OWN syndrome is the most common inherited chromosomal disorder, with a frequency of 1 in 700 live births. Three cytogenetic variants cause the disorder: trisomy 21 (accounting for 95% of all cases), chromosomal translocation (4% of all cases), and mosaicism with trisomy 21 (1% of all cases). Phenotypic expression of the syndrome includes mild-to-moderate mental retardation, craniofacial–skull base abnormalities, cardiovascular disorders, gastrointestinal problems, and immunological deficiency.11

Of particular importance to surgeons who treat spinal disorders in children is the high rate of craniocervical instability reported in patients with Down syndrome. Atlantoaxial instability has been reported in 10 to 30% and OC instability in 8 to 63% of patients with Down syndrome.

Despite the alarmingly high incidence of craniovertebral instability in this patient population, relatively few research articles have been published on the topic, and no morphological studies have been completed prior to this report.

In 1996, Uno and colleagues6 reported significant anteroposterior occipitocervical instability (Oc–C1) motion (1–9 mm, mean 2.3 mm) in 75 patients with Down syndrome compared with age-matched control individuals (mean 1.3 mm). Earlier, Tredwell and associates5 reported Oc–C1 instability in 43 (61.4%) of 64 asymptomatic patients with Down syndrome; instability was defined as greater than 4 mm of subluxation on flexion–extension radiographs. The authors emphasized that multidirectional instability, including rotatory instability, may be present in these patients. In 1992, Menezes and Ryken7 reported their surgical experience in 18 symptomat-ic patients with Down syndrome, 50% of whom had OC instability and rotatory subluxation requiring fusion. In their study, instability was defined as subluxation greater than 7 mm at the Oc–C1 joint complex. In 2000, Taggard, et al.,14 reported Oc–C1 instability in 16 (44%) of 36 patients with Down syndrome who were treated for craniovertebral junction abnormalities.
In the current study we compare morphological characteristics of the C-1 SAS in patients with Down syndrome with those in age-matched control individuals to assess OC joint anatomy and to identify potential predictive factors for instability.

**Clinical Material and Methods**

Our study population consisted of eight patients with Down syndrome and one patient with congenital Oc–C1 instability (two girls and seven boys); in our control group were 15 age-matched individuals (one girl and 14 boys). The ages of the participants in the study and control groups ranged from 2.9 to 15.9 years and from 4.3 to 15.9 years, respectively. The age-matched control participants were evaluated to rule out a diagnosis of os odontoideum or cervical trauma. All individuals included in the study underwent high-resolution CT imaging of the cervical spine, which was performed using 1-mm contiguous sections from the skull base to C-7.

**Image Filtering**

Image data were initially passed through an anisotropic diffusion filter using the open-source imaging package Insight Toolkit (version 1.6; Kitware, Inc., Albany, NY) developed under the sponsorship of the National Library of Medicine. The anisotropic filter reduced noise within the image while preserving the edges of the bone. A confidence-connected filtering process was subsequently performed to reduce noise within the data set further.

**Region-Growing Segmentation and Antialiasing**

Isolation of the C-1 vertebra was accomplished by using a region-growing segmentation algorithm (Insight Toolkit). To begin segmentation, an SD was specified and a seed point was picked within the C-1 vertebral body. The region to be included in the segmentation was grown out from the seed point until the intensity of the adjacent voxels no longer lay within the designated SD range. Using an antialiasing filter (Insight Toolkit), the steplike appearance caused by the gaps between the CT slices was reduced.

**Surface Mapping**

Surface map values were calculated on a voxel-by-voxel basis by measuring the angle generated between a vector oriented vertically and at the normal of each voxel. The tangent of each angle was taken and saved for every voxel within the image data set. A graduated color scale was then applied at each voxel point to correspond with the tangent value of each voxel (red = horizontal surface, blue = vertical surface). Surface maps for patients with Down syndrome were compared with those for age-matched controls.

**Morphometric Analysis**

Measurements were made in sagittal reconstructions of the cervical spine to determine the length and depth of the SAS of C-1. To obtain the length, measurements were taken along the midline of the lateral mass of C-1 from the anterior to the posterior aspect of the SAS. The depth was calculated by dropping a perpendicular line from the length measurement to the inferiormost portion of the C-1 SAS (Fig. 1). To normalize for variations in sizes of the individual C-1 vertebra, the depth was divided by the length measurement.

**Statistical Analysis**

Descriptive statistics were used to compare the normalization ratios obtained by morphometric analysis of the C-1 SAS. A Student t-test was used to compare the two groups, and the right and left C-1 SAS measurements were combined within groups to increase statistical validity. Statistical significance was achieved at a probability value less than 0.05.

**Results**

Morphometric analysis of the C-1 SAS in eight patients with Down syndrome and one patient with congenital instability at Oc–C1 yielded statistically significant differences compared with measurements of the C-1 SAS in age-matched controls (Table 1). The mean normalized depth/
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Length ratio for the study group was 0.083 ± 0.04 (mean ± SD, range 0.015–0.164) and that for the age-matched controls was 0.202 ± 0.08 (range 0.05–0.33, p < 0.001).

Qualitative visual inspection of the surface mapping revealed differences when patients with Down syndrome were compared with age-matched controls. The C-1 SAS of patients with Down syndrome was markedly less sloped than that of age-matched control individuals in all but one instance. These findings correlated with both a visual inspection of the sagittal CT reconstructions and with the normalized ratios obtained by measuring the C-1 SAS along the midline of the lateral mass. The sagittal CT reconstructions clearly depicted a generalized flattening of the C-1 SAS of the patients with Down syndrome along the x and y axes compared with the normal cup-shaped C-1 SAS seen in the age-matched controls (Fig. 2). A comparison of the patient with congenital Oc–C1 instability and an age-matched control (Pair E) demonstrated an essentially normal left C-1 SAS in the patient; however, the right C-1 SAS of the control individual was noted to be very steeply sloped in one dimension (Fig. 3).

Discussion

Craniocervical instability is likely an underreported presentation among patients with Down syndrome that should be familiar to pediatricians and to surgeons who specialize in spinal problems in children. Our review of the current literature found relatively few references reporting the incidence of OC instability, and no anatomical studies of joint morphology in this patient population are available for review. In 1961, Spitzer and colleagues were the first to report craniocervical instability in a population of patients with Down syndrome after finding evidence of instability in nine of 29 patients in their study. In 1981, Hungerford, et al., reported the next documented case of Oc–C1 instability in a patient with Down syndrome who presented with worsening quadriaparesis that improved after fusion. Several other case reports followed that documented similar patient presentations.

In 1990, Gabriel, et al., retrospectively reviewed the incidence of Oc–C1 translation in 73 patients with Down syndrome by using techniques described by Wiesel and Rothman. They reported that 63% of patients had anteroposterior translation of 1 mm or greater, independent of age. As noted earlier, similar results were reported by Tredwell, et al., Menezes and Ryken, and Taggard, et al. Taggard and colleagues noted that Oc–C1 instability was coexistent with atlantoaxial dislocation in 15 of 36 patients.

Treatment recommendations for patients with Oc–C1 instability have been published by several authors. Brockmeyer suggested surgical fusion if patients present with greater than 8 to 10 mm of subluxation at the Oc–C1 level, even if they are asymptomatic. Taggard, et al., used a variety of reference techniques to determine abnormal Oc–C1 motion and based the decision to perform fusion in patients on abnormal movement combined with evidence of neural

### Table 1

<table>
<thead>
<tr>
<th>Representative Pairing</th>
<th>Patient’s C-1 SAS†</th>
<th>Age-Matched Control’s C-1 SAS‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>A</td>
<td>0.021</td>
<td>0.042</td>
</tr>
<tr>
<td>B§</td>
<td>0.108</td>
<td>0.120</td>
</tr>
<tr>
<td>C</td>
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<td>0.073</td>
</tr>
<tr>
<td>D</td>
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<td>0.070</td>
<td>0.048</td>
</tr>
<tr>
<td>F</td>
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<td>0.164</td>
</tr>
<tr>
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<td>0.117</td>
</tr>
<tr>
<td>I</td>
<td>0.086</td>
<td>0.059</td>
</tr>
</tbody>
</table>

* Data represent probability values < 0.001 (Student t-test).
† The overall mean ± SD for the nine patients was 0.083 ± 0.043.
‡ The overall mean ± SD for the 15 age-matched controls included in the final statistical analysis was 0.202 ± 0.076.
§ Pairing depicted in Fig. 2.

Fig. 2. Sagittal CT reconstructions used for a comparison of a patient having Down syndrome with an age-matched control (see Pairing B in Table 1). Left: A C-1 reconstruction with a surface map overlay on the SAS. The color scale ranges from red (flat) to blue (highly sloped surface). Note the relative lack of blue and green tones in the C-1 SAS of the patient with Down syndrome compared with that of the age-matched control. Right: A C-1 reconstruction with normalized values after measurement of the C-1 SAS. Note the lack of curvature of the C-1 SAS in the patient with Down syndrome compared with that of the age-matched control.
Congenital OC instability in children with Down syndrome

Fig. 3. Sagittal CT reconstructions used to compare the patient with congenital OC instability and an age-matched control. Left: A C-1 reconstruction with a surface map overlay on the superior articular surface. The color scale ranges from red (flat) to blue (highly sloped surface). Note the relatively normal left C-1 SAS and the very sloped right C-1 SAS (dark blue), which has little contour (that is, cupping of the surface). Right: A C-1 reconstruction showing normalized values after measurement of the C-1 SAS. Note the lack of curvature of the right C-1 SAS compared with that of the age-matched control.

We evaluated the C-1 SAS in patients presenting with greater than 8 mm of subluxation on flexion–extension radiographs. Morphometric analysis of the C-1 SAS consistently demonstrated the absence of the normal concave shape of the C-1 SAS when viewed in the sagittal dimension. Normalized ratios of the C-1 SAS (defined as depth/length) were abnormal compared with those of age-matched controls. The joint was analyzed further using a surface map that allowed 3D visualization of the joint anatomy with superimposed gradients that defined the angulation of the joint surface. Qualitative assessment of surface imaging correlated with the quantitative measurements obtained at the C-1 SAS. The 3D visualization was qualitative in this study, and techniques are being developed to automate and assess quantitatively the 3D C-1 SAS modeling to improve accuracy.

Variations in the anatomy of the C-1 SAS could logically account for the OC–C1 instability demonstrated in our patients. Under normal conditions, the occipital condyle is seated within the cup-shaped C-1 articulation. Anterior and lateral translation is restricted by the walls of the C-1 articular surface. In the setting of Down syndrome, the normal cup-shape of the C-1 SAS is altered, revealing a flat joint that is unable to prevent anterior or lateral subluxation independently. Stability in our patient population is likely to be predominantly provided by ligaments that support the Oc–C1 joint, namely the capsular membrane, the anterior and posterior Oc–C1 membranes, and the tectorial membrane. Although these ligaments are quite strong, it is unlikely that over time they could support and restrain movement completely. We believe that subluxation at the Oc–C1 junction in patients with Down syndrome is a direct result of the absence of curvature at the C-1 SAS.

Based on this hypothesis, the concept of ligamentous laxity and the development of delayed instability can also be explained. In a study of patients with Down syndrome who were followed up serially with dynamic imaging, it was demonstrated that delayed instability—defined as progressive subluxation with an increased atlantodens interval—is possible. Likewise, Tredwell and associates stated that compression, craniovertebral architecture, and osseous maturation. Overall, specific recommendations for fusion based on the degree of motion have been difficult to define and have relied largely on anecdotal evidence; likewise, patients presenting with neurological symptoms such as myelopathy are often treated surgically even though lesser degrees of subluxation are present.

The biomechanics of the OC junction are complex, and we refer the reader to a paper by White and Panjabi for a detailed description of the traditional biomechanical concepts regarding this region in healthy adults. In summary, the majority of the stability at the Oc–C1 level is provided by the cup-shaped joint formed by the occipital condyle and the C-1 SAS. Capsular ligaments provide support at the condylar/C-1 SAS joint. The anterior and posterior Oc–C1 membranes as well as the tectorial membrane provide significant support at this level; additionally, the alar and apical ligaments provide minor support. Normal craniovertebral motion, as described by White and Panjabi, is classified into directions of flexion–extension, lateral bending, and lateral rotation. In healthy adults at the Oc–C1 level, 25° of motion occurs with flexion–extension, 5° of motion occurs with lateral bending, and 5° of axial rotation is permissible. White and Panjabi defined Oc–C1 instability in adults as greater than 2 mm of subluxation on dynamic imaging. Alternative descriptions of normal motion at the Oc–C1 junction have been described; el-Khoury, et al., asserted that the tip of the odontoid should remain directly below the basion during flexion and extension.

In contrast to the extensive documentation of the joint in adults, knowledge regarding the functional development of this joint in children is scanty, and few researchers have explored the normal degree of motion seen in infants and children. In assessing Oc–C1 motion in 22 neonatal and infant cadavers, Gilles and colleagues found multiaxial motion. They suggested that final modeling and functional development occurs during maturation. Likewise, White and Panjabi noted that the Oc–C1 segment is relatively unstable in children. To our knowledge, no author has assessed the shape of the OC junction during development.
“upper cervical instability in Down syndrome at the Oc–C1 and atlantoaxial levels is a reflection of the generalized ligamentous laxity of these children.” If one assumes that the shape of the C-1 SAS is altered and fails to provide mechanical support to prevent subluxation, it seems probable that over time the ligaments supporting the joint will either fail or lose tensile strength. It is our contention that ligamentous laxity is a result of altered osseous anatomy and not the reverse.

Our study results provide the first description of altered anatomy at the C-1 SAS, suggesting a mechanism by which Oc–C1 instability occurs in children with Down syndrome. The current study provides a simple method of analyzing the morphological aspects of the C-1 SAS using reconstructed sagittal CT images. Knowledge of abnormal development at the C-1 SAS may prove useful in the future as a screening test for instability and may help guide recommendations regarding the need for OC fusion in the setting of OC and upper cervical spine instability. It is important to note that the current study is preliminary and includes a limited patient cohort. Additionally, the patients included had evidence of greater than 8 mm of subluxation on dynamic imaging. It is likely that lesser degrees of subluxation are encountered in symptomatic patients. A correlation of the degree of subluxation and the shape of the C-1 SAS is needed to define a threshold for characterizing vertebrae in a patient as unstable and as requiring surgical fusion. Likewise, variations in neural canal width, degree of subluxation, and evidence of spinal cord signal abnormalities are important variables that should guide treatment recommendations and be incorporated into any definition of instability. The current study also fails to account for cartilaginous tissue at the joint complex that may provide additional stability. Finally, additional healthy individuals will need to undergo evaluation to define the range of normal variation seen with maturation, and comparisons between male and female patients will be needed as standards are developed regarding the shape of the C-1 SAS. As discussed earlier, Gilles and colleagues noted multiaxial movement at the Oc–C1 joint in all 24 pediatric cadaveric specimens they studied, which led them to conclude that normal maturation, including final modeling and functional development of the craniocervical junction, occurs after birth.

Demonstrating morphological changes at the C-1 SAS that correlate with instability may provide a new means by which to diagnose instability in patients with Down syndrome and offer more explicit criteria for recommending cervical fusion than that supplied by close clinical observation. Alterations in joint anatomy presumably influence the likelihood of ligamentous instability occurring over time; however, this issue has yet to be adequately addressed.

**Conclusions**

On the basis of high-resolution CT imaging used to assess the C-1 SAS, we report the first description of differences in the anatomy of the Oc–C1 joint that likely lead to instability in this patient population. A comparison of patients who have Down syndrome with age-matched controls demonstrates a flattened or “rocker bottom” joint in patients with Down syndrome who present with greater than 8 mm of subluxation at Oc–C1. The findings presented in this paper suggest a hypothesis that explains the mechanism of subluxation and provides a standard means to assess the shape of the C-1 SAS joint for the purposes of screening this patient population. Developmental population-based studies are needed to define the normal range of anatomy seen at the Oc–C1 joint in children.

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**References**


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