Study Title: Fusion rate and clinical outcomes following 1 or 2 level open Transforaminal Lumbar Interbody Fusion for degenerative disc disease with novel 3-D printed titanium cages with pedicle screw fixation

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1. Introduction

1.1 Study Purpose

To evaluate the fusion rate and clinical outcomes at 1 year of 20 patients with DDD who undergo a 1 or 2 level TLIF with Tritanium® PL cage and pedicle screw fixation. The proposed case series will build on the body of clinical and radiological evidence for this implant in TLIF patients. It will also provide pilot data for future studies that will compare the Tritanium ® cage to PEEK.

1.2 Background

TLIF addresses a range of painful degenerative pathology including DDD and spondylolisthesis. PEEK cages are the standard of care for use in TLIF, however titanium cages have shown good results compared to PEEK in the literature.[1]

1.3 Device

Tritanium ® PL is an intervertebral body fusion device indicated for use with autograft and/or allogenic bone graft comprised of cancellous and/or corticocancellous bone graft when used as an adjunct to fusion in patients with degenerative disc disease (DDD) at one level or two contiguous levels from L2 to S1. The Tritanium ® PL cage is a 3D manufactured titanium cage designed with angled serrations for bidirectional fixation and to maximize surface area for endplate contact with the implant. The cage is also designed to address the potential for subsidence into the endplates.

The Tritanium® PL Cage was cleared for marketing under 510(k) K160955

1.4 Study Objectives

- Primary Objective
  - Assess fusion at 1 year post-operatively on CT
- Secondary Objectives

- Assess pain and functional outcomes using VAS and ODI (validated patient reported outcomes)
- Assess hardware placement and fusion with plain radiographs collected at 2 weeks, 6 months and 12 months post-op.
- Monitor adverse events

2. Study Hypothesis

The Tritanium PL cage will produce satisfactory fusion rates due to its highly porous material designed for bone in-growth and biologic fixation. TLIF fusion rate, adverse events and patient reported outcomes will be qualitatively comparable to PEEK results in the literature.

3. Study Methods

3.1 Study Design

Prospective, non-randomized (single arm) single-center study to evaluate the post-operative radiographic and patient outcome variables of the Tritanium PL cage compared to literature reported outcomes for traditional PEEK cage for interbody fusion treatment of degenerative disc disease (DDD).

3.2 Treatment Group

20 patients requiring an open 1 or 2 level TLIF will make up the study population. Eligible patients will have lumbar (L2-S1) degenerative disc disease (may have up to grade 1 spondylolisthesis), and/ or degenerative scoliosis. DDD is defined as back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies. The DDD patients may also have up to Grade I spondylolisthesis at the involved level(s). These patients should be skeletally mature and have six months of non-operative therapy.

3.3 Primary Study Endpoint

Fusion status at 1 year

4. Study Population

4.1 Sample size

20 patients will be enrolled in the study. Outcomes from this pilot study may be used to design larger controlled trials.

4.2 Inclusion and Exclusion Criteria

Patients must meet all of the inclusion criteria and none of the exclusion criteria in order to be eligible to enter the study.

- Inclusion Criteria
  - Subject has one or more of the following diagnoses:
    - Degenerative disc disease (DDD) at one level or two contiguous levels from L2 to S1.
      - DDD may also include up to Grade I spondylolisthesis at the involved level(s).
      - Note: DDD is defined as back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies.
    - Degenerative scoliosis for which the Tritanium PL cage will be used as an adjunct to fusion.
  - Skeletally mature and ≥ 18 years old at time of enrollment
  - Completed at least 6 months of non-operative therapy prior to surgery
  - Willing and able to sign a study specific consent and comply with the requirements of the protocol including follow up visits and imaging.

- Exclusion Criteria
    - >2 levels requiring surgical intervention
    - Non-degenerative pathology including tumor, trauma, post-laminectomy kyphosis
    - Psudeoarthrosis at the index level
    - Previous fusion at the levels to be treated or at adjacent level
    - Any abnormality present which affects the normal process of bone remodeling including, but not limited to, severe osteoporosis involving the spine, bone absorption, osteopenia, primary or metastatic tumors involving the spine, active infection at the site or certain metabolic disorders affecting osteogenesis.
    - History of osteoporotic fracture
    - History of an endocrine or metabolic disorder known to affect bone and mineral metabolism
    - Inadequate tissue coverage over the operative site or taking medications that may interfere with bony/soft tissue healing including chronic steroid use
    - Known allergy to titanium or cobalt chrome or may be sensitive to materials
    - Rheumatoid arthritis or other autoimmune disease or a systemic disorder such as HIV, active hepatitis B or C or fibromyalgia
    - Lumbar kyphosis- lumbar lordosis < 20°

- Degenerative scoliosis >20° OR any other pathology scoliosis (idiopathic, congenital, posttraumatic, iatrogenic)
- Active systemic infection or infection at the operative site
- Marked local inflammation
- Any open wounds
- Pregnant, or intends to become pregnant during the study
- Current smokers
- Subject is class 3 obese (BMI >40) or overweight and can produce loads on the spinal system which can lead to failure of the fixation of the device or to failure of the device itself
- Any mental or neuromuscular disorder which would create an unacceptable risk of fixation failure or complications in postoperative care
- Any neuromuscular deficit which places an unsafe load level on the device during the healing period
- Any other medical or surgical condition which would preclude the potential benefit of spinal implant surgery, such as the presence of tumors, congenital abnormalities, elevation of sedimentation rate unexplained by other diseases, elevation of white blood cell count (WBC), or marked left shift in the WBC differential count.
- Any condition of senility, mental illness, or substance abuse.
- Involved in current spinal litigation that may interfere or influence patient self-assessment of function and pain

- Physical or mental condition that may interfere or influence patient self-assessment of function and pain.
- Incarcerated at the time of study enrollment

4.3 Study Duration

Study subjects will be expected to participate in this study for 12 months following surgery, with follow-up evaluations at initial post-op (2 weeks), 3 months, 6 months, and 12 months.

5. Study Objectives/Outcomes

5.1 Primary Study Objective

Evaluate fusion status at 1 year (12 months)

- Radiographic Assessment of Fusion

  Radiographic assessments by CT scan and AP/ lateral x-rays at the 12 month visits include overall assessment of fusion. Fusion will be graded by the Principle Investigator taking into account signs such as:

  • Bony Bridging

  • Radiolucency

  • Development of Pseudoarthrosis

5.2 Primary Safety Objectives

- The evaluation of all adverse events including device related, procedure related and additional serious adverse events.
- Evaluation and reporting of additional surgical intervention at the operative site including revision and/or device removal

All adverse events will be documented on a continuous basis and reviewed by the Bone and Joint Clinical Research Staff. Information regarding all device failures including implant breakage, subsidence, migration, or expulsion will be captured.

5.3 Secondary Objectives

Secondary objectives are expected to further define the patient outcomes for effectiveness of the surgery and device in this population.

5.3.1 Oswestry Disability Index

The Oswestry Disability Index (ODI) is the most commonly used outcome measure in patients with low back pain. It has been extensively tested, showed good psychometric properties, and applicable in a wide variety of settings. This validated patient-reported outcome measure is a 10 item questionnaire that evaluates disability and functional impairment associated with back problems. A total ODI score is determined by adding the scores of the individual questions and dividing that total by the maximum possible score to yield a percentage. Therefore, the ODI score ranges from 0% to 100%. A higher score corresponds to a greater disability.

5.3.2 Visual Analog Scale

The severity of back and leg pain will each be evaluated in all study subjects using a 10 cm visual analog scale (VAS).

6. Study Enrollment and Follow Up Visits

6.1 Screening visit

Consecutive patients who potentially meet the inclusion/exclusion criteria for the study will be screened for eligibility. Patients who agree to participate in the study will sign an IRB approved Informed Consent form. Consenting patients who meet the inclusion/exclusion criteria will complete preoperative demographics and subject

questionnaires (ODI and VAS). Patients will have recent (appropriate for surgical planning by the PI) AP, Lateral and Flex/Ext x-rays.

6.2 Follow Up Visits

Patients will return to clinic to complete subject questionnaires (ODI and VAS) at 2 weeks, 3 months, 6 months, and 12 months postoperatively. Plain radiographs (AP and Lateral views) will be obtained at 2 weeks, 6 months and 12 months. A CT scan will also be obtained at 12 months.

7. Hospitalization/Surgical Technique/Discharge

Subjects will be admitted to the hospital according to the Principle Investigator's standard for an instrumented posterolateral fusion in conjunction with a TLIF surgery. Prophylactic antibiotics, preoperative planning, patient positioning and anesthesia will be carried out in accordance with the institution's and Investigator's standard of care.

7.1 Surgical Approach

The surgeon performs a midline incision and standard posterior exposure to decorticate the transverse processes bilaterally to accommodate graft for the posterior fusion. The spinous processes and interspinous ligaments can usually be left intact, which minimizes epidural scarring and provides a larger surface area for the posterior fusion.

After exposure, pedicle screws are placed bilaterally. Fluoroscopy or other strategies may be used to aid in proper screw positioning. Distraction may then be performed using the surgeon's preferred method to open the posterior portion of the disc space, if needed.

7.2 Transforaminal Lumbar Interbody Fusion (TLIF)

For the TLIF procedure, access to the disc space is gained via a triangular working window. The window is formed by the traversing nerve root and thecal sac on the medial side, the exiting nerve root from the proximal vertebral level on the lateral side, and the superior aspect of the pedicle of the distal vertebra forms the base of the triangle. The surgeon performs a laminotomy, laminectomy and/or facetectomy (partial or total) along with removal of the ligamentum flavum to provide access to the disc space. Care should be taken to preserve the facets as much as possible and remove only enough bone as needed to provide access for introduction of the interbody spacer and to decompress and mobilize the nerve root as necessary. If decompression of the contralateral side of the spinal canal is required, the TLIF procedure can be modified to include a central laminectomy.

After exposure of the posterior aspect of the disc, an incision is made in the annulus through which the discectomy and endplate preparation are performed. Endplate preparation consists of removal of the cartilaginous endplate down to bleeding bone. The Tritanium PL interbody cage is then introduced.

Once the interbody implant is in place and bone graft added to the disc space, distraction is released and compression is applied to the pedicle screw to load the anterior implant and restore lordosis to the spine.

7.3 Surgical Close and Recovery

Standard procedures and precautions are to be followed for closure of the surgical incision and postoperative recovery. The patient is typically mobilized out of bed the day after surgery; bracing is not required but can be used according to

surgeon preference. The subject may be instructed to return to normal activity at the discretion of the Investigator.

8. Data Collection

All data collected for the study will be maintained on Case Report Forms and stored in a secure location at the Bone and Joint Clinic of Baton Rouge. All data will also be stored in discreet fields in a database.

8.1 Baseline Data – A preoperative history and physical to include demographics and diagnosis data will be taken at the screening/baseline visit after Informed Consent is obtained. Baseline data will include:

- Date of Visit
- DOB
- Gender
- Height and Weight
- Tobacco Use
- Diagnosis
- Affected levels
- AP, Lateral, and Flex/EXT x-rays
- Back and Leg VAS
- ODI

8.2 Surgery Data.

- Implanted System Details
- Surgery Detail/Concomitant Procedures
- Surgery Time (initial incision to closure)

- Perioperative Antibiotic Use
- Estimated Blood Loss
- Intra-operative complications, if any

8.3 Follow up data

- AP, Lateral x-rays (2 weeks, 6 weeks and 12 months)
- Back and Leg VAS (2 weeks, 6 weeks, 3 months and 12 months)
- ODI (2 weeks, 6 weeks, 3 months and 12 months)
- CT (12 months)
- Adverse Events (if applicable)

9. Benefits and Risks

9.1 Potential Benefits

There is no guarantee that the subject will experience any immediate or direct benefits from the surgery, the Tritanium ® device or from taking part in this study.

9.2 Risks

Potential risks include those associated with any spinal surgery resulting in neurological, cardiovascular, respiratory, gastrointestinal compromise, or death.

9.3 Mitigation of Risks

Operative and acute periprocedural risks for the patients enrolled in this study are mitigated by the operating orthopedic spine surgeon being trained and experienced in the proper surgical technique to perform the surgery and to implant the respective device. Long-term risks such as device failure or pseudoarthrosis are mitigated by proper patient selection and by following accepted standard of care in this population for spinal fusion surgery.

10. Statistical Methods

The purpose of this study is to build upon the available data for the Tritanium implant in this on-label population. Descriptive statistics will be used to summarize demographics and baseline and surgical variables.

Change in in VAS and ODI will be determined and the percentage of patients exceeding the MCIC (minimally clinical important change) will be reported for each outcome. The MCIC to be used for each patient reported outcome are derived from Parker, et al, *J Neurosurgery Spine*, 2011.[2]

- VAS – Leg pain- 2.8
- VAS – Back Pain- 2.1
- ODI – 14.9

The fusion rate will be reported and qualitatively compared to TLIF fusion rates in the literature.[3]

11. References

1. Nemoto O, Asazuma T, Yato Y, Imabayashi H, Yasuoka H, Fujikawa A. Comparison of fusion rates following transforaminal lumbar interbody fusion using polyetheretherketone cages or titanium cages with transpedicular instrumentation. *Eur. Spine J.* 2014;23(10):2150-5. doi:10.1007/s00586-014-3466-9.

2. Parker SL, Adogwa O, Paul AR, et al. Utility of minimum clinically important difference in assessing pain, disability, and health state after transforaminal lumbar interbody fusion for degenerative lumbar spondylolisthesis. *J. Neurosurg. Spine* 2011:1-7. doi:10.3171/2010.12.SPINE10472.

3. Khan NR, Clark AJ, Lee SL, Venable GT, Rossi NB, Foley KT. Surgical Outcomes for Minimally Invasive vs Open Transforaminal Lumbar Interbody Fusion. *Neurosurgery* 2015;77(6):847-874. doi:10.1227/NEU.0000000000000913.