# Preliminary Case Studies of a New Processed Cellular Allograft Derived from Umbilical Cord Blood (UCB) in Challenging Spinal Fusion Patients

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**Citation**

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**Abstract**

Case histories in unique patient populations can be a useful bridge before larger more comprehensive studies can be undertaken. A new fluid allograft product (BioBurst, Burst Biologics, Boise, ID) has performed beyond expectations in the cases presented here, with rapid consolidation of the bone graft and greater than expected bone volume. These early highly encouraging results in challenging patients show the potential of BioBurst Fluid as a valuable adjunct for spinal fusion and justify further research and clinical studies.

## INTRODUCTION

Among the current challenges for spine surgeons are relatively high-risk patients who have undergone multiple decompressive procedures and spinal fusion surgeries as well as patients who adhere to deleterious life-style choices such as tobacco use, or are encumbered with other risks such as obesity, diabetes, or advanced age. For this patient population, there have been no large randomized studies to determine the best approach to improve quality of life, as the pathologies are variable and the techniques used must be specialized for each individual patient. For these individuals, ethical concerns would preclude randomization unless clinically equivalent modalities are being compared.

The typical randomized controlled clinical trial by its very nature needs to be performed with a homologous population with a specific anatomical location and standardized surgical technique with the limited use of additional surgical adjuncts. Consequently, high success rates are frequently reported as study results report on single level procedures and patients with first time surgeries. Challenging patients are, for the most part, excluded from these types of studies. As such, many hospital systems and insurance carriers cite the lack of real world data for patients.[1] These real world outcomes for spinal fusion continue to be determined by individual risk factors in a general population such as smoking, multilevel involvement (particularly 3 or more levels) and other co-morbidities which include, among others, advanced age, diabetes, osteoporosis, and spinal deformity.[2,3,4]

In recent years, large databases obtained from either hospital systems or third-party payers have been used to determine patient outcomes particularly with respect to cost-effectiveness and pharmaco-economics. However, they are limited with respect to newer treatment options which have become available, in which sufficient numbers of patients are not yet of record.[1,5] Prospective patient registries, first developed as post-marketing surveillance tools suggested by the Food and Drug administration, are now being developed to address the need for realistic data from a varied population.[6,7,8] These also require time for sufficient enrollment and follow-up, and thus the newest treatments or advances first come to light through reports of individual case histories.

Stem cell treatments and the advent of minimally manipulated tissue products have been an exciting area of growth over the past ten years and has greatly expanded the research and focus of orthobiologic products.[9,10,11,12] Umbilical Cord Blood (UCB), a rich source for stem cells, growth factors, and cytokines has shown great potential for

treatment of a variety of pathologies and disease states with many clinical studies underway. [13,14]

Mesenchymal stem cells (MSCs) have been found in the nucleated fraction of umbilical cord blood in addition to hematopoietic stem cells and leukocytes. [15] MSCs are multipotent stromal cells that can differentiate into various regenerative cell types such as osteoblasts and chondrocytes, among many others. [16,17] UCB derived cells seem to be in a more primitive state, with proposed higher telomerase activity, and thus have the highest proliferative potentials when compared with MSCs from bone marrow and adipose tissues.[18,19,20] UCB cells are not exposed to environmental mutagens as much as adult derived cells and therefore are less likely to possess mutated DNA structures. [21]

Recently, a new comprehensive processing methodology (Progenokine®, Smart-Surgical Inc. dba Burst Biologics, Boise, Idaho) was developed with particular focus on preserving the integrity of UCB cells and protecting cell viability. One aspect of this new processing methodology employs non-toxic media which protects cell viability and avoids the use of DMSO which has been shown to cause side effects such as emesis, chills, rigor, and cardiovascular events. [22,23,24] As a result, the cells are allowed to continue to self-renew after a freeze thaw cycle and avoid the apoptotic cell fate. [25] Using this process, an injectable/fluid allograft stem cell product derived from UCB (BioBurst Fluid®, Burst Biologics, Boise, ID) was developed and is commercially available as a minimally manipulated tissue under CFR 1271 for homologous use.

Smart-Surgical Inc. dba Burst Biologics began as a research organization prior to having commercially available products and advanced laboratory research remains the main driver for the goals of the organization. A better and more comprehensive understanding of the complex mechanisms of cell biology, the functions of cell mediation and communication, will enable the organization to optimize the use of their products and further educate health care practitioners.

As an example, BioBurst Fluid contains cytokines that have been extensively studied and found to play a critical role in vasculogenesis and angiogenesis (ANG1, VEGFa, VEGFb, FGF-1). [26,27,28] Those cell functions are critical in supporting bone growth, consolidation, and remodeling, all critical to the spinal fusion process. [29] Other cytokines which are present (IL-8, MCP-1, MIP-1beta) in BioBurst are currently under study in the laboratory and are thought to be involved in signaling the recipients stem cells to mobilize to the area where bone growth is required. [30,31,32] The greater the understanding of the mechanisms involved, the greater the opportunity for better patient outcomes.

## METHODS

The authors practice often includes referrals from other spine practices, particularly those cases in which there has been one or more prior surgeries and/or fusions, adjacent level disease, pseudarthrosis, and failed back syndrome. Additional surgery may be necessary to treat the pathology and afford the patient better quality of life. The following three cases are representative of patients presenting a challenge to any spine surgeon.

## RESULTS

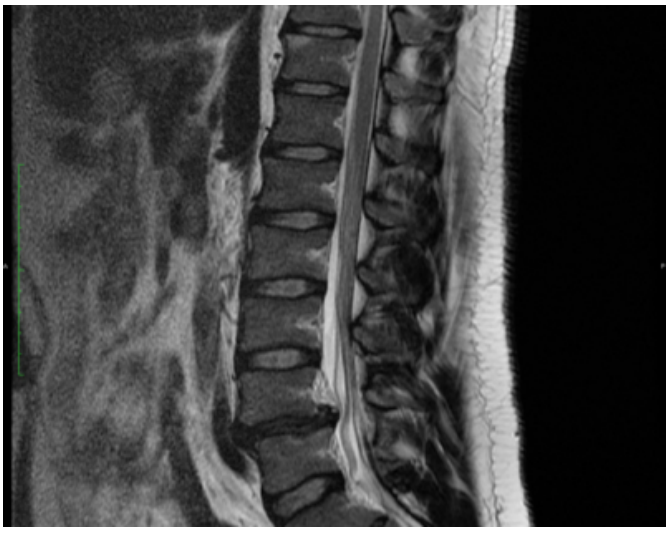
Along with meticulous surgical technique and rigid spinal instrumentation, the author has selected BioBurst Fluid to augment and enhance the fusion process.

***Case Number 1:***

A 38-year-old man who worked in a cafeteria presented with lower back and radicular pain. MRI shows Grade 1 spondylolisthesis with severe foraminal stenosis (Figure 1).

**Figure 1**

MRI of L4-L5 foraminal stenosis



Surgery was performed and included L4-L5 decompression with complete facetectomies and Transforaminal Lumbar Interbody Fusion (TLIF) with 30cc of Burst allograft mixed with 3cc of BioBurst Fluid to aid the fusion process. At 6 months the patient had relief of symptoms and returned to

work. Radiographs show excellent placement of instrumentation and early bone consolidation in both the interbody and posterolateral grafts (Figures 2 and 3).

**Figure 2**

AP L4-L5 shows early consolidation of PLF graft

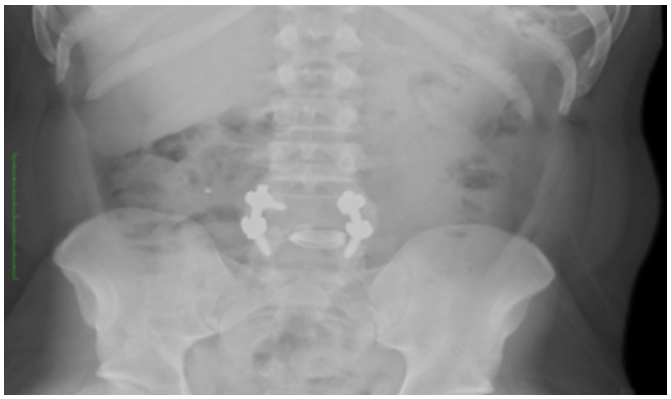
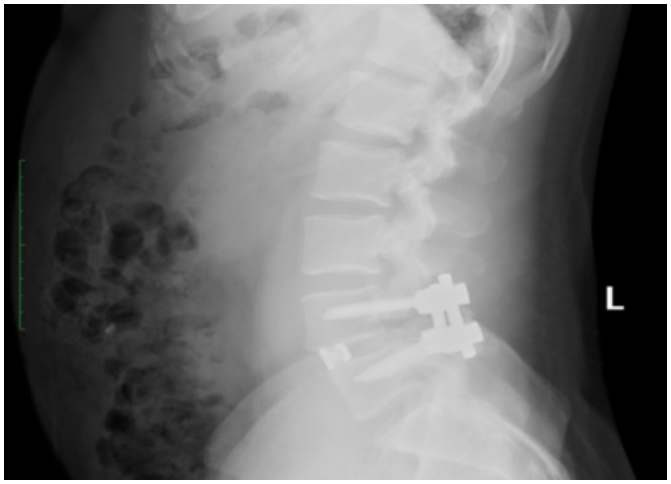


**Figure 3**

Lateral L4-L5 shows early consolidation of interbody graft




***Case Number 2:***

A 51-year-old female presented with low back and left leg pain. Imaging showed spondylolisthesis at L4-L5 with central and foraminal stenosis (Figure 4). The patient was unresponsive to both physical therapy and pain management programs. Patient underwent a L4-S1 TLIF and did well for six weeks post-op, then had sudden onset of worsening symptoms. Imaging showed a failed TLIF (Figure 5).

**Figure 4**

MRI showing L4-L5 spondylolisthesis with central and foraminal stenosis

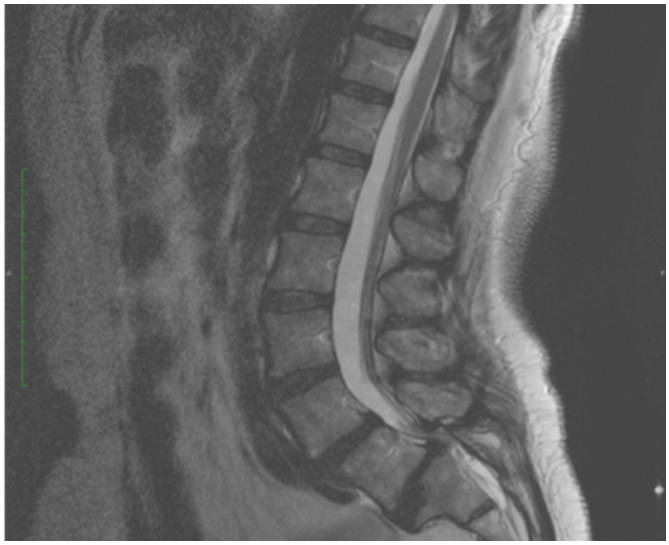
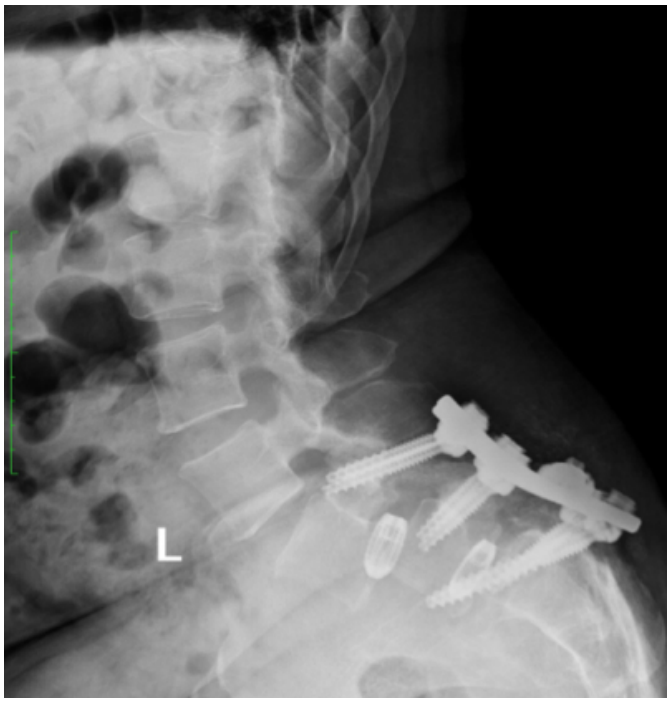


**Figure 5**

Lateral view of failed TLIF




The surgery was revised via a posterior revision L2-Ilium along with a second stage Anterior Lumbar Interbody Fusion (ALIF) at L3-L4 and L4-L5 a few days later. Both of surgeries used Burst allograft and BioBurst Fluid to aid the fusion process at a 10 to 1 ratio with 80cc used posteriorly and 20cc anteriorly. The post-op 6-month radiographs (Figure 6 and Figure 7) show significant fusion

consolidation within the interbody grafts as well as the posterior gutters. The patient's symptoms have improved significantly.

**Figure 6**

Lateral view of revised construct showing significant interbody fusion consolidation

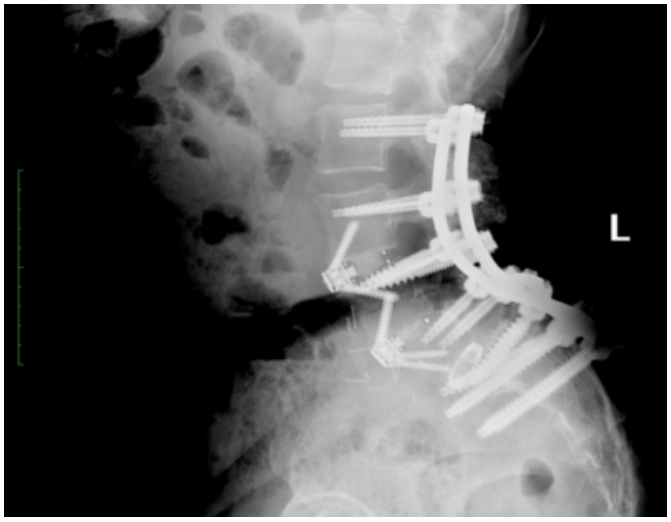
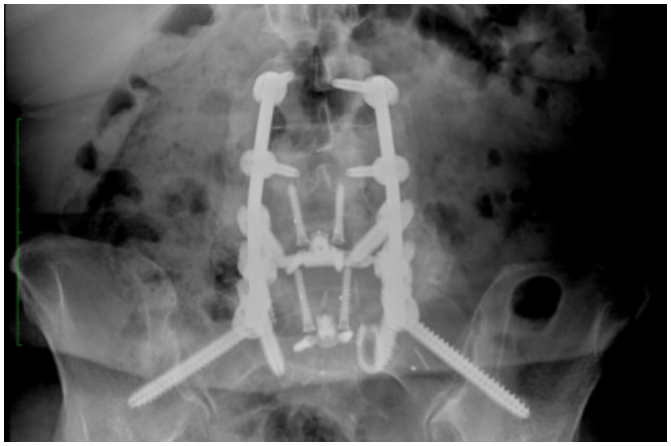



**Figure 7**

AP view of revised construct showing significant posterior fusion consolidation



***Case Number 3:***

A 64-year-old male with previous L2-L5 fusion presented with low back and right leg pain. An ALIF was performed at L5-S1 to stabilize the collapsed disc and indirectly decompress the foramen at L5-S1. The fusion failed and the patient underwent a second ALIF procedure and subsequently the sacrum collapsed (Figure 8 and Figure 9).

**Figure 8**

Lateral view of failed ALIF with sacrum collapse

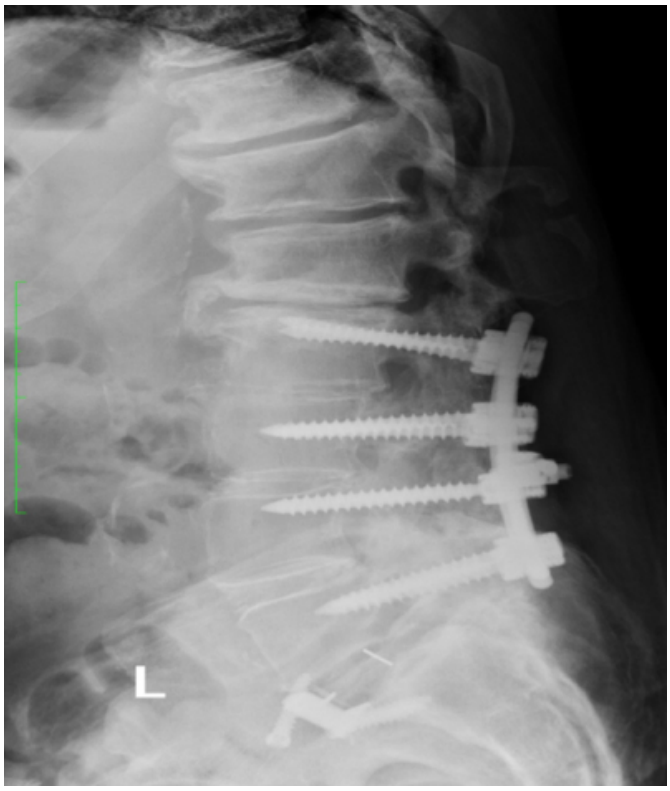
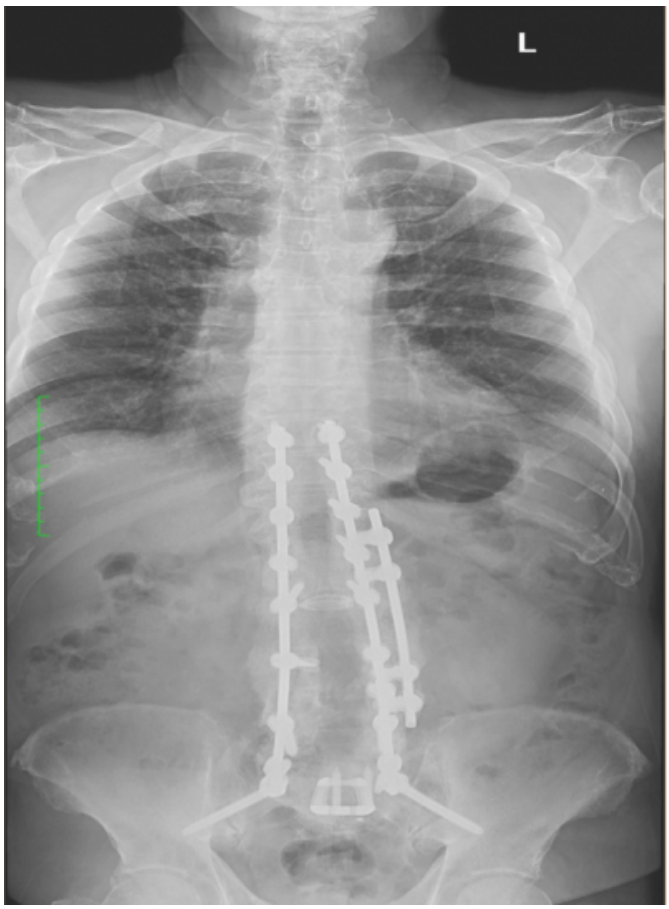


**Figure 10**

7-month AP radiograph shows substantial fusion consolidation in posterior gutters.



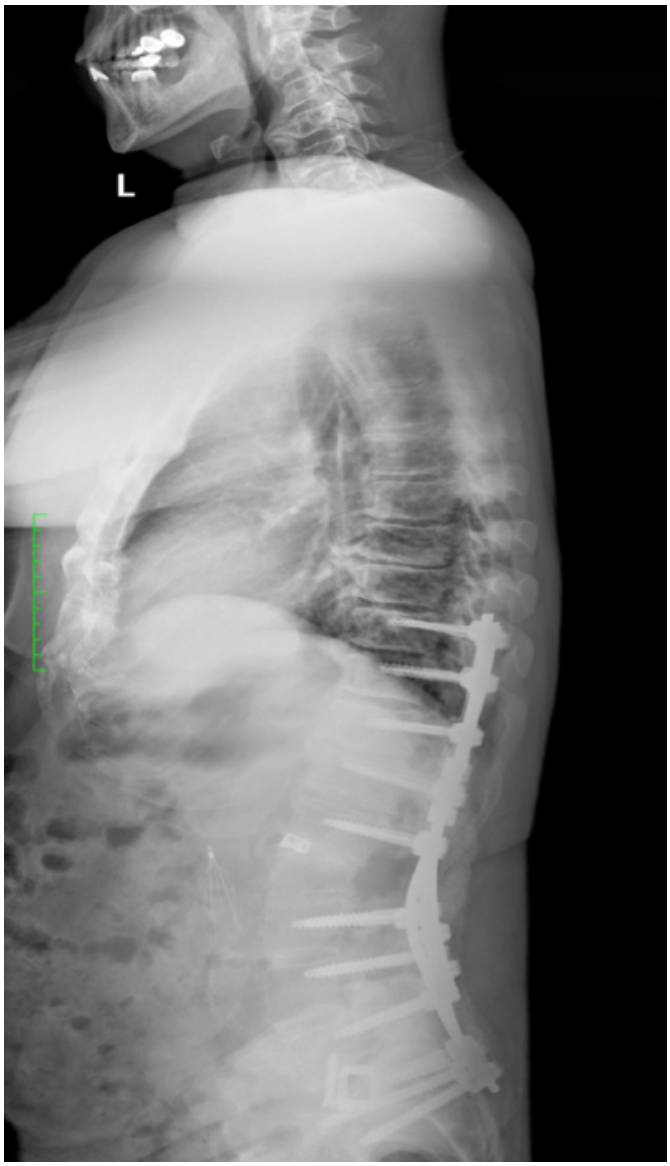

Based on initial post-op films the patient had significant sagittal balance issues and eventually required T9-Ilium fusion with a 3CO spacer at L2. 100cc of Burst allograft along with 10cc of BioBurst Fluid to aid the fusion process were used. At 7 months the patient had significant resolution of low back and leg pain. AP and Lateral radiographs at 7 months show significant progression to fusion in both interbody grafts and posterolateral gutters (Figure 10 and Figure 11).

## DISCUSSION

The majority of literature discussing radiographic and clinical success rates for spine surgery and fusion in particular display a great deal of variation despite the previously mentioned effort to observe and study a homogenous population.1,33 Comparison and compilation of study results is complicated and limited by differences in study design, success criteria, and methods of assessment. 34 Patients who present with risk factors known to limit fusion success such as greater than two levels fused, multiple fusion and/or decompressive attempts, pseudarthrosis repair or construct revision, and smoking, are generally not included in larger clinical trials. 2,3,4,35 Case histories in unique patient populations can be a useful bridge before larger more comprehensive studies can be undertaken.

**Figure 11**

7-month lateral radiograph shows substantial fusion consolidation with interbody grafts.




The new injectable/fluid allograft product (BioBurst, Burst Biologics, Boise, ID) has performed beyond expectations in the cases presented here, with rapid consolidation of the bone graft and greater than expected bone volume. These early highly encouraging results in challenging patients show the potential of BioBurst Fluid as a valuable adjunct for spinal fusion and justify further research and clinical studies.

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