Radiographic analysis of fusion success with Integra Collagen Ceramic Matrix, as compared to autograft use, in posterolateral lumbar spine arthrodesis

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ABSTRACT

Study Design: Retrospective, single center, non-randomized study.

Objectives: To evaluate the efficacy of Integra Collagen Ceramic Matrix (Collagen / β-TCP Composite) bone void filler in posterolateral lumbar fusions.

Methods: All patients treated with Integra Collagen Ceramic Matrix (CCM) putty and/or strip during posterior or transforaminal lumbar fusion surgery between April 2007 – December 2007, and who had CT Scan images at 1 year post surgery were considered for inclusion in the study. Medical records of these patients were analyzed, and data was collected on all subjects who met the eligibility requirements. Fine-cut CT scans with sagittal and coronal reconstructions were interpreted by an independent radiologist blinded to treatment.

Results: Of the 18 patients, 9 patients (50%) underwent single level fusion procedures, 5 patients (28%) had 2-level fusion surgery, 3 patients (17%) had 3-level surgery and 1 patient (5%) underwent a 4-level procedure. Fusion rates were 100% for all evaluable single level and 2-level cases. Overall fusion rate was 93.5% (29/31) of all evaluable levels. When comparing the two posterolateral sides, the autograft side and Integra CCM side resulted in nearly identical fusion rates: 29 of 31 evaluable levels (93.5%) at the autograft side and 28 of 30 evaluable levels at the Integra CCM side (93.3%) No significant differences were observed for the fusion scores in patients that received Integra CCM Putty versus Integra CCM Strip. There were no Adverse Device Effects noted. Two patients experienced Serious Adverse Events resulting in prolonged hospitalization. These SAEs were unrelated to the devices used, and resolved without residual effect. None of the 18 patients required re-operations for revision, removal or supplemental fixation.

Conclusion: Integra CCM is an effective and safe alternative for the use of autograft in posterolateral lumbar fusions, with fusion rates similar or better than those reported with autograft and other bone graft alternatives.

Keywords: lumbar fusion, bone substitute, bone marrow aspirate, mineralized collagen, collagen ceramic matrix, Integra Mozaik™, OsteoStrux™, Integra OS™

INTRODUCTION

Posterolateral spine fusion with pedicle screw fixation is a common surgical procedure for treating patients with intractable low back pain or leg pain, caused by degenerative disc disease with stenosis and/or spondylolisthesis. The goal is to form a fusion mass spanning the affected transverse processes by placing a bone graft on either side of the vertebral column[4].

Disclosure:
This study was funded in part by a research grant from the Integra LifeSciences Corporation (Plainsboro, NJ). FDA status: the device that is subject of this manuscript is cleared for use in the extremities, spine and pelvis. This includes posterolateral fusion, the surgical procedure examined in this study[9;10].

The use of autograft, for which the bone is typically harvested from the subject's iliac crest, has been an established standard for years. However, the use of autograft is associated with several shortcomings and complications including increased operating time and blood loss associated with the separate incision, limited tissue availability, variable tissue quality, and significant incidence of donor site morbidity and pain. In recent years, the inherent limitations of autograft have led to the increased use of alternatives that either reduce or eliminate the need to harvest autogenous bone[1].

Integra Collagen Ceramix Matrix was developed to mimic the composition and pore structure of natural human bone. The product consists of a framework of highly purified type-I collagen and porous β-Tricalcium Phosphate (TCP) granules in a 20:80 ratio

(by weight). The microarchitecture of Integra Collagen Ceramix Matrix (CCM) collagen is specifically engineered for osteoconductivity by encouraging vascularization and cell ingrowth while the TCP provides resistance to compression and a source of mineral during bone formation. The three dimensional pore structure of the product quickly imbibes fluids, making it easy to combine with bone marrow aspirate. Integra CCM guides the regeneration of bone across a critical defect site into which the strip or putty is implanted. New bone forms in apposition to the matrix surface when the graft is placed in direct contact with viable host bone. Ultimately the matrix is resorbed and remodeled into bone[8].

METHODS

The study was a retrospective review of the clinical and radiographic records of patients who underwent single-level or multi-level lumbar fusion at one spine center. Waiver of Consent and Waiver of Authorization (HIPAA) were received for this study from the Western Institutional Review Board. All patients that underwent posterior or transforaminal lumbar fusion surgery from April 30, 2007 until December 10, 2007, and for whom Integra CCM (strip and/or putty) was used were considered for inclusion in the study. Inclusion criteria for this study were single-level or multi-level PLF, PLIF or TLIF cases in patients over 18 years of age that underwent surgery more than a year ago. Exclusion criteria included use of medication known to influence bone metabolism (such as prolonged steroid use) and participation in another clinical trial.

For all patients, the surgical procedures involving Integra CCM and autograft were similar: Posterolateral use of Integra CCM was limited to the symptomatic side. Autograft was used at the contralateral side. This allowed for a comparison of fusion rates between Integra CCM and autograft. For the posterolateral fixation with Integra CCM, following decompression, decortication of bone on the vertebral bodies and transverse processes was performed to achieve a bleeding surface. Bone marrow aspirate (BMA) was obtained from the anterior iliac crest by using an aspiration needle. A sufficient volume of BMA concentrate was obtained and applied to Integra CCM Strip or Putty according to the product instructions. The volume of the aspirate was sufficient to adequately hydrate the Integra CCM Strip or Putty to obtain proper handling, which is approximately a 1:1 volume/volume ratio. Following instrumentation (if applicable), Integra CCM was applied and good contact with the native decorticated bone was achieved (~5cc per side per level).

Data collection included the subject demographics and medical history, surgical procedure and follow-up procedure details, device related adverse events, and available post surgery CT-scans. The interpretation of fusion results based on fine-cute CT-scans (sagittal and coronal reconstructions) was performed by an independent radiologist blinded to treatment. Fusion mass on each side was evaluated separately. Judgment of fusion was based on the presence or absence of definitive, uninterrupted bridging of well mineralized trabecular bone between the transverse processes. Interpretation of fusion scored as either "fused", "not fused" or "unable to discern".

RESULTS

Patients and procedures

Based on the eligibility requirements and CT-scan availability at approximately 12 months after surgery, 18 patients were included in this analysis. These patients (12 males and 6 females) had a mean age of 57.8 years (range 33 - 83 years). All 18 patients had one or more negative confounding factors or co-morbidities, such as Smoking (2/18 patients, 11.11%), Diabetes (2/18 patients, 11.11%), Osteopenia (1/18, 5.5%) and Osteoporosis (2/18 patients, 11.11%). Of the 18 patients, 9 patients (50%) underwent single level fusion procedures, 5 patients (28%) had 2-level fusion surgery, 3 (17%) had 3-level surgery and 1 patient (5%) underwent a 4-level procedure. The total number of fusion levels across the 18 patients was 32.

Integra CCM Strip or Putty was implanted in the posterolateral space in all evaluable patients, and autograft at the contralateral side. Thirty-two spinal levels were operated on, with one-sided posterolateral use of CCM at each level, corresponding to 32 sides. There were 23 sides repaired using CCM Strip and 9 sites treated with CCM Putty. All product applications (Strip and Putty) were mixed with Bone Marrow Aspirate (BMA) in a 1:1 concentration. Sixteen of 18 Patients (88.9%) received instrumentation in the Interbody and /or Posterolateral spaces. Fourteen patients received a combination of interbody (cage) and posterolateral instrumentation (pedicle screws and rods) at one or more levels. Two patients received posterolateral instrumentation only. Two patients underwent uninstrumented fusion, one 2-level fusion

and one 3-level fusion. Three patients received rh-BMP2 in the interbody space.

Fusion Results

Posterolateral fusion was determined at 32 levels, therefore 64 posterolateral locations were evaluated for fusion masses. Three of those locations could not be evaluated due to metal artifacts in the CT, and were labeled "unable to determine" by the radiologist. It concerned two sides of a L4-L5 level in one patient, and a unilateral side of a L5-S1 of another patient. When scoring individual posterolateral locations, 55 of the evaluable sides (61) were scored "fused" (90.2%). On a per level basis, 29 of the 31 evaluable levels were fused (93.5%), when considering that a fusion mass on either posterolateral side would likely result in a biomechanically stable fusion. On a per patient basis, 15/18 patients (83.3%) had successful fusion of all concerned levels. All evaluable single level and 2-level cases achieved fusion of all concerned levels. In the 3-level cases, 8 of the 9 levels fused (88.9%). A patient with a 3-level procedure (L3-S1) did not show fusion at the level L5-S1. In the one 4-level case, only 2 of the four levels (50%) were determined "fused" (Figure 1). In this patient that underwent 4-level surgery (L1-L5), fusion scores were "not fused" for L1-L2 and L4-L5.

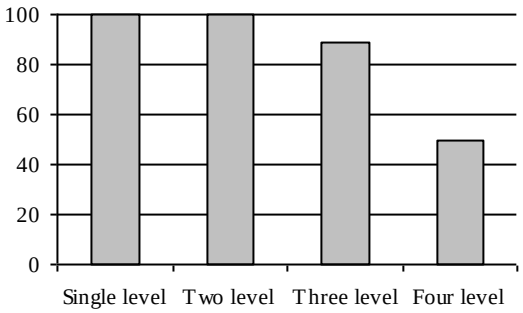

Figure 1: Percent fusion rate of all concerned levels

When comparing the two posterolateral sides, the autograft side and Integra CCM side resulted in nearly identical fusion rates (Table 1). The fusion rates were 29/31 (93.5%) at the autograft side and 28/30 (93.3%) at the Integra CCM side (p = NS; Fisher's exact test). No significant differences were observed for the fusion scores in patients that received Integra CCM Putty versus Integra CCM Strip. Integra CCM Putty was used for 9 levels in 7 patients. Integra CCM Strip was used for 23 levels in 11 patients. Per level fusion rate for Integra CCM Putty was 7 out of 8 evaluable levels (87.5%) (one level could not be interpreted from the CT scans) whereas the per level fusion rate for Integra CCM Strip was 21/23 or 91.3% (p = NS; Fisher's exact test).

Table 1: Fusion rates per evaluable posterolateral (PL) side

Level	Number evaluable PL sides	Integra CCM PL sides fused (%)	Autograft PL sides fused (%)
L1-L2	2	0 (0)	0 (0)
L2-L3	2	1 (100)	1 (100)
L3-L4	12	6 (100)	6 (100)
L4-L5	28	13 (92.9)	13 (92.9)
L5-S1	17	8 (100)	9 (100)
Total	61	28 (93.3)	29 (93.5)

A trend towards higher fusion rate with use of instrumentation could be observed. Fusion was achieved in 4 out of the 5 levels (80%) in 2 patients without instrumentation (no interbody or posterolateral instrumentation). Fusion rate in the levels with posterolateral instrumentation but without interbody instrumentation was 6/8 (75%). Fusion rate in the levels with both posterolateral instrumentation and interbody instrumentation was 18 out of 18 evaluable levels (100%), whether or not rh-BMP2 was used in the interbody space. However no statistically significant differences were observed between these subgroups (p = NS; Fisher's exact test).

A bone stimulator was used in 3 out of 18 patients. In this patient group 7 out of 9 levels fused. In comparison 21 out of 22 evaluable levels fused in patients without postoperative use of bone stimulation (P=NS; Fisher's exact test).

The two patients in the study that were active smokers had 100% fusion of all levels (4 levels in total). Of the two patients with diabetes, one had a fusion success rate of 2/3 levels (uninstrumented), while the other showed fusion of 2/2 levels but 3 out of 4 posterolateral sides.

Safety outcomes

Adverse Device Effect and Serious Adverse Events (SAEs) were collected from the patient records. Two patients experiences Serious Adverse Events resulting in prolonged hospitalization. One patient experienced a bacterial infection with pseudomonas, and needed treatment with IV antibiotics. Another patient experienced significant blood loss during surgery, resulting in hypoxemia. Both SAEs were determined as not related to the device, and both resolved without residual effect.

Based on the information in the patient records, none of the 18 patients required re-operations for revision, removal or supplemental fixation.

DISCUSSION

When performing surgical treatment of degenerative disc disease of the lumbosacral spine, the goal is to achieve a solid fusion. Posterolateral fusion can be achieved by placing bone graft between the transverse processes at either side of the vertebrae. Although the use of autologous bone graft from the iliac crest is still considered the gold standard, surgeons have become increasingly aware of the disadvantages associated with the graft harvest, such as significant and prolonged donor site morbidity and pain. This has led to the use of alternative bone grafts, such as allografts and ceramics, but also the use growth factors, such as rh-BMP2.

Integra Collagen Ceramix Matrix (CCM) was developed to provide an alternative to autologous bone graft. Both putty and strip versions are resorbable bone void fillers made from a porous highly purified collagen matrix that have high purity β-tricalcium phosphate (TCP) granules dispersed throughout. The microarchitecture of Integra CCM collagen is specifically engineered for osteoconductivity by encouraging vascularization and cell ingrowth while the TCP provides resistance to compression and a source of mineral during bone formation. Integra CCM Putty is designed as a moldable and packable carrier, and Integra CCM Strip is designed as a carrier with a fixed shape and dimension that can be cut to size.

This retrospective study was performed to evaluate the efficacy of Integra CCM in posterolateral instrumented lumbar fusions, in a routine clinical practice setting. Eighteen patients with CT scans available at 12 months post surgery or beyond are included in this evaluation. Of the 18 patients, 9 patients (50%) underwent single level fusion procedures, 5 patients (28%) had 2-level fusion surgery, 3 (17%) had 3-level surgery and 1 patient (5%) underwent a 4-level procedure.

The overall fusion rate in this study was similar or greater than the reported fusion rates with autograft or other bone graft products. Indeed, on a per patient basis, 15/18 patients (83.3%) had successful fusion of all concerned levels, whereas when scoring each vertebral level separately, 29 of the 31 evaluable levels were fused (93.5%). More importantly, all evaluable single level and 2-level cases achieved 100% fusion.

In comparison, recent published studies on the fusion rates at 12 months in single level instrumented posterolateral fusion with autograft range from 65% [6] to 83% [7] as determined by CT scans. The use of a demineralized bone matrix graft (Grafton® DBM) in combination with autograft showed a radiographic fusion rate at 24 months of 42% and 60% in prospective [3] and retrospective studies in posterolateral fusion respectively [12]. Reported fusion rates with β-TCP / autograft composites in single and two-level instrumented posterolateral fusion at 1 year are 96.2% and 92.5% respectively, based on X-ray and CT evaluation. Similar fusion rates (93.3%) were also reported with Type I collagen / hydroxyapatite bone grafts imbibed with BMA in a study on instrumented posterolateral fusion. This latter study excluded smokers and results were interpreted by X-ray at 2 years.

Published fusion rates vary (widely) between studies. This can be largely explained by variability in study design such as single versus multiple level surgeries, type and amount of bone graft used and whether or not instrumentation was used. Furthermore, the imaging methodology and criteria used for assessing fusion impact the interpretation of the fusion outcome. In fact, in the study by Dimar 2nd et al.,[7] the authors showed that using CT only is a more stringent method than using radiographs (and CT). Using the first method, they showed a fusion rate of 71.5% for single level instrumented posterolateral fusion with iliac crest autograft at 12 months, whereas the second method resulted in an estimated fusion rate of 82.5%. In the current evaluation, only CT images were used for the interpretation of fusion.

The impact of instrumentation has been shown by Andersen et al.[2] This group reported fusion rates in posterolateral fusion (both single and multilevel procedures) using fresh frozen allograft with or without instrumentation (screws & rods), and showed

a success rate of 81% in the patients with instrumentation and only 58% in the group without instrumentation. In the current study, a trend towards higher fusion rate with use of instrumentation could be observed, but this was not significant.

Overall, the fusion rate observed in this study is similar to the ones reported with other synthetic bone void fillers, and numerically better than some of the reported fusion rates with certain DBM products and autograft. Certainly when considering that this study did not exclude smokers or comorbidities such as diabetes, the fusion rate of 100% in the single level and two level cases is remarkable. Furthermore there was only one 3-level case that did not have successful fusion of all levels (only 2/3), but this was a case without instrumentation. Other 3-level cases also showed 100% fusion.

The key limitations of the study are the facts that this is a retrospective study, and that a left / right performance of autograft and Integra CCM may not be entirely independent. On the other hand, left / right comparison allows for a comparison in a small study population[11]. The study population used here is a good representation of the average patient undergoing lumbar fusion surgery in a routine clinical practice. Therefore this study supports the use of Integra CCM in such a diverse population with good fusion results for most of those patients. An additional limitation of this study is that it only looked at fusion outcomes and not clinical outcomes. However, the correlation between clinical results (such as functional outcome and pain outcome) and fusion results has been shown in several other studies[4;5], supporting the connotation that the results of this study have clinical significance.

Further analysis of the current data set and future prospective studies are suggested to further confirm the results of this study.

CONCLUSION

In this retrospective study it was shown that Integra Collagen Ceramic Matrix mixed with BMA results in posterolateral fusion rates comparable as those obtained with autograft, in a left / right intrapatient comparison. Of all patients undergoing single or two-level PLF, PLIF or TLIF procedures, the posterolateral fusion rate was 100%. These results suggest that Integra CCM is an effective and safe alternative for the use of autograft in posterolateral lumbar fusions.

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