Author's response to reviews

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

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Version: 3 Date: 2 February 2015

Author's response to reviews: see over
Dear Sir/ Madam,

Thank you for providing revision comments regarding this systematic review manuscript for publication. We apologise for missing the deadline by a few days, and are very pleased to offer this work for additional review by your editorial team.

Anterior cervical discectomy and fusion (ACDF) is the primary surgical treatment of cervical spondylosis. Although the gold standard has been previously considered autograft, the development of safe, efficacious cage implants has led to their predominance. Research on cage design outcomes has expanded over the past decade into exploring a wider scope of possible modifications to not only shape, but plating, biomaterials and protein addition. However a lack of standardisation makes design optimisation between these research fields difficult to unify.

By reviewing the historical trends in design and assessing the current, market available features, we aim to improve an understanding of cage design optimisation. Although other reviews on ACDF exist, these are broader in scope and have focused on either surgical techniques or biomaterials. With the growing amount of research on cage implants, this review provides a timely and necessary consolidation on which research based design integration and optimisation may take place.

All authors have read and approved the manuscript and there are no arrangements, financial or otherwise that may be construed as a conflict of interest.

Thank you for your time in assessing our manuscript. We look forward to your response.

Thank you and Regards,
Elizabeth Chong
Reviewer's report
Title: The design evolution of Interbody Cages in Anterior Cervical Discectomy and Fusion
Version: 2
Date: 15 December 2014
Reviewer: jiaquan luo
Reviewer's report: Minor Essential Revisions
Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: no

Reviewer 1: The author reviewed 180 articles and include 64 articles for analysis. The author concluded that current research was focusing on the promotion of osseointegration through bioactiviation 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. The article was well written. Revisions are requested for publication.

Comments:
1. Databases such as PubMed, Medline, Embase and Cochrane were included in the analysis. What is the Orthopedics China Biological Medicine Database?

It is not clear as to what the reviewer is referring to in this comment. If it was a question regarding the inclusion of The Orthopedics China Biological Medicine Database, it was not included in this search as this was a primarily English language article.

More detail on limits of the search were added.
Line 111 added text "available in the English language " and removed text “on languages"

2. Tables should be 3-line tables.

An attempt was made to reformat the relevant table, however it could not be performed without sacrificing data or easy comprehension. As this is not a requirement of the journal formatting, it is preferred that tables are kept in current form in order to not reduce viewer understanding.

3. As you mentioned bioactivity osseointegration of cage in your article, recently, David F. Williams, editor-in-Chief of Biomaterials, published one article titled there is no such thing as a biocompatible material(Biomaterials35(2014)10009-10014). In that article, David F. Williams suggest that we simply substitute ‘biocompatible system’ for ‘biocompatible material’. This would go a long way to removing the fundamental difficulty of equating biocompatibility with a material
property. What’s your comment?

Thank you for the suggested article, it is an excellent suggestion and the reference has been included. Edits have also been made with regards to the article’s opinion as it does work towards devising a clearer lexicon in regards to biomaterials, an issue will become increasingly relevant with the expanding field of bioactivation of surfaces.

Line 253 text deleted “biocompatible,”
Line 253 text added “biomaterial”
Line 254 text added “, that can undergo surface modification to improve osseointegration and cell adhesion”
Reference Included

4. There are some errors that should be corrected. Such as keywords:
Anterior Cervical Discectomy Fusion means ACDF.

Although ACDF is an initialism of Anterior Cervical Discectomy and Fusion, simple searches of both keywords yield different results (e.g. Pubmed 1/2/15, “ACDF” displays 554 results, while “Anterior Cervical Discectomy Fusion” displays 1403). Though results do overlap, and thus a systematic or even a thorough search of the literature would make these differences obsolete, catering to a cursory, non-research driven search would make the difference between the two keywords meaningful.

Further edits made:
Abbreviations added:
ICBG = Iliac Crest Bone Graft
CF-P = Carbon Fibre Reinforced Polymer

Text edited for clarity.
Line 48 grammar “showed” to “have displayed”
Line 86 text deleted “unresponsive”
Line 87 text added “who are unresponsive to conservative management”
Line 90 substituted text “for” with “of”
Line 91 text deleted “In most cases,”
Line 92 pluralisation of “outcome”
Line 94 replaced text “with” for “via”
Line 128 text added “into a graft sized slightly”
Line 128 text deleted “with a slightly” and “diameter”
Line 129 text added “. Insertion was”
Line 129 text deleted “with insertion”
Line 130 text deleted “allowed” “,”
Line 130 text added “utilised a similar” and “and”
Line 135 text deleted “type” and “improves”
Line 135 text added “increased”
Line 136 text deleted “increasing”
Line 136 text added “thereby improving”
Line 137 text added “In 1960,”
Line 137 text deleted “in 1960”
Line 138 text deleted “This technique has”
Line 138 text added “A technique which later”
Line 153 spelling corrected “spondylotic”
Line 235 text added “can”
Line 242 tense corrected “progresses” to “progress”
Line 295 text added “,” and “cervical canal area and”
Line 296 text deleted “cervical canal area”
Line 315 text added “Originally,”
Line 316 text added “however” and “the requirement of”
Line 326 text moved “lateral”
Line 327 text moved “laterally”
Line 334 text added “, as well as”

Reviewer's report
Title: The design evolution of Interbody Cages in Anterior Cervical Discectomy and Fusion
Version: 2
Date: 28 December 2014
Reviewer: Jiaming Liu
Reviewer's report: Major Compulsory Revisions
The author 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. It's an interesting topic. However, there are some comments for the author.

1. “Keywords”: “Anterior Cervical Discectomy Fusion” is duplicate with “ACDF”, please delete one of them.

See above response to Reviewer 1’s 4th comment.

2. “Background”: in this section, the author used many sentences to introduce “ACDF”. The author should focus on the interbody cage, and used more sentences to introduce “cage design”.

More detail focusing on cage design added in Abstract and Background.
Line 36 added text “Compared to their graft counterparts”
Line 99 added text “Initially, market available cage materials and designs varied dramatically, with a selection between ceramic and alloy materials in threaded and non-threaded designs. This has shifted dramatically through the years, with modern designs conforming to a non-threaded, wedge shaped profile, and a choice between titanium alloy and the newer, polyetheretherketone (PEEK) materials.”

3. “Methods”: the author just only used one word “cervical fusion implant design” to search the related articles. Is it really enough? Are there any useful articles missed?

Although this was the only keyword for the systematic search, prior to creating this search term, non-systematic searches were performed in order to develop an appropriate search term. These included usages of basic, non-specific terms such as “ACDF”, “Anterior Cervical Discectomy Fusion”, “Anterior Cervical Discectomy Fusion Cage”, “Cervical implant design” and “Cervical cage” to determine the
usefulness of such terms. These yielded a large volume of results with very few of interest to design and development. In addition any articles deemed relevant to design that were missed from our specific keyword were added through manual searches of article reference sections (As shown in Table 1).

Line 107 text added “After performing initial, non-systematic searches using the terms “Anterior Cervical Discectomy Fusion”, “ACDF” and “Cervical Fusion” in conjunction with the terms “cage”, “design” and “implant”, we”

4. “Results”: this section is too simple. The “inclusion criteria” and “exclusion criteria” are not clear. The process of the article selection did not introduction. No information is described about the included articles.

A description of article selection was added

Line 116 text added “Articles were selected based on their detail and relevance to the topic of cage design; both clinical and laboratory studies were included. Laboratory studies comparing cage designs and materials that were controlled and reliable were utilised to inform theoretical advantages of specific designs.”

With additional text added to clarify inclusion and exclusion criteria:
Line 119 phrase changed from “inclusion criteria was prospective and retrospective studies” to “The inclusion criteria of clinical studies were prospective and retrospective designs”
Line 120 text added “patients requiring ACDF in the treatment of degenerative cervical disease, patient”
Line 121 text substituted “greater” for “larger”
Line 121 text added “individual patients” and “implanting cages filled with allograft with or without anterior plating”
Line 121 text deleted “utilising” and “plated or non-plated cage designs with allograft and no additional proteins”
Line 123 text added “, using additional proteins to promote fusion and ossification, or those that did not report on fusion rates, clinical outcomes and/or complication rates”
Line 125 text deleted “and any information absent on fusion, clinical outcomes and complications.”

5. “Discussion”: in this section, the author should introduce the advantage and disadvantage of different cage devise. However, some of them are not clear. The section “anterior plating” is not important in this article. The emphasis of the article is cage device, so some contents of the section could be deleted. The author gave some introductions about the future design of the interbody cage. However, there were no some views or opinions of the author self. No limitation of the article was described in the article.

Edits made to “Cage Design Evolution” clarify the advantages and disadvantages of different cage designs, with summary sentences added.

Line 145 text edited from “limitations of autogenous grafts are important” to “Limitations of the autogenous graft are an”
Line 146 abbreviation added “ICBG”
high levels of
and
“graft” “. Of particular interest is the efficacy in treating cervical spondylosis which is reviewed in the following section”
“; and”
“consisted of” to “was”
“with the advantages of”
“limit on”
“addition, in”
“, but not compared to their non-threaded counterparts”
“Both aim to mimic healthy anatomy of the cervical spine, while increasing segmental stiffness and surface area contact.”
“, with few differences in their overall advantages and disadvantages”
“due to their ability to mimic healthy cervical anatomy, thereby improving surface contact whilst maintaining initial stability”
“the inherent flaws of”
“However, some information can be gleaned from following”
“, which” and “a non-threaded”
Anterior Plating section kept due to its relevance to modern cage designs which now integrate anterior plates into the stand-alone design.

Edits made to “Cage Materials” in reflection of the both Reviewer 1’s suggestions and to clarify the discrepancies between advantages portrayed in clinical versus laboratory based studies.

“; this has not clearly transferred into the clinical setting due to the difficulty in determining and controlling for other surgical factors, including”
“However,”

Edits made to
“reduce complication rates by promoting early”
“cage”

Author opinions added on the trends of cage designs and optimisation.
“Although the variance in cage design availability has reduced significantly since their first introduction, the amount of research into cage implants has grown. This has trended away from comparing shape designs and fixation to exploring the possibilities posed by the innate material properties, additional growth proteins and the chance for complex 3D printed shapes and streamlined plating designs. Thus although conclusion have been made regarding the optimal cage design
in terms of human anatomy, design optimisation needs to become a focus in order to yield the cumulative benefits of each field in an ideal design.”

Assessment of paper’s limitation was provided
Line 401 text added “This paper is not without its limitations, the current search criteria were chosen in order to focus solely on design without performing a full review of all cage related literature. By doing so there will naturally be some articles of relevance not included in the review, however it was determined satisfactory for this article’s purpose.”

Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests'