In vivo segmental motion of the cervical spine in rheumatoid arthritis patients with atlantoaxial subluxation

R. Takatori[1], D. Tokunaga[1], N. Inoue[2,3], H. Hase[1], T. Harada[1], H. Suzuki[3], H. Ito[4], T. Nishimura[4], H.S. An[2], T. Kubo[1]

[1]*Department of Orthopaedics and* [4]*Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan;* [2]*Department of Orthopedic Surgery, Rush University Medical Center, Chigago, USA;* [3]*Department of Mechanical Engineering, Doshisha University, Japan.*

Abstract

Objective

The dynamic mechanism underlying cervical spine involvement in rheumatoid arthritis (RA) remains unidentified. The purpose of the current study was to determine the in vivo *cervical segmental motion in RA patients with atlantoaxial subluxation (AAS) using a patient-based three-dimensional magnetic resonance imaging (MRI) computer model.*

Methods

Healthy volunteers and RA patients with AAS (all females, n=10) underwent MRI examination of the cervical spine. Each vertebral body from the occipital bone (Oc) to the first thoracic vertebra (T1) was reconstructed from slices of T2-weighted sagittal MR images in the neutral, flexion, and extension positions. Using volume merge methods, each reconstructed vertebral body was virtually rotated and translated. Rotational segmental and translational segmental motions were obtained in three major planes.

Results

Overall, the axial translational motions in the RA group were lower than those in the healthy volunteers; however the axial translational motion at only C1-C2 during flexion was at the same level as that in the healthy volunteers and was greater on the bottom side than that at other intervertebral levels. The frontal rotational motions at C1-C2 during extension were greater in the RA patients than those in the healthy volunteers ($p<0.05$).

Conclusion

The atlantoaxial joints in the RA patients with AAS showed great frontal rotational motion during extension and great axial translation on the bottom side during flexion. The current noninvasive MRI-based method could be useful in evaluating the 3-D dynamic mechanism underlying cervical involvement in RA in vivo.

Key words

Segmental motion, atlantoaxial subluxation, cervical spine, rheumatoid arthritis, magnetic resonance imaging.

Ryota Takatori, MD; Daisaku Tokunaga, MD, PhD; Nozomu Inoue, MD, PhD; Hitoshi Hase, MD, PhD; Tomohisa Harada, MD; Hiromi Suzuki, MS; Hirotoshi Ito, MD, PhD; Tsunehiko Nishimura, MD, PhD; Howard S. An, MD; Toshikazu Kubo, MD, PhD.

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Please address correspondence and reprint requests to: Ryota Takatori, MD, Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan.
E-mail: r-taka@koto.kpu-m.ac.jp

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Introduction

Cervical spine involvement in rheumatoid arthritis (RA) occurs at a high frequency. It is observed in 30%-80% of RA patients (1-5), and the atlantoaxial joint is most commonly involved. Chronic inflammation leads to atlantoaxial instability and subluxation (1-5), and further progression may lead to myelopathy due to spinal cord compression by the odontoid and pannus or to sudden death respiratory muscle paralysis with cranial settling (6-8). Furthermore, subaxial subluxation (SS) leads to instability of the affected segment in the subaxial area.

As described above, cervical spine instability in RA is an important factor that results in severe limitation in the activities of daily living (ADL) in RA patients if the patients have symptoms such as myelopathy; however, the cervical involvement may not be detected because even patients with severe disorders often have no symptoms, and the dynamic mechanism underlying cervical spine involvement in RA remains unidentified. Many reports have investigated cervical spine instability with the use of radiographs (9, 10). In RA patients, it is generally evaluated using the lateral view of radiographs obtained during flexion and extension movements (10-13). Further analyses of the dynamic mechanism of cervical spine involvement in RA were performed with cineradiography (14) and a biplanar roentgenogram (15). However, three-dimensional (3-D) measurements are required to estimate static and dynamic changes in a rheumatoid cervical spine, particularly the upper cervical spine, *in vivo*.

Using cadaveric spines, Panjabi *et al.* performed 3-D assessments of the movements of the upper cervical spine (16). Recently, the use of a personal computer with advanced image-processing technology for 3-D assessment of segmental motion in the spine was reported (17-20). These methods allowed *in vivo* 3-D motion analysis of a subject-based 3-D computer model; however, there were no reports on the cervical spine in RA.

The purposes of the current study were to assess the *in vivo* cervical segmental motion in healthy volunteers and RA patients with atlantoaxial subluxation (AAS) and to elucidate the instability pattern accompanying AAS during neck flexion and extension; these goals were accomplished using a subject-based 3-D magnetic resonance-imaging (MRI) computer model.

Subjects and methods

Subjects

All assessments were performed after the study was approved by the Ethics Committee of Kyoto Prefectural University of Medicine, and informed consent was obtained from all subjects. The participants included 10 healthy volunteers (all females, 35-56 years of age; mean age, 41.6 years; the control group) and 10 RA patients (all females, 36-72 years of age; mean age, 61.6 years; the RA group) who were diagnosed with AAS based on radiographic evaluation. All patients had been diagnosed with RA based on the criteria put forth by the 1987 American College of Rheumatology. There was a significant difference in age between healthy volunteers and RA patients ($p<0.01$, Table I). No significant difference was found in body mass index (BMI) between healthy volunteers and RA patients (Table I).

Radiographic evaluation

Lateral images of RA patients were taken during flexion and extension and anterior–posterior images were taken in the open-mouth position (Fig. 1). The anterior atlantodental interval (AADI), the Ranawat value, and the Redlund-Johnell value were measured using analysis software for digital imaging (21-23). AAS was defined as AADI >3mm, and vertical subluxation (VS) was defined as a Ranawat value <13 mm or Redlund-Johnell value <32 mm (for female subjects). SS was defined as greater than 3.5 mm of translation of one vertebral body on another (10, 24). Furthermore, atlantoaxial impaction (AAI) was evaluated using the Sakaguchi-Kauppi method (25, 26).

MRI evaluation

The axial and sagittal images (T1- and T2-weighted, respectively) of the cervical spine in the neutral supine position

Table I. Characteristics of the subjects (mean ± SEM).

	Healthy volunteers	RA patients	*p*-value
Age	41.6 ± 2.0	61.6 ± 3.4	$p<0.01$
BMI (body mass index)	21.5 ± 0.9	21.2 ± 1.0	ns
Total motion in flexion (Oc–T1)			
Frontal rotation (degree)	28.7 ± 2.1	28.4 ± 2.6	ns
Sagittal translation (mm)	58.9 ± 1.4	27.7 ± 6.9	$p<0.001$
Axial translation (mm)	-18.8 ± 1.5	-0.7 ± 3.0	$p<0.001$
Total motion in extension (Oc–T1)			
Frontal rotation (degree)	-46.3 ± 2.1	-30.9 ± 3.2	$p<0.001$
Sagittal translation (mm)	-40.1 ± 2.4	-20.9 ± 5.8	$p<0.04$
Axial translation (mm)	-12.6 ± 1.7	-9.1 ± 2.0	ns

Frontal rotation; flexural side: plus, extensional side: minus. Sagittal translation; anterior side plus, posterior side: minus. Axial translation; top side: plus, bottom side: minus.

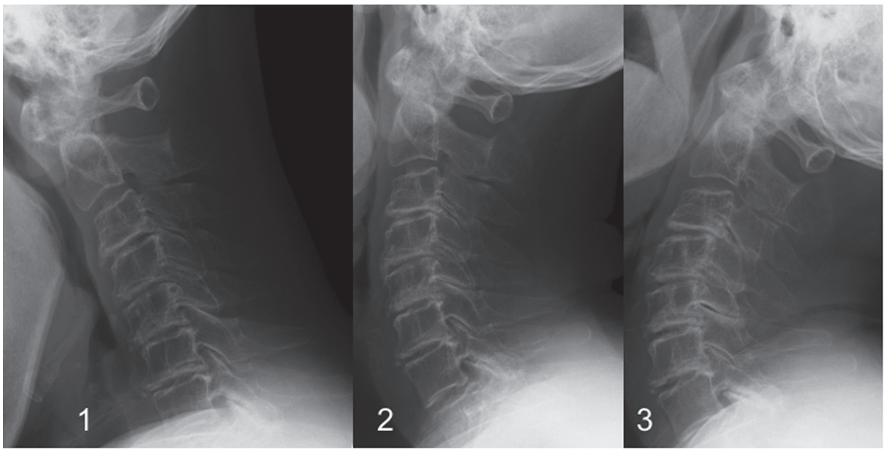

Fig. 1. The lateral view of radiographs in (**1**) flexion, (**2**) neutral, and (**3**) extension positions (an example of an RA patient).

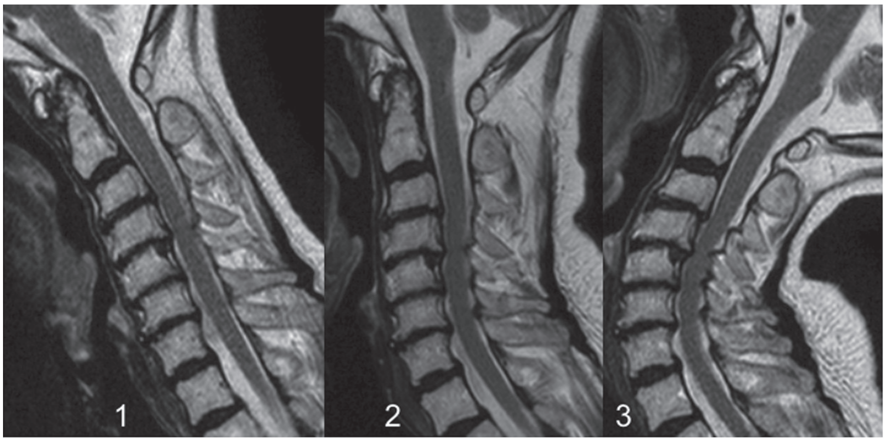

Fig. 2. The T2-sagittal midline view of MRI in (**1**) flexion, (**2**) neutral, and (**3**) extension positions (an example of an RA patient).

using a pillow on the head and neck were obtained with a 1.5 T clinical scanner with a head-neck coil (Gyroscan Intera; Philips Medical Systems, Best, Netherlands). Additionally, the T2-weighted sagittal MR images during flexion and extension were obtained using our protocols to evaluate changes in the cervical spine during flexion and extension movements in the supine position (Fig. 2). For range of motion (ROM) in ADL without pain, images in the flexion position were taken using a pillow on the head, and images in the extension position were taken using a pillow on the neck. The examination with an attendant doctor was to be canceled if the patient had pain while under the supervision of the doctor; however, there were no cancellations of the examination in any cases in this study. The slices of T1-weighted sagittal MR images were obtained with turbo spin-echo (TSE) sequence (TR/TE = 710/10 ms; echo train length = 3; FOV = 250x250 mm; slice thickness/gap = 3/0.3 mm, 15 slices; acquisition matrix 256x512; number of averages = 2). The slices of T2-weighted sagittal MR images were also obtained with turbo spin-echo (TSE) sequence (TR/TE = 3540/110 ms; echo train length = 49; FOV = 250x250 mm; slice thickness/gap = 3/0.3 mm, 15 slices; acquisition matrix 320x512; number of averages = 4).

3-D reconstruction of MR images

To identify segmental motion between two vertebral bodies in flexion and extension of the cervical spine, 3-D image data with location information was reconstructed from 2-D DICOM image data from an MRI examination. The following process and analysis were performed.

1. Constructing the 3-D MRI computer model

The slices of T2-weighted sagittal MR images in the neutral, flexion, and extension positions were all imported into a 3-D reconstruction software package (Mimics; Materialise Co., Ltd. Yokohama, Japan), and a threshold level was selected to define the shell of the bone marrow (Fig. 3). Each vertebral body from the occipital bone (Oc) to the first thoracic vertebra (T1) was segmented based on the threshold level. Detailed vertebral shapes, such as facet joints, were reconstructed along with manual operation.

2. Analysis of segmental motion between each of two vertebral bodies

To analyze the segmental motion of two vertebral bodies, a point-cloud data set for each body was created with Mimics software for volume merging, using the custom software program previously described by Ochia *et al*. (18, 19). In the volume merge method, a vertebral body in the neutral position was virtually rotated and translated toward the same body during flexion or extension. These rotations and translations of the vertebral body were performed at increments of 0.05° and 0.05 mm, respectively. The segmental motions were classified into rotational and translational motions. Three rotational axes were examined: frontal rotation (flexion/extension), sagittal rotation (lateral bending), and axial rotation; frontal rotation was regarded as the main rotational segmental motion. Total frontal rotational motion was evaluated using the sum of the frontal segmental motions from Oc-C1 to C7-T1. Translational segmental motion was subsequently calculated in three directions; frontal, sagittal, and axial translation, and estimated for each translation (Fig. 1). The terms left/right, anterior/posterior, and top/bottom are used to express the sides in frontal, sagittal, and axial translation, respectively. The total of these motions was evaluated using the squares of the translational motions from Oc -C1 to C7-T1.

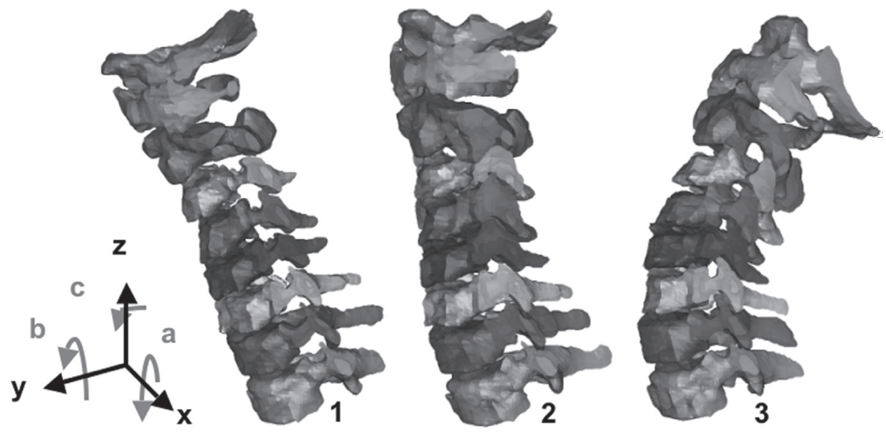

Fig. 3. The patient-based 3D MRI computer models of the cervical spine from Oc to T1 in (**1**) flexion, (**2**) neutral, and (**3**) extension positions were reconstructed (an example of a RA patient). Three rotational axes (**a**: frontal rotation, **b**: sagittal rotation, and **c**: axial rotation) and three directions (**x**: frontal translation, **y**: sagittal translation, and **z**: axial translation) were determined.

Statistical analyses

Differences in the segmental motions at intervertebral levels were compared using the Kruskal-Wallis test. Differences in the segmental motions between healthy volunteers and RA patients with AAS were compared using the Mann-Whitney U test. The correlations between age and each total motion were assessed using Spearman's correlation due to the significant difference in age between the two groups. The cutoff value for significant difference (p-value) was defined as $p<0.05$. All analyses were conducted using the StatView program package (Version 5.0; SAS Institute Inc., Cary, NC).

Results

Segmental motions in the healthy volunteers

In the control group, there were significant differences in the frontal rotational and sagittal and axial translational segmental motions at intervertebral levels during flexion and extension ($p<0.01$, Figs. 4, 5, and 6). The axial and sagittal rotational segmental motion and frontal translational motion showed no significant differences at the intervertebral levels, and the magnitude of these motions was very low. Frontal rotational segmental motions were greater at the lower intervertebral levels (C5-C6 to C7-T1) during flexion, and at Oc-C1 and the middle intervertebral levels (C3-C4 to C5-C6) during extension. On the other hand, sagittal translational motion increased from C7-T1 to Oc-C1 during flexion and extension, and axial translational segmental motions were greater on the bottom side at Oc-C1 and the middle intervertebral levels (C2-C3 to C4-C5) during flexion and at the upper intervertebral levels (C2-C3 and C3-C4) during extension.

Radiographic assessment in RA patients

The averaged anterior atlantodental interval (AADI) in flexion, neutral, and extension positions was 6 mm (range, 5-10 mm), 5 mm (range, 4-7 mm), and 2 mm (range, 1-5 mm), respectively. All cases showed AAS in the neutral position and unstable AAS with changes in AADI during motion. Eight cases showed reducible AAS which was reduced during extension, and 2 cases showed non-reducible AAS which has spontaneous subluxation. The average Ranawat value was 17 mm (range, 15-19 mm), and the average Redlund-Johnell value was 41 mm (range, 35-50 mm); therefore AAS deformity was detected in all the patients, but no VS or SS deformities were detected in any of the patients. Eight cases showed grade 1 AAI, 2 cases showed grade 2 AAI, and there were no cases that showed grade 3 or 4.

Segmental motions in the RA patients and a comparison between the control group and the RA group

Similar to the findings in the healthy volunteers, there were significant differences in the contribution among the intervertebral levels in the frontal rotational, and sagittal and axial translational segmental motions during flexion and extension in the RA patients ($p<0.05$, Fig. 4, 5, and 6). There tended to be greater ranges of frontal rotational motion at the middle intervertebral levels (C3-C4 to C6-C7) during flexion and at the C1-C2 level during extension. On the other hand, the sagittal translational segmental motions at the upper intervertebral levels were greater than those estimated at the lower intervertebral levels during flexion and extension, and the axial translational segmental motions were greater on the bottom side at C1-C2 during flexion and at Oc-C1 during extension.

Compared with the control group in terms of total motion, total sagittal and axial translational motions during flexion in the RA group were significantly lower than those observed in the control

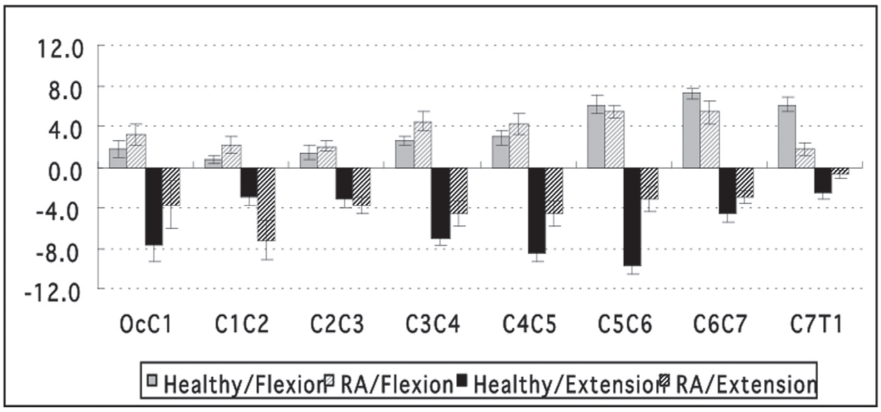

Fig. 4. Frontal rotational segmental motion of the cervical spine (unit: degrees; flexural side: plus, extensional side: minus). The data of each segment in flexion and extension were compared with the data of each segment in the neutral position, respectively.

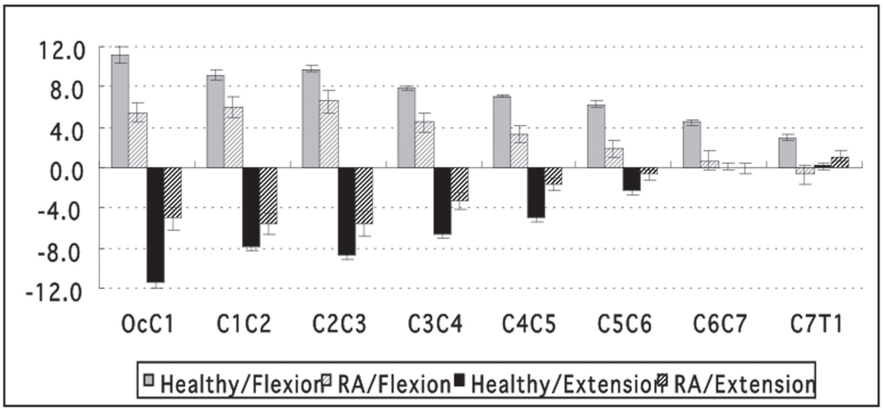

Fig. 5. Sagittal translational segmental motion of the cervical spine (unit: mm; anterior side: plus, posterior side: minus). The data of each segment in flexion and extension were compared with the data of each segment in the neutral position, respectively.

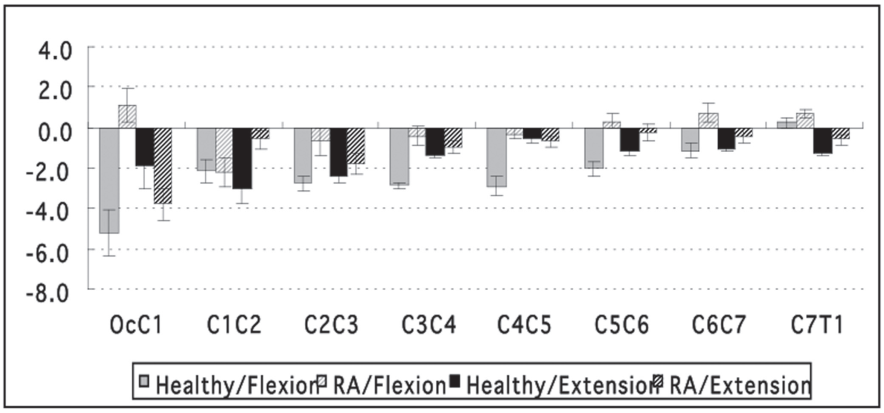

Fig. 6. Axial translational segmental motion of the cervical spine (unit: mm; top side: plus, bottom side: minus). The data of each segment in flexion and extension were compared with the data of each segment in the neutral position, respectively.

group ($p<0.001$, Table I). Total frontal rotational motion and total sagittal motion in the RA group during extension movements were lower than those observed in the control group (frontal rotation: $p<0.001$; sagittal translation: $p<0.04$; Table I). Total axial and sagittal translation during flexion were negatively correlated with age (axial translation: Rho=0.55, $p<0.02$; sagitttal translation: Rho=0.55, $p<0.02$), therefore these motions were lower at higher age. There were significant differences between the RA group and control group in these motions after correcting for age.

A comparison of the frontal rotational segmental motion between the two groups revealed that the values at the C6-C7-T1 levels during flexion and those at the C4-C5-C6 and C7-T1 levels during extension were lower in the RA group than those in the control group ($p<0.05$, Fig. 4). Conversely, the frontal rotational segmental motions at the C3-C4 level during flexion and at the C1-C2 level during extension were greater in the RA group than those in the control group ($p<0.05$, Fig. 4). The sagittal translational segmental motions from all levels during flexion and at the Oc-C1 and C3-C4 to C5-C6 levels during extension were lower in the RA group than those in the control group ($p<0.05$, Fig. 5). The axial translational segmental motions in the RA group were lower on the bottom side at Oc-C1 and C3-C4 to C6-C7 during flexion ($p<0.02$, Fig. 6) and at C1-C2 during extension than those in the control group ($p<0.01$, Fig. 6).

Discussion

The current study demonstrated that noninvasive techniques involving the application of the volume merge method in a 3-D MRI computer model provided accurate measurements of the 3-D segmental motion of the cervical spine in RA patients with AAS *in vivo*.

This study demonstrated the total main rotational and translational motions of the cervical spine during flexion and extension. Total main rotational motion reflects the ROM during head–neck mobility, and total translational motion reflects the intervertebral mobility during flexion and extension (9, 18, 19). In RA patients with AAS, the ROM of extension and the intervertebral mobility during flexion and extension were considered to decrease when compared to those observed in the control group. Hakkinen *et al*. reported that neck muscle strength and mobility are decreased in patients with atlantoaxial disorders (27). Therefore, in the participating RA patients, decreasing head-neck mobility was considered to reflect a loss of neck muscle strength and function of the joints. If pathologically great segmental motion exists at some level under conditions in which overall cervical spine mobility is decreased, the instability occurred at that level would greatly affect the mobility.

Regarding the relationship between age and motion, total axial and sagittal translational motion during flexion were lower at higher age, therefore cervical spine mobility was decreased at higher age. There were significant differences between the RA group and control group in these motions after correcting for age. However, the cervical spine motions were affected by not only rheumatoid changes but also degenerative changes. Furthermore, even though the subjects were protected from pain in the examination, a subject's tolerable limit of discomfort might affect the total motion of the cervical spine.

In the current study, all RA patients had unstable AAS, which showed subluxation at the neutral position, and no VS. The atlantoaxial joints in patients with AAS showed greater frontal rotational motion than those in the control group during extension. Using flexion/extension MRI, Karhu *et al*. reported that in the neutral position, the C1 vertebra was more flexed in the RA patients than in the healthy subjects, and RA patients demonstrated greater extension in the upper cervical spine than that observed in the healthy subjects (28). In the current study, the range of the AADI in RA patients was 4 to 7 mm; these patients were considered to have an AAS deformity in the unstable stage. These results indicated that the atlantoaxial joints in the RA patients with AAS showed great frontal rotational motion during extension and great axial translation on the bottom side during flexion. For this reason we considered that rotational motion, not only sagittal translational motion, during neck extension resulted in a spontaneous reduction of the subluxation, which can be attributed to the remaining intact periodontoid-ligamentous and capsular structures during AAS progression (1).

There are several reports on the natural history of the cervical spine involvement in RA (1-5). Regarding the natural history of upper cervical spine involvement in RA, particularly in the atlantoaxial joints, it is known that anterior subluxation occurs first and then vertical (bottom) subluxation (2, 4). Oda *et al*. reported that reducible AAS occurred first, and the irreducible change in preceding anterior atlantoaxial subluxation was a sign of the start of vertical subluxation (2). Fujiwara *et al*. showed a positive correlation between the C1-C2 angle and the AADI and a negative correlation between the Oc-C1 angle and the AADI in the natural history of RA in radiographs, suggesting that the atlas not only shifts forward, but it also slips down at a decline from the axis (3). It is important for prognostication and determination of treatment criteria to identify the pathological motion at the time AAS occurs, which is a comparatively early stage. AADI measured on a radiograph is a simple and useful parameter in evaluation of rheumatoid involvement of the cervical spine. Based on the current results, however, cervical spine instability in AAS occurs not only in the direction of sagittal translation. In fact, the instability of the cervical spine in these patients with AAS showed great rotational motion and translational motion on the bottom side. This suggests that the deformity will progress in these directions. This complex motion should be a concern when patients with AAS are treated either conservatively or operatively. We believe that it is important to evaluate not only the sagittal translational motion, but also the axial translational and frontal rotational motions in the atlantoaxial joints during the unstable stage of cervical spine involvement in RA. The current results were obtained by the evaluation of a limited number of subjects; therefore further prospective large-scale studies are necessary to verify these results.

Three-dimensional models are generally obtained from CT images or MRI. A CT-based model would be better suited for 3-D evaluation because it shows the bony surface more accurately than the MRI model, and it is very useful in surgical planning at the clinic. However, the amount of radiation from CT should be taken into consideration, and CT can not be used on all patients in the comparatively early stage. Thus, if information on the motion of the vertebral body could be obtained from MRI, it would be more useful for earlier diagnosis of cervical involvement in osteoarthritis and RA (29). Furthermore, MRI has the potential to produce a 3-D evaluation of soft tissues and nerves. T2-weighted sagittal MR images of the cervical spine during flexion and extension positions are useful for evaluating the dynamic factors underlying spinal cord compression (30, 31). Therefore we use T2-weighted images in osteoarthritis and RA patients with cervical involvement. Duerinckx *et al*. used midline sagittal T2-weighted MR images for dynamic analyses of cervical spine motion during flexion and extension (32). In this study, we presumed that T2-weighted images could be used to reconstruct 3-D images and that the current noninvasive MRI-based method could be used for dynamic assessment of the vertebral body. Furthermore, the coupled motion associated with flexion and extension motion was minimal in the RA patients in our study. However, asymmetrical destruction of the vertebral body and facet joint may occur during the progressive stages of RA and thus cause complex coupling segmental motions during various cervical motions (15, 33). Although this new method is not necessary for every RA patient in clinical practice, it could be useful in evaluating the complex segmental motion of the cervical spine in severe cases because of the ability to measure 6 degrees of freedom with a 3-D model. This method also provides important information for determining the appropriate operative procedure and the area necessary to evaluate the relationship between the complex motions and the neural findings of the images. The method requires a standard MRI examination and general-purpose software, and is reproducible in general facilities. At the present, original software has the advantages of accuracy and convenience of analysis, however, general-purpose software can also be used for analysis. Furthermore, developments in medical imaging equipment and analysis software will make it possible to easily analyze a patient's motions in general facilities using this method in the near future. This method is highly effective because there is no radiation, it provides detailed motion analysis, and it may be applied to other joints not only limited to the cervical spine. The current study was limited in that only changes during flexion and extension could be analyzed. Future studies should include assessments of pathological motion of the cervical spine during other motions, such as sagittal rotation and axial rotation, to identify other pathological conditions. This could lead to a system architecture that provides objective evaluations of prognostication, appropriate intervention timing, and methods of conservative or operative therapy.

References

1. HALLA JT, HARDIN JG, VITEK J *et al.*: Involvement of the cervical spine in rheumatoid arthritis. *Arthritis Rheum* 1989; 32: 652-9.
2. ODA T, FUJIWARA K, YONENOBU K, AZUMA B, OCHI T: Natural course of cervical spine lesions in rheumatoid arthritis. *Spine* 1995; 20: 1128-35.
3. FUJIWARA K, YONENOBU K, OCHI T: Natural history of upper cervical lesions in rheumatoid arthritis. *J Spinal Disord* 1997; 10: 275-81.
4. DREYER SJ, BODEN SD: Natural history of rheumatoid arthritis of the cervical spine. *Clin Orthop* 1999; 366: 98-106.
5. NEVA MH, KOTANIEMI A, KAARELA K, LEHTINEN JT, BELT EA, KAUPPI M: Atlantoaxial disorders in rheumatoid arthritis associate with the destruction of peripheral and shoulder joints, and decreased bone mineral density. *Clin Exp Rheumatol* 2003; 21: 179-84.
6. BODEN SD, DODGE LD, BOHLMAN HH *et al.*: Rheumatoid arthritis of the cervical spine. A long-term analysis with predictors of paralysis and recovery. *J Bone Joint Surg Am* 1993; 75: 1282-97.
7. MIKULOWSKI P, WOLLHEIM FA, ROTMIL P *et al.*: Sudden death in rheumatoid arthritis with atlanto-axial dislocation. *Acta Med Scand* 1975; 198: 445-51.
8. YASZEMSKI MJ, SHEPLER TR: Sudden death from cord compression associated with atlanto-axial instability in rheumatoid arthritis. A case report. *Spine* 1990; 15: 338-41.
9. ORDWAY NR, SEYMOUR RJ, DONELSON RG *et al.*: Cervical flexion, extension, protrusion, and retraction. A radiographic segmental analysis. *Spine* 1999; 24: 240-7.
10. ROCHE CJ, EYES BE, WHITEHOUSE GH: The rheumatoid cervical spine: signs of instability on plain cervical radiographs. *Clin Radiol* 2002; 57: 241-9.
11. KAUPPI M, ANTTILA P: A stiff collar for the treatment of rheumatoid atlantoaxial subluxation. *Br J Rheumatol* 1996; 35: 771-4.
12. KAUPPI M, NEVA MH: Sensitivity of lateral view cervical spine radiographs taken in the neutral position in atlantoaxial subluxation in rheumatic diseases. *Clin Rheumatol* 1998; 17: 511-4.
13. ZIKOU AK, ALAMANOS Y, ARGYROPOULOU MI *et al.*: Radiological cervical spine involvement in patients with rheumatoid arthritis: a cross sectional study. *J Rheumatol* 2005; 32: 801-6.
14. HINO H, ABUMI K, KANAYAMA M *et al.*: Dynamic motion analysis of normal and unstable cervical spines using cineradiography. An *in vivo* study. *Spine* 1999; 24: 163-8.
15. IAI H, GOTO S, YAMAGATA M *et al.*: Three-dimensional motion of the upper cervical spine in rheumatoid arthritis. *Spine* 1994; 19: 272-6.
16. PANJABI M, DVORAK J, DURANCEAU J *et al.*: Three-dimensional movements of the cervical spine. *Spine* 1988; 13: 726-30.
17. LIM TH, ECK JC, AN HS *et al.*: A noninvasive, three-dimensional spinal motion analysis method. *Spine* 1997; 22: 1996-2000.
18. OCHIA RS, INOUE N, RENNER SM *et al.*: Three-dimensional *in vivo* measurement of lumbar spine segmental motion. *Spine* 2006; 31: 2073-8.
19. OCHIA RS, INOUE N, TAKATORI R, ANDERSSON GB, AN HS: *In vivo* measurement of lumbar segmental motion during axial rotation in asymptomatic and chronic low back pain subjects. *Spine* 2007; 32: 1394-1399.
20. ISHII T, MUKAI Y, HOSONO N *et al.*: Kinematics of the upper cervical spine in rotation. *Spine* 2004; 29: E139-44.
21. HINCK VC, HOPKINS CE: Measurement of the atlanto-dental interval in the adult. *Am J Roentgenol* 1960; 84: 945-51.
22. RANAWAT CS, O'LEARY P, PELLICCI P *et al.*: Cervical spine fusion in rheumatoid arthritis. *J Bone Joint Surg Am* 1979; 61: 1003-10.
23. REDLUND-JOHNELL I, PETTERSSON H: Radiographic measurements of the cranio-vertebral region. Designed for evaluation of abnormalities in rheumatoid arthritis. *Acta Radiol Diagnosis* 1984; 25: 23-8.
24. WHITE AA, PANJABI MM: The problem of clinical instability in the human spine: a systematic approach. *In* WHITE AA, PANJABI MM (Eds.): *Clinical Biomechanics of the Spine*. 2nd ed., Philadelphia, JB Lippincott 1990: 277-378.
25. KAUPPI M, SAKAGUCHI M, KONTTINEN YT, HAMALAINEN M: A new method of screening for vertical atlantoaxial dislocation. *J Rheumatol* 1990; 17: 167-72.
26. KAUPPI M, SAKAGUCHI M, KONTTINEN YT, HAMALAINEN M, HAKALA M: Pathogenetic mechanism and prevalence of the stable atlantoaxial subluxation in rheumatoid arthritis. *J Rheumatol* 1996; 23: 831-4.
27. HAKKINEN A, NEVA MH, KAUPPI M *et al.*: Decreased muscle strength and mobility of the neck in patients with rheumatoid arthritis and atlantoaxial disorders. *Arch Phys Med Rehabil* 2005; 86: 1603-8.
28. KARHU JO, PARKKOLA RK, KOSKINEN SK: Evaluation of flexion/extension of the upper cervical spine in patients with rheumatoid arthritis: an MRI study with a dedicated positioning device compared to conventional radiographs. *Acta Radiol* 2005; 46: 55-66.
29. ZIKOU AK, ARGYROPOULOU MI, ALAMANOS Y *et al.*: Magnetic resonance imaging findings of the cervical spine in patients with rheumatoid arthritis. A cross-sectional study. *Clin Exp Rheumatol* 2005; 23: 665-70.
30. CONDON BR, HADLEY DM: Quantification of cord deformation and dynamics during flexion and extension of the cervical spine using MR imaging. *J Comput Assist Tomogr* 1988; 12: 947-55.
31. LAIHO K, SOINI I, KAUTIAINEN H *et al.*: Can we rely on magnetic resonance imaging when evaluating unstable atlantoaxial subluxation? *Ann Rheum Dis* 2003; 62: 254-6.
32. DUERINCKX AJ, YU WD, EL-SADEN S *et al.*: MR imaging of cervical spine motion with HASTE. *Magn Reson Imaging* 1999; 17: 371-81.
33. NEVA MH, KAARELA K, KAUPPI M: Prevalence of radiological changes in the cervical spine--a cross sectional study after 20 years from presentation of rheumatoid arthritis. *J Rheumatol* 2000; 27: 90-3.