

Compressive osseointegration for endoprosthetic reconstruction

Lindsay Parlee,¹ Ryland Kagan,¹ Yee-Cheen Doung,¹ James B. Hayden,¹ Kenneth R. Gundle^{1,2}

¹Department of Orthopedics and Rehabilitation, Oregon Health and Science University; ²Operative Care Division, Portland VA Medical Center, OR, USA

Abstract

This review summarizes the biomechanical concepts, clinical outcomes and limitations of compressive osseointegration fixation for endoprosthetic reconstruction. Compressive osseointegration establishes stable fixation and integration through a novel mechanism; a Belleville washer system within the spindle applies 400-800 PSI force at the bone-implant interface. Compressive osseointegration can be used whenever standard endoprosthetic reconstruction is indicated. However, its mode of fixation allows for a shorter spindle that is less limited by the length of remaining cortical bone. Most often compressive osseointegration is used in the distal femur, proximal femur, proximal tibia, and humerus but these devices have been customized for use in less traditional locations. Aseptic mechanical failure occurs earlier than with standard endoprosthetic reconstruction, most often within the first two years. Compressive osseointegration has repeatedly been proven to be non-inferior to standard endoprosthetic reconstruction in terms of aseptic mechanical failure. No demographic, device specific, oncologic variables have been found to be associated with increased risk of aseptic mechanical failure. While multiple radiographic parameters are used to assess for aseptic mechanical failure, no suitable method of evaluation exists. The underlying pathology associated with aseptic mechanical failure demonstrates avascular bone necrosis. This is in comparison to the bone hypertrophy and ingrowth at the bone-prosthetic interface that seals the endosteal canal, preventing aseptic loosening.

Introduction

Substantial periarticular bone loss, whether secondary to tumor resection or as the consequence of trauma or multiple

arthroplasty revisions, presents reconstructive challenges. As an alternative to ablative procedures, limb salvage with endoprosthetic reconstruction is an option for patients. While various types of implants are available, compressive osseointegration fixation offers an alternative to cemented or non-cemented intramedullary stems.¹ This technology exploits the principals of Wolff's law to create a stable, high pressure bone implant interface that theoretically avoids stress shielding.²⁻⁴

This technology has the potential to decrease the rate of aseptic mechanical failure, preserve bone stock and allows for stable short-segment fixation.^{2,5,6} In addition to existing bone loss, in some clinical scenarios there may be advantages to preserving or avoiding instrumenting the intramedullary bone. Primary bone tumors have their highest incidence in adolescents and young adults. Limb salvage, a procedure in which the tumor is resected and the limb is spared, is offered to nearly 70-85% of these patients.⁷⁻⁹ The 5-years survival in these patients is reported as high as 70-80%; however, the all cause revision rates after limb salvage is higher than after primary arthroplasty. Therefore, those patients who are young at diagnosis will likely require multiple implant replacements in their lifetimes.¹⁰⁻¹⁵ Inevitably bone stock is lost with each revision, and this may be minimized with compressive osteointegration endoprosthetic reconstruction, offering an advantage over traditional stemmed fixation. As a relatively new technology the aim of this review is to summarize the biomechanical concepts, clinical outcomes and limitations of compressive osseointegration fixation for endoprosthetic reconstruction.

Compressive osseointegration fixation

The ZimmerBiomet Compress® (Warsaw, IN, USA) (Figure 1) has been FDA approved since 2003. Unlike other intramedullary stems, compressive osseointegration fixation uses a novel compressive force that results in immediate stabilization as it applies an axial force at the bone-implant interface.⁷ Compression is achieved through a stacked, spring loaded Belleville washer system that creates a force of 400-800 PSI. This force is adjusted based on the cortical width; an inadequate force can lead to failure due to loosening while an excessive force may result in failure due to periprosthetic fracture.¹⁶ An appropriate compressive force results in hypertrophy and osseointegration at both the bone implant

Correspondence: Kenneth Gundle, 3181 SW Sam Jackson Park Road, Mail Code OP-31, Portland OR 97239, USA.
Tel.: 503-494-6400 - Fax: 503-346-6844.
E-mail: gundle@ohsu.edu

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interface and bone surrounding the implanted spindle in accordance to Wolf's Law.^{2,4,7,17,18}

Compressive osteointegration fixation consists of three key components: anchor plug, spindle, and adaptor. The anchor plug is fixed in place using five transverse pins. The length of these pins is based on the bicortical distance at the level of the anchor plug.¹⁹

Once the anchor plug is secure, the spindle size is selected based on the diameter of the remaining bone. The minimal cortical width is measured, because less than 2.5 mm width is a relative contraindication.¹⁹ The spindle is chosen by a combination of bone diameter and cortical thickness. Key to spindle selection is choosing the size that is closest to the measured diameter, but slightly larger than the measured width. There are four spindle sizes, including one designed for use in the metaphyseal flare, for a

bicortical length up to 45 mm.¹⁹ The spindle contains the compressive washers that eventually apply a force at the bone-implant interface. The force applied (400-800 lb) is determined according to the cortical thickness (Table 1). Prior to attachment of the spindle, the ostomy site is reamed to contour the bone such that it matches the spindle. The spindle is aligned prior to tightening the compression nut within the spindle. The compression nut then transfers the pre-loaded force to the anchor plug, creating the desired force between the bone and implant. If alignment is incorrect, this can easily be reversed and rotated.¹⁹

Once the spindle is in place, antirotation pins are used to limit rotational force at the bone-implant interface. The use of three antirotation pins in the collar is recommended whenever possible. The site of antirotation pin placement in the collar is decided based on both the spindle and sleeve size (Figure 2). After the spindle is in place, an adaptor is attached to the spindle.¹⁹ The adaptor is selected based on the anatomic location of the bone resection and endoprosthetic reconstruction. An example of a distal femoral adaptor is shown in Figure 1.¹⁹

Current postoperative recommendation after implanting a compressive osseointegration device in the lower extremity is restricted touch-down weight-bearing for six weeks. After six weeks, some authors advise to increase weight-bearing by 25% each week, such that full ambulation without assistive devices is achieved 3 months postoperatively. However, only 49% of patients followed this protocol in one series.⁷ Other authors allow for full weight-bearing as tolerated after six weeks.^{1,10} As there is no way to definitely confirm that the implant is stable, this timeframe may be arbitrary and is similar to recommendations following implantation of uncemented stems. Zimel *et al.* found that hypertrophy may not be visualized on imaging at 3 months, and advises caution with weight-bearing until radiographic evidence of fixation is seen.²⁰ Questions remain about the time to achieve stability of compressive osseointegration implants, and whether initial weight-bearing restrictions influence outcome. Even though weight-bearing is limited postoperatively, active-assisted and active range of motion and muscle

Table 1. Compressive force.

Cortical Thickness (mm)	Force (lb)
0.0 – 2.4	Not indicated
2.5 – 3.9	400
4.0 – 5.4	600
5.5 and above	800

strengthening can be started immediately after surgery.

Indications

Compressive osseointegration can be used whenever standard endoprosthetic reconstruction is indicated, such as for limb salvage in patients with bone tumors.¹¹ Limited remaining bone stock poses a considerable barrier for stemmed implants that compressive osseointegration fixation circumnavigate. A unique feature of compressive osseointegration fixation is the short length of the implanted spindle allowing for use with minimal remaining bone stock. Typical sites of use include the proximal or distal femur, proximal tibia, and humerus. It has been suggested that compressive osseointegration requires approximately 8 cm of resected bone at the distal femur, 13 cm at the proximal femur, 15 cm at the proximal tibia and 12 cm at the

proximal humerus.^{2,5,6,10,13,17,21} Case reports also describe custom implants utilizing this technology for fixation in the pelvis.²² In addition to oncologic indications, compressive osseointegration has been used for endoprosthetic reconstruction in the setting of acute fractures, as well as mal-unions and non-union.¹⁰ Compressive osseointegration is also indicated for revision of unsuccessful osteotomy, arthrodesis, or revision total joint arthroplasty.¹⁹

The manufacturer described contraindications include active infection, neurologic or mental condition rendering the patient unable or unwilling to follow postoperative care instructions, vascular insufficiency, poor bone quality or quantity (less than 2.5mm cortical thickness), latent infections, and pathologic soft tissue or skeletal conditions that prevent stable device fixation.¹⁹ Additional contraindications frequently cited in the literature include diffuse metastatic disease and prior radiation

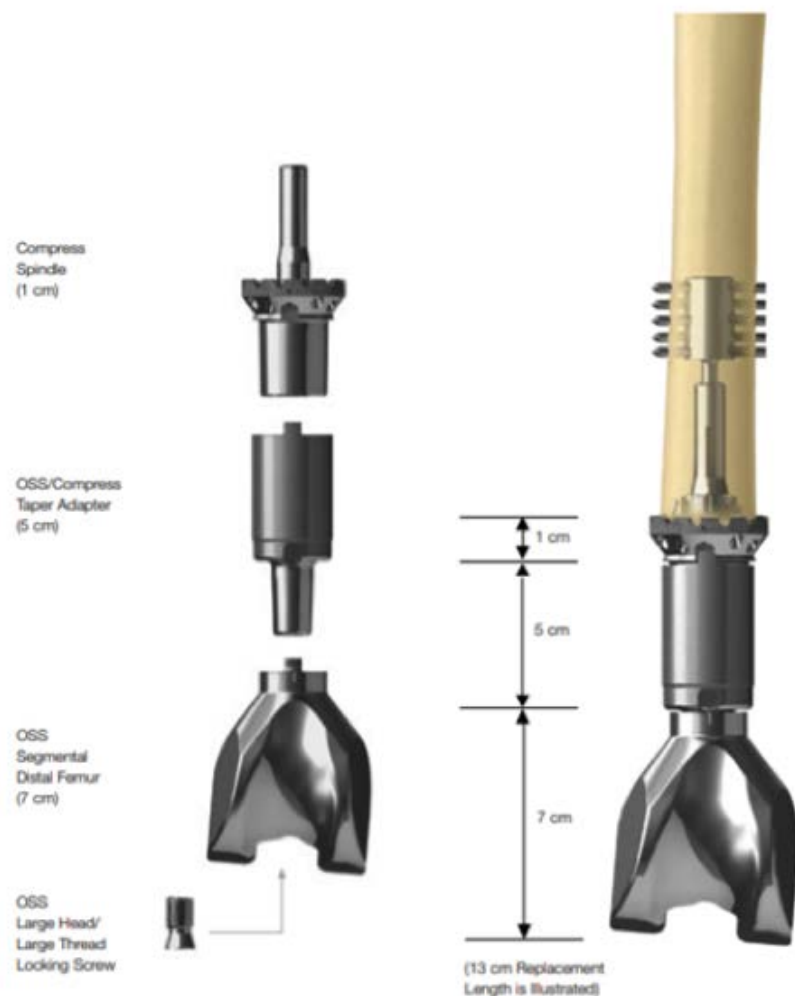


Figure 1. Compress® components with distal femoral adaptor. Image used with permission of Zimmer-Biomet.

at the operative site. One study found that radiation was associated with increased risk of overall failure ($p < 0.003$), but not aseptic mechanical failure.¹ There is less consensus among surgeons regarding other potential contraindications, such as age. Some centers suggest age greater than 50 years as a contraindication while others have suggested an older age such as 70 years.^{5,6,11,23} Other suggested contraindications include life expectancy less than 10 years, systemic medical conditions that impair bone healing, extra articular resection of knee, inadequate soft tissue envelope that cannot be reconstructed, and metastatic disease mandating immediate weight-bearing to be relative contraindications.^{1,6,7,11,20}

Outcomes

Understanding and classifying failure mechanisms is critical to design improvement and failure reduction of compressive osseointegration devices. As such, a number of studies have attempted to describe and classify different types of compressive osseointegration implant failures. Goldman *et al.* describes these failures as either mechanical or non-mechanical. Non-mechanical failures include those due to infection, soft tissue failure, or tumor progression. Mechanical failures, often referred to as aseptic failures are those related to the device.⁷ The device can fail at a number of locations, including the anchor plug, spindle sleeve or fixation pins.¹¹ Non-device related mechanical failures include periprosthetic fracture, failure of the spindle to in-grow, and aseptic loosening.⁷

Equally important to classifying failure is understanding the pathophysiologic mechanism and presentation of aseptic failure. Multiple studies have identified a pathologic pattern in the bone surrounding implants that aseptically fail. The bone quality, after removal of osseointegration devices that experienced aseptic loosening, was found to have underlying avascular necrosis of the bone.^{2,4,11} In contrast, in the devices removed due to tumor recurrence or infection, there was bone growth at the bone-prosthetic interface that sealed the endosteal canal to particulate debris; this may reduce the likelihood of aseptic loosening after six to twelve months.^{4,24} In a separate multi-center study, osteonecrosis was also found after removal of the compressive osseointegration devices that experienced aseptic failures following periprosthetic fracture.²⁵

Aseptic failure should be suspected

when a patient presents with specific signs and symptoms. Healey *et al.* noted that the signs and symptoms of a proximal femur compressive osseointegration device failure include thigh tenderness that is worse with the hip rotated to the 90-90 position (supine, hip flexed and knee flexed).¹¹ Radiographic evaluation should be done in these patients. However, as a result of the unique biomechanical mechanism by which it establishes fixation and stabilization, aseptic failure of compressive osseointegration devices radiographically present different than long-stemmed implants. A number of radiographic parameters have been suggested to evaluate compressive osseointegration device fixation, including bone hypertrophy at the bone-implant interface, a parameter when present represents stable integration.^{1,9,13,14,20} Radiographic parameters suggestive of failure include a progressive gross decrease in the distance between the anchor plug base and the top of the spindle sleeve,²³ deformation of the implant that suggests bending or breaking of the device,¹¹ and bony atrophy at the bone implant interface.¹¹ Ultimately, the authors of previous investigations admit that currently there is no suitable methodology for evaluating aseptic mechanical failure of this technology.¹¹

In a study of eighteen patients who were revised to a compressive osseointegration device following failure of their long-stem cemented or uncemented implants, all eighteen patients explicitly stated feeling more comfortable with their compressive osseointegration implants; this may suggest improved stability and fixation over their prior devices.¹¹ In addition to patient reports of stability, multiple studies that have used Musculoskeletal Tumor Society (MSTS) scores report favorable functional outcomes with compressive osseointegration devices. Zimel *et al.* reports an average MSTS score of twenty-seven out of thirty, which is consistent with scores reported in other

studies in which the compressive osseointegration was used for distal femoral reconstruction.^{20,26-32}

Unlike long-stemmed implants that are prone to aseptic failure over time, compressive osseointegration technology may escape this tendency by avoiding stress shielding.^{30,33-35} Pedtke *et al.* found no difference in aseptic failure at five years, in age and indication matched patients.²³ There was, however, a greater overall survival at five years with compressive osseointegration stems (83.5%) relative to the cemented intramedullary stem (66.6%).¹¹ These findings are consistent with those found in a large multicenter review of 2,174 traditional long-stem implants that likewise reported the survival from aseptic failure to be 88%.³⁶

These devices do however differ in the average time at which aseptic failure occurs. One study found that the average time to aseptic loosening was 88 months for cemented intramedullary implants, in contrast to an average of 8.3 months to failure for compressive osseointegration devices.⁵ Other investigators have likewise found that aseptic loosening tends to occur early with compressive osseointegration implants, most often within the first two years.^{5,11,36} An important distinction is that aseptic failure becomes more likely over time in long-stem implants.^{30,33-35} Compared to an uncemented press-fit that had an 85% 5-years survival and 71% 10-years survival, with aseptic loosening as the number one cause of failure, compressive osseointegration devices had an 88% 5-years survival with no aseptic failures beyond one year.²¹ Goldman *et al.* looked specifically at the implanted spindle and found that when removal for infection or amputation was excluded from analysis, there were no spindle failures beyond 5 years. In this study, the overall 5-years survival was 91%, with spindle failures happening within the first 2 years only.⁷ While multiple studies have shown that revisions due to aseptic failure

Spindle Size	Inner Array	Middle Array	Outer Array
30 mm	13-15 mm Sleeve	-	-
38 mm	13-15 mm Sleeve	13-19 mm Sleeve	13-23 mm Sleeve
44 mm	13-15 mm Sleeve	13-22 mm Sleeve	13-28 mm Sleeve
Elliptical (37x49 mm)	13-15 mm Sleeve	13-20 mm Sleeve	13-27 mm Sleeve




Figure 2. Antirotation pin site selection.

are uncommon after implantation of a compressive osseointegration stem, revision for other reasons may occur. A retrospective study of 127 patients who received distal femoral compressive osseointegration endoprostheses at one institution between 1996 and 2013 found that the 5-years unplanned reoperation-free survival was only 57% and 10-years unplanned reoperation-free survival was 50%.^{7,29,36-54} Likewise, Calvert *et al.* found that at 2 years, the all-cause revision of any component of the compressive osseointegration implant was 32%.⁵ A large multicenter review of 2174 endoprostheses (mostly long-stem cemented) implanted between 1974 and 2008 found that the all cause failure for endoprostheses was 25%, with a 12% rate of aseptic failure. This suggests that reoperation may be more common after use of a compressive device, a potential drawback when compared to cemented stems.³⁶

Rates of survival from aseptic mechanical failure have proven to be fairly stable even as studies have had longer periods of surveillance (Table 2). In 116 patients from a single institution, 95% of patients were free from aseptic mechanical failure at eighteen months, 93% at four years, and overall there were zero aseptic mechanical failures in the proximal femur.¹⁰ In another study of 82 patients, the 5-years survival from aseptic failure was 85%, and the 10-years survival was 80%.¹¹ A previous literature review notes the 10- to 15-years survival from aseptic failure in the compressive osseointegration implants was as high as 84-89% (Table 2).^{5,11,21}

While mechanical aseptic failures have been repeatedly found to occur early with compressive osseointegration, no specific

variables or risk factors have been reported to correlate with increased rates of mechanical failure.^{5-7,10,11,21} Likewise, no patient demographic variables have been found to be associated with aseptic mechanical failure.⁵ Other studies have concluded that age, BMI, and sex are not associated with failure.^{6,7} Monument *et al.* found no oncologic variables associated with aseptic mechanical failure, including diagnosis, neoadjuvant, adjuvant, post-operative radiation.⁶ There was some difference in the rate of bone hypertrophy in patients receiving chemotherapy. Patients who do not receive chemotherapy initially have faster hypertrophy with increased cortical width at three and six months postoperatively.^{6,18} Despite this initial difference, hypertrophy typically catches up in the chemotherapy group, with no difference between the groups seen by twelve months.¹⁸ While Kagan *et al.* found that there is an increase in failure for patients receiving radiation, the average age of the population in this study was higher than in others studies that did not find a similar association.^{1,5,6,10,11,18,21}

When indicated, revision of a Compress device involves removing a small amount of bone, averaging 3mm or less in one series.⁵⁵ This contrasts with the tedious removal of cemented stems, particularly when aiming to eradicate residual cement in the setting of infection.⁵⁶ Well ingrown uncemented stems are often morbid and challenging to remove, frequently involving extended osteotomies and complex revision techniques.⁵⁷ While ingrown stems may be retained, this likely limits the success of infection eradication.⁵⁸ In the setting of a stemmed megaprosthesis, the degree of bone loss after failure and

explanation often limits reconstructive options.²⁰ When patients go on to repeated surgery, bone loss can ultimately lead to amputation versus a total femur or total humerus prosthesis.^{59,60} Minimizing bone disruption and protecting residual bone stock at the time of revision are advantages of compressive osseointegration.

A number of compressive osseointegration device-related variables have been evaluated throughout the literature, such as compressive force, antirotation pins, and resection length. In a study of 41 patients with compressive osseointegration implants, the most common compression force used for fixation was 600 PSI. In the 18% of subjects who had 400 PSI and the twelve percent who had 800 PSI force used for compression, no correlation between aseptic loosening and applied compressive force was found.²¹ Other studies have since confirmed this finding as well as concluded that other variables, such as resection length, site other than the distal femur, use of antirotating pins, spindle length, and compressive force all have no association with aseptic mechanical failure. These studies, however, may be underpowered.^{5,6} While a resection length greater than fourteen centimeters (40% total length) has been found to be a risk for early failure in long-stem prostheses, a similar association has not been found for devices employing compressive osseointegration.⁶¹

Antirotation pins are thought to improve rotational stability, which may make early ambulation safer and reduce the risk of aseptic mechanical failure. However, there is a theoretical increase in risk of fracture at the pin site due to interruption of periosteal blood flow that could delay

Table 2. Literature review: rate and average time to aseptic mechanical failure.

Study	Year	N=	Location	Follow Up (years)	Overall failure (%)	AMF (%)	Average time to AMF (months)
Avedian <i>et al.</i> ¹⁸	2007	24	Distal femoral	2	-	0	-
Farfalli <i>et al.</i> ²¹	2009	41	Distal femur	5	-	12	< 12
O'Donnell ⁵⁷	2009	16	Proximal tibia	2	12.5	6.3	38
Pedtke <i>et al.</i> ²³	2012	26	Distal Femoral	5	26.9	3.8	22
Healey <i>et al.</i> ¹¹	2013	82	Distal Femoral	5 10	15 20	15 1	<60 >60
Calvert <i>et al.</i> ⁵	2014	50	Femoral; proximal humerus; proximal tibia; intercalary femoral	2 5	32 44	14 11	<12 30
Monument <i>et al.</i> ⁶	2015	22	Femoral				
Goldman <i>et al.</i> ⁷	2016	79	Distal femoral	5 10	43 50	9 9	23
Zimel <i>et al.</i> ²⁰	2016	71	Distal Femoral	5 10	29 29	11 11	5 5
Kagan <i>et al.</i> ¹	2017	116	Lower extremity	1.5 4	22 25	5 7	6.3

osseointegration.⁶² Despite this possibility, antirotation pins have not been found to impact overall survival.^{5,6,62} A cadaveric study found that adding additional antirotation pins resulted in an increase in the torque required to cause failure in compressive osseointegration devices implanted into the femur. The manufacturer suggests the use of three anti-rotation pins, yet the greatest increase in torque was between zero and one pin.⁶² Fractures at pin sites have been seen. However, in a study where antirotation pins were used in fifteen of fifty (30%) patients, aseptic failure rate was 6.7% compared to 17.1% in those who did not have antirotation pins. While this difference was not statistically significant ($p=0.33$), antirotation pins were not found to increase aseptic failure.⁵ In another study that looked at periprosthetic fracture, five out of six patients with periprosthetic fractures were located above the anchor plug, with only one resulting from the use of antirotation pins.²⁵ While no single device variable seems to cause an increased risk of aseptic failure, there does seem to be an increased risk of aseptic failure associated with surgeons who have done less than five reconstructions using compressive osseointegration devices.^{5,24,36}

Compressive osseointegration has primarily been used in the distal femur. However, surgeons have successfully used this implant in various bones throughout the body. Survivorship differs at these locations, likely due to differences in mechanical forces.¹⁰ For example, overall and aseptic failure of the distal femur and proximal tibia is increased relative to the proximal femur, whereas, the overall rate of failure at the proximal humerus, proximal femur, and proximal tibia are comparable. Despite similar rates of failure at these sites, the mechanism of failure at each site may differ in fundamental failure mechanism.⁵

One study found that fifteen of sixteen individuals who underwent endoprosthetic reconstruction with compressive osseointegration in the proximal tibia experienced initial osseointegration. Despite this initial success, the longevity of compressive osseointegration fixation at the proximal tibia remains ambiguous. Currently it is thought that the chance of failure at the proximal tibia between two to five years is 3-4%.^{32,38,63-66} In addition, there may be a time delay to stable fixation in the proximal tibia, with an increased risk of failure prior to 6 months, possibly due to its subcutaneous location.¹⁰

While not widespread practice, case reports providing evidence of successful use of compressive osseointegration in sites other than the lower extremity have been

published. In a multi-case study, three patients had revisions of allografts with standard elbow prostheses with compressive osseointegration.³² One patient had this used in the proximal ulna.³² While transient radial nerve palsy occurred in two of the three patients, both patients regained functional range of motion, with radiographic evidence of bone hypertrophy in the humeral cortex. Similar to use at the proximal tibia, the durability of compressive osseointegration at the humeral cortex is unknown; however, it is thought to be a viable option when there is significant bone loss at the distal humerus.⁶⁷

Conclusions

Compressive osseointegration is being used with greater frequency for limb salvage in patients with primary bone tumors, and remains an option for patients with significant bone loss related to revision arthroplasty or fracture non-union. Since it has a short anchor plug, compressive osseointegration offers a surgical option when limited bone remains, or when multiple future revisions are anticipated. Bone quality, bone thickness, prior radiation, and inability to tolerate limited weight-bearing are factors that must be considered when deciding whether to use compressive osseointegration for a patient.

Due to its design, compressive osseointegration demonstrates a pattern of failure different than traditional long-stem implants. Whereas traditional long-stem implants have an increased risk of aseptic loosening and failure over time due to stress shielding, compressive osseointegration implants tend to fail early, in the first two years after implantation. Despite this difference, overall survival of compressive osseointegration implants from aseptic failure is comparable to traditional stemmed implants.

Future research should focus on understanding the unique mechanisms of failure of compressive osseointegration in various anatomic sites. In addition, more long term follow up is needed so we can better understand survivorship of these devices at various anatomic locations. Finally, further research needs to be done to clarify the indications and contraindications for the use of compressive osseointegration.

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