Advances in Customised Medical Prostheses through Additive Manufacturing with an Emphasis on Hip Replacement and Cervical Implants

D. Dimitrov, M. B. Bezuidenhout, G. Marcantonio
Laboratory for Rapid Product Development, Department of Industrial Engineering, University of Stellenbosch, South Africa

Abstract
This paper analyses the state-of-the-art in customised medical prosthesis with a focus on hip replacement and cervical implants. Based on this analysis, the Selective Laser Melting process in the proprietary form of LaserCUSING is applied to investigate the enhancement on certain properties of hip and cervical cage implants. A special attention is given to the possibilities for the manufacture of a hip implant with surface features; from which antimicrobial loaded bone cement can be eluted. Discussed is also the suitability of the surfaces obtained by LaserCUSING for osseointegration, which forms the prerequisite for successful fusion of cervical cage implants.

Keywords
Additive Manufacturing, LaserCUSING, Hip Implants, Spine Implants

1 INTRODUCTION
The evolution of rapid prototyping technologies into additive manufacturing (AM) enables the direct manufacturing of functional parts from various metallic powders. The layer-by-layer approach of AM ensures optimal use of material. It also allows the development of complex three dimensional geometries for mass customisation of medical implants. Near net shape parts of almost 100% density and comparable mechanical properties can be obtained with appropriate process parameters.

An annual increase in hip replacement surgeries emphasizes the importance of implant longevity. Obstacles that impair the life expectancy of hip implants are the large mismatch of elastic moduli between metallic implants and natural bone, and the occurrence of prosthetic infection, the latter being the worst. Prosthetic infection is currently treated with complex surgical procedures causing much discomfort for the patient. Severe cases can end in amputation or even mortality.

In standard cervical cage implants currently used in anterior cervical discectomy and fusion (ACDF) surgery, subsidence is a major issue. Factors affecting subsidence are notably the shape of the implant and the preparation of the endplates during surgery. The development of a customised implant aims to reduce the rate of subsidence by distributing the load more effectively across the endplate/implant interface.

2 CUSTOMISED MEDICAL IMPLANTS
2.1 Hip Implants
Hip implants are largely manufactured from wrought material by subtractive processes. Custom designing and manufacturing for specific cases with short lead times is not yet applied in clinical practice. This leads to situations where surgeons often have to choose an implant as close as possible to the patient’s geometry and then further tailor the implant and bone to match as best as possible during surgery [1].

Furthermore, evidence is showing that the number of primary total hip replacement surgeries performed in the United States is increasing annually [2]. With an average functional lifetime of 10 – 15 years for hip replacement implants, especially in younger patients [3], emphasis can be placed on the need for the enhancement on certain properties in order to increase implant longevity and reduce the risk of implant failure. Amongst two of the most prevalent failure modes of hip replacement implants is the occurrence of aseptic loosening due to an increase in micromotions between the implant and bone interface [4]. It is argued that micromotions and consequently aseptic loosening is attributed to an inadequate primary stability of the implant, directly after surgery, and the stress shielding phenomenon at a later time after surgery. A second serious obstacle is the probability of implant infection.

2.1.1 Aseptic Loosening
The primary stability of an implant is an indication of the relevant micro-motions between the bone and implant surface. Micro-motions are a result of physical loading on the implant directly after surgery and before osseointegration have occurred [5]. When the primary stability of an implant is insufficient, micro-motions can exceed 150μm, which cause the formation of a fibrous tissue layer between the implant and bone leading to inadequate osseointegration and an increased probability of failure [4].
Stress shielding of the femur occurs due to the high stiffness of the femoral stem. After surgery, the natural distribution of stresses and strains in and around the bone at the site of implantation is disturbed and altered. Most of the load from normal activity is transferred from the endoprosthetic head via the femoral stem of the implant to the distal femur and not via the proximal femur bone tissue itself [6]. This sudden change can cause the bone to remodel and resorb. The significance of the occurrence of bone resorption due to stress shielding is shown in studies of Schramm et al. [7]. The study comprised of a ten year follow up on patients who received total hip arthroplasties with conventional implants of which the stems were tapered. In 64 of the 89 (72%) studied hips some reduction of bone density in the proximal femur was observed.

Customisation strategies for hip implants to target aseptic loosening include both the geometrical and functional customisation of implants. Geometrically customised implant designs have shown promise for improving the primary stability. Various finite element models have been developed in order to study the effect that a customised geometry will have on the primary stability and stress shielding [5] [8]. Ruben et al. [8] developed a three dimensional shape optimisation procedure to increase primary stability and decrease proximal bone loss. With additive manufacturing, such optimised implants could be manufactured for each patient with a complex or abnormal anatomy in short lead times.

Extensive investigations into the incorporation of lattice structures to reduce the stiffness of an implant and consequently stress shielding also yielded promising results. Complex lattice structures with varying unit cells to model a patient’s bone more closely can be designed and manufactured with additive manufacturing technologies (Figure 1).

Due to the nature of the lattice structure, bone ingrowth is also promoted by having open pores. However, a possible concern of such structures is that in the case of a necessary revision surgery, too much bone ingrowth becomes a major complication in removing the prosthesis during surgery.

2.1.2 Infection

Implant infection currently poses one of the greatest challenges in orthopaedic surgery [10]. It is estimated that the infection rate for primary hip replacement surgeries is generally less than 2% and possible infection rates as high as 17% has been reported for revision surgeries [11]. With over 400,000 total hip and knee replacement surgeries performed per year in the US alone [2], the significance of even a 2% infection rate is considerably high. Immediately following a total hip replacement surgery, a process dubbed "race to the surface" initiates where there is a race between tissue integration and the adhesion of bacterial cultures onto the implant to create a biofilm [12]. A biofilm is a specialized extracellular matrix which envelops the bacterial strain and is resistant to the human immune system as well as antibiotics. Thus the only way of removing a biofilm is through surgical procedures and removal of the implant [13].

Current surgical procedures for the treatment of infection involve the removal of the implant, a thorough debridement, followed by a prolonged period of intravenous antibiotics, which typically lasts six weeks to three months. In this period, a temporary spacer with antibiotic loaded bone cement is implanted to help eradicate infection by eluting antibiotics locally at the site of infection. Only after the administering of antibiotics, a new functional implant is inserted again [14]. Given the nature of the infection, this procedure cannot guarantee that there will be no re-infection [15]. It is therefore argued that infection prevention is a very important strategy in ensuring implant success.

The use of antibiotic-loaded bone cement as a prophylaxis for bacterial colonisation is an accepted practice; however, debates exist about the possible dangers of this strategy to allow bacteria to mutate and become resistant [16]. Recent research has shown the possibilities of customising implant surfaces with alternative coatings containing nanotechnology. Amongst these are silver nanoparticles. Zhao et al. [17] have found that the silver nanoparticles could kill all the bacteria in the suspension around the sample during the first days of their study. It also retained antimicrobial ability for up to 30 days without significant decline. Another promising alternative to conventional antibiotics is the use of antimicrobial peptides. In vivo studies performed with an antimicrobial peptide, nisin F, infiltrated bone cement confirmed the efficacy of such a strategy [18].

It is thus apparent that promising results have been obtained for the customisation of a total hip replacement femoral stem for antimicrobial efficacy. However, due to the limitations of the current manufacturing processes for hip implants, the focus
remained on coatings on the exterior of the implant. A novel idea has been put forward by Mueller et al. [19] to apply additive manufacturing in order to create internal cavities from which antimicrobial substances can be eluted (Figure 2).

A specific interest is to further investigate features in which an antimicrobial loaded bone cemented can be embedded. Not only would such a strategy reduce the probability of bacterial colonisation but the bone cement can also be loaded with osteoconductive cells, promoting osseointegration. By embedding bone cement into the implant, the possibility also exist for maintaining sufficient structural and especially fatigue properties. This however, needs to be verified.

A functionally customised implant to prevent bacterial colonisation could also be used in treatment and revision surgeries. In the case of chronic infection, the complex two-stage procedure, which involves the implantation and removal of a temporary spacer, could be substituted with a procedure in which an antimicrobial infiltrated, fully functional implant is used after debridement. This could potentially reduce hospitalisation time for the patient and operating theater occupation time for each case of chronic infection, leading to a reduction in cost for both the patient and medical aid companies.

Figure 2 - Total hip replacement femoral stem with internal channels [19].

2.2 Spinal Implants

Back pain can be caused grouped into three categories [20]:

- Pinched nerves often due to herniated or deteriorated discs.
- Musculoskeletal pain
- Infections occur in the vertebrae

A common cause for patients requiring spinal surgery is degenerative disc disease (DDD). DDD is a natural part of ageing where the water content of the nucleus fibrosus reduces over time. This causes the disc to dry up and reduces its load carrying capability.

Various surgical techniques are available to treat back pain. Table 1 summaries the number of operative procedures listed by Eager et al. across 2069 cases [21]. It is apparent that fusion is a common surgery that is carried out right across the spine. The use of cage devices for interbody fusion in the lumbar and cervical spine has rapidly increased in recent years [22]. Advantages of using a cage device in place of conventional fusion includes the restoration of disc height.

Table 1 - Types of operative procedures (N = 2069)

<table>
<thead>
<tr>
<th>Procedure type</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACDF</td>
<td>323</td>
</tr>
<tr>
<td>Anterior/Posterior Cervical Fusion</td>
<td>59</td>
</tr>
<tr>
<td>Anterior/Posterior Lumbar Fusion</td>
<td>59</td>
</tr>
<tr>
<td>Spinal Decompression (any level, no fusion)</td>
<td>121</td>
</tr>
<tr>
<td>Single-Level TLIF or PLIF</td>
<td>377</td>
</tr>
<tr>
<td>Resection of Lesion (with or without fusion)</td>
<td>210</td>
</tr>
<tr>
<td>Multi-Level Cervical or Cervicothoracic Fusion</td>
<td>203</td>
</tr>
<tr>
<td>Multi-Level Thoracolumbar or Lumbar Fusion</td>
<td>532</td>
</tr>
<tr>
<td>Thoracic Fusion</td>
<td>97</td>
</tr>
<tr>
<td>Release of Tethered Cord</td>
<td>15</td>
</tr>
<tr>
<td>Other</td>
<td>73</td>
</tr>
</tbody>
</table>

Table 1 also indicates that the lumbar spine is the most affected. Extensive research has already been conducted on the lumber spine to the extent that there are disc devices for total disc replacement (TDR). De Beer investigated the possibility of a customised lumbar disc replacement with matching end-plate geometry [20]. The cervical spine however has not been as extensively researched which leaves room to investigate aspects such as customised implants.

2.2.1 Existing Cervical Cage Implants

There are three types of anterior surgical interventions for the treatment of DDD: discectomy alone (ACD), discectomy with fusion (ACDF) and discectomy with fusion and instrumentation (ACDFI) [23].

Marjorie et al. [24] showed that ACDF was the most common surgery carried out for the cervical spine between 1992 and 2005. Marawar et al. [25] analysed that over three periods between 1990 to 2004, the number of estimated discharges of ACDF surgeries in North America increased from 59 952 between 1990-1994, to 260 804 between 1995-1999, to 451 166 between 2000-2004, making the total number of discharges over 15 years to be 771 932. Figure 3 shows the surgical trends of the cervical spine between 1992 and 2005.
Cervical cage devices are used in ACDF when the intervertebral disc needs to be removed due to myelopathy, herniation or DDD. Originally they were fabricated using titanium alloys, but the industry has shifted to polyetheretherketone (PEEK) as the material of choice for mass production of standard implants. These devices are designed to fit rigidly between the vertebrae to restore its original spacing and promote osteointegration for successful fusion. Because they are standardized, they do not ensure a perfect fit and could loosen after surgery. Surgeons often have to run through a few sizes to find the implant that fits best, sometimes at the expense of damaging the end-plates of the adjacent vertebrae [26]. The risk with using cage devices however is subsidence.

2.2.2 Subsidence

Subsidence is a phenomenon that occurs after intervertebral discectomy surgery, where the cage device collapses into the lower adjacent vertebra. In research conducted by van Jonborgen et al. and Barsa & Suchomel, subsidence was defined as cage migration of 3mm or more into the adjacent vertebral body [26] [27]. Both performed radiographs post-surgery and 6 months post-surgery (Figure 4). Out of 100 patients, Barsa and Suchomel found 18 patients with subsided cages, while van Jonborgen found 10 cages out of 106 implanted had subsided (9%) [26] [28]. This shows that there is a need for a cage device which will lower the frequency of revision surgery due to post-operative complications such as subsidence. Cage design, end plate preparation (damage kept to a minimum) and stress distribution at the cage-end plate interface are suggested as the main factors of subsidence [26] [27] [28]. Van Jonborgen goes on to suggest that a modified cage design with improved and extended lower contact surface could be expected to reduce subsidence.

3 RESEARCH AVENUES

3.1 Hip Implant

An investigation into the efficacy of certain features to elute antimicrobial loaded bone cement is to follow in order to establish the best geometry and geometrical patterns for such features. Similar to Figure 2, focus will remain on the femoral component only.

A Concept Laser M2 LaserCUSING machine will be used to build Ti-6Al-4V samples with different features for testing. Figure 5 shows two conceptual ideas of typical surface patterns that could also be tested. Detailed designs regarding the type of features, geometry and pattern will depend on typical elution kinetics of different antimicrobial substances. Important factors include the release rate of the antimicrobial substance as well as its effective volume in an agar solution.

The samples with the antimicrobial bone cement filled features will be subjected to Staphylococcus aureus incubation while submersed in an agar solution. By having a control sample, conclusions can be made about the effect of different geometries and patterns on the possibility of preventing Staphylococci to colonise on the material surface.
3.2 Cervical Cage Implant

Here again the Selective Laser Melting (SLM) method will be used to produce individual parts with complex geometries whilst maintaining the mechanical properties to standard parts manufactured by conventional methods such as casting. Figure 6 shows two different designs for a possible custom cervical cage implant. The first has a network-type structure for bone to attach onto to promote osseointegration. The other has a custom profile at the top and bottom to match the patient’s vertebrae.

![Possible custom cervical cage designs](image)

**Figure 6 - Possible custom cervical cage designs**

In order for a customized cervical implant to be feasible, a strong working relationship between medicine and engineering must exist, where Medical Image Processing (MIP), Computer Aided Design (CAD) and AM are involved in an integrated process chain to minimise time and cost. The effectiveness of this process chain has to be studied and benchmarked against the current conventional ACDF surgical method. Figure 7 shows the design flow to be investigated for developing customised implants.

![Flow diagram for developing customised cervical implant](image)

**Figure 7 - Flow diagram for developing customised cervical implant.**

A customised cervical cage device will be developed and a cost analysis conducted on surgery time & fabrication to determine the principle feasibility of the approach. The custom implant will be tested on cadaver specimens with the aid of Stellenbosch University’s Tygerberg Medical Campus.

4 CONCLUSION AND OUTLOOK

This paper discusses the state-of-the-art regarding customisation in hip replacement and cervical cage implants. Based on this, the objective is to develop a hip replacement implant with features within which to embed antimicrobials in order to potentially improve not only the probability of implant success, but also the complex treatment procedures of implant infection. For cervical cage implants, the aim is to determine the suitability of the surfaces obtained by Additive Manufacturing, which could aid in osseointegration, the prerequisite for successful fusion of cervical cage implants. The research avenues further aim to utilise and analyse LaserCUSING as an enabler to fabricate customised medical implants.

5 REFERENCES


6 BIOGRAPHY

Dimiter Dimitrov obtained his PhD degree in Technical Sciences (Manufacturing Engineering) from the Technical University of Dresden. In 1999 he was appointed Professor in Advanced Manufacturing at the University of Stellenbosch, South Africa.

Martin Bezuidenhout is currently an M.Eng (Research) student at the University of Stellenbosch. His research project focuses on the application of LaserCUSING to incorporate features in hip replacement prostheses for infection prevention.

Graziano Marcantonio is a student at the University of Stellenbosch, studying M.Eng (Research) in Engineering Management. His research investigates the customisation of cervical cage implants using LaserCUSING.