aprevo®

Personalized Interbody Fusion Device

Clinical Data Summary

carlsmed®

To Whom it May Concern:

I am writing on behalf of Carlsmed regarding coverage for our aprevo® device for your Medicare Advantage (MA) plan enrollees. Aprevo® is a Breakthrough-Designated Technology that is cleared by the Food and Drug Administration (FDA) and received New Technology Add-on Payment (NTAP) status from the Centers for Medicare & Medicaid Services. Traditional Medicare beneficiaries have benefited from access to this Breakthrough technology since 2021, and their MA counterparts are entitled to the same. As CMS noted in recent rulemaking regarding the MA Program, "[w]hen deciding whether an item or service is reasonable and necessary for an individual patient, [CMS] expect[s] the MA plan to make this medical necessity decision in a manner that most favorably provides access to services for the beneficiary and align with CMS's definition of reasonable and necessary as outlined in the Medicare Program Integrity Manual, Ch. 13, section 13.5.4." 88 Fed. Reg. 22,120, 22,188 (Apr. 12, 2023).

The following clinical dossier provides information on this Breakthrough technology, its clinical use, clinical publications, and other information that we believe will be useful to you as you process claims for the aprevo® and related procedures for MA plan enrollees. Given the Breakthrough Device Designation for aprevo®, prior NTAP status, coverage for traditional Medicare beneficiaries, and strong clinical evidence described in the attached, we trust that your MA plan enrollees will be eligible for coverage for the technology and related procedure, particularly when this information is viewed in a manner that most favorably provides access to services for the beneficiary.

If you have any questions or need any additional information, please do not hesitate to contact me at align-patient-access@Carlsmed.com.

Sincerely,

Sharon V. Schulzki
Chief Clinical Officer

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Executive Summary

The aprevo® patient specific lumbar interbody fusion devices are an FDA designated Breakthrough Technology, cleared for use in adult patients suffering from debilitating degenerative conditions of the lumbar spine. This technology received a CMS New Technology Add-on Payment (NTAP) in 2021. CT imaging studies and surgeon specifications are used to create both a personalized surgical plan and the patient specific aprevo® implants to achieve the plan. The devices are designed to match the irregular surfaces of each patient's bone as well as provide the precisely prescribed alignment during surgery.

Lumbar fusion surgery is associated with a significant rate of complications and costly revisions ranging from 20% to over 40% with each revision representing an added cost of >$100,000. In adult spinal deformity surgery, postoperative spinal malalignment has been shown to have the greatest negative impact on clinical outcomes compared to the impact of all other complications and is a significant predictor of revision surgery. Patients undergoing 1-3 level fusions for less severe lumbar degenerative pathologies are similarly impacted by post-operative spinal malalignment, with studies showing that those who are not restored to the appropriate alignment exhibit a 10-times higher risk of requiring revision surgery. Many patients having a suboptimal distribution of lower spine curvature (lordosis) have been worsened by lumbar fusion surgery and this group exhibited a revision rate within the first year of over 19%.

Traditional stock interbody fusion cages create suboptimal alignment of the intervertebral space which negatively impacts segmental and global alignment of the lumbar spine. Failure to achieve the optimal functional alignment for each patient has been shown to cause adjacent segment failure or device related complications leading to poor outcomes and the need for revision surgery.

The peer reviewed published studies described in this document present data on over 530 patients treated with patient-specific aprevo® devices, demonstrating an unmatched level of precision in their surgically achieved alignment compared to the use of stock devices. In addition, early data from the 350 patient COMPASS™ Registry showed the rate of revision surgery attributable to mechanical complications or radiographic malalignment following spinal deformity surgery was 1.5%, whereas a separately published study on 997 patients treated with stock devices showed a revision rate for the same causes by 1-year follow-up of 9.7%.

The application of personalized medicine to spine fusion surgery is a necessary step toward improving care, reducing costs and increasing patient satisfaction. One-in-five older adults regret their decision to undergo spinal deformity surgery, and almost twice as many patients who regret surgery experienced a postoperative complication. Among patients with degenerative conditions who require a revision lumbar fusion surgery, over 29% regret the choice to have the second surgery.

The importance of achieving optimal patient specific alignment to reduce the risk of mechanical complications and costly revision surgery cannot be overstated. The aprevo® personalized interbody devices improve surgical outcomes by enabling surgeons to more reliably achieve their patient-specific alignment goals, reducing both implant related complications and revision surgery, and improving patient satisfaction.

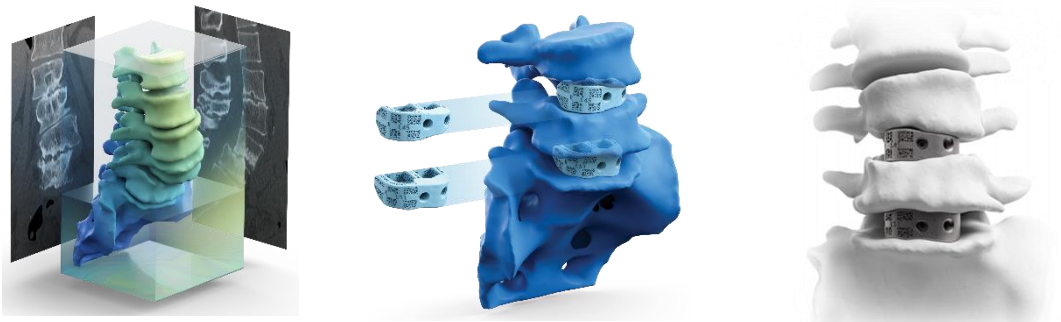
Patient Specific Interbody Devices

Technology Description

The aprevo® patient specific lumbar interbody fusion devices are an FDA designated Breakthrough Technology. These devices are FDA cleared for use in adult patients suffering from debilitating degenerative conditions of the lumbar spine, such as degenerative disc disease (DDD), disc herniation, spondylolisthesis, degenerative scoliosis/kyphosis, spinal stenosis, and failed previous fusion. The aprevo® patient specific devices have been in clinical use since February 2021, and received a CMS New Technology Add-on Payment which became effective October 2021.

Patient specific lumbar interbody fusion devices are designed from patient CT imaging studies and surgeon specifications. Carlsmed's proprietary FDA cleared software utilizes an AI-based algorithm to segment spinal structures and render a 3D model, including each vertebral body and three-dimensional endplate mapping. The surgeon's treatment and alignment goals are determined and translated to a surgical plan in which the vertebral bodies adjacent to the disc spaces being treated are positioned to achieve these goals. The negative space arising between the vertebral endplates is mapped to define the geometry of the device and the superior and inferior device surfaces are matched to the topography of the cranial and caudal vertebral endplates. The implants are manufactured of titanium alloy using an additive manufacturing process. Carlsmed creates the personalized surgical plan and fabricates the patient specific devices in approximately four weeks (Figure 1).

Patient specific implants are designed to match the patient's bony anatomy, and to provide precise alignment as dictated in the surgical plan for both intervertebral and overall lordosis, foraminal height, and coronal correction. Matching the device surfaces to the unique topography of the patient's endplates allows the desired alignment to be achieved because this attribute overcomes the unpredictable contact seen with stock devices, which interferes with achieving optimal fit and alignment.



1(A) 1(B) 1(C)

Figure 1. (A) CT images are used to create a 3-dimensional lumbar spine model from which each vertebral body is individually segmented, and the endplate anatomy is mapped. (B) The surgeon's goals are translated to a 3D plan in which the vertebral bodies are positioned to achieve the desired alignment. The negative space arising between the vertebral endplates is mapped. This is used to define the geometry of each personalized device, including conforming to the contours of the endplates. (C) Sterile patient-specific titanium alloy implants are delivered to the operating room, ready for surgery.

The design of each device is personalized to achieve the planned alignment through its geometry and anatomical fit, as well as provide features to facilitate insertion based on the characteristics of the disc space and the operating preferences of the surgeon. The devices are manufactured in single patient production lots with up to three device heights (plus: up to 2mm added height, nominal and minus: up to 1mm reduced height) provided for each fusion level to support an optimal fit based on segment mobility. (Figure 2)

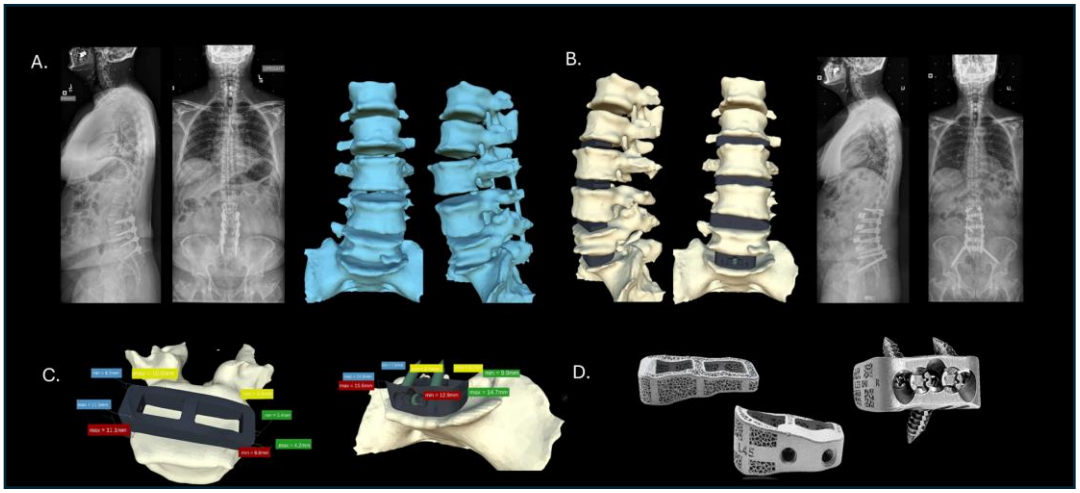


Figure 2. Case example. The patient is a 65-year-old male with persistent symptoms, adjacent segment disease, and global sagittal malalignment following a previous postero-lateral lumbar fusion. (A) AP and lateral views of preoperative X-Ray and 3D reconstruction models (blue). (B) AP and Lateral views of the 3D reconstruction plan (beige) and post-operative X-Ray. (C) Example of personalized implant geometry for lateral and anterior approaches, with colored tags specifying implant dimensions. Device geometry was derived from mapping the intervertebral space of the corrected alignment with superior and inferior implant surfaces matching vertebral endplate topography. (D) Images of sample implants for lateral and anterior approaches.

Clinical Data Supporting the use of Personalized Interbody Devices

<u>The High Risk of Revision Surgery with Stock Devices</u>

Lumbar fusion surgery is associated with a significant number of complications and costly revisions creating an unsustainable burden on the US healthcare system. In a study published by Martin et al.[1] the 11-year revision surgery rate among 2,345 adults who underwent inpatient lumbar fusion surgery for *degenerative* spine disorders was **20.1%**, with most reoperations having a diagnosis suggesting device complications or pseudarthrosis. In a review of 21 studies published by Chrastil et al.[2] the overall revision rate among patients receiving a lumbar fusion to treat *degenerative* lumbar conditions was **18.2%**. In 2022, Akinturk et al,[3] published a meta-analysis of 79 publications comprising 26,207 adult spinal *deformity* patients with a minimum of 1-year follow-up. The number of reported complications was 9138 representing **34.5%** of patients, with implant failure and radiographic malalignment as the most common, and an average revision rate of **17.8%.** In a longitudinal comparative cohort study comprised of 122 adult spinal *deformity* patients with a minimum of five years of follow-up, **31%** underwent revision surgery by year five.[4]

Mechanical and radiographic complications have a profound effect on the cost-utility of adult spinal deformity surgery. In a study of 244 adult spinal deformity patients published by Williamson et al.[5] patients who developed a mechanical or radiographic complication accrued the highest overall costs of $130,482 and $103,982, respectively. Another study by Zuckerman et al.[6] estimated the cost of revision surgery for rod fracture/pseudoarthrosis at $67,000 - $87,000, with an estimated incidence of 35% and an estimated intervention rate of 65%. Numerous studies point to postoperative malalignment and implant related mechanical complications as the two main factors contributing to high revision surgery rates and poor outcomes.

Postoperative Malalignment

Postoperative spinal malalignment has been shown to have the greatest negative impact on clinical outcomes in adult spinal deformity surgery**.** A retrospective cohort study by Krol et al.[7] showed that 317/762 (42%) of patients exhibited radiographic complications, which negatively impacted Oswestry Disability Index (ODI) and Scoliosis Research Society (SRS) scores more than any other complication. They concluded that the most detrimental contributors to poor long-term outcomes were almost exclusively related to poor radiographic correction, loss of correction post-operatively, and mechanical failure.

Achieving the necessary alignment to address a patient's condition and improve the chances of a successful outcome requires careful planning and precise execution of the surgery. In a 2023 study published by Smith et al.,[8] a group of experienced surgeon investigators of the International Spine Study Group measured planned versus achieved alignment in 266 complex adult spinal deformity patients having a mean number of 14 levels fused. The study showed that, at 6 weeks post-op, only 31.5% of cases achieved the targeted PI-LL mismatch within 5° (Figure 3), with a mean overcorrection of 4.6°. A similar percent of cases (30.4%) missed the planned PI-LL mismatch by >15°. This data demonstrates that even highly experienced surgeons are frequently unable to correct alignment when stock cages are used. The authors noted that, although patient-specific rods may help to lock in desired alignment, deformity correction primarily occurs through osteotomies and through release and realignment of the disc spaces, where interbody fusion devices are placed.

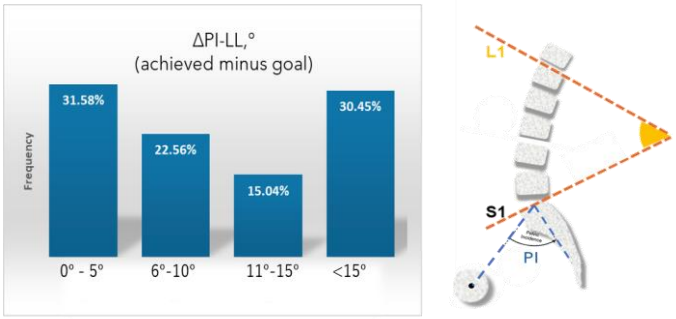
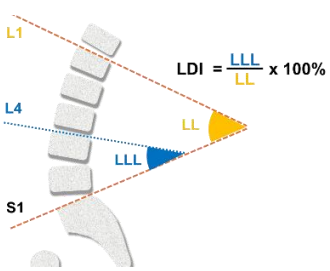


Figure 3. (Left) Histogram summarizing the distribution of 266 patients treated surgically for adult spinal deformity based on difference between the surgeon's preoperative goals for PI-LL and achieved PI-LL. PI = pelvic incidence, LL = lumbar lordosis. (Right) Depiction of PI and LL measurements.

Malalignment is not a deformity-only problem. Leveque et al.[9] evaluated pre- and postoperative spinopelvic parameters of nearly 600 patients having 1 or 2 level fusions for degenerative conditions. They found that 30% of patients exhibited malalignment preoperatively and 28% still had malalignment after surgery. In the same study, among the 173 patients with pre-operative malignment, 71% were not corrected by surgery. Patients undergoing 1-3 level fusion for lumbar degenerative pathology, who are not restored to the appropriate lordosis based on age and pelvic parameters exhibited a 10-times higher risk for requiring revision surgery.[10] Phan

et al.[11] conducted a meta-analysis investigating the relationship between spinopelvic alignment parameters and the development of adjacent level disease following lumbar fusion for degenerative disease in 1,113 patients. Their findings showed a strong association between spinal malalignment and the development of adjacent level pathology. This suggests that spine surgeons should routinely pay attention to maintaining or restoring appropriate lordotic alignment in patients undergoing surgery for lumbar degenerative disease, even those without overt deformity. Tempel et al.[12] demonstrated that a PI-LL mismatch of >11 degrees has a positive predictive value of 75% for the development of symptomatic adjacent level disease requiring revision surgery.

In addition to the role of spinopelvic parameters, a suboptimal distribution of lordosis is associated with a high risk for revision surgery. Lordosis Distribution Index (LDI) quantifies the ratio between the L4-S1 lordosis and L1-S1 lordosis. A poor post-op LDI is defined as one that is either hyperlordotic (>80%) or hypolordotic (<50%). Bari, et al.[13] studied 149 short segment fusion patients having an LDI distribution across hypo/normal/hyper of 24%, 62%, 13%, respectively. Patients presenting with a hypolordotic distribution (LDI < 50) were generally not improved to normal LDI. (Figure 4) This postoperative condition was associated with an increased risk of revision surgery at 1-year (p = 0.04) and the 1-year revision rate in these patients was 19.4%.



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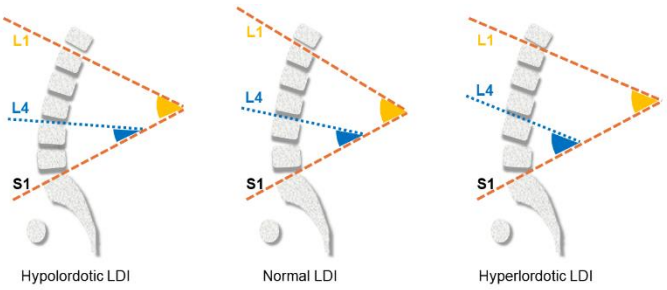

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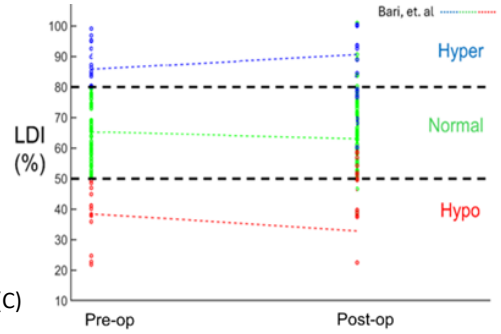

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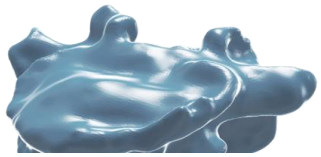
Figure 4. (A) Definition of lordosis distribution index. (B) Depiction of hypolordotic LDI (<50%), normal LDI (50%-80%) and hyperlordotic LDI (>80%). (C) LDI pre-op and post-op comparisons for each patient group, showing that the patients with preoperative hypolordotic distribution (red) were generally worsened, as were the patients in the preoperative hyperlordotic LDI group (blue).

Stock interbody fusion cages create unpredictable and often suboptimal alignment of the intervertebral space which negatively impacts segmental and global alignment of the lumbar spine. As discussed above, failure to achieve the optimal functional alignment for each patient has been shown to cause adjacent segment failure or device related complications leading to poor outcomes and the need for revision surgery. Although stock devices are commercially available in a wide range of lordotic angles, multiple clinical studies have demonstrated a poor association between the lordotic shape of a cage and the intervertebral alignment it produces. Oikonomidis et al.[14] showed that among 138 patients, a flat non-lordotic cage produced the predicted no change in lordosis (average pre-op 27° and post-op 26°), however a 10° lordotic cage produced an average additional lordosis of only 1°. Lovecchio et al. [15] showed that among 17 patients, a 10° cage produced an incremental lordosis of only 1.6°, and among 57 patients,

a 20° cage produced only 3.4° of added lordosis. Mathew et al.[16] evaluated 53 patients who received 6° cages, showing an average incremental lordosis of 10.9° while the patients receiving 20° cages demonstrated an average incremental lordosis of only 8.6°.

Vertebral endplate variability is one potential explanation for the significant discrepancy between the lordotic angle of stock cages and the intervertebral lordosis they create. Stock devices, which are essentially flat and uniform on the upper and lower surfaces, do not achieve a precise fit against the irregular bony topography of vertebral endplate surfaces. Vertebral endplate abnormalities are common in lumbar fusion patients, especially the elderly. In a study of 1564 endplates in 133 subjects with Modic changes on MRI, 27.8% of all endplates exhibited defects, with 31% of L4-L5 and 49% of L5-S1 endplates exhibiting a defect.[17] (Figure 5).



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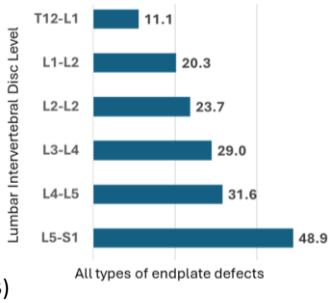

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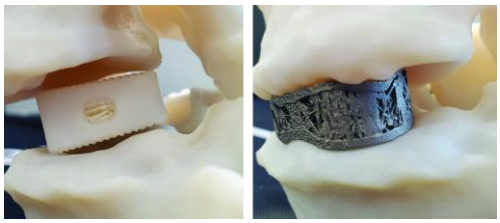


5 (C)

Figure 5. (A) Example of vertebral endplate irregularity (left). (B) Prevalence and distribution of endplate defects in the lumbar spine. Data presented are prevalence rates, referring to the total samples studied for that specific disc level.[17] (C) Model comparing the fit of stock interbody device to a patient specific interbody device.

Implant Related Complications

One of the main complications that can occur following implantation of a stock cage is pseudarthrosis, which is defined as complete absence of continuous bony trabeculation between adjacent vertebrae, peri-implant radiolucency, and/or motion on dynamic flexion-extension films. Achieving a solid fusion improves long-term clinical results with respect to back and lower limb symptomatology.[18] In a meta-analysis by Chun et al.[19] the published rates of pseudarthrosis in procedures using stock interbody devices was found to range from 0% to 30%, with an average of 10.7% among patients treated for degenerative disc disease (DDD) or other degenerative lumbar conditions. Because pseudarthrosis can contribute to excessive stress on the posterior rods, rod fracture is considered a proxy for pseudarthrosis. This phenomenon is particularly prevalent among patients with adult spinal deformity (ASD). Odogwa et al.[20] reported a rod fracture rate of 19.2% in 198 patients. Gupta et al.[21] measured a rod failure rate of 21% in 647 ASD patients with an average time to failure of 2.2 years.

Another implant-related complication that can necessitate revision surgery is subsidence. Subsidence of the implant occurs when the interbody cage penetrates the vertebral endplate and intrudes into the vertebral body following surgery. In these situations, intervertebral height restoration may be reduced or lost. In addition, the cage may fail to maintain segmental lordosis leading to malalignment. The previously noted meta-analysis by Chrastil et al.[2] reviewed 21 studies describing complications associated with posterior and transforaminal lumbar interbody fusion to treat patients with spondylolisthesis, degenerative scoliosis, severe instability, pseudarthrosis, recurrent disk herniation, and painful degenerative disc disease. The

overall reported complication rate averaged 36.4% (range 8% to 80%) and the average subsidence rate was 26.5%.

Adjacent segment pathology can be a consequence of malalignment and is characterized by a composite score including disc height loss, endplate sclerosis, osteophyte presence, and spondylolisthesis at the lumbar level adjacent to a fusion. Zigler et al.[22] reported the 5-year results of a prospective lumber disc replacement trial in which changes in the adjacent level were observed in 28.6% of the single level fusion patients treated for DDD in the control group. Among patients without adjacent-level disease (ALD) preoperatively, new findings of degeneration at five years post-treatment were apparent in 23.8% of patients in the control group.

Numerous clinical and non-clinical studies have shown that the features of patient specific interbody devices can reduce the risk of implant related complications in lumbar fusion surgery. A combination of clinical, cadaveric and FEA data has demonstrated that patient specific devices:

- achieved the planned correction more reliably; [23]
- decreased posterior rod loads by 28%; [24]
- provided a significant increase in contact area between the interbody cage and vertebral endplate to improve graft loading; [25]
- produced substantially less stress concentration on the endplate which directly impacts subsidence risk; [26]
- minimized the stress increase inside the adjacent disc and facets, which is known to contribute to adjacent level disease and/or failure; [27] (Figure 6) and
- reduced postoperative subsidence and subsidence-related pain in patients who received personalized devices versus stock devices. [28]

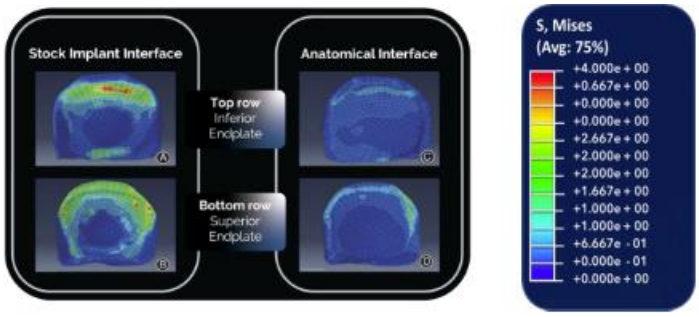


Figure 6. Comparison of Von Mises endplate stress contours between anatomical and stock devices on C4 inferior endplate and C5 superior endplate. Stress signal was recorded by the film sensor in the interface between the inferior surface of the cage and superior endplate of C5. [27]

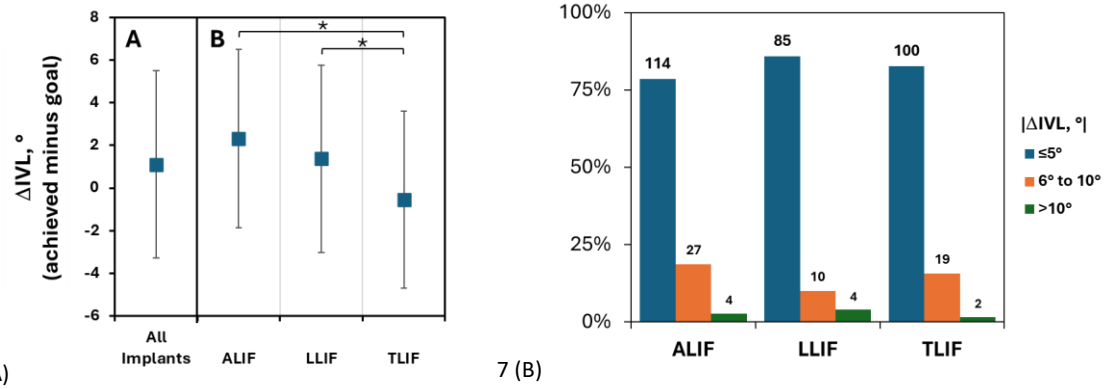
In summary, stock interbody devices fail to equip surgeons with the essential tools required to achieve optimal correction of spinal alignment and reliable fusion of interbody spaces, contributing to an unacceptable level of malalignment, implant related complications and costly revision surgery.

Personalized Interbody Device Clinical Data

Peer reviewed published clinical data has demonstrated the following benefits of aprevo® personalized interbody devices:

- A study of **365 personalized interbody levels in 217 patients** showed **82%** of levels **achieved targeted IVL alignment within 5° and 97% within 10°.**[29]
- Among **135 patients** with degenerative conditions, aprevo® patients showed a **52% increase in alignment restoration** of malaligned patients ($p<0.05$) compared to a separately published study using stock devices.[30]
- **A study of 111 aprevo® patients** with degenerative conditions showed a **21% LDI improvement in hypolordotic** patients ($p = 0.030$) [31] and a **75% Increase** in number of hypolordotic LDI patients **achieving normal LDI** compared to stock device data.[13]
- A publication on **65 adult spinal deformity** patients showed **a 42% improvement** in achieving targeted PI-LL within 5° compared to stock devices ($p=0.046$) and a **50% reduction** in missing targeted PI-LL by >15° compared to stock devices ($p=0.012$).[32]
- **Data from a CT study showed 94%** average implant to **vertebral endplate contact** at 1-year follow-up and **95.8%** of personalized interbody levels with **zero subsidence at 1-year** follow-up on CT. [33]
- Early data from the IRB approved COMPASS™ registry showed a **1.5% revision** rate due to mechanical complications or radiographic malalignment in an **adult spinal deformity** cohort at 12-wk to 1-year follow-up.[34] A separately published analysis on 997 patients showed a **revision rate of 9.7%** for mechanical/implant related complications or radiographic malalignment **with stock devices** by **1-year follow-up**.[35]

Sadrameli et al.[29] conducted a retrospective study of 217 patients with spinal deformity or degenerative conditions receiving aprevo® personalized interbody devices. The desired intervertebral lordosis angle (IVL) was prescribed into the device design for each personalized device (IVL goal). Standing postoperative radiographs were measured and the IVL offset was calculated as IVL achieved minus IVL goal. In this patient population, 365 personalized interbody fusion devices were implanted with anterior (n=145, ALIF), lateral (n=99, LLIF), and transforaminal (n=121, TLIF) approaches. Among the 365 treated levels, IVL offset was 1.1° ± 4.4° (mean ± SD). The targeted intervertebral lordosis was achieved within 5° of plan in 299 levels (81.9%). The achieved IVL offset within 5° based on approach was 85.9% of LLIFs, 82.6% of TLIFs, and 78.6% of ALIFs. Only ten levels (2.7%) missed the planned IVL by >10°. (Figure 7) These results are a stark contrast to the previously demonstrated unpredictability of alignment achieved with stock devices.[14,15,16]



7(A) 7 (B)

Figure 7. (A) IVL offset for all levels treated and for levels treated with ALIF, LLIF, or TLIF with personalized interbody implants. (B) Distribution of the magnitude of IVL offset stratified by implant type.

Asghar et al.[30] evaluated the impact of personalized interbody implants in correcting PI-LL mismatch compared to the previously described study by Leveque et al.[9] in which stock implants were used. In this study, the authors assessed radiographic preoperative and postoperative spinopelvic alignment (PI-LL) in patients who underwent one- or two-level lumbar fusions with aprevo® personalized interbody implants for degenerative (non-deformity) indications. The aim was to assess the incidence of malalignment (PI-LL ≥ 10°) both before and after fusion surgery and to determine the rate of alignment correction in this population. There were 135 patients included in this study. Among the 52 pre-operatively malaligned patients, alignment was restored in 23 (44.2%) representing a statistically significant increase in the "restored" group (p=0.046). In contrast to the study by Leveque et al., in which 71% of malaligned patients were not corrected by surgery, this represents a 52% increase in alignment restoration of preoperatively malaligned patients, and 21% decrease in patients for whom alignment was not restored (p< 0.05). (Figure 8)

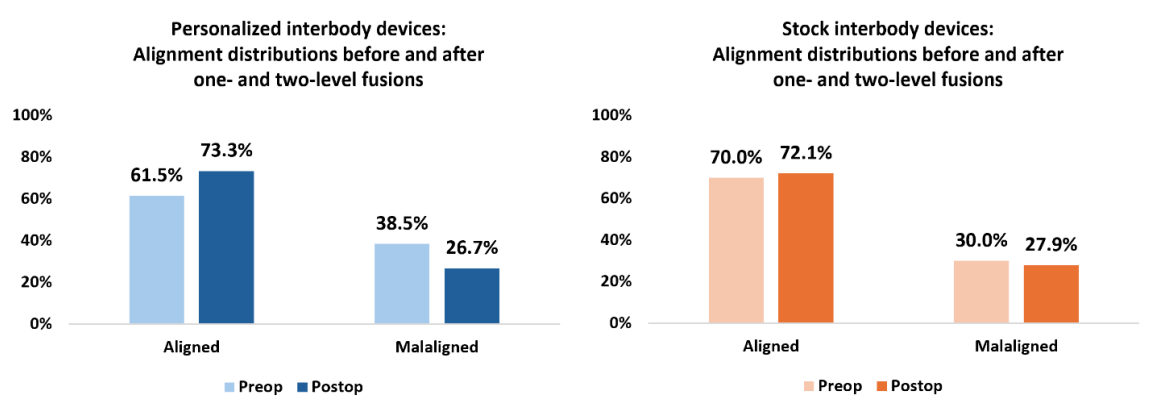


Figure 8. Changes in spinal alignment parameters for the entire cohort of one- and two-level fusion patients at pre and postoperative time points, including lumbar lordosis (LL), pelvic incidence (PI), and the calculation of PI minus LL (PI-LL). Comparison between personalized interbody devices (left) and stock interbody devices, right.

A study by Mullin et al.[31] evaluated radiographic measurements within 6-months of surgery from 111 consecutively treated patients diagnosed with degenerative spinal conditions and treated with short-segment fusion of L4-L5, L5-S1 or L4-S1 using aprevo® personalized interbody implant(s). They compared intervertebral lordosis for treated and untreated levels as well as Lordosis Distribution Index (LDI) pre- and postoperatively. Patients with a preoperative hypolordotic distribution (LDI<50%), showed a statistically significant increase in LDI postoperatively, approaching the normal LDI range (LDI 50-80%) (p=0.030). Likewise, patients with hyperlordotic distribution preoperatively (LDI>80%) experienced a decrease in LDI postoperatively, trending toward the normal range, although the changes were not statistically significant.

The previously described study by Bari et al.,[13] documented a **worsening of LDI** in both the hypolordotic and hyperlordotic LDI groups, and a 1-year revision rate in the **hypolordotic LDI group of 19.4%.** In contrast to these findings, patients receiving aprevo® personalized interbody devices demonstrated a statistically significant increase in LDI. Furthermore, 43% of patients in the hypolordotic group improved to an LDI within the normal range, representing a 75% increase in number of hypolordotic LDI patients achieving normal LDI compared to the patients studied by Bari et al. (Figure 9)

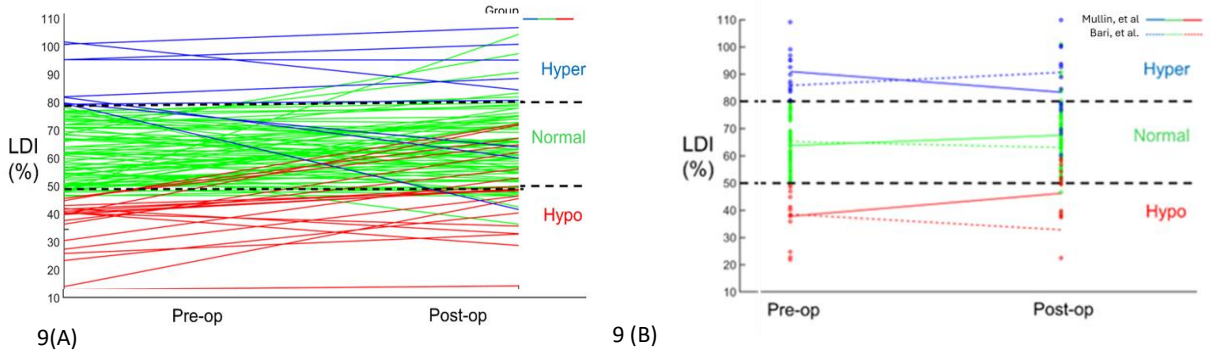
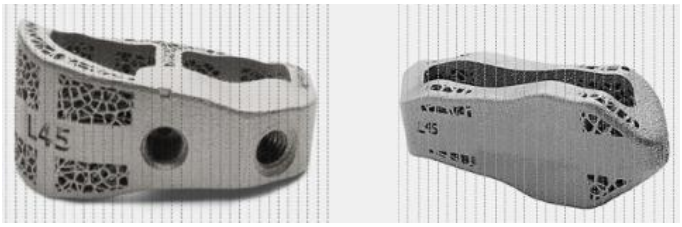


Figure 9. (A) LDI pre-op and post-op comparisons for each patient, showing a substantial number of patients in the hypolordotic group (red) improving to an LDI within the normal range. (B) LDI comparisons for different distribution groups. The preoperative to postoperative changes in LDI for each group as reported by Bari, et al.[13] are also shown.

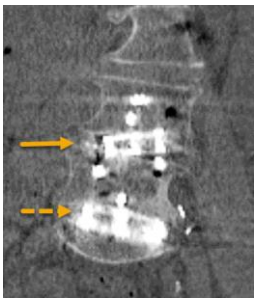
A study by Ames et al.[33] used 1-year post-op CT imaging to evaluate the implant-endplate contact area, fusion, subsidence, and achievement of planned alignment correction in a series of 15 patients receiving 24 aprevo personalized interbody devices including 2 patients receiving a hybrid construct (1 aprevo® + 1 stock cage). The authors noted that irregular endplate morphology is a risk factor for both cage subsidence and migration because it impacts the fit between the uniform surface of stock cages and the unique anatomy of each patient's vertebral endplate surfaces.[36] In addition, increased contact between an interbody cage and the adjacent endplate has been shown to improve post-operative disc height maintenance and angular correction.[37]

Three-dimensional thin-section (1 mm) CT scans of each patient were performed at approximately one year follow-up. Multiplanar reconstructions (MPR), including axial, coronal, and sagittal images were produced. An independent spine surgeon evaluated all CT slices for the contact area of the implant to the endplate, cage subsidence, and degree of fused local bone inside cages. These parameters were analyzed for every coronal and sagittal slice at the superior and inferior endplates (coronal CT slices shown in Figure 10A). The area of the implant in intimate contact with the endplate (i.e., no discernable gaps) was compared to the total available contact surface to determine the implant-endplate contact area ratio.

The assessment of contact between the personalized aprevo® implant and the vertebral endplates found an average contact of 94%. The endplate-implant contact for the two stock ALIF cages was also evaluated with an overall average of 81%. The average contact with the superior endplate was 95% (note that there was implant subsidence) and the average contact against the inferior endplate was 68%. Previous studies have shown that patient-specific cages increased the contact area between the cage and the endplate by up to 74% compared to commercially available cages, resulting in better utilization of the cage's total area, improved load sharing across the endplate and significantly lower contact stress.[38]



10 (A)



10 (B)

Figure 10. (A) Illustration of coronal CT slices for representative ALIF and TLIF personalized interbody implants. (B) Two-level implantation showing moderate subsidence of stock cage into superior endplate at L4-L5. The solid yellow arrow indicates the level treated with a stock implant. The dashed yellow arrow indicates the level treated with a personalized interbody cage.

The presence of complete fusion was assessed using the Bridwell scale.[39] Bridwell Grade I on CT images was observed in 100% of the levels implanted with personalized interbody implants. For the two levels implanted with stock cages, both were assessed as Grade II, i.e. graft intact, but not fully remodeled and incorporated. With regard to subsidence, Grade I (moderate) subsidence was found in one level implanted with a personalized interbody device (4.2%). Both stock implants were assessed as having subsided into the endplates, one with Grade I (Figure 10(B)) and the other with Grade II (high-grade). Subsidence may lead to increased pain and loss of correction; however, it can also increase endplate to implant contact, which may have contributed to 95% average contact against the superior endplate in the two stock devices. The personalized interbody devices had a mean offset between planned and achieved intervertebral alignment of 1.3°, demonstrating that a high level of alignment precision was achieved.

The authors concluded "This one-year follow-up CT analysis of personalized interbody cages provides a unique opportunity to assess implant-to-endplate contact. Personalized interbody devices appear to offer a high level of endplate to implant contact at one-year follow-up, which may contribute to improved interbody fusion rates, less subsidence, maintenance of alignment, and potentially decrease the risk of implant-related complications."

A study performed by the International Spine Study Group (ISSG) and previously reported by Smith et al.[8] demonstrated that surgeons failed to achieve alignment goals in nearly two-thirds of 266 Complex Adult Deformity Surgery (CADS) cases. Smith et al.[32] subsequently assessed whether personalized interbody devices are associated with improved rates of achieving goal alignment following adult spinal deformity (ASD) surgery. The authors assessed the effectiveness of aprevo® personalized interbody devices in achieving goal alignment following ASD surgery based on a multicenter cohort of 65 patients and compared the rates of achieving goal alignment to their previously published study using stock interbody implants. A case example is presented. (Figure 11)

Data describing achieved versus planned PI-LL mismatch from the previously described 2023 study published by Smith et al.[8] was compared to a radiographically matched patient group receiving aprevo® personalized interbody devices.[32] Mean offsets (SD) were 0.9° (5.2°) for intervertebral lordosis (IVL), 0.1° (4.7°) for intervertebral coronal angle (IVCA), and 0.1 mm (2.3 mm) for intervertebral posterior disc height (IVPH). (Figure 12) The comparison showed that the percentage of cases achieving the targeted lordosis within 5° (Figure 12) increased by 41.6% (44.6% vs. 31.5%) versus the cases using stock devices (p=0.046). In addition, there was a 50% decrease in cases in which the planned PI-LL mismatch was missed by >15° versus ISSG study (p=0.012). (Figure 13)

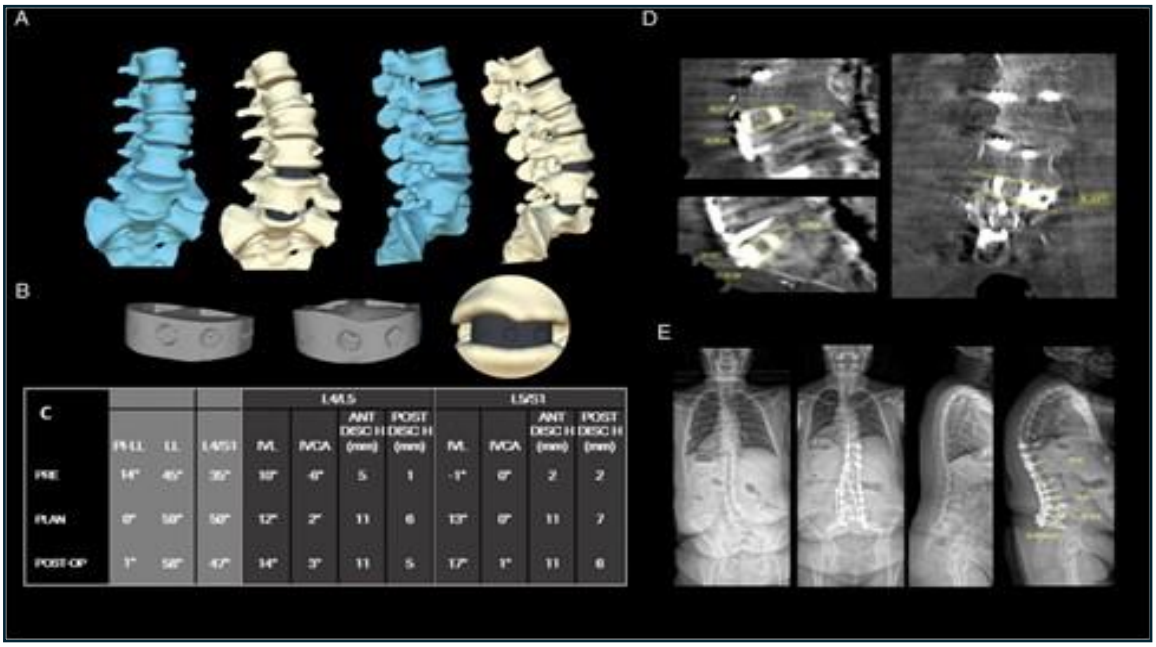
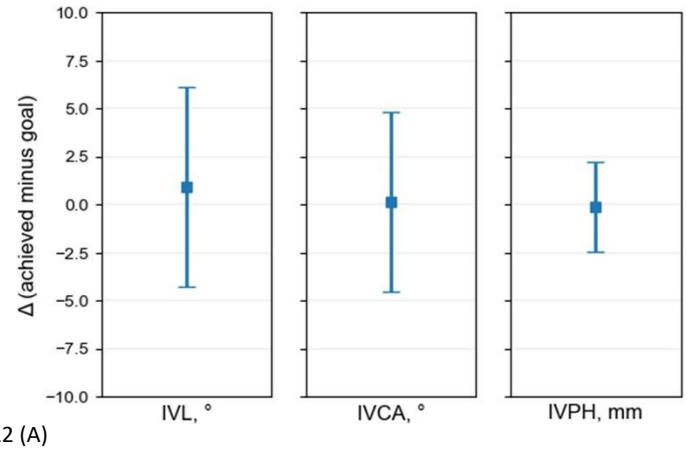
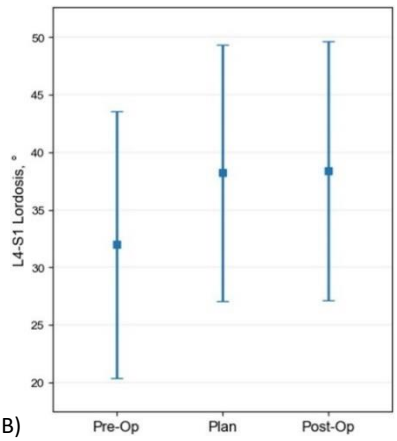


Figure 11. Patient example illustrating achieved vs planned alignment. Patient is a 53-year-old woman with global sagittal malalignment (adult spinal deformity with fractional curve at lumbosacral junction). (A) Shown are antero-posterior (AP) and lateral 3D reconstruction views of preoperative (blue) and planned (beige) alignment. (B) Geometry of personalized implants for L4/5 and L5/S1 which was derived from mapping the intervertebral space of the corrected alignment with superior and inferior implant surfaces matching vertebral endplate topography. (C) Table of preoperative, planned, and postoperative alignment for pelvic incidence to lumbar lordosis mismatch (PI-LL), lumbar lordosis (LL), L4-S1, and intervertebral space planning for L4-L5 and L5-S1. (D) One-year postoperative CT showing fusion, implant contact, and alignment in lateral and coronal views. (E) Preoperative and postoperative standing x-rays with AP and lateral views. IVL = intervertebral lordosis angle; IVCA = intervertebral coronal angle; ANT DISC H = anterior disc space height; POST DISC H = posterior disc space height.

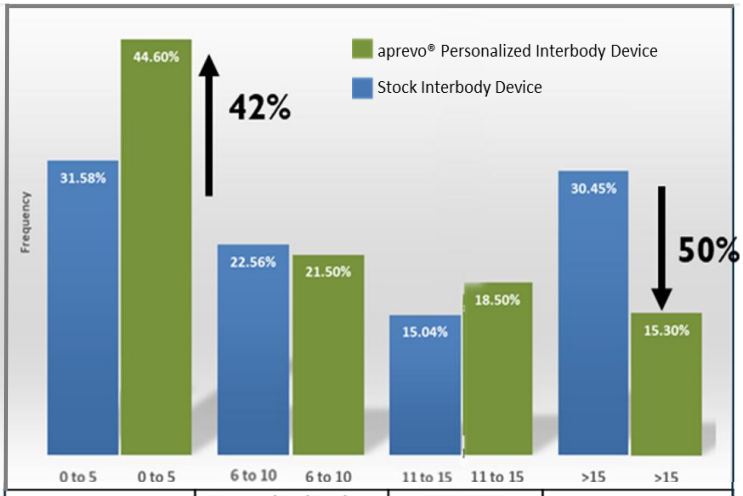


12 (A)



12 (B)

Figure 12. (A) Segmental alignment offset between achieved and goal for all levels treated with personalized interbody implants for 65 adults surgically treated for spinal deformity. Mean offsets (SD) are 0.9° (5.2°) for intervertebral lordosis (IVL),0.1° (4.7°) for intervertebral coronal angle (IVCA), and −0.1 mm (2.3 mm) for intervertebral posterior disc height (IVPH). (B) L4-S1 lordosis in 65 adult spinal deformity patients treated surgically with personalized implants. Baseline (Pre-Op) mean = 32° ± 11.6°, goal (Plan) 38.2° ± 11.1°, and achieved (Post-Op) 38.4° ± 11.3°.



|ΔPI-LL| Group	Personalized Implant Patients (n)	ISSG CADS Patients (n)	p-value
0° to 5°	**29**	**84**	**0.046**
6° to 10°	14	59	0.822
11° to 15°	12	40	0.514
>15°	**10**	**82**	**0.012**

Figure 13. Percentage distribution of the magnitude of offsets of the PI-LL achieved compared to the plan for 65 subjects with adult spinal deformity treated with personalized implants based on a 3D preoperative plan compared to 266 patients treated with stock implants through the International Spine Study Group (ISSG) Complex Adult Deformity Surgery (CADS) analysis. PI = pelvic incidence; LL = lumbar lordosis.

Lastly, a group of investigators in the 350 patient IRB approved multi-center Clinical Outcome Measures in Personalized aprevo® Spine Surgery (COMPASS™) registry recently published interim study results for a sub cohort of patients diagnosed and surgically treated for adult spinal deformity.[34] The study included 65 patients from 9 centers with mean follow-up of 14.7 months. Index surgeries were comprised of implantation of median 2 personalized interbody devices by anterior, lateral, or transforaminal approaches and with median 8 posteriorly instrumented levels. The percentage of patients starting in the **severe (++) PI-LL** modifier category was **reduced from 55% preoperatively to 12%** postoperatively, with **38% improving from preoperative moderate (+) or severe (++) PI-LL modifiers to a PI-LL modifier of zero**. This compares favorably to results by Moal et al.[40] who reported that **only 13% of patients improved** from preoperative moderate or severe PI-LL modifiers to modifier zero. Mean preoperative PI-LL decreased significantly from 21.0± 16.2° to 7.1 ± 12.7° postoperatively ($p<0.001$). Similarly, T1PA decreased from 25.0 ± 10.1° to 17.7 ± 9.0° ($p<0.001$), whereas PT did not change significantly. (Figure 14)

Complications occurred in 13 patients (19.4%), including one mechanical complication requiring revision 9 months post-surgery with no complications related to the personalized interbody devices. Importantly, the rate of reoperation for mechanical complications in the current study was **1.5%,** with **only a single revision due to proximal junctional kyphosis** that occurred 9 months postoperatively. (Table 1) This excludes 2 revisions for screw malpositions.

The **1.5% revision rate with aprevo®** compares very favorably to a separately published analysis on 997 patients by Lafage et al.[35] showing a revision rate of **9.7%** for mechanical complications or radiographic malalignment **with stock devices by 1-year follow-up**. (Table 2) The authors noted that the greatest number of reoperations (N = 101) was recorded during 6-weeks to 1-year post-op, with the majority attributed to x-ray imbalance (N = 58) and implant failure (N = 29). Other publications report rates of reoperation for mechanical complications between 10% and 32% over post operative periods of 1 to 2 years.[41,42]

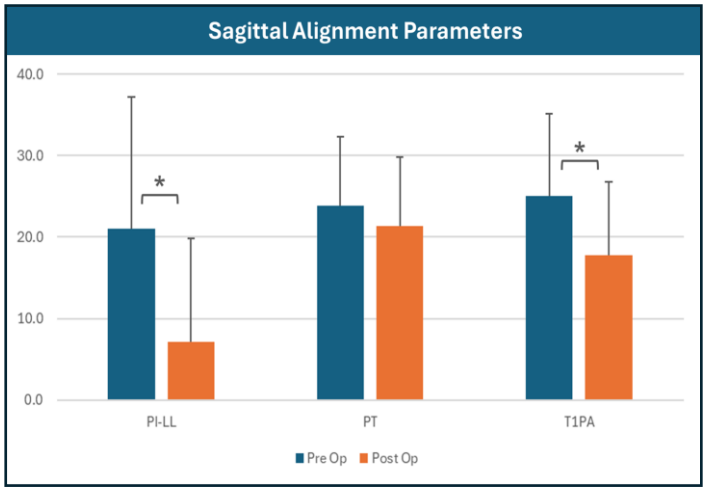


Figure 14. Mean preoperative PI-LL decreased significantly from 21.0± 16.2° to 7.1 ± 12.7° postoperatively (p<0.001). Similarly, T1PA decreased from 25.0 ± 10.1° to 17.7 ± 9.0° (p<0.001), whereas PT did not change significantly.

Category	≤ 90 days Post Op		> 90 days Post Op	
	No. Pts. (%)	No. Events	No. Pts. (%)	No. Events
Medical AE	6(9%)	8	3(4%)	4
Medical Complication (SAE)	2(3%)	2 [a]		
Surgical AE	6(9%)	9	1(2%)	1 [b]
Surgical Complication (SAE)				
Prolonged surgery/recovery	8(12%)	8 [c]		
Reoperation	2(3%)	2 [d]	1(1.5%)	1 [e]

Notes:
[a] postoperative DVT (2)
[b] adjacent segment disease treated nonoperatively, 18 months post op (1)
[c] vascular injury (2), dural tear (2), pneumothorax (1), anemia (1), seroma (1), lymphocele (1)
[d] screw malposition or loosening (2)
[e] Mechanical complication: adjacent segment disease with PJK (1), reoperation 9 months post op

None of reported AEs or complications were related to personalized interbody devices.
Abbreviations: AE, adverse event; SAE, serious adverse event; DVT, deep vein thrombosis; PJK, proximal junctional kyphosis.

Table 1. Adverse Events (AEs) and Complications (SAEs).[34]

MAJOR COMPLICATIONS AND REOPERATION RATES WITH STOCK DEVICES			
	MAJOR COMPLICATIONS	MAJOR with Reoperation	MAJOR without Reoperation
Implant Failure	48 (4.81%)	**29** (2.91%)	19 (1.91%)
Implant Dislodgement/malposition	14 (1.5%)	**10** (1%)	4 (0.5%)
X-ray imbalance	67 (6.72%)	**58** (5.82%)	9 (0.9%)
Total	129 (12.9%)	**97 (9.7%)**	32 (3.2%)

Table 2. Major complications and reoperation rates for implant failure or radiographic imbalance occurring between six weeks and one-year postoperative (n=997 patients).[35]

Conclusion

The application of personalized medicine to spine fusion surgery is a necessary step toward improving care, reducing costs and increasing patient satisfaction. One-in-five older adults regret their decision to undergo spinal deformity surgery, and almost twice as many patients in the high decisional regret group experienced a postoperative complication compared with the low decisional regret group.[43] A study by Du et al.[44] showed that on multivariate analysis, only revision surgery was independently associated with increase in risk for medium–high decisional regret (p=0.041). Remarkably, among patients receiving a lumbar fusion for degenerative conditions, a significantly higher number of patients undergoing revision fusion (29.4%) exhibited high regret compared to the number of primary fusion patients exhibiting regret (5.6%), (p=0.026).[45] (Figure 15)

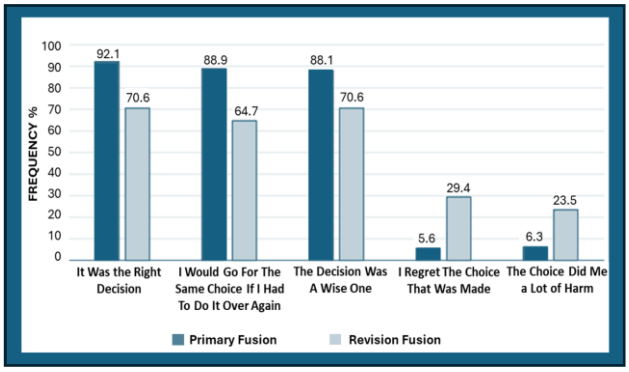


Figure 15. Responses to the Ottawa Decisional Regret Questionnaire among primary fusion and revision fusion patients.[45]

The importance of achieving optimal patient specific alignment to reduce the risk of mechanical complications and revision surgery cannot be overstated. Even though surgeons have an increasing level of clinical outcomes data to determine their surgical goals for each patient, numerous studies have demonstrated that they lack the tools to achieve these goals intraoperatively.

The aprevo® personalized interbody devices improve surgical outcomes by enabling surgeons to more reliably achieve their patient-specific alignment goals, reducing both implant related complications and costly revision surgery, and improving patient satisfaction.

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