Artificial cervical disc arthroplasty has been introduced to limit the development of ASD that can occur with ACDF. By direct decompression along with disc height and neuroforaminal restoration, ACDF has achieved a success rate of over 90%, with resolution of symptoms and return to normal daily activities after surgery.3 However, immobility of the fused level has been associated with accelerated degeneration at levels adjacent to the fused site, which is a major long-term concern with ACDF surgery.1,9,12,18,23 Evidence of ASD has been shown in many biomechanical studies in which removal of segmental motion increases stiffness at the fused segment, resulting in elevated stress at adjacent levels, where degeneration is potentially accelerated.8 Therefore, artificial disc arthroplasty, by preserving segmental motion and alleviating the stress burden at adjacent levels, is believed to decrease the propensity for ASD. The concept has been supported by early clinical outcomes showing that artificial cervical discs were capable of preserving segmental motion8,19 with improved pain and function scores.2

Despite its encouraging short-term outcomes with artificial cervical disc arthroplasty, however, there are concerns regarding complications related to device design as well as subsidence, dislocation, and instability due to misalignment.1 In our previous work, we analyzed 3 different disc prostheses—Bryan (Medtronic, Inc.), Prestige LP (Medtronic, Inc.), and ProDisc-C (Synthes, Inc.)—using an image-based FE method to investigate the propensity for ASD.

Analysis of load sharing on uncovertebral and facet joints at the C5–6 level with implantation of the Bryan, Prestige LP, or ProDisc-C cervical disc prosthesis: an in vivo image-based finite element study

Heesu Kang, M.S.,1–3 Paul Park, M.D.,1 Frank La Marca, M.D.,1,3 Scott J. Hollister, Ph.D.,1–3 and Chia-Ying Lin, Ph.D.1,3

1Spine Research Laboratory, Department of Neurosurgery, and 2Department of Biomedical Engineering, University of Michigan Medical School; and 3Department of Mechanical Engineering, University of Michigan, Ann Arbor, Michigan

Object. The goal of this study was to evaluate and compare load sharing of the facet and uncovertebral joints after total cervical disc arthroplasty using 3 different implant designs.

Methods. Three-dimensional voxel finite element models were built for the C5–6 spine unit based on CT images acquired from a candidate patient for cervical disc arthroplasty. Models of facet and uncovertebral joints were added and artificial discs were placed in the intervertebral disc space. Finite element analyses were conducted under normal physiological loads for flexion, extension, and lateral bending to evaluate von Mises stresses and strain energy density (SED) levels at the joints.

Results. The Bryan disc imposed the greatest average stress and SED levels at facet and uncovertebral joints with flexion-extension and lateral bending, while the ProDisc-C and Prestige LP discs transferred less load due to their rigid cores. However, all artificial discs showed increased loads at the joints in lateral bending, which may be attributed to direct impinging contact force.

Conclusions. In unconstrained/semiconstrained prostheses with different core rigidity, the shared loads at the joints differ, and greater flexibility may result in greater joint loads. With respect to the 3 artificial discs studied, load sharing of the Bryan disc was highest and was closest to normal load sharing with the facet and uncovertebral joints. The Prestige LP and ProDisc-C carried more load through their rigid core, resulting in decreased load transmission to the facet and uncovertebral joints. (DOI: 10.3171/2010.3.FOCUS1046)

Key Words • cervical disc arthroplasty • joint load sharing • facet joint • uncovertebral joint • cervical spine

Abbreviations used in this paper: ACDF = anterior cervical discectomy and fusion; ASD = adjacent-segment disease; FE = finite element; ROM = range of motion; SED = strain energy density; STL = stereolithography.

Unauthenticated | Downloaded 04/24/24 05:41 AM UTC
of subsidence caused by device design.13 Based on the hypothesis that subsidence is related to high implant-interface stress, prostheses with a flexible core (nucleus) were shown to have less likelihood of subsidence, by absorbing high strain energy. However, this raised additional concerns regarding load sharing by facet and uncovertebral joints at the treated level, due to reduced loads transferred to the device’s core causing greater shared load burdens for the facet and uncovertebral joints. Given that proper placement of implants in arthroplasty provides better restoration of the natural kinematics of the joint,1 investigating how the underlying articular mechanism of an artificial disc impacts the biomechanical environment of the spinal segment should help achieve better performance of the prosthesis.

In this extended study, load sharing at the facet and uncovertebral joints was analyzed and compared among segments implanted with Bryan, Prestige LP, and ProDisc-C artificial discs. Using an in vivo image-based FE method, we computed von Mises stresses and the levels of strain energy density (SED). In addition, a spinal segment with an intact, healthy intervertebral disc was modeled and analyzed as a control reference. An underlying assumption in this study was that uncovertebral joints would be preserved at the time of implantation to avoid the possibility of segmental instability after total disc replacement with bilateral uncovertebral joint resection.5,20 The goal of our study was to evaluate the potential consequences of load sharing on the joints after total cervical disc replacement using different implant designs.

Methods

Artificial Disc Models

Figure 1 illustrates STL models of the Bryan, Prestige LP, and ProDisc-C cervical disc prostheses used in this study (STL is a standard file format for solid freeform fabrication). The Bryan and ProDisc-C models consist of upper and lower endplates and a polymeric nucleus, whereas the Prestige LP disc is composed of upper and lower endplates, with a ball-trough-type metal-on-metal joint. The disc core of the Bryan disc is made of polyurethane, while the ProDisc-C core is polyethylene. The Bryan disc, unlike the ProDisc-C and Prestige LP, relies on a tight fit between its designed geometry and the concavity of the vertebral bodies rather than an explicit fixation mechanism. In general, artificial disc endplates have a porous coating to enhance bone-implant integration. In this study, it was assumed that the bony endplates and artificial disc endplates were fully integrated so that no relative motion was allowed between them.

In Vivo Image-Based FE Modeling

We built in vivo FE models, using an image-based FE modeling and analysis technique, based on a patient with left C-6 radiculopathy secondary to degenerative disc disease and spondylosis of the C5–6 segment. The advantage of an image-based FE modeling and analysis technique is that it can provide fast modeling with accuracy sufficient to capture actual anatomy in clinical settings. All inclusion criteria for enrollment in the FDA’s Investigational Device Exemption trials for a possible total disc arthroplasty were met in this patient.15 The protocols for image acquisition and processing were approved by the institutional review board of the treating institution.

Segmentation was conducted based on image densities using region-growing and masking tools in Simpleware ScanIP software (Simpleware Ltd.). Using these tools with properly chosen threshold values, vertebral bodies were segmented into masks for cortical shells and cancellous cores. Uncovertebral joints and facet joints were added as separate masks based on anatomical knowledge. All masks generated during segmentation could be automatically converted to 3D stereolithography (STL) models. Design models of Bryan, Prestige LP, and ProDisc-C prostheses were also prepared in STL format. In addition to the artificial disc model designs, an intact model of the intervertebral disc was also created. The intact disc model consisted of an outer replica of the annulus fibrosus and an inner core representing the nucleus pulposus.

To process the STL models of spine units with artificial discs, 3D voxel elements (8-node hexahedral elements) were created using Voxelcon (Quint Corp.), an image-based FE software application. Each STL model was imported in an orderly manner, such that vertebral bodies were imported first followed by disc endplates, as the latter imported components would replace any previous ones when creating voxels in Voxelcon. Using this method, we were able to conduct Boolean operations among components with geometrical overlap to further reduce modeling time. Voxel FE models for the C5–6...
spinal segment with the 3 prostheses and the control are presented in Fig. 2. The size of the artificial discs was carefully chosen to fit the intervertebral disc height. The placement of each artificial disc was determined such that the resultant instantaneous axis of rotation was close to the region found in a previous FE study. Furthermore, artificial disc endplates were placed parallel to the vertebral endplates with direct contact to cancellous bone. The unit voxel element size was 0.3 mm, and the total number of voxel elements was approximately 1,000,000 for all models so as to incorporate the full details of the complicated vertebral body geometries.

Table 1 presents material properties for spinal units, the 3 artificial disc components, and the natural intervertebral disc. The material properties in our study were determined based on those used in the previous FE studies of biomechanics including cervical spine FE models. Linear isotropic material properties were assumed in the Voxelcon solver. Static analysis was conducted by imposing 1.5 Nm of flexion, extension, and lateral bending moments, with 73.6 N of axial precompression superior to

<table>
<thead>
<tr>
<th>Components</th>
<th>Young Modulus (MPa)</th>
<th>Poisson Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>cortical bone</td>
<td>12,000</td>
<td>0.3</td>
</tr>
<tr>
<td>cancellous bone</td>
<td>100</td>
<td>0.3</td>
</tr>
<tr>
<td>facet joints</td>
<td>5</td>
<td>0.45</td>
</tr>
<tr>
<td>uncovertebral joints</td>
<td>5</td>
<td>0.45</td>
</tr>
<tr>
<td>intervertebral disc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>annulus fibrosus</td>
<td>3.4</td>
<td>0.4</td>
</tr>
<tr>
<td>nucleus pulposus</td>
<td>1</td>
<td>0.49</td>
</tr>
<tr>
<td>Bryan endplates (titanium)</td>
<td>110,000</td>
<td>0.3</td>
</tr>
<tr>
<td>nucleus (polyurethane)</td>
<td>25</td>
<td>0.45</td>
</tr>
<tr>
<td>Prestige LP endplates</td>
<td>110,000</td>
<td>0.3</td>
</tr>
<tr>
<td>(titanium carbide)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ProDisc-C endplates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(cobalt chromium)</td>
<td>210,000</td>
<td>0.3</td>
</tr>
<tr>
<td>core (polyethylene)</td>
<td>800</td>
<td>0.3</td>
</tr>
</tbody>
</table>
C-5, with constraints on the inferior endplate of C-6. The axial precompression force and moments were implemented as equivalent load distribution and load couples, respectively.

Biomechanical Comparison

Static analyses were conducted on the C5–6 spine units with the 3 different artificial disc implants and the intact intervertebral disc to investigate load levels shared by the uncovertebral and facet joints. The von Mises stress and SED were calculated to measure loads shared by the uncovertebral and facet joints. Shared loads at the C5–6 segment with the 3 different artificial disc implants were compared with those of the intact intervertebral disc as the control. Shared loads at the facet joints were investigated only in extension and lateral bending moments because facet joints are not considered to carry tensile loads. The rotation angle was measured by the Cobb method (Fig. 3), which is frequently adapted for radiographic assessments.16

Results

Analyses of Load Sharing at the Facet Joints

Table 2 presents average von Mises stresses and SED levels at the facet joints of C5–6 for the Bryan, Prestige LP, ProDisc-C, and intact discs under either extension or lateral bending moment. Relative load and energy levels of the segmental unit with the artificial discs are illustrated in Figs. 4 and 5, which were normalized to the values of the intact spinal unit. Under extension moment, the von Mises stress at loaded facet joints in the spinal segment with the Bryan prosthesis reached 0.554 MPa, which was similar to that of the intact intervertebral disc (0.481 MPa). In contrast, when the Prestige LP and ProDisc-C discs were used, the facet joints of the spinal segments were found to have much lower levels of von Mises stresses (0.03568 MPa and 0.1015 MPa, respectively), which were 7.4% and 21.1% of the intact model. Under lateral bending moment, von Mises stresses also showed a similar distribution of higher values occurring with the Bryan and intact discs (0.314 MPa and 0.249 MPa, respectively), whereas values with the Prestige LP and ProDisc-C discs were much lower (0.0743 MPa and 0.153 MPa, respectively). However, the stress difference is smaller in lateral bending than in extension. When the energy absorbed by the joints was measured by SED, facet joints with the Bryan disc absorbed more strain energy (32.43 × 10⁻⁶ J/mm³) than the Prestige LP (0.155 × 10⁻⁶ J/mm³) and ProDisc-C (1.17 × 10⁻⁶ J/mm³). The SED comparison clearly demonstrated that discs with rigid cores resulted in lower SED levels, since less motion and deformation at the joints was permitted (Fig. 5).

Analyses of Load Sharing at Uncovertebral Joints

Load sharing at the uncovertebral joints was evaluated and compared under flexion, extension, and lateral bending moments. The average von Mises stresses and SED levels indicate higher transferred loads and absorbed energy at uncovertebral joints with the Bryan
Joint stress after cervical disc arthroplasty

prosthesis in flexion and extension moments, as opposed to the joints with Prestige LP or ProDisc-C disc (Figs. 6 and 7). As presented in Table 3, the average von Mises stresses of the Bryan model in flexion and extension moments (0.5137 and 0.3999 MPa, respectively) were 125% and 100% of those of the intact model (0.4095 and 0.3974 MPa), whereas stress levels of the Prestige LP (0.1056 and 0.1024 MPa) and ProDisc-C (0.1419 and 0.1513 MPa) models were 26% and 36% of those in the intact model. In lateral bending, the average von Mises stresses with the Prestige LP (0.2867 MPa) and ProDisc-C (0.3302 MPa) were similar to those of the control (0.3116 MPa), but were only slightly greater than half of the value measured with the Bryan disc. The SED levels of all loaded joints with the artificial discs (20.25, 20.14, and 30.93 × 10^–6 J/mm^3, for the Prestige LP, ProDisc-C, and Bryan discs, respectively) were substantially greater than in the control (6.435 × 10^–6 J/mm^3).

**Load Displacement Responses**

Due to the limited properties of the voxel element in the current modeling technique, facet joints were modeled as linear solid elements rather than contact elements that carry only compressive loads. This resulted in a stiff response in the ROM along flexion-extension, as presented in Table 4. The ROM in the C5–6 spinal unit of the control was 3.1° in 1.5 Nm flexion and extension moments. The Bryan disc spinal unit showed a similar ROM (2.9°) to that of the control. Spinal units with the Prestige LP and ProDisc-C discs presented stiff responses in ROM, presumably due to their rigid cores (0.43° and 0.64°, respectively).

**Discussion**

The study goal was to evaluate the effect of artificial disc designs on load sharing at the facet and uncovertebral joints. Although we did not conduct a kinematics study, the stability of unconstrained/semiconstrained artificial discs relies on the remaining joints and soft tissues to some extent. In fact, the Bryan and Prestige LP discs are considered unconstrained or semiconstrained designs, and the ProDisc-C is semiconstrained with a fixed axis of rotation. This suggests that the core material stiffness can play a major role in the comparison of the load sharing of the artificial discs. Therefore, our image-based FE analysis with static loading conditions can reflect possible complications related to the cervical disc arthroplasty.

Cervical disc arthroplasty has been purported to limit the potential long-term complication of ASD after spinal fusion. Although promising outcomes have been reported from short-term investigations, many concerns for the “artificial” preservation of segmental motion still remain with regard to subsidence or migration of the device, as well as degeneration of joints at the treated and adjacent

---

**TABLE 3: Average von Mises stresses and SED levels for all disc models evaluated by flexion, extension, and lateral bending at uncovertebral joints**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bryan</th>
<th>Prestige LP</th>
<th>ProDisc-C</th>
<th>Intact</th>
</tr>
</thead>
<tbody>
<tr>
<td>von Mises stress (MPa)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>flexion</td>
<td>0.5137</td>
<td>0.1056</td>
<td>0.1419</td>
<td>0.4095</td>
</tr>
<tr>
<td>extension</td>
<td>0.3999</td>
<td>0.1024</td>
<td>0.1513</td>
<td>0.3974</td>
</tr>
<tr>
<td>lateral bending</td>
<td>0.4696</td>
<td>0.2867</td>
<td>0.3302</td>
<td>0.3116</td>
</tr>
<tr>
<td>SED (10^{-6} J/mm^3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>flexion</td>
<td>19.94</td>
<td>5.507</td>
<td>5.534</td>
<td>8.715</td>
</tr>
<tr>
<td>extension</td>
<td>16.56</td>
<td>2.503</td>
<td>5.363</td>
<td>10.64</td>
</tr>
<tr>
<td>lateral bending</td>
<td>30.93</td>
<td>20.25</td>
<td>20.14</td>
<td>6.435</td>
</tr>
</tbody>
</table>

---

**Fig. 6.** Comparison of average von Mises stresses at uncovertebral joints of C5–6 spine segment with Bryan, Prestige LP, and ProDisc-C prostheses, normalized to the von Mises stress of the intact intervertebral disc.

**Fig. 7.** Comparison of average SED at uncovertebral joints of C5–6 spine segment with the Bryan, Prestige LP, and ProDisc-C prostheses, normalized to the SED of the intact intervertebral disc.
levels. Van Ooij et al.\textsuperscript{22} reported facet joint arthrosis due to abnormal segmental motion in 11 of 27 patients who had persistent symptoms after cervical disc arthroplasty. Abnormal segmental motion has been thought to create excessive load burden on the facet joints and therefore may induce early degeneration. A late complication that has been reported up to 18 years after artificial disc arthroplasty is facet joint degeneration, which has been hypothesized to result from instability caused by removal of anterior longitudinal ligaments.\textsuperscript{15} According to these prior investigations and our previous findings, we hypothesized that arthroplasty with an unconstrained prosthesis may accentuate the instability and possibly result in facet degeneration over time. The instability can then induce an increased shared load at the remaining joints, which can cause deterioration of the joint.

For the Bryan disc, which has a flexible polyurethane core, there would be a higher propensity for the implant to transfer loads to the facet joints after disc replacement, since the implant is allowed greater ROM for a given constraint from the surrounding tissues. Our results indicate that with the Bryan disc, the facet joints bore greater loads compared with the other artificial discs. As a consequence, stress levels at the facet joints with the Bryan disc were 0.55 MPa in extension moment and 0.31 MPa in lateral bending moment, which were higher than those with the ProDisc-C disc (0.10 MPa in extension and 0.15 MPa in lateral bending) and orders of magnitude higher than those with the Prestige LP disc (0.036 MPa in extension and 0.074 MPa in lateral bending). However, the stress level at the facet joints with the Bryan disc was comparable to the intact model (0.48 MPa in extension and 0.25 MPa in lateral bending), suggesting that the biomechanics are similar to the inherent state.

Low load sharing at the facet joints with the Prestige LP and ProDisc-C discs, which have greater core rigidity, can also be problematic with respect to disuse osteopenia of the joints. Although these artificial discs can provide better stability to the treated spine segment, the low load sharing can result in further degeneration of the remaining joint tissue. Trouillier et al.\textsuperscript{21} studied the effect of artificial disc implantation on facet loading at the operated and adjacent levels by observing subchondral bone density using CT osteoabsorptiometry. They concluded that decreased subchondral bone density of the facet joints may be related to joint load reduction associated with artificial disc arthroplasty, compared with preoperative abnormal facet loads. In the current study, our results agreed with their observations. The high degree of stiffness of the prosthetic disc nucleus results in greater load to the anterior of the implanted discs and therefore adversely alleviated the default loads originally shared by the facet joints. These findings may provide valuable insight when making decisions about the most appropriate artificial disc for a given condition.

Because the artificial discs in this study are unconstrained or semiconstrained designs, uncovertebral joints may be preserved with arthroplasty to increase the stability of the segmental motion. Uncovertebral joints, along with the facet joint and intervertebral disc, provide stability and guidance for cervical spine segmental motion.\textsuperscript{21} It has been shown that the ROM increases at the cervical segment after the uncovertebral joints are resected, especially in extension and lateral bending modes.\textsuperscript{5,11,20} Uncovertebral joint resection can be performed during implantation to facilitate insertion of the device or to resolve symptoms related to foraminal stenosis. A study of the effect of uncovertebral joint excision on stability after total disc replacement suggested that the unilateral resection of uncovertebral joints can be beneficial for decompression of intervertebral disc space as well as restoration of ROM.\textsuperscript{5} However, total disc replacement after bilateral resection of uncovertebral joints may result in hypermobility, which in turn may cause accelerated degeneration of the joints and potentially, in the long term, growth of osteophytes. Thus, we assumed the preservation of the uncovertebral joints in our study to investigate possible effects of device design on joint degeneration.

Excessive loads on the uncovertebral joints after disc arthroplasty may also lead to joint degeneration. Our results show that the average von Mises stresses at the uncovertebral joints for flexion-extension moments with the Bryan discs were up to 25% greater than those of the intact disc model (Fig. 6). The SED at uncovertebral joints with the Bryan disc was dramatically increased to 230% of that in the intact model, suggesting that the joints were overstimulated (Fig. 7). Conversely, SEDs at the uncovertebral joints of the cervical units with ProDisc-C and Prestige LP discs were found to be much lower (Fig. 7), which might indicate offloading of the joints which, in turn, may interfere with normal kinematics of the segmental motion. The difference in SED is thought to be due to the greater rigidity of the 2 designs, thus shielding a significant amount of stress borne by the uncovertebral joints after implantation of the Bryan disc.

The proportion of increased SED in the uncovertebral joints was much greater with the Bryan disc when the loading mode was lateral bending (Fig. 7). Nearly 5–10 times greater SEDs normalized to the intact segmental unit were observed compared with the Prestige LP and ProDisc-C discs in flexion or extension, whereas the normalized SED in the uncovertebral joints with the Bryan disc was 2–3 times more when the loading was switched to lateral bending. These results could be explained by impingement of the edges of the artificial disc endplates into the uncovertebral joint space, thus elevating the contact stress. It should be emphasized that the design of the endplate of the artificial disc should be geometrically compatible with the uncinate process, which is known to be the densest region in the superior surface of cervical vertebrae,\textsuperscript{14} to avoid undesired collision dur-

<table>
<thead>
<tr>
<th>Table 4: Measurement of Cobb angles in sagittal flexion-extension for all disc models</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disc Model</strong></td>
</tr>
<tr>
<td>Bryan artificial cervical disc</td>
</tr>
<tr>
<td>Prestige LP artificial cervical disc</td>
</tr>
<tr>
<td>ProDisc-C artificial cervical disc</td>
</tr>
<tr>
<td>intact model</td>
</tr>
</tbody>
</table>
Joint stress after cervical disc arthroplasty

ing segmental motion. Moreover, as uncovertebral joints are pivotal to segmental motion in the cervical spine, the overhanging endplates of the artificial disc would create obstacles for the joints to articulate under certain motion modes, such as lateral bending. The Prestige LP and Pro-Disc-C discs may therefore have less tolerance for mal-positioning within the disc space, since the instantaneous centers of rotation in both devices are fixed. Malaligned centers would magnify the excessive loads shared by the joints. Alternatively, Bryan discs are designed with a flexible core that allows an offset along the transverse plane, which may actually counter the iatrogenic impact of disc replacement, although it does appear to result in greater load sharing by the uncovertebral joints.

The purpose of the current study was to understand how the implant design of a particular artificial disc affects coordination of load sharing among the artificial and segmental joints at the treated level, which is of paramount importance for the modern spine surgeon as more devices become available for implantation. Learning the possible underlying mechanisms that alter load sharing after disc arthroplasty as well as how certain implant designs can predispose the implant to failure will help the surgeon navigate the increasing array of implant options available. Finite element analysis may serve as an important tool to help determine the differences between disc designs, as clearly shown in the 3 types of artificial discs analyzed in this study.

Study Limitations

Since our FE model involved a single motion segment, analysis of the adjacent segments could not be performed. Given that the potential benefit of arthroplasty is prevention of ASD, comparison of different artificial disc designs on the adjacent-segment facet and uncovertebral joints warrants further study. Another limitation of our study is that current image-based analysis only allows linear modeling and analysis. Nevertheless, the results of our study provide valuable information concerning probable changes in shared loads and stresses at the facet and uncovertebral joints after disc replacement using different implants. Furthermore, the image-based analysis used in our study allows reconstruction of in vivo models in a rapid and efficient fashion. Future studies will be extended to include a multilevel FE model of spine motion segments and nonlinear ligamentous elements to increase the accuracy of the simulation.

Conclusions

The device core/nucleus material stiffness as well as device endplate design appear to affect the load transmission to the remaining facet and uncovertebral joints. The load sharing of the Bryan disc was the highest of the 3 discs evaluated and was closest to normal load sharing with the facet and uncovertebral joints. The high degree of stiffness of the prosthetic disc nucleus in the Prestige LP and ProDisc-C resulted in decreased load sharing with the facet and uncovertebral joints.

Disclosure

Dr. Park is a consultant to Medtronic, but has no personal financial or institutional interest in any of the materials or devices described in this article.

Author contributions to the study and manuscript preparation include the following. Conception and design: F La Marca. Acquisition of data: H Kang. Analysis and interpretation of data: C Lin, H Kang, P Park. Critically revising the article: C Lin, P Park, F La Marca, S Hollister. Reviewed final version of the manuscript and approved it for submission: F La Marca. Study supervision: C Lin.

Acknowledgments

The authors thank Dr. Miriam Adam and Mrs. Holly Wagner for assistance with manuscript preparation.

References

16. Mummneni PV, Burkus JK, Haid RW, Traynelis VC, Zde-

Address correspondence to: Chia-Ying Lin, Ph.D., Department of Neurosurgery, University of Michigan Medical School, Biomedical Science Research Building, Room 5007, 109 Zina Pitcher Place, Ann Arbor, Michigan 48109. email: lincy@umich.edu.