatView for Windows Version 5.0 data analysis software (SAS Institute Inc, Cary, NC, USA). The level of significance applied was $p < 0.05$.

Results

1) Relation between the preoperative radiographic LLD and the perceived LLD

The pelvis in natural standing position inclined to the affected side in excess of two degrees in 54.2% (tilt-affected-side group), horizontal in 40.7% (horizontal group), and inclined to the unoperated side in 5.1% (tilt-unoperated-side group) preoperatively. Causes of inclination to the unoperated side were severe adduction contracture of the affected side hip joint, or lumbar scoliosis. The relation between the radiographic LLD and the perceived LLD in each group is shown in Table Ⅰ. In tilt-affected-side group, the absolute value of the perceived LLD was significantly smaller than that of the radiographic LLD ($p < 0.0001$). In horizontal group, there was significant difference between the radiographic LLD and the perceived LLD ($p = 0.03$), although the difference was smaller than that of Tilt-affected-side group. In tilt-unoperated-side group, the perceived LLD was greater than the radiographic LLD in one of three cases, and the difference between the perceived LLD and the radiographic LLD was not significant ($p = 0.52$).

The relation between the radiographic LLD and the perceived LLD in each group according to the lumbar bending range is shown in Table Ⅱ. The absolute value of the perceived LLD was smaller than that of the radiographic LLD in all the groups, and there was significant difference in mid group.

2) Sequential change of the perceived LLD and the radiographic LLD

The sequential change of the perceived LLD is shown in Figure 4. In 41 cases (70 %), the patients described they felt that the affected side was longer at the time of hospital discharge, and the postoperative perceived LLD decreased with time. The change with time was statistically significant ($p < 0.0001$).

In 12 cases (20.0%), the perceived LLD persisted at two years after the surgery (Table Ⅲ). In all of the 12 cases, the patients felt that the affected side was longer, and no case felt that the affected side was shorter. Eleven of 12 cases were osteoarthritis secondary due to dysplastic hip, and one case was traumatic osteoarthritis. No case of rapidly destructive coxarthrosis or idiopathic osteonecrosis of the femoral head felt LLD at two years after surgery.

In all the cases, there was no change of the postoperative radiographic LLD after three months to two years.

3) Relation between the postoperative perceived LLD and the preoperative lumbar bending range

In tilt-affected-side group, five of eight cases in rigid group perceived the LLD at two years postoperatively, and the average perceived LLD in rigid group was 4.6 (0-15.0) mm. In mid group, 2 of 15 cases perceived the LLD, and the average perceived LLD in mid group was 0.7 (0-5.0) mm. In flexible group, one of nine cases

Table 2. Relation between preoperative radiographic LLD and preoperative perceived LLD in each group according to lumbar bending range.

	n	preop. radiographic LLD (mm)	preop. perceived LLD (mm)	
flexible group	13	-13.0 ± 10.2	-10.8 ± 2.4	p = 0.56
mid group	34	-10.3 ± 9.2	-4.6 ± 5.6	p < 0.0001
rigid group	12	-9.3 ± 7.9	-6.9 ± 7.9	p = 0.18
		(average ± SD)		(paired t-test)

perceived the LLD, and the average perceived LLD in flexible group was 0.6 (0-5.0) mm. There was significant difference among these groups in the average perceived LLD (p = 0.013). Post hoc test revealed significant difference between rigid group and mid group (p = 0.023), and between rigid group and flexible group (p = 0.037) (Figure 5).

In horizontal group, no case perceived the LLD in flexible group (n = 2) and rigid group (n = 4) at two years postoperatively, and 3 of 18 cases perceived the LLD in mid group. The average perceived LLD in mid group was 0.7 (0-5.0) mm, and there was no significant difference among the three groups classified according to the lumbar bending range.

In tilt-unoperated-side group, there were two cases of flexible group and one case of mid group. One case of mid group perceived the LLD, and the postoperative radiographic LLD in the case was 5.5 mm.

4) Factors affecting the postoperative perceived LLD

In eight cases of tilt-affected-side and rigid group, there was no significant difference in the postoperative radiographic LLD between the cases with the perceived LLD postoperatively and the cases without the perceived LLD. The difference in the radiographic leg lengthening also was not significant between the two groups. On the other hand, the lengthening beyond perceived LLD was significantly greater in the cases with the perceived LLD (p = 0.025) (Table Ⅳ).

In 18 cases of horizontal and mid group, the differences in the postoperative radiographic LLD, in the radiographic leg lengthening and in the lengthening beyond perceived LLD were not significant between the cases with the perceived LLD and the cases without the perceived LLD, although the postoperative radiographic LLD tended to be greater in cases with the perceived LLD than in the cases without the perceived LLD (Table Ⅴ). For the three cases perceiving the LLD at two years postoperatively, the postoperative radiographic LLD was 5.1 mm or more (see Table Ⅲ).

In other subgroups, cases with the perceived LLD postoperatively were none to only two cases. Therefore, statistical analyses were not performed.

Discussion

Goodman et al. reported that preoperative accurate planning and a number of intraoperative cues to assess reproduction of the preoperative plan were helpful to prevent postoperative LLD [3]. Bose also described that the precise reproduction of the intraoperative position of the femur (abduction/adduction) and the use of an intraoperative measurement device assisted in equalization of leg length during surgery [5]. However, these articles aimed at radiographic equality of the leg length, and none of them mentioned the difference between the radiographic LLD and the perceived LLD. Konyves and Bannister revealed that the patients with the perceived LLD after THA had significantly lower hip function. However, they also aimed at the radiographic leg length equalization to avoid perception of the LLD [10]. In cases with the horizontal pelvis preoperatively where the compensatory lumbar scoliosis is none or minimum, radiographic equalization of the leg length would achieve satisfactory results. In fact, in horizontal group in the current study, all three cases who perceived the LLD postoperatively had the postoperative radiographic LLD greater than 5.0 mm, whereas no patient perceived the LLD if the postoperative radiographic LLD was 5.0 mm or less. On the other hand, in cases with preoperative pelvic tilting due to severe anatomical deformation such as secondary osteoarthritis due to developmental dysplasia of the hip, which is the commonest etiology of the osteoarthritis of the hip in Japan, the radiographic equalization of the leg lengthening cannot always

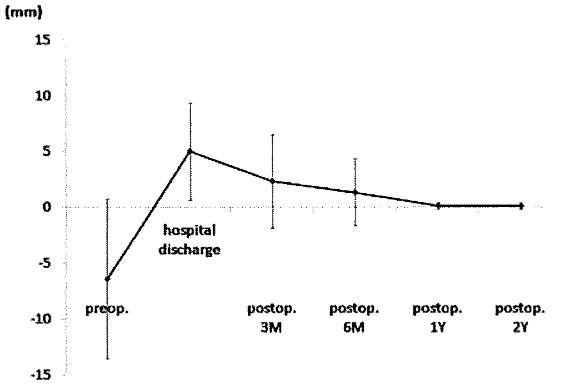


Figure 4. Sequential change of the perceived LLD.
The average perceived LLD at hospital discharge was 5.0 (0-20.0) mm, and the perceived LLD decreased with time. The data are given as average ± SD.

Table 3. Cases with perceived LLD at 2 years after surgery.

Age	Sex	pelvic tilting	lumbar lateral flexibility	preop. perceived LLD (mm)	preop. radiographc LLD (mm)	postop. radiographic LLD (mm)	radiographic leg lengthening (mm)	lengthening beyond perceived LLD (mm)	perceived LLD at 2 years postop. (mm)
51	F	tilt-affected-side	flexible	-10.0	-16.8	-0.9	15.9	5.9	5.0
67	F	tilt-affected-side	mid	0.0	-5.2	5.2	10.4	10.4	5.0
64	M	tilt-affected-side	mid	-5.0	-7.8	6.9	14.7	9.7	5.0
61	F	tilt-affected-side	rigid	-5.0	-5.3	6.2	11.5	6.5	10.0
75	F	tilt-affected-side	rigid	-5.0	-7.0	4.3	11.3	6.3	2.5
65	F	tilt-affected-side	rigid	-5.0	-6.9	5.2	12.1	7.1	5.0
67	F	tilt-affected-side	rigid	-5.0	-21.1	-0.9	20.2	15.2	15.0
86	F	tilt-affected-side	rigid	-2.5	-9.6	0.0	9.6	7.1	5.0
74	F	horizontal	mid	0.0	-2.5	5.1	7.6	7.6	2.5
72	F	horizontal	mid	-2.5	-4.3	5.2	9.6	7.1	5.0
65	F	horizontal	mid	-12.5	-11.5	7.1	18.6	6.1	5.0
61	F	tilt-affected-side	mid	0.0	-2.7	5.5	8.2	8.2	2.5

Table 4. Comparison between cases with perceived LLD and cases without perceived LLD in tilt-affected-side and rigid group.

	n	postop. radiographic LLD (mm)	radiographic leg lengthening (mm)	lengthening beyond perceived LLD (mm)	
perceived LLD (+)	5	3.0 ± 1.0	12.9 ± 1.7	8.4 ± 1.4	(average ± SD)
perceived LLD (-)	3	2.3 ± 0.3	11.6 ± 4.9	3.3 ± 1.3	
		p = 0.76	p = 0.46	p = 0.025	
		(Mann-Whitney test)			

Table 5. Comparison between cases with perceived LLD and cases without perceived LLD in horizontal and mid group.

	n	postop. radiographic LLD (mm)	radiographic leg lengthening (mm)	lengthening beyond perceived LLD (mm)	
perceived LLD (+)	3	5.8 ± 1.1	12.0 ± 5.9	6.9 ± 0.8	(average ± SD)
perceived LLD (-)	15	3.8 ± 4.2	9.4 ± 4.4	6.2 ± 4.1	
		p = 0.40	p = 0.51	p = 0.95	
		(Mann-Whitney test)			

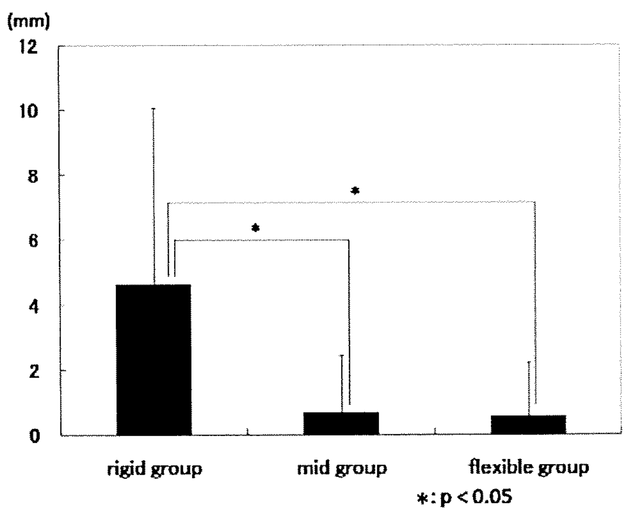


Figure 5. The postoperative perceived LLD in tilt-affected-side group by the group of the preoperative lumbar bending range. The data are given as average ± SD.
The perceived LLD of rigid group was significantly greater than those of other groups.

achieve the satisfactory result. In tilt-affected-side group in the current study, there were three cases of which the perceived LLD was 5mm or more although the radiographic LLD was within 1mm (see Table Ⅲ). The current study suggested that the preoperative perceived LLD works as a reference to determine the amount of leg lengthening in THA.

The factors related to the perceived LLD include the radiographic LLD, the contracture of the hip joint, the inclination of the pelvis due to the scoliosis of the lumbar spine, and the flexion contracture of the knee joint. In THA, leg lengthening and release of the contracture of the affected side is possible, and the pelvic inclination is expected to be more horizontal postoperatively. By predicting the degree of postoperative pelvic inclination, it would be possible to determine the adequate amount of leg lengthening. The lumbar spinal lateroflexion to the affected side taken preoperatively in this study is a simulation of the situation where a pelvis becomes horizontal in connection with the leg lengthening and the release of the contracture of the affected hip after THA. Cases with high lumbar flexibility to the affected side seem to have high reversibility of the pelvic inclination, so the pelvis becomes horizontal due to leg length equalization, resulting in the disappearance of the perceived LLD. On the other hand, cases with low lumbar flexibility to the affected side seem to have low reversibility of the pelvic inclination, so the inclination of the pelvis remains after THA; thus resulting in a situation where the perceived LLD remains (Figures 6 and 7). In this study, cases with rigid lumbar spine felt LLD at a high rate after THA, and cases with flexible lumbar spine felt LLD at a lower rate. The results can be explained by the abovementioned mechanisms.

The reason that most of the patients felt the affected side was longer immediately after THA would be related to the pelvic inclination. Adduction restriction of the affected side hip joint due to tight hip abductors, which is often seen immediately after THA, accelerates

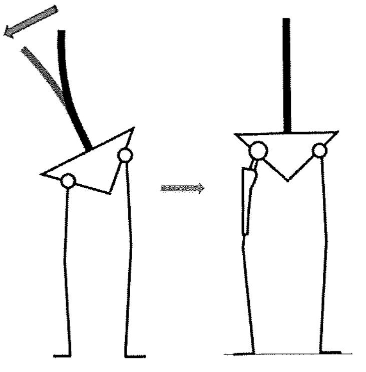


Figure 6. Cases with high flexibility to the affected side of lumbar spine.
The pelvis becomes horizontal due to leg length equalization, resulting in the disappearance of the perceived LLD.

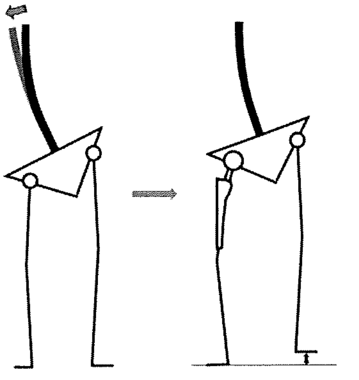


Figure 7. Cases with low flexibility to the affected side of lumbar spine.
The inclination of the pelvis remains after THA, resulting in a situation where the perceived LLD remains.

pelvic inclination and causes this perception of LLD [7]. As the hip abductors are stretched and relaxed by postoperative rehabilitation, the pelvic inclination would decrease and the perceived LLD found immediately after the surgery would diminish. In fact, 70% of the cases felt the LLD at the time of hospital discharge, and only 20 % of the cases felt the LLD at two years after surgery in this study.

In patients with hip joint disease, the affected hip is usually restricted in abduction [11], and tends to be adducted in the supine position. However, this study showed that, in standing position, the pelvis tended to incline the affected side downward and the affected hip tended to become abducted in the majority of the cases. This is explained as compensation for the leg shortening of the affected side. In such cases (tilt-affected-side group), the perceived LLD was smaller than the radiographic LLD. In only three cases (tilt-unoperated-side group), even in standing position, the pelvis inclined towards the contralateral side downward, and the affected hip was in adduction.

The present study has some limitations. First, it is not a randomized study. We started this study after we hypothesized that the preoperative lumbar lateral flexibility would be helpful as a guideline of the optimal amount of leg lengthening. As a result, we took care not to lengthen the leg too much in some cases with rigid lumbar spine. Secondly, although the morbidity period may be a factor of the reversibility of the pelvic inclination, it was not evaluated in the current study. Finally, the ideal amount of the lengthening beyond perceived LLD could not be decided in the current study. However, the lengthening beyond perceived LLD in the cases with the perceived LLD was 8.4 ± 1.4 (6.3 to 15.2) and that in the cases without the perceived LLD was 3.3 ± 1.3 (-0.9 to 5.4) in tilt-affected-side and rigid group (see Table Ⅳ). Furthermore, all 12 cases with the postoperative perceived LLD received the leg lengthening beyond perceived LLD of 5.9 mm or more (see Table Ⅲ). Therefore, the leg lengthening beyond perceived LLD within 5 mm might be acceptable.

There is no publication, to our knowledge, that addresses the adequate amount of leg lengthening in planning of THA in order to avoid postoperative perceived LLD. Our study suggested that the preoperative evaluation of lateral flexibility of lumbar spine and perceived LLD is helpful in determining the optimal amount of leg lengthening in THA. In cases with preoperative pelvic inclination downward to the affected side and with rigid lumbar spine, amount of leg lengthening should not be excessively greater than preoperative perceived LLD. In other cases, lengthening the leg to the same length as the contralateral side rarely results in postoperative perceived LLD.

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OPLLによる脊髄障害への電気生理学的アプローチ

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連続型や混合型の骨化を有する後縦靱帯骨化症（ossification of posterior longitudinal ligament：OPLL）では，MRIなど各種画像診断のみでは障害責任高位を正確に診断することは困難である。術前に脊髄機能を知ることは重要であり，このような場合，電気生理学的な脊髄機能診断が有用である。

また，脊椎靱帯骨化症の症例ではほかの疾患に比して手術中に脊髄障害をきたす危険性が高く，安全に手術をおこなうには脊髄モニタリングが必須である。

Updates of Ossification of Posterior Longitudinal Ligament.

Electrophysiological diagnosis of spinal cord dysfunction in ossification of posterior longitudinal ligament.

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Shigenori Kawabata, Atsushi Okawa, Shoji Tomizawa, Kenichi Shinomiya

It is extremely difficult to make a correct diagnosis of the responsible lesion in multilevel continuous and mixed-type ossification of the posterior longitudinal ligament (OPLL) even after magnetic resonance imaging (MRI). Understanding the function of the preoperative spinal cord is crucial for surgical planning and electrophysiological diagnosis of spinal cord function is useful in such cases. Also, intraoperative spinal cord monitoring is required for cervical OPLL surgery because OPLL patients show postoperative neurological deterioration more frequently than any other pathogenesis.

はじめに

後縦靱帯骨化症（ossification of posterior longitudinal ligament：OPLL）は重篤な脊髄障害の原因となることが多く，適切な診断に基づいた治療方法が求められる。脊髄圧迫があるが機能障害をきたしていない症例や，骨化巣が多椎間に

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及ぶ場合は，各種画像診断や神経学的所見のみでは診断が困難であることも多く，電気生理学的検査が確定診断の助けとなる。

また脊椎靱帯骨化症例では，ほかの疾患に比して手術中に脊髄障害をきたす危険性が高く，安全に手術をおこなうには術中脊髄モニタリングが有用である。

頸椎OPLL症例における電気生理学的診断[1)2)]

脊髄の電気生理学的機能診断法としては，体性感覚誘発電位（SEP），末梢神経伝導検査（M波，F波），経頭蓋磁気刺激－筋誘発電位，針筋電図検査などが一般的におこなわれている。これらの検査法で大まかに脊髄機能障害の有無が診断でき，OPLLによる脊髄圧迫により脊髄機能障害が起きているかの診断に有用である。

多椎間におよぶOPLLで詳細に脊髄機能障害高位を診断する必要がある場合は，これらの検査では高位診断は困難であり，脊髄誘発電位測定が必要となる。脊髄誘発電位は体表からでは測定が困難であるため，脊髄近傍のくも膜下腔・硬膜外腔，椎間板内，黄色靱帯内などに電極を設置する必要がある（図1）。胸髄刺激後の脊髄刺激脊髄誘発電位（SP-SCEP）では後索・後側索を上行する

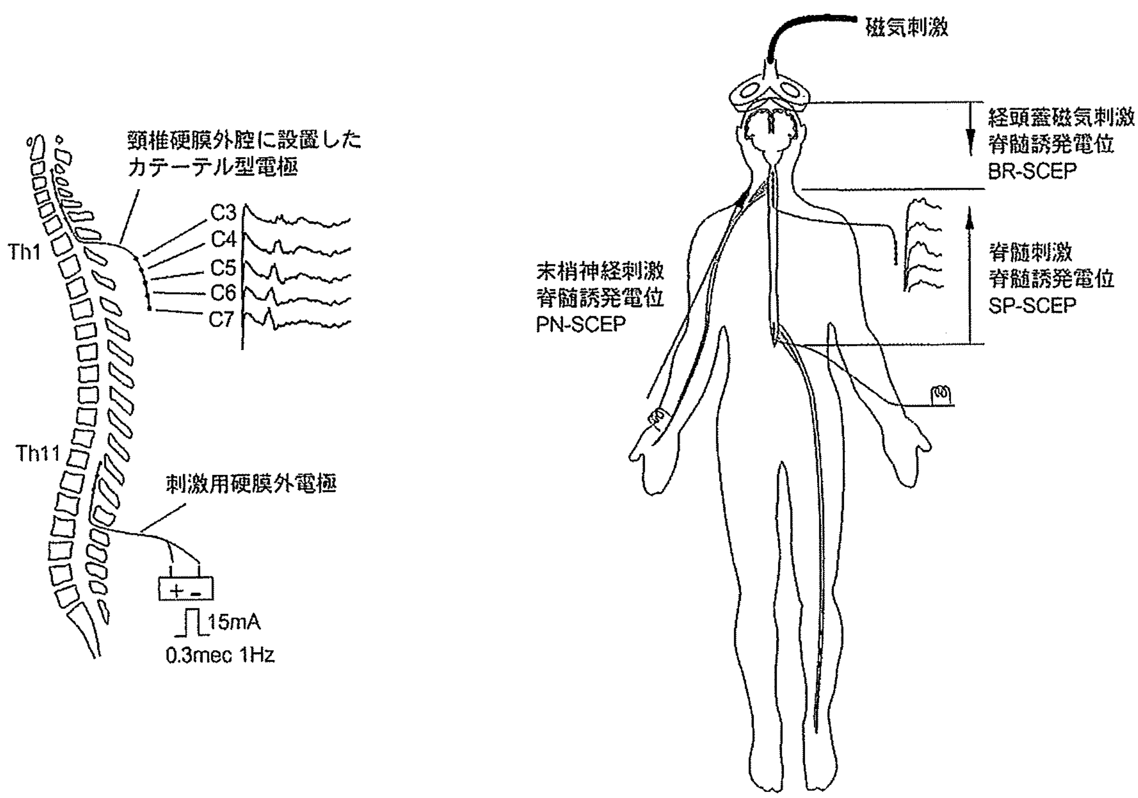


図1　各種脊髄誘発電位の模式図

記録電極は，硬膜外腔・くも膜下腔・黄色靱帯・椎間板内など脊髄近傍に設置する。脊髄・脳・末梢神経を刺激し，脊髄誘発電位を記録する。

（筆者ら作成）

OPLL：ossification of posterior longitudinal ligament（後縦靭帯骨化症），SEP：体性感覚誘発電位

電位，脳を電気または磁気で刺激することで索路を下行する経頭蓋刺激脊髄誘発電位（BR-SCEP）を記録できる。上肢末梢神経幹刺激後の脊髄誘発電位（PN-SCEP）では髄節性電位（神経根枝の電位，シナプス電位，索路の電位の混合電位）を記録することができる。これらの電位の振幅の変化や

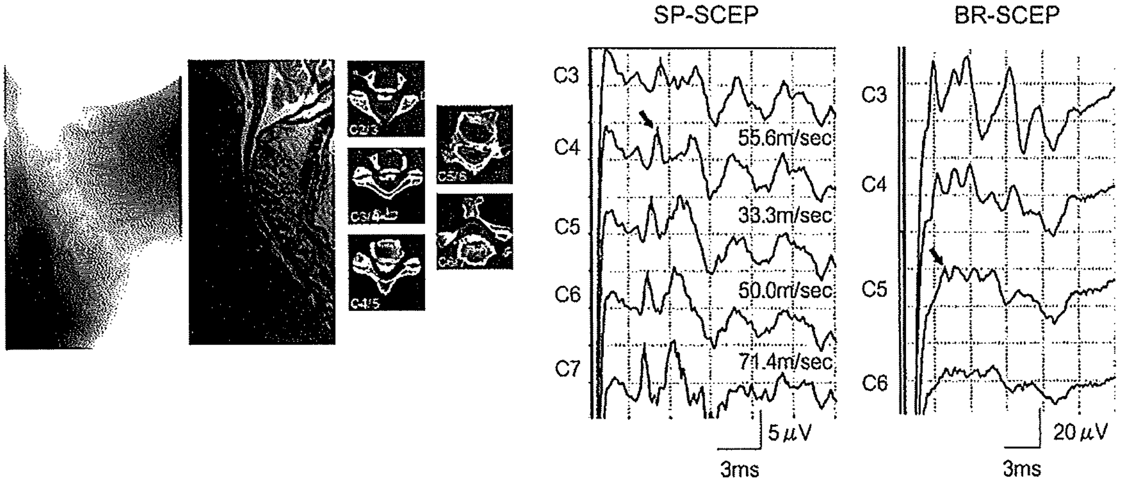


図2　症例1　72歳男性 C2-6，6-7 OPLL

主訴：四肢しびれ，歩行障害，膀胱直腸障害
上行性のSP-SCEP，下行性のBR-SCEPともに最狭窄部のC4/5で電位変化があり，機能障害部位と診断される。
（筆者ら作成）

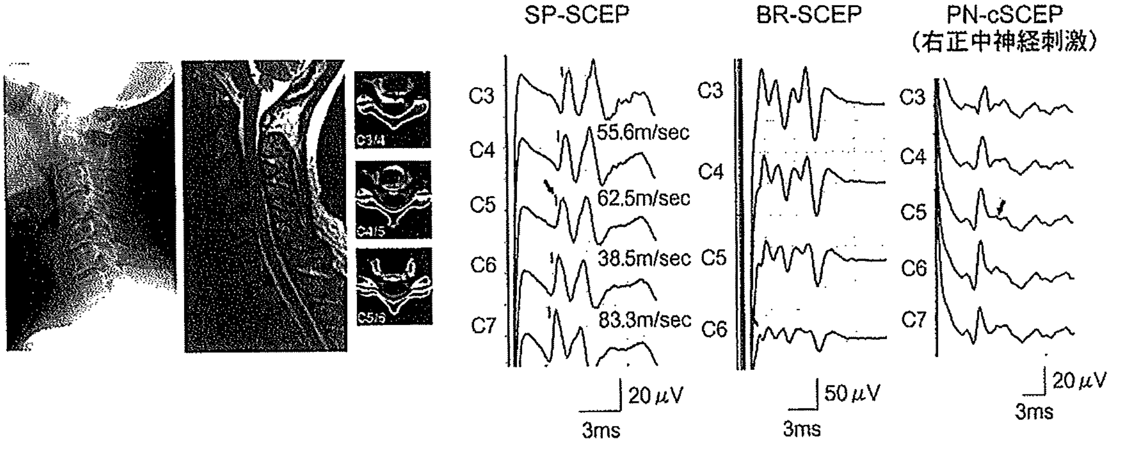


図3　症例2　56歳女性 混合型 OPLL C2-4，5-6

主訴：頸部痛，四肢しびれ
最狭窄部はC3/4であるが，電位測定ではC5/6障害の診断であった。　（筆者ら作成）

BR-SCEP：経頭蓋刺激脊髄誘発電位，PN-SCEP：脊髄誘発電位，SP-SCEP：脊髄刺激脊髄誘発電位

潜時遅延をみることで，多椎間におよぶOPLLにおいても，詳細に脊髄機能障害部位を診断することができる（図2,3）。

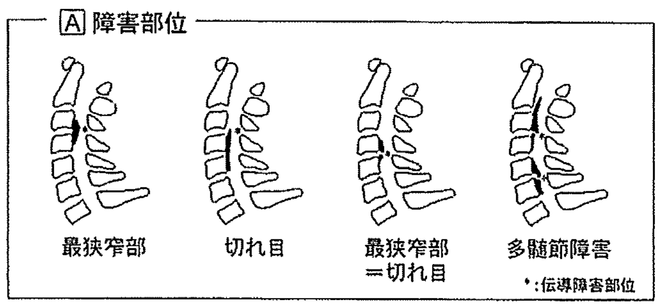
OPLLの形態と脊髄障害高位の関係[3)4)]

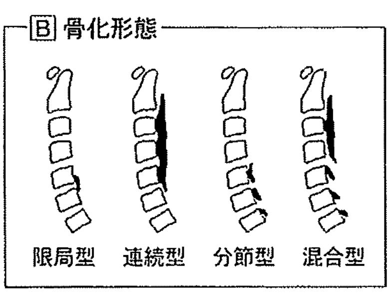
当院の頸椎OPLL患者について，脊髄誘発電位による脊髄障害高位診断結果と骨化形態の関係について検討した。骨化形態が限局型の症例はすべて骨化に一致した最狭窄高位で障害を認めた。連続型骨化の症例では障害タイプは多様で，骨化の切れ目や骨化の上下端など動的因子が関与する部位で機能障害をきたす例，最狭窄部で機能障害をきたす例，両者が混合し多髄節で障害されている例があった。分節型・混合型でも同様に多様な障害タイプを呈したが，特に多髄節障害は混合型OPLLに多かった（図4）。このように，頸椎OPLLによる脊髄障害の原因は動的因子と静的因子の両因子がともに関与し複雑な症状を呈していることが少なくない。

OPLL症例における術中脊髄モニタリング（図5，6）[5)6)]

広範囲の骨化や骨化占拠率の大きい靱帯骨化症では除圧手術中の神経障害の危険も高い。当院で1997～2003年に頸椎OPLLの手術を行った73例中5例（6.4%）に術後神経症状の悪化を認めている。内訳は脊髄障害3例，C5麻痺が1例，遅発性C5麻痺1例であった。これはそのほかの脊髄症手術例の神経合併症（1.5%）に比べ明らかに多かった。

術中障害の回避には術中脊髄モニタリングが有用である。我々はBR-SCEP，経頭蓋電気刺激筋誘発電位（BR-MSEP），SEPを組み合わせてモニタリングをおこなっている。術中のモニタリング





C	最狭窄部	切れ目	最狭窄部＝切れ目	多髄節障害	計
限局型	4	—	—	—	4
連続型	1	2	—	1	4
分節型	3	1	2	—	6
混合型	—	5	3	6	14
計	8	8	5	7	28

図4　骨化形態と障害高位の関係

伝導障害部位を骨化との関係から上記Aの4つのタイプに分類し，骨化形態との相関を検討した。

（筆者ら作成）

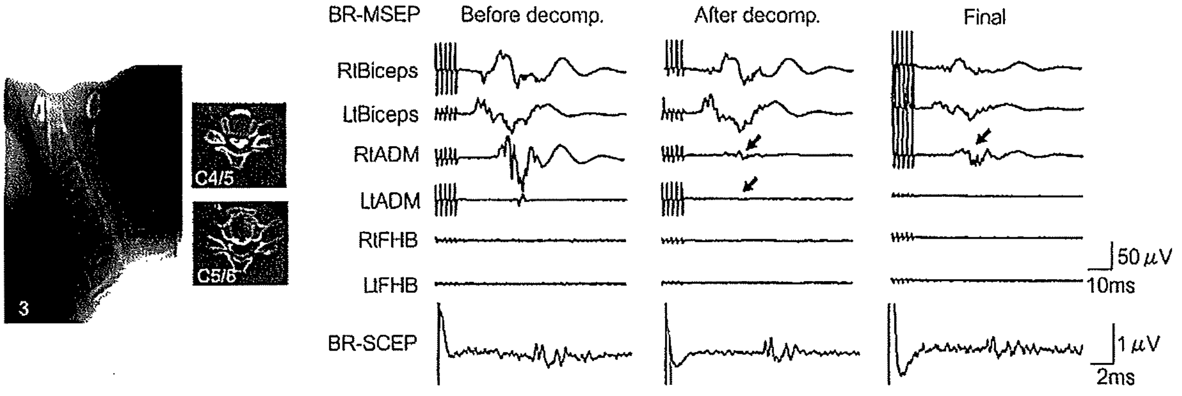


図5　症例3　58 歳男性 C4-6 連続型 OPLL C3-7 前方除圧固定施行

骨化除圧直後に左 ADM 波形の消失。最狭窄部である C5 椎体の除圧が不十分と考え除圧を追加したが，手術終了時も振幅の改善は認められなかった。両 FHB は手術開始時より導出が不良であったが，終了時左はほとんど消失している。術後，左上肢筋力低下と歩行障害が出現した。

（筆者ら作成）

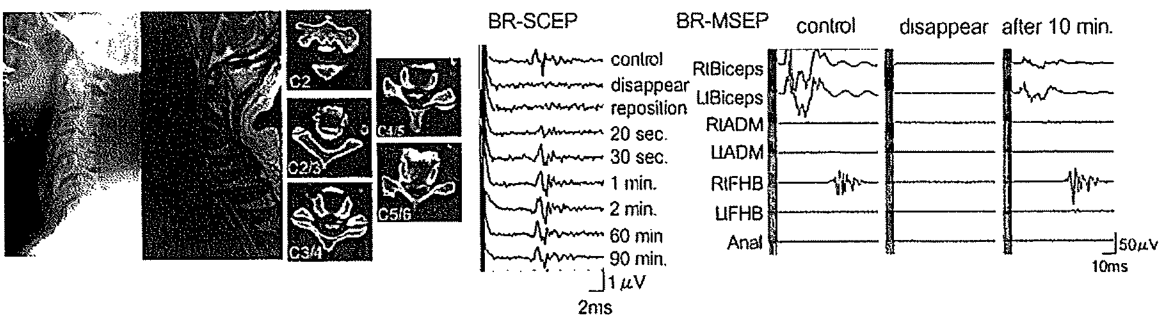


図6　症例4　64 最男性 C2-6 混合型 OPLL 後方除圧術施行

椎弓展開時に脊髄誘発電位が消失。手術操作を休止し待機したが電位回復せず，8分後頸椎の屈曲姿位が原因であるが可能性を考えて，屈曲位から中間位へと矯正を行ったところ，直後から電位の回復を認めた。筋誘発電位も同様に，すべての筋電位が消失したが頸椎姿位矯正後電位の回復を認めた。術後に，脊髄障害を認めなかった。

（筆者ら作成）

により術者にアラームをだすことで，術後神経障害を回避したと思われる症例は5例あり，神経障害の原因は除圧操作2例，移植骨による頸椎伸長1例，頸椎姿位2例であった。アラームにより手術操作を休止し原因に対処することで術後神経障害は起こらなかった。術中モニタリングにより神経障害の原因が明らかになることは，手術手技の向上にもつながる。2004 年以降，当施設で OPLL 手術後の神経障害悪化は頸髄の片側の髄節障害1例のみであり，モニタリングにより手術の

BR-MSEP：経頭蓋電気刺激筋誘発電位

安全性が向上したことを特筆したい。

おわりに

OPLLは診断・手術ともに他疾患に比べ困難であることが多い。電気生理学的手法を駆使することで，OPLL診療の質を向上させることができる。

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Bone Regeneration with Autologous Plasma, Bone Marrow Stromal Cells, and Porous β-Tricalcium Phosphate in Nonhuman Primates

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To potentiate the bone formation capability of bone marrow stromal cell (BMSC)/β-tricalcium phosphate (β-TCP) constructs, we devised an autologous plasma-based construct. We tested its effectiveness and investigated the effects of its components on a monkey ectopic bone formation model. The autologous plasma (platelet-rich plasma, PRP, or platelet-poor plasma, PPP)/BMSC/β-TCP construct (R group or P group) showed significantly more bone formation at 3 and 6 weeks after implantation than a conventional BMSC/β-TCP construct using a culture medium (M group). There was no significant difference between the P and R groups. Moreover, the P group constructs with a 10-fold lower cell concentration yielded equivalent bone formation to the M group at 5 weeks after implantation. To elucidate the effect of fibrin and serum contained in the plasma, five constructs were prepared using the following cell vehicles: autologous serum+fibrinogen (0, 1, 4, or 16 mg/mL) or phosphate-buffered saline+fibrinogen (4 mg/mL). The serum+fibrinogen (4 mg/mL, physiological concentration of monkeys) construct showed the most abundant bone formation at 3 weeks after implantation, though at 5 weeks no statistical difference existed among the groups. Autologous plasma efficiently promoted osteogenesis of BMSCs/porous β-TCP constructs, and both fibrin and serum proved to play significant roles in the mechanism.

Introduction

The supply of autologous bone grafts is insufficient to repair large bone defects. Harvesting these bone grafts has risks of infection, nerve damage, and cosmetic disability.[1,2] Despite the development of various porous ceramics with osteoconductivity,[3] including hydroxyapatite (HA) and tricalcium phosphate (TCP), by themselves, these ceramics have little osteoinductivity[4,5] and are insufficient to repair massive bone defects. To overcome these problems, bone tissue engineering methods have been developed that combine bone marrow stromal cells (BMSCs) with porous ceramic scaffolds. BMSCs are easily isolated from bone marrow and have a proliferative capability and multilineage differentiation potential, including the capacity for osteogenic differentiation.[6,7] There are many reports that demonstrate the *in vivo* bone formation capability of BMSC/porous ceramic constructs.[8–14]

Although a variety of strategies to prepare BMSC/porous ceramic constructs have been contrived, practical methods have still not been established. In well-accepted techniques, after suspended in culture medium, BMSCs were seeded into porous ceramics, and the cells were cultured on porous ceramics for a few hours,[8–10] 1 week,[12,13] or 2 weeks[11,14] to attach the cells to the scaffolds and induce osteogenic differentiation of the cells. In these constructs, it is probable that BMSCs proliferated two-dimensionally by creeping along the surface of the pores, and the nutrient was supplied from the culture medium at the early stage of implantation. Considering that the range of nutrient diffusion from surrounding tissue is limited within the surface area of cell/scaffold construct,[15–18] BMSC survival after implantation could be impaired at the center of the constructs.

To provide preferable environments to BMSCs seeded into porous ceramics, we devised a construct that utilized autologous plasma of either platelet-poor plasma (PPP) or

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