Title: The design evolution of Interbody Cages in Anterior Cervical Discectomy and Fusion

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Abstract:

**Background:** Anterior cervical discectomy with fusion is a common surgical procedure for patients experiencing pain and/or neurological deficits due to cervical spondylosis. Although iliac crest bone graft remains the gold standard today, the associated morbidity has inspired the search for alternatives, including allograft, synthetic and factor/cell-based grafts; and has further led to a focus on cage fusion technology. Cage interbody implants have enhanced biomechanical properties, with designs improving each year to maximise biocompatibility and osseointegration. We present a systematic review examining the historical progress of implant designs and performance, as well as an update on the currently available designs and the potential future of cervical interbody implants.

**Methods:** We performed a systematic review using the keywords “cervical fusion implant design”, with no limits on year of publication. Databases used were PubMed, Medline, Embase and Cochrane. In addition, the search was extended to the reference lists of selected articles.

**Results:** 180 articles were reviewed and 64 articles were eligible for inclusion. Exclusion criteria were based around study design, implant information and patient cohorts. The evolution of cage implant design has been shaped by improved understanding of ideal anatomy, progress in materials research and continuing experimentation of structural design. Originally, designs varied primarily in their choice of structure, however long term studies showed the overall advantages of non-threaded, wedge shaped cages in complementing healthy anatomical profiles, and thus focus has shifted to refining material utilisation and streamlining anterior fixation.
Conclusions: Evolution of design has been dramatic over the past decades; however an ideal cage design has yet to be realised. Current research is focusing on the promotion of osseointegration through bioactivation of surface materials, as well as streamlining anterior fixation with the introduction of integrated screws and zero profile designs. Future designs will benefit from a combination of these advances in order to achieve ideal disc heights, cervical alignments and fusions.

Keywords: Anterior Cervical Discectomy Fusion, Review, ACDF, Interbody, Cage, Design, Evolution

Abbreviations:

ACDF = Anterior Cervical Discectomy and Fusion

Ti = Titanium

PEEK = Polyetheretherketone

AP = Anterior-posterior

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Author contributions

EC performed systematic search strategy and selected full articles for review and wrote the first draft.

MP supervised systematic review and reviewed selected articles for review and contributed to manuscript preparation.
RM conceptualised the review, supervised systematic review and contributed to manuscript preparation.

WW supervised systematic review and contributed to manuscript preparation.
**Background**

Age-related degeneration of the cervical spine is evident in over 50% of the middle-aged population and is the most common cause of neural dysfunction[1]. Although the majority of cases are asymptomatic, changes such as disc herniation, osteophyte formation and hypertrophied ligaments may compress the cervical neuraxis to result in cervical pain, radiculopathy, or myelopathy[2]. First line treatment is conservative; however surgery is indicated in unresponsive symptomatic patients.

Anterior cervical decompression and fusion (ACDF) is one of the most widely used surgical treatments for patients with cervical spondylosis[3]. It is also an indicated treatment in cases for cervical realignment, trauma and neoplasm[4]. In most cases, ACDF achieves stabilisation and solid arthrodesis with good-to-excellent clinical outcome and minimal surgical risks. The anterior approach to cervical decompression was first described by Cloward[5], and Robinson and Smith[6] in the 1950s. Both described an anterior approach with a longitudinal incision along the anterior border of the sternocleidomastoid muscle to allow for soft tissue dissection and annular incision. Following discectomy and removal of any compressive structures, fusion was then achieved using an autogenous graft. Although technical modifications have been made over the years this procedure is still standard today, leaving improvements in fusion rates and clinical outcomes to be generated through changes in implant design and material[7]. This article reviews the evolution of cervical interbody implant designs and assesses future research directions.

**Methods:**

We performed a systematic review of the literature using the following protocol: we searched the databases PubMed, Medline, Embase and Cochrane using the keywords “cervical fusion implant design” for articles published up to March 2014. There were no limits on language or species.
Results:

180 abstracts were searched for relevance and, of these, 52 articles were selected for analysis. Inclusion criteria was prospective and retrospective studies with patient cohorts greater than 30, utilising plated or non-plated cage designs with allograft and no additional proteins. Exclusion criteria included studies with non-degenerative disease cohorts and any information absent on fusion, clinical outcomes and complications. In addition, the search was extended by manually searching the reference sections of relevant articles; this added 12 publications (Table 1).

Discussion:

Historical Evolution: Bone Grafts to Fusion Devices

The first anterior cervical interbody techniques were introduced by Cloward, and Robinson and Smith in the 1950s. Cloward’s procedure involved insertion of a dowel graft following decompression. Required bone was harvested from the iliac crest of the patients or via allograft bone bank and was then pre-cut with a slightly wider diameter and shorter than the drill hole, with insertion achieved through distraction and force[5]. Robinson and Smith’s approach allowed initial distraction, anterior decompression and fusion with the support of a horseshoe graft harvested from the patient’s iliac crest.

Autograft interbody designs have since evolved to improve stability and distraction. In 1969, Simmons and Bhalla[8] described the benefits of a keystone type graft, which improves distraction height by locking into a prepared defect, increasing stability and fusion. Bailey and Badgley in 1960 expanded the usage of ACDF to treat neoplasm and instability through the usage of onlay strut grafts. This technique has evolved into anterior cervical corpectomy[9]. Limitations of autogenous grafts are important considerations in all of these procedures. Iliac crest bone harvesting is associated with short and long-term morbidity at the harvest site, including pain, wound drainage, infection, haematomas, nerve injury and iliac crest fractures or deformity[10]. Initially, alternative
graft materials were sought as a method of circumventing donor site limitations. However, not only did autograft remain superior in fusion, subsidence and extrusion rates but each alternative involved its own limitations[2, 11]. As a result, the focus has switched towards cage implants and graft substitutes as viable alternatives to autograft (Figure 1).

Figure 1: Historical perspectives on ACDF implants
A) Cloward Dowel Graft B) Smith-Robinson Based Rectangular Implant C) Simmons-Bhalla Keystone D) Bailey-Badgley Onlay Strut

Cage fusion technology was proposed by Bagby in 1988. Developed to treat spondylitic cervical myelopathy in horses, the Bagby Bone Basket was a cylindrical device made of fenestrated, hollow, stainless steel designed to allow bone ingrowth in an incompressible spacer[12]. This technology was soon trialled on humans in the lumbar spine and by the 90s was being adapted to the cervical region. Stand-alone designs have since become the mainstay of ACDF, achieving excellent safety, primary stability and long-term fusion results without the limitations and morbidity associated with ICBG graft options[7, 13]. Of particular interest is the efficacy in treating cervical spondylosis which is reviewed in the following section[14, 15].

Cage Design Evolution:
The basic design of cages involves a small, hollow implant featuring lateral, upper and/or lower windows to a central cavity filled with either autologous bone, allograft bone or osteoinductive materials[16]. Historically, cage designs can be divided into threaded (screw), and non-threaded cages (vertical rings and box-shaped), with anterior plating applied by surgeon preference. Each type confers individual advantages and disadvantages and an examination of their development allows for insight into future technology. Table 2 contains a comparison of clinical and radiological
outcomes of different overall cage types, however it must be taken into consideration that different sample sizes and surgeon cohorts have been included.

**Threaded:**

**Screw Cages**

Screw cages are based on Cloward’s procedure and were some of the earliest available cages. The BAK-C (Sulzer Spinetech, Minneapolis, MN), released in 1994, consisted of a porous, titanium-alloy cylinder packed with surgical site bone-graft[14]. The device was received with considerable success due to its safety and immediate stability, showing significantly higher stiffness and accelerated fusion when compared to both non-threaded and iliac crest bone graft models[17]. However, studies soon revealed disadvantages of the screw design: decreased maximum distractible height due to the tolerated lateral width of adjacent vertebrae and higher levels of cage subsidence due to vertebral endplate weakening. In vitro biomechanical studies comparing screw designs to tricortical bone graft showed screw designs to be less stable during flexion, extension and bending[18, 19].

**Non-Threaded:**

**Box-Shaped**

Box-Shaped and vertical ring cages resemble Smith-Robinson’s horseshoe graft. Initial designs were rectangular boxes with roughened contact surfaces to improve anchorage[20]. This design demonstrates greater segmental stiffness in all directions compared to both intact segments and tricortical bone grafts[18]. Further improvements to surface fit have improved cage anchorage through mimicking the inverse shape of the vertebral endplate’s concave contour[21, 22]. By early 2000, box-shaped cages began incorporating trapezoidal and wedge-shaped designs[14, 16]. Trapezoidal cages inversely match vertebral endplates to increase cage stability in lateral bending,
flexion and axial rotation[23], whilst wedge-like designs utilise an anterior slope, with a 1-2mm higher anterior to posterior height, to achieve better restoration of natural cervical lordosis[24, 25].

**Vertical Ring Designs**

In vitro studies have shown little intragroup variation in screw and vertical ring designs; however, one study reported vertical ring designs as having greater control over extension and bending. Compared to intact motion segments, vertical ring designs are reported to have lower rotation stiffness due to the decreased surface area of endplate-implant interface[18].

From a biomechanical perspective, non-threaded cages remain superior to threaded cages; however, new designs are constantly emerging to improve the inherent flaws of each design by adapting to the natural dimensions of disc space. An early attempt to bridge the difference between a Cloward and Smith-Robinson type design focused on cage dislocation or non-union with instability. The WING cage (Medinorm AG, Germany) attempted a compromise, featuring a cylindrical centre and two lateral flat wings[23]. The cylindrical middle allowed for contact with cancellous bone, with the lateral wings increasing the area of contact with adjacent vertebrae to resist excessive subsidence[23]. Although it achieved good clinical outcomes and fusion rates, the implant was reported to have decreased initial bone contact and primary lateral instability, showing no meaningful advantage over plain screw or box designs[14, 26].

The clinical literature comparing different cage shapes is limited, with only one paper reviewing the overall results in a single surgeon cohort[14]. Trends in usage can be seen to have favoured wedge-shaped, trapezoidal cages; this can be attributed to ease of implantation, greater segmental stiffness and restoration of healthy cervical lordosis.

**Anterior Plating**
Stand-alone designs are known to receive good-to-excellent fusion rates with single level ACDF. These results are not achieved in multi-level ACDF, with rates of non-union reported up to 40% in 3-level fusions[27-29]. Anterior plating has been adopted to improve fusion rates and reduce chances of non-union and pseudoarthrosis in multi-level ACDF. Anterior metal fixation of bone graft has been employed since 1970, when Schurmann and Busch described the usage of a steel rod reaching adjacent vertebrae[30]. Since then several anterior stabilisation techniques have been described, with a majority of surgeons using the now standardised technique of Caspar plating[31, 32]. Generally, cervical plate fixation improves fusion rates through stabilisation and is associated with improved lordotic alignment, increased disc height, improved fusion rates and lower subsidence rates in both single and multi-level fusions[32, 33]. Anterior plating is not without limitations and is associated with additional complications over stand-alone cage procedures, the most common being early postoperative dysphagia, which in rare cases progresses to chronic dysphagia. Other complications include screw migration resulting in soft tissue damage and adjacent-level degeneration in cases of inappropriately sized or misaligned plates[34].

Cage Materials

Evolution of cage materials has accompanied the changes in design. The field of biomaterials study is widespread and volume constraints dictate that only large trends will be reviewed (see Table 3). Three materials have primarily been used in the manufacture of cage implants: carbon fiber reinforced polymers (CF-P), titanium (Ti) and polyetheretherketone (PEEK). CF-P cages were initially trialled, achieving high rates of fusion and good-to-excellent clinical outcomes however have largely been superseded by PEEK due to its superior elastic modulus[35-38].

Ti and its alloys were one of the first materials to be utilised for cages in the 1980s. Used by the orthopaedic world since the 1940s, Ti is a biocompatible, robust material with excellent corrosion resistance and a low density[39]. PEEK cages were introduced in the 1990s by AcroMed as an
alternative to Ti cages; they provide the advantages of radiolucency and an elastic modulus close to bone thereby avoiding the stress shielding associated with Ti[40]. Today, controversy exists between the utilisation of Ti versus PEEK cages. Although PEEK has theoretical advantages, the roles of endplate preparation, area of contact and overdistraction are rarely controlled for in studies. A majority of studies have reported improved fusion rates, lower subsidence rates and radiolucency with PEEK versus Ti cages[41-44], with one long-term study by Chen et al reporting limited differences in the early postoperative period, but better maintenance of intervertebral height, cervical lordosis and clinical outcomes by PEEK cages in 7-year follow up[45].

Cage Design Optimisation

Anatomy

Understanding the healthy and pathological anatomy of the cervical spine is vital in optimising the design of cervical cage implants. The first published anatomical studies of the cervical spine in relation to the anterior approach were written in the 90s and have since been quantitatively expanded upon through the use of imaging technology.

Important measurements in reference to ACDF include height, anterior-posterior (AP) diameter and width of the cervical disc space (see table 4). Disc heights from C2/3 to C6/7 are approximately 1/3 of the vertebral height, with no dependence on age in healthy subjects[46]. In the cervical spine each disc is thinner posteriorly than anteriorly, with the greatest height in the midline, contributing to healthy cervical lordosis, an important consideration in design[47]. Distracted disc height is significantly greater, with the disc space opening nearly 4mm to accommodate cages of up to 10mm. The AP diameter increases inferiorly, with shortest depth at C2/3 increasing by 3mm at C6/7. The lateral width of the disc space also increases inferiorly; in ACDF, implant width is limited by the uncovertebral joint and corresponding endplate concavity.

Pathology
In degenerative change, disc space narrowing causes tension in adjacent ligaments and compression of the neuraxis leading to symptomatic cervical spondylosis (Figure 2). The incidence of cervical spondylosis is reported to be as high as 76-82%, however a majority of these individuals are asymptomatic[48]. Classically, cervical spondylosis is believed to involve a combination of nucleus pulposus protrusion, osteophyte formation, and fibrosis, most frequently effecting the C5/6, C6/7 and C4/5 levels, in order of decreasing occurrence[49, 50]. Radiographic findings are often poorly correlated to symptomatology; however, visualisation of severe changes, including large osteophyte formation, marked disc space narrowing, sclerosis of vertebral plates and posterior subluxation, are more often associated with pain and discomfort[51]. Macroscopically there is loss of foraminal height and area, cervical canal area, and flattening of the end plate as the uncinated processes enlarges and flattens to lose its sharp, tapered configuration[52, 53].

**Figure 2: Degenerative Changes of the Cervical Spine**

A) Healthy cervical vertebrae and disc; B) Changes of cervical spondylosis (Disc herniation, osteophyte formation and disc space narrowing leading to reduction in neural foramen size)

Cage Dimensions

Modern cage designs have begun targeting individual design features and dimensions to ensure maximal clinical and fusion outcomes. Due to the variation of disc space height between cervical levels and individuals, cage implants are available in a variety of sizes. From surgical experience the author is familiar with variance in only the height of implants, with lateral and AP dimensions remain largely uniform within company models.

Cage Height

Cervical cages relieve neuraxis compression through the restoration of disc space height, thereby reversing the loss of foraminal height and area, and cervical canal diameter[48, 54, 55]. The goal of
adequate distraction must be tempered by the complications of overdistraction, which is related to
non-union, postoperative neck pain and poor clinical outcomes due to an increase in contact
pressures between graft and cervical end plates. Smith-Robinson grafts were recommended to be
10-15mm in height[6]; modern grafts are smaller to circumvent vertebral modification[56]. In
1993, An et al demonstrated that ideal distraction height is dependent on baseline disc height, with
maximal changes in foraminal height achieved in 2mm of distraction above baseline[48]. Modern
cages adhere to this and available heights ranging between 5-8mm with trial spacers utilised during
surgery to determine ideal cage height.

Cage Width and Length

Cervical implant width and length ensure maximal surface contact and stability of ACDF. These
dimensions are dictated by cervical anatomy; too small an implant would provide inadequate
stability and too large an implant would result in damage to the surrounding structures[50].
Although disc space lateral width can range between 20-30mm in the cervical spine, cage implant
width is limited by the uncovertebral joint laterally, with ideal placement contacting bilaterally with
the uncinated processes[22, 57]. Smith-Robinson recommended implants of 14mm in width and
depth, acknowledging the need to modify based on individual requirements[6]. Modern cage
designs reflect these dimensions, with lateral widths ranging between 12-20mm and depths ranging
between 12-16mm[34].

Modern Cage Designs

An ideal cage design would restore healthy alignment and disc height and achieve immediate post-
operative stability, high-fusion rates and low complication rates. Recent cage designs have
attempted to promote osseointegration and thus fusion through modification of cage surfaces. Ti
and its alloys can be modified to increase surface roughness through plasma beam and electron
spray techniques[39]. In vitro experimentation has shown this increases total protein and alkaline
phosphatase levels, thereby increasing osteogenic cell differentiation[58]. The improved bioactivity
of Ti can be utilised in combination with the elastic modulus and radiolucency of PEEK through the
creation of composite Ti/PEEK spacers[59, 60]. Clinically available composite spacers, such as the
Combo ® (A-SPINE Asia, Taiwan), combine PEEK bodies with Ti-endplates (Figure 3) to
theoretically augment bone-implant fusion, however there is a dearth in the literature on their
comparative efficacy when compared to established clinical and radiographic baselines for Ti or
PEEK cages. This requirement for large, long-term clinical studies to verify the relative efficacy of
a new cage design is complicated due to the variety of spacers available on the market and the speed
at which new designs are released.

![Figure 3: Composite Ti/PEEK Cage](image)

Combo ® cage (A-SPINE Asia, Taiwan) demonstrating ridged titanium endplates on a PEEK
interbody spacer

Another focus in the improvement of cage designs is the streamlining of anterior plating into a
stand-alone cage[61]. Zero-Profile cages utilise an integrated, low profile plate design to avoid
implant-to-soft tissue impact, reducing dysphagia rates and other plate-associated
complications[34], whilst maintaining good clinical and fusion outcomes[62, 63]. Two main
designs currently utilise the zero-profile plate system (Figure 4). The Zero-P (Synthes CmbH
Switzerland, Oberdorf, Switzerland) was approved by the United States Food and Drug
Administration in 2008 and is composed of a PEEK body attached to an anterior plate containing
four holes with internal screw treads of either 14 or 16mm lengths. A second approach to zero-
profile plating is adopted by the ROI-C cervical cage (LDR Holding Global Corporation, France),
which combines a PEEK body with a self-locking, guided plate system, allowing insertion of plates
directly into adjacent vertebrae through the disc space, obviating any need for external hardware.
No studies currently exist comparing the efficacy of the two.
Figure 4: Low Profile Integrated Plating

A) Zero-P cervical cage V) ROI-C cervical cage C) Radiograph demonstrating Zero-P placement
D) Radiograph demonstrating ROI-C placement

The combination of integrated low-profile plating and Ti/PEEK composite cages is the next logical step in cage design and is currently undergoing experimental design by Kasios (Kasios Biomaterials, France). The design utilises a PEEK body with partial titanium endplates, a low-profile titanium plate and dual opposed locking screws (Figure 5). In addition it features a preloaded osteoconductive graft of beta-tricalcium phosphate.

Recent studies have also explored the development of absorbable designs utilising polyactic acid (PLLA)-polyglycolic acid (PGLA) copolymers and poly(L-lactide-coD,L-lactide), these exhibit the necessary rigidity at the time of implantation with gradual degradation to promote bone formation and solid arthrodesis. In addition, complete postoperative absorption allows improved radiological assessment. However, these benefits are still theoretical, with studies showing high levels of stand-alone cage dislocation requiring revision surgeries[64].

Figure 5: Future Designs

New design integrating a Ti/PEEK composite cage with a low profile plate (Kasios Biomaterials, France)

Conclusion

The evolution of ACDF implant design from bone graft to composite cages has been dramatic; however an ideal implant has yet to emerge. Although there are numerous new designs, difficulties in gathering clinical evidence comparing available models is a limitation in determining the
superiority of any one implant. Regardless, trends exist, with shapes favouring wedge-shaped
trapezoidal boxes, dimensions reflecting healthy anatomy and a preference towards PEEK bodies.
These trends reflect a mixture of clinical evidence and surgical experience, two important factors
that continue to influence the ongoing development of ACDF implants. Continued experimentation
and integration will be required to achieve further refinement and can be seen in the most recent
step of combining bioactive Ti/PEEK composites with the latest zero-profile technology.
References


Table 2: Clinical and radiological outcomes of different cage designs

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<tr>
<th>Titanium Cage Type</th>
<th>Good-to-Excellent Clinical Outcome (%)</th>
<th>Fusion rate at 12 months (%)</th>
<th>Complication Rates (%)</th>
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<td>Threaded[7, 14, 17, 18]</td>
<td>80-94.4</td>
<td>91-99</td>
<td>11.8-20</td>
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<td>Non-Threaded[14, 19, 20]</td>
<td>75-87</td>
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Table 3: Clinical and Radiological Outcomes of different Cage materials

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<th>Cage Material</th>
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<th>Fusion rate at 12 months (%)</th>
<th>Subsidence (%)</th>
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<td>Titanium[26, 41, 48-50]</td>
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<td>93-100</td>
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Table 4: Cervical Disc Measurements;

Measurements were compiled using weighted averages from studies of adult radiographs and cadavers; however a lack of reporting on age, gender and racial variation limits the value of such data [46-51]
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<td>(2.09-3.81)</td>
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Additional files provided with this submission:

Additional file 1: Table 1.docx, 15K
http://www.biomedcentral.com/imedia/8652555461426956/supp1.docx