



3D Printing Impact on the Orthopedic Shoulder Replacement Global Supply Chain

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3D Printing Impact on the Orthopedic Shoulder Replacement Global Supply Chain

Abner M. Ward, MD, MBA, FACS, FAAOS

A Thesis in the Field of Biotechnology Management
for the Degree of Master of Liberal Arts in Extension Studies

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Abstract

The goal of this work was to investigate a novel new technology being used to improve total shoulder replacements in patients with difficult to treat anatomy. The new technology is the use of three-dimensional (3D) implant creations that can be tailored to a patient's specific shoulder defects as opposed to shelf, standard size implants. The project will help provide management direction to improve the efficiency in the global supply system so that surgeons in various parts of the world may have access to surgical components in the shortest time without significant delay. The study findings were that hindrances to 3D adoption for just-in-time surgical usage primarily include difficulties with sterilization and lack of a global validation metric when performed at multiple international centers, as opposed to one location in a single country. This research topic has a direct clinical impact to improve patient quality of life and decrease their period of pain and suffering, while awaiting a total shoulder replacement.

Dedication

This effort is dedicated to: my sons, Aksel Ward, Brayan Tierney, Leo Ward and Rex Ward; my wife, Yifan Lu; my god-mother, Emma Washington; and mother, Mary Cotey.

Acknowledgements

This thesis would not have been possible without the support of my friends and family.

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I.

Introduction

In 2011, more than 50 million people in the United States reported that they had been diagnosed with some form of arthritis, according to the National Health Interview Survey. Simply defined, arthritis is inflammation of one or more of your joints. In a diseased shoulder, inflammation causes pain and stiffness. Although there is no cure for arthritis of the shoulder, there are many treatment options available to improve a patient's quality of life. One such treatment option to manage pain and stay active is a shoulder replacement. The three forms of shoulder replacement are: hemiarthroplasty; total shoulder arthroplasty/replacement; and reverse total shoulder arthroplasty/replacement. This paper is not intended to learn about the various surgical techniques to perform shoulder replacements but is instead focused on the management research problem of how to supply more unique, patient anatomy specific implant components to the surgeons who use them in the least amount of time for some of the most technically complex cases in total shoulder replacement. This paper took a close look at a novel new technology for implant creation, which is the use of three-dimensional (3D) implants that can be tailored to patient's specific shoulder defects as opposed to shelf, standard size components. The project will help provide management direction on ways to improve the efficiency in the global supply system so that surgeons in various parts of the world may have access to surgical implants in the shortest time. This research topic has direct clinical impact to improve patient quality of life, by decreasing pain and suffering following surgery. (1)

II.

Definition of Terms

- Arthroscopy—Procedure that uses special cameras and equipment to visualize, diagnose and treat problems inside a joint.
- Fusion—a "welding" process by which bones are fused together with bone grafts and internal devices (such as metal rods) to heal into a single solid bone. Also known as Arthrodesis.
- Internal fixation—a method to hold the broken pieces of bone in proper position with metal plates, pins or screws while the bone is healing.
- Joint replacement (partial, total and revision)—When an arthritic or damaged joint is removed and replaced with an artificial joint called a prosthesis.
- Orthopedic Surgery—Field of medicine relating to nonoperative and operative treatment of medical conditions related to the musculoskeletal system.

- Osteotomy—the correction of a bone deformity by cutting and repositioning the bone.
- Reverse total shoulder arthroplasty--In a reverse total shoulder replacement, the socket and metal ball are opposite a conventional total shoulder arthroplasty. The metal ball is fixed to the glenoid and the plastic cup is fixed to the upper end of the humerus. A reverse total shoulder replacement works better for people with rotator cuff tear arthropathy because it relies on different muscles, outside the rotator cuff, to move the arm.
- Soft tissue repair—The mending of soft tissue, such as torn tendons or ligaments.
- Shoulder Hemiarthroplasty—Just the head of the humerus is replaced by an artificial component.
- Sterilization--Destroy or eliminate all forms of microbial life by physical or chemical methods.
- Three-Dimensional (3D) printing—Use of digital files to print three dimensional objects from plastics and metals. Also known as additive manufacturing.

- Total shoulder arthroplasty—Both the head of the humerus and the glenoid are replaced. A plastic "cup" is fitted into the glenoid, and a metal "ball" is attached to the top of the humerus.

III.

Background

During my time in graduate school I have been tantalized by the concepts from Management E-5012, Systems Thinking class where read Nassim Taleb's book, "Antifragile". (2) I have thought deeply and hard about the concept of antifragility and the benefit of shocks on a system along with using it to grow when exposed to disorders, stressors, risks and uncertainty. The book has helped me grasp the positive effect of antifragility as opposed to the common intellectual viewpoint of being a negative hinderance. Then I began to relate how some systems are stuck in impasses and that randomness is necessary to unlock and set them free. In my industry, Orthopedic Surgery, we have a very well-defined supply chain of upstream and downstream products to create our musculoskeletal implants. Due to my expertise as an Orthopedic Shoulder and Elbow surgeon, I have been able to attend multiple domestic and international conferences, in the field, along with private industry events to test early implants and give design feedback. Currently, I have an affiliation with Lima Corporate, an Italian company that designs and manufactures implants for knee, hip, shoulder, and small joints, based in San Danielle, Italy, and doing business in the United States. This company was unique to me due to their early use of three-dimensional (3D) implant creations that could be tailored to patient's specific glenoid anatomical defects as opposed to using generalized, average body morphologic implants. The idea of using an

implant that could disrupt the traditional supply chain was novel to me, thus I have decided to further delve into this topic and use it for my thesis. In March 2018 I attended the American Academy of Orthopedic Surgeons (AAOS) national conference in New Orleans, Louisiana and at the conference, I had the chance to handle several of Lima's 3D constructed implants that were not readily available in the United States. Then, in September 2018, I traveled to San Danielle, Italy and met the lead engineers and administration of Lima. I had an opportunity to learn this new process of producing customized implants and having the possibility to distribute worldwide in a short time period. These two experiences further solidified that this disruptive technology could have a large impact on the current global implant supply change for the medical design industry.

Orthopedic surgery or orthopedics, also spelled orthopaedics, is the branch of surgery concerned with conditions involving the musculoskeletal system. Orthopedic surgeons use both surgical and nonsurgical means to treat musculoskeletal trauma, spine diseases, sports injuries, degenerative diseases, infections, tumors, and congenital disorders. (3)

Nicholas Andry coined the word in French as *orthopédie*, derived from the Ancient Greek words ὀρθός *orthos* ("correct", "straight") and παιδίον *paidion* ("child"), and published *Orthopedie* (translated as *Orthopædia: Or the Art of Correcting and Preventing Deformities in Children*) in 1741. The word was assimilated into English as *orthopædics*; the ligature æ was common in that era for *ae* in Greek- and Latin-based words. Though, as the name implies, the discipline was initially developed with attention to children, the correction of spinal and bone

deformities in all stages of life eventually became the cornerstone of orthopedic practice.

(3)

Early Orthopedics

Many developments in orthopedic surgery have resulted from experiences during wartime. On the battlefields of the Middle Ages the injured were treated with bandages soaked in horses' blood which dried to form a stiff, but unsanitary, splint.

Originally, the term orthopedics meant the correcting of musculoskeletal deformities in children. Nicolas Andry, a professor of medicine at the University of Paris coined the term in the first textbook written on the subject in 1741. He advocated the use of exercise, manipulation and splinting to treat deformities in children. His book was directed towards parents, and while some topics would be familiar to orthopedists today, it also included “excessive sweating of the palms” and freckles. (3)

Jean-André Venel established the first orthopedic institute in 1780, which was the first hospital dedicated to the treatment of children's skeletal deformities. He developed the club-foot shoe for children born with foot deformities and various methods to treat curvature of the spine. (3)

Advances made in surgical technique during the 18th century, such as John Hunter's research on tendon healing and Percival Pott's work on spinal deformity steadily increased the range of new methods available for effective treatment. Antonius Mathijssen, a Dutch military surgeon, invented the plaster of Paris cast in 1851. However, up until the 1890s, orthopedics was still a study limited to the correction of deformity in children. One of the first surgical procedures developed was percutaneous tenotomy. This involved cutting a tendon, originally the Achilles tendon, to help treat deformities

alongside bracing and exercises. In the late 1800s and first decades of the 1900s, there was significant controversy about whether orthopedics should include surgical procedures at all. (3)

Modern Orthopedics

Examples of people who aided the development of modern orthopedic surgery were Hugh Owen Thomas, (**Fig. 1**) a surgeon from Wales, and his nephew, Robert Jones. Thomas became interested in orthopedics and bone-setting at a young age and, after establishing his own practice, went on to expand the field into general treatment of fracture and other musculoskeletal problems. He advocated enforced rest as the best remedy for fractures and tuberculosis and created the so-called 'Thomas Splint', to stabilize a fractured femur and prevent infection. He is also responsible for numerous other medical innovations that all carry his name: 'Thomas's collar' to treat tuberculosis of the cervical spine, 'Thomas's manoeuvre', an orthopedic investigation for fracture of the hip joint, Thomas test, a method of detecting hip deformity by having the patient lying flat in bed, 'Thomas's wrench' for reducing fractures, as well as an osteoclast to break and reset bones. (3)

Thomas's work was not fully appreciated in his own lifetime. It was only during the First World War that his techniques came to be used for injured soldiers on the battlefield. His nephew, Sir Robert Jones, had already made great



Figure 1. Hugh Owen Thomas, a pioneer of modern orthopedic surgery.

advances in orthopedics in his position as Surgeon-Superintendent for the construction of the Manchester Ship Canal in 1888. He was responsible for the injured among the 20,000 workers, and he organized the first comprehensive accident service in the world, dividing the 36-mile site into 3 sections, and establishing a hospital and a string of first aid posts in

each section. He had the medical personnel trained in fracture management. He personally managed 3,000 cases and performed 300 operations in his own hospital. This position enabled him to learn new techniques and improve the standard of fracture management. Physicians from around the world came to Jones' clinic to learn his techniques. Along with Alfred Tubby, Jones founded the British Orthopaedic Society in 1894. (3)

During the First World War, Jones served as a Territorial Army surgeon. He observed that treatment of fractures both at the front and in hospitals at home was inadequate, and his efforts led to the introduction of military orthopedic hospitals. He was appointed Inspector of Military Orthopaedics, with responsibility over 30,000 beds. The hospital in Ducane Road, Hammersmith became the model for both British and American military orthopedic hospitals. His advocacy of the use of Thomas splint for the initial treatment of femoral fractures reduced mortality of compound fractures of the femur from 87% to less than 8% in the period from 1916 to 1918. (3)

The use of intramedullary rods to treat fractures of the femur and tibia was pioneered by Gerhard Küntscher of Germany. This made a noticeable difference to the speed of recovery of injured German soldiers during World War II and led to more widespread adoption of intramedullary fixation of fractures in the rest of the world. However, traction was the standard method of treating thigh bone fractures until the late 1970s when the Harborview Medical Center in Seattle group popularized intramedullary fixation without opening up the fracture. (3)

The modern total hip replacement was pioneered by Sir John Charnley, expert in tribology at Wrightington Hospital, England in the 1960s. He found that joint surfaces

could be replaced by implants cemented to the bone. His design consisted of a stainless-steel one-piece femoral stem and head and a polyethylene, acetabular component, both of which were fixed to the bone using PMMA (acrylic) bone cement. **(Fig. 2)** For over two decades, the Charnley Low Friction Arthroplasty and its derivative designs were the most-used systems in the world. This formed the basis for all modern hip implants. (3)



Figure 2. X-ray of a hip replacement.

The Exeter hip replacement system (with a slightly different stem geometry) was developed at the same time. Since Charnley, there have been continuous improvements in the design and technique of joint replacement (arthroplasty) with many contributors, including W. H. Harris, the son of R. I. Harris, whose team at Harvard pioneered uncemented arthroplasty techniques with the bone bonding directly to the implant.

Knee replacements using similar technology were started by McIntosh in rheumatoid arthritis patients and later by Gunston and Marmor for osteoarthritis in the 1970s developed by Dr. John Insall in New York utilizing a fixed bearing system, and by Dr. Frederick Buechel and Dr. Michael Pappas utilizing a mobile bearing system.

External fixation of fractures was refined by American surgeons during the Vietnam War but a major contribution was made by Gavril Abramovich Ilizarov in the USSR. He was sent, without much orthopedic training, to look after injured Russian soldiers in Siberia in the 1950s. With no equipment he was confronted with crippling conditions of unhealed, infected, and malaligned fractures. With the help of the local bicycle shop he devised ring external fixators tensioned like the spokes of a bicycle. With this equipment he achieved healing, realignment and lengthening to a degree unheard of elsewhere.

His Ilizarov apparatus is still used today as one of the distraction osteogenesis methods.

Modern orthopedic surgery and musculoskeletal research has sought to make surgery less invasive and to make implanted components better and more durable. (3)

Training

In the United States, orthopedic surgeons have typically completed four years of undergraduate education and four years of medical school. Subsequently, these medical

school graduates undergo residency training in orthopedic surgery. The five-year residency is a categorical orthopedic surgery training. (3)

Selection for residency training in orthopedic surgery is very competitive. Approximately 700 physicians complete orthopedic residency training per year in the United States.

About 10 percent of current orthopedic surgery residents are women; about 20 percent are members of minority groups. There are approximately 20,400 actively practicing orthopedic surgeons and residents in the United States. According to the latest 2011-2012 Occupational Outlook Handbook published by the United States Department of Labor, between 3–4% of all practicing physicians are orthopedic surgeons. (3)

Many orthopedic surgeons elect to do further training, or fellowships, after completing their residency training. Fellowship training in an orthopedic sub-specialty is typically one year in duration (sometimes two) and sometimes has a research component involved with the clinical and operative training. Examples of orthopedic sub-specialty training in the United States are:

- Hand and Upper Extremity
- Shoulder and Elbow
- Total Joint Reconstruction (arthroplasty)
- Pediatric Orthopedics
- Foot and ankle surgery
- Spine surgery
- Musculoskeletal oncology
- Surgical Sports Medicine

- Orthopedic Trauma (**Fig. 3**)



Figure 3. Orthopedic Trauma X-ray of a pelvis fracture repair.

These specialty areas of medicine are not exclusive to orthopedic surgery. For example, hand surgery is practiced by some plastic surgeons and spine surgery is practiced by most neurosurgeons. Additionally, foot and ankle surgery is practiced by board-certified Doctors of Podiatric Medicine (D.P.M.) in the United States. Some family practice physicians practice sports medicine; however, their scope of practice is non-operative. (3)

After completion of specialty residency/registrar training, an orthopedic surgeon is then eligible for board certification by the American Board of Medical Specialties or the American Board of Orthopedic Surgery. Certification by the American Board of Orthopaedic Surgery or the American Osteopathic Board of Orthopedic Surgery means that the orthopedic surgeon has met the specified educational, evaluation, and examination requirements of the Board. The process requires successful completion of a standardized written exam followed by an oral exam focused on the surgeon's clinical and surgical performance over a 6-month period. In Canada, the certifying organization is the Royal College of Physicians and Surgeons of Canada; in Australia and New Zealand it is the Royal Australasian College of Surgeons. (3)

In the United States, specialists in hand surgery and orthopedic sports medicine may obtain a Certificate of Added Qualifications (CAQ) in addition to their board primary certification by successfully completing a separate standardized examination. There is no additional certification process for the other sub-specialties. (3)

Practice

According to applications for board certification from 1999 to 2003, the top 25 most common procedures (in order) performed by orthopedic surgeons are as follows:

1. Knee arthroscopy and meniscectomy (**Fig. 4**)
2. Shoulder arthroscopy and decompression
3. Carpal tunnel release
4. Knee arthroscopy and chondroplasty
5. Removal of support implant
6. Knee arthroscopy and anterior cruciate ligament reconstruction
7. Knee replacement
8. Repair of femoral neck fracture
9. Repair of trochanteric fracture
10. Debridement of skin/muscle/bone/fracture
11. Knee arthroscopy repair of both menisci
12. Hip replacement
13. Shoulder arthroscopy/distal clavicle excision
14. Repair of rotator cuff tendon
15. Repair fracture of radius (bone)/ulna (**Fig. 5**)
16. Laminectomy
17. Repair of ankle fracture (bimalleolar type)
18. Shoulder arthroscopy and debridement
19. Lumbar spinal fusion

- 20. Repair fracture of the distal part of radius
- 21. Low back intervertebral disc surgery
- 22. Incise finger tendon sheath
- 23. Repair of ankle fracture (fibula)
- 24. Repair of femoral shaft fracture
- 25. Repair of tibial fracture (**Fig. 6**)

A typical schedule for a practicing orthopedic surgeon involves 50–55 hours of work per week divided among clinic, surgery, various administrative duties and possibly teaching and/or research if in an academic setting. (3)



Figure 4. Radiography of knee used in work up for knee arthroscopy.



Figure 5. Orthopedic implants to repair fractures to the radius and ulna. Note, the visible break in the ulna. (right forearm)



Figure 6. Anterior and lateral view x-rays of fractured left tibia with internal fixation after surgery.

Arthroscopy

The use of arthroscopic techniques has been particularly important for injured patients. Arthroscopy was pioneered in the early 1950s by Dr. Masaki Watanabe of Japan to perform minimally invasive cartilage surgery and reconstructions of torn ligaments. Arthroscopy allows patients to recover from the surgery in a matter of days, rather than the weeks to months required by conventional, 'open' surgery. It is a very popular technique. Knee arthroscopy is one of the most common operations performed by orthopedic surgeons today and is often combined with meniscectomy or chondroplasty. The majority of upper extremity outpatient orthopedic procedures are now performed arthroscopically. (3)

Arthroplasty

Arthroplasty is an orthopedic surgery where the articular surface of a musculoskeletal joint is replaced, remodeled, or realigned by osteotomy or some other procedure. It is an elective procedure that is done to relieve pain and restore function to the joint after damage by arthritis or some other type of trauma. As well as the standard total knee replacement surgery, the uni-compartmental knee replacement, in which only one weight-bearing surface of an arthritic knee is replaced, is a popular alternative. Joint replacements are available for other joints on a variable basis, most notably the hip, shoulder, elbow, wrist, ankle, spine, and finger joints. (3)

In recent years, surface replacement of joints, in particular the hip joint, have become more popular amongst younger and more active patients. This type of operation

delays the need for the more traditional and less bone-conserving total hip replacement, but carries significant risks of early failure from fracture and bone death.

One of the main problems with joint replacements is wear of the bearing surfaces of components. This can lead to damage to surrounding bone and contribute to eventual failure of the implant. Use of alternative bearing surfaces has increased in recent years, particularly in younger patients, in an attempt to improve the wear characteristics of joint replacement components. These include ceramics and all-metal implants (as opposed to the original metal-on-plastic). The plastic chosen is usually ultra-high-molecular-weight polyethylene, which can also be altered in ways that may improve wear characteristics.

(3)

Epidemiology

Between 2001 and 2016, the prevalence of musculoskeletal procedures drastically increased in the U.S, from 17.9% to 24.2% of all operating room procedures performed during hospital stays. (3)

In a study of hospitalizations in the United States in 2012, spine and joint procedures were common among all age groups except infants. Spinal fusion was one of the five most common operating room procedures performed in every age group except infants younger than 1 year and adults 85 years and older. Laminectomy was common among adults aged 18–84 years. Knee arthroplasty and hip replacement were in the top five OR procedures for adults aged 45 years and older. (3)

A major problem that I have personally encountered in my practice, as an Orthopedic Shoulder Surgeon, is in fixing the bones of patients with osteoporosis. The

same holds for revising Total Shoulder replacements and the subsequent lack of suitable bone at the scapula glenoid, where the glenoid component of a Total Shoulder replacement would interface with the humeral component. Currently, the standard implants for revision glenoid components often do not fit patient's anatomy well due to a loss of bone when removing prior implants. Thus, the standard implants that are built for the masses do not often match the anatomy of specific individual patients well. Because surgeons are using glenoid components that are not well tailored to the patient, the opportunity to be more productive and complete a greater number of surgical cases in a set time period is lower, since working on one patient longer to fit standard implants to unique patient's anatomy. With longer operative times, there is a higher risk for surgical site infections, and poorer outcomes. Thus, in order to improve efficiency and outcomes, a better implant system was needed. This led to the usage of 3D implants in Orthopedic Shoulder surgery to create a better revision glenoid component fit.

The 3D printing industry, or “additive manufacturing”, has increasingly captured mainstream interest due to the multitude of breakthroughs and applications being developed. 3D printers obtain printing information from a digital file and inject materials in successive patterns to build a three-dimensional solid object from plastics and metals.

(Fig. 7)



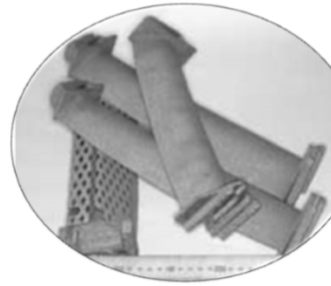
Figure 7. Engine component for Formula 1 racecar made with 3D technology.

From this methodology, a variety of products can be manufactured from a single 3D printer (**Fig. 8**). This reduces the number of steps in the production chain which enables manufacturing companies to achieve significant savings on logistics and production costs. Companies that use 3D printing can find additional savings from sustainable business practices and the decrease in production waste. This revolutionary way has several advantages over conventional production techniques including decreasing manufacturing expenses and lowering complexity in manufacturing. Additional benefits include: rapid prototyping; high degree of component customization; flexibility to change design; reducing time to market; reduce tooling, machining and waste materials; and making it possible to manufacture parts with cellular structures. Applications of 3D printing include in medical implants, and the automotive and aerospace industry. Currently, 3D printing is poised to benefit the production of medical devices and disrupt the healthcare; supply chain overall. (4,5)

➤ Medical implants



➤ Aerospace



➤ Automotive

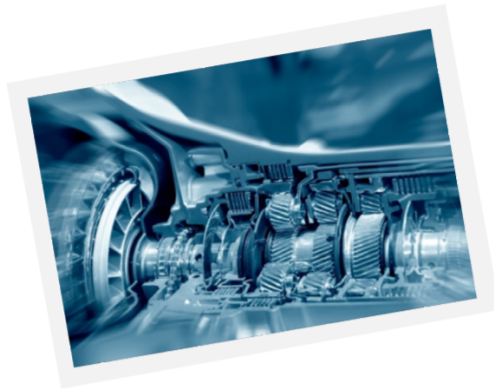


Figure 8. Example of 3D components currently produced.

The biggest advantage that 3D implants bring is optimizing supply chains. Today, traditional supply chains follow SCOR model (plan, source, make, deliver, return), with each step requires significant resources. (6) 3D technology transforms the supply chain in the following ways: First, the technology allows a more rapid vetting out of designs prior to starting production. By quickly locating designs flaws, the technology allows more rapid redesigning and prototyping, which results in shorter design cycles and better product design. Second, the technology speeds up assembly by creating custom, inexpensive, and quality manufacturing aids. Third, 3D printing allows custom thermoforming patterns that allow designs of varying thickness, patterns of varying sizes, and patterns requiring unique shapes. Fourth, the 3D production turnaround is shorter than a conventional process; there is little to no time lost. Design files are sent straight to a printer for fabrication and then post-process distribution is performed as needed. Fifth, and last, the technology allows the creation of virtual inventory. Designs can be stored on computer files, USB, or the cloud, and accessed whenever needed just in time to manufacture and ship straight to the consumer. This would result in greatly decreasing warehouse held product inventory thus costs for maintaining large storage facilities. Overall, 3D printing can improve the efficiency of the supply chain to boost productivity and lead to ripple effects across multiple industries, including healthcare. (7)

Specific to healthcare, 3D printing has been used in the production of prosthetic implants and limbs, along with prosthetic dentistry. 3D printing in health care shows the following improvements comparing to traditional medical implant manufacturing:

Customization: 3D printing can create implants that are customized to patient and fits in their anatomy

Lead Time: 3D printing enables rapid design and prototyping, and allows feedback from doctors and patients to speed up the design process. It is possible to iterate the design process based on direct feedback from the surgeon who will operate and use the implant and print a new one for assessment in a couple of hours.

Cost: 3D printing enables surgeons to make changes before its final production, therefore lowers the cost of defective product; also custom and complex implants are now printed at a smaller scale, which means the production is more efficient and cost-effective.

Sterilizability: Sterilizability is an important property for medical materials such as implants. 3D printing uses a lot of materials that are sterilizable.

Complexity: 3D printing is able to design and print much more complex medical implants comparing to traditional manufacturing process. (8)

In sum, the 3D printing has the potential to help health care professionals to increase the level of understanding of the disease involved, and provide the patient-specific implants and optimize the surgical process and cost. (9) It is estimated that by 2019, 3D printing will be considered a critical tool in healthcare and used in more than 35 percent of all surgical procedures requiring prosthetic and implant devices within the body. (10) It was also estimated that by 2019, 10 percent of people in the developed world will be living with a 3D printed item on or in their body. (10) Researchers project that the 3D market could have an impact up to \$550 billion dollars a year by 2025. Though, it is unlikely the technique will fully supplant current mass production practices, but instead will serve as a complementary process. (11)

Lima Corporate is a global medical device company based out of San Danielle, in northern Italy, and provides reconstructive Orthopedic implants to surgeons looking to improve their patient's quality of life. The company's product range includes large joint revision and primary implants, along with complete extremity solutions for difficult musculoskeletal fractures and oncologic tumor reconstructions. Recently, the company celebrated the 10th year of using 3D technology for their Trabecular Titanium (TT) implants. Currently the company is the pioneer and leader in 3D printing technologies applied to Orthopedics. Lima was able to partner with another company, Electron Beam Melting (EBM), to develop the technology and help address the functional limits of the coatings applied to traditional prosthetic implants. Lima also partnered with another company, Arcam, to further develop the potential of the TT technology and use Arcam's knowledge and experience with 3D printing in other industries. As a result of the Arcam partnership, Lima began to acquire the machinery and production designs to create prototypes for studying the effects of materials that could potentially mimic trabecular bone. This experience with Trabecular Titanium highlighted the versatility of the technology. The geometries produced with EBM technology immediately revealed that the new material exceeded the limits of traditional machining production processes. In 2007, the first acetabular (i.e., hip implant) cup, the Lima Delta TT Cup, was born with the objective to satisfy the demands of surgeons for better implant performance and outcomes. Once approved, the Delta TT Cup was implanted for the first time in Italy. Since then the cup has been widely available on the global market. Following the past 10 years' experience, Lima developed a product portfolio covering different anatomical areas from hips to extremities as well as tailored solutions for patient specific needs

utilizing TT. The 10-year milestone helps show the companies endearing commitment and support of new technologies to develop solutions to help assist surgeons in restarting patient motion. (4, 12)

The EBM process technology involves several steps, features, and benefits. The process involves powder deposition (**Fig. 9**), followed by 3D model loading, and then layer by layer melting with a high energy electron beam. An important feature is that occurs in a vacuum process which leads to no contamination and better material properties. (**Fig. 10, 11, and 12**) A few benefits of EBM process are that can create a precise shape of the component. (4, 12, 13)



Figure 9. Base powder used in 3D implant creation

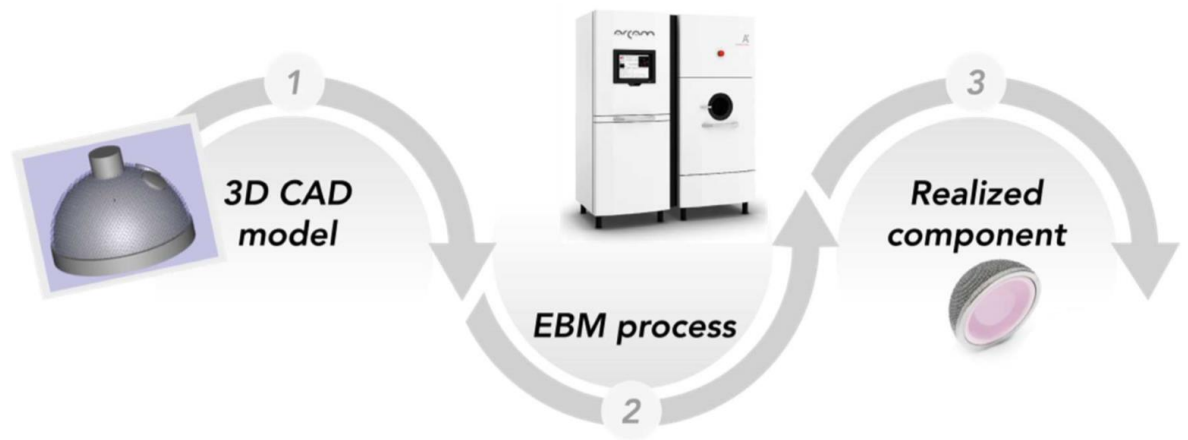


Figure 10. Schematic of 3D component design process.



Figure 11. On the left, actual 3D printer opened showing the implant productions site. On the right, is a blueprint of the 3D printer mechanism.



Figure 12. 3D printer with door closed.

The Lima implant that sparked my interest particularly about 3D technology, and the guiding impetus for this thesis, was the company's glenoid component for total shoulder replacements. The shoulder is made up of the humeral head and the glenoid. In shoulder replacement, the humeral head and glenoid need to be replaced to provide a decrease in pain from a usually arthritic and irregular shoulder. The 3D glenoid implant could be custom form fitted to reproduce the anatomy of patients with complex glenoid wear or those needing revision surgeries, which are usually much more difficult surgeries to perform than primary procedures. Prior to this implant, surgeons had to find glenoid implants that were close enough to patient's native anatomy, but not identical. However, now with 3D technology, surgeons can now exactly reproduce defects in patient's anatomy that will in turn better fit their orthopedic needs. (4, 12, 13)

Chapter IV.

Materials and Methods

In this study it was not possible to perform in vitro or in vivo studies on 3D implants and needed to rely on industry third party resources for information gathered. When using vendor information there may be the risk of systematic biases from using industry third-party data.

Using 3D technology brings great opportunity in the orthopedic surgical industry, meanwhile, it also poses some challenges, such as: implant variation; inconsistent sterilization and establishing a consistent validation process if manufacture in multiple locations. Implant variation from one location to another could adversely affect patient outcomes, if not well standardized. As previous research shows, the two most governing factors that affect 3D implant variation are design and materials. (14) However, the biggest problem identified has been the sterilization process for 3D implants.

Regulatory sterilization standards can vary around the world and are difficult to gauge since there is not a standardized international protocol. This study will propose a solution to create a more consistent global sterilization process standard. First, will perform a market analysis of different sterilization processes. Second, will make a comparative analysis on the pros and cons of the most prevalent sterilization methods. Third, will examine the leading 3D implant manufacturer, Lima Corporate's process to sterilize and validate implant quality. Fourth, and finally, will interview industry leading

Orthopedic Shoulder and Elbow Surgeon experts at the 2019 American Shoulder and Elbow Conference, which I attended as a member. Will use this peer data to develop an acceptable tolerance level and specification for 3D glenoid implant sterilization. By performing the aforementioned steps, this study will recommend a start point to standardize the 3D implant sterilization process.

Chapter V.

Results

Market Assessment of Current Sterilization Process: We looked at a 2018 industry market analysis of the sterilization industry that compiled data from some of the key participants, such as Steris, Getinge Group, 3M, Sortera Health, and Advanced Sterilization Products (15). The global sterilization equipment market accounted for \$7.32 billion USD in 2017 and is expected to reach \$11.67 billion USD by 2024 with a compound annual growth rate of 6.9% between 2019 and 2024. The sanitization process of sterilization can include chemical or mechanical cleansing of materials by using chemicals, heat, and radiation. The selection of the sterilization method depends upon the heat sensitivity of the product want to use. (15)

Over the period from 2017 to 2024 the analysis shows good growth in the sterilization market primarily fueled by medical procedures. North America and Europe are the most mature regions for the sterilization equipment market and expect to remain in the same position for the near future. North America is the largest consumer for sterilization products and accounts for 35% of global market share, followed by Europe. The market demand in both regions is seen as a little stagnant due to being in the maturity stage of industrialization. While on the other hand, developing markets such as China and India will help drive growth and are the most promising future markets. Though, growth in these regions could potentially be stymied by government regulation, increased

costs, and lack of awareness. In 2017, Asia Pacific and Latin America collectively held approximately 30% of the global sterilization market demand. Technological developments in Asia Pacific and Latin America are spurring the growth. China is the largest consumer, followed by India in the Asia Pacific Region. Asia Pacific market sterilization demand is projected to grow at a 7.9% compound average growth rate. While in Latin America, Brazil is the regional leader. (15)

The global sterilization equipment market is segmented into five types: pharmaceutical companies; hospitals & clinics; educational institutes; food & beverage industry; and others. The sterilization equipment market was dominated by pharmaceutical products and food industries in 2017. The sterilization of 3D glenoid components falls under the pharmaceutical industry, for grouping purposes. (15)

Analyzing the market, the global sterilization equipment market is segmented into four types: heat sterilization equipment (i.e., dry heat sterilization and moist heat/steam sterilization equipment); chemical sterilization (i.e., ethylene oxide sterilization, hydrogen peroxide sterilization, ozone-based sterilization, formaldehyde sterilization, and others); filtration sterilization; and ionizing radiation sterilization (i.e., e-beam radiation sterilization, gamma sterilization, and others). The heat sterilization equipment segment contributes for more than 40% of all sterilization equipment sales market. The dry heat and moist heat sterilization equipment are predicted to be the strongest future growth segments. (15)

Comparative Analysis of the Sterilization Process: The three most common types of sterilization found by market analysis were: steam with an autoclave; using ethylene oxide gas (ETO); and use of hydrogen peroxide gas plasma (PO). Each has their own

pros and cons. The benefit of steam is that it is non-toxic, has high lumen penetration, and only needs a short processing time of 4-30 minutes. A drawback to steam is that the high temperatures used from 121-132°C may cause melting or warping. The benefit of ETO is that only need low temperatures of 37-60°C and provides adequate lumen penetration. The cons of ETO are that devices should be rinsed before use, there is a potential health risk to personnel, has a long processing time of 10-24 hours, and is restricted from being used in CA, NY, and MI. The pros of PO are that it is non-toxic, needs only low temperatures of 37-44°C, has a medium processing time of 52 minutes, and adequate lumen penetration. The drawbacks of PO are that it has a material-dependent lumen penetration. (16)

Case Study: Lima Corporate. The company at the forefront for 3D sterilization is Lima Corporate. The company currently uses the inert gas, EO, for their 3D implant sterilization. When I interviewed the CEO, Mr. Luigi Ferrari, at the corporate headquarters, he discussed with me that the biggest reason the company has identified to use EO is because this gas can be used with various polymers in the 3D printing process that are sensitive to heat and moisture and would not cause as detrimental an effect as other gases they tested in the past. When I spoke with some of the lead engineers, they relayed that after treating the 3D implants with EO, the products are aerated to eliminate any residues that may be trapped within the scaffolds and could detrimentally alter the material properties.

Interview with Industry Experts. When attended the 2019 American Shoulder and Elbow Surgeons (ASES) Annual Meeting, in New York City, from October 16-19, I had the chance to interact and interview several leaders in the field, along with discussing the

products with vendors selling the products. When interviewed Mr. Nicholas Olson, Group Product Manager at Stryker Orthopedics, he told me that his company currently uses a third-party company, named Materialise, to produce 3D glenoid implants for difficult revision shoulder replacements. The basic information that garnered from Mr. Olson was that 3D technology is rapidly improving and has the ability to create surgical implants that can anatomically reproduce human glenoid anatomy. However, he did mention that there is still a concern that the 3D products are not at the same sterility level as the currently used machine casted implants that have been widely available for a longer period of time. Stryker uses a combination of ETO and gamma sterilization. During the meeting, I was also able to meet with Dr. Frank A. Cordasco and Dr. Robert Hotchkiss, from the Hospital for Special Surgery (HSS). They relayed that HSS had just began construction for a new joint venture with Lima Corporate, and were very excited about the progress in innovation, but the hospital had not begun producing 3D implants for use in patients yet. (17)

Chapter VI.

Discussion

The US market for shoulder arthroplasty implants is worth over 40% of the entire global market for all types of minor orthopedic replacement implants and is growing at 6.6% per year. (19) Boosted by the increase in the US's elderly baby boomer population and a linked rise in proximal humerus fractures, by 2021 the shoulder replacement implant market in the US will be worth \$982 million. The main driver for the shoulder replacement implant market in the US is the increase in the size of the population aged 65 years and over, of whom more than 50% suffer from arthritis. Proximal humerus fractures (i.e., fractures of the upper arm bone near the shoulder) are one of the most common shoulder injuries and mainly due to osteoporosis in people over 70 years old. The global incidence rate for proximal humerus fractures has been steadily increasing by 15% per year. Of proximal humerus fractures, 5% require shoulder arthroplasty, either with partial shoulder replacement, or a reverse total shoulder replacement. As have more surgeries, will increase the risk for secondary revisions that need more complicated glenoid components, compared to primary surgeries. (18)

Hindrances to 3D usage for just in time implants include issues with consistent sterilization and difficulty with how to validate if performed at multiple centers, as opposed to one location in one country. The process of sterilization, with inert gasses, at multiple locations around the world, just before a 3D implant is placed into a human, is

likely the greatest hindrance for worldwide implant supply chain delivery. Regulatory sterilization standards can vary around the world and are difficult to always gauge, even when using the same protocols. Along with the sterilization process the validation of the process can be different from one location to another, especially if dealing with a plant in western Europe versus one in East Asia or North America. The risk of an improperly sterilized implants can be catastrophic and lead to infections that necessitate implant removal, secondary surgeries, along with incurring additional, financial strain, and significant pain and suffering for the patient to undergo further surgery.

Upon reviewing the research on 3D implant sterilization methodologies, I would recommend using the inert gas, ETO, as the global standard. The gas has proven success from the global leading company, LimaCorporate, and has been accepted by many industry experts.

In conclusion, the development of 3D printing for the global Orthopedic supply chain has been an absolute game changer for the international Orthopedic shoulder surgical community. The concepts of antifragility and shocking the status quo to create insightful gains are uncommon in medical device sales, due to the industry often following extremely conservative parameters. However, the 3D technology presented in this paper is promising to create those type of gains and be instrumental in disrupting the international Orthopedic shoulder implant supply chain process.

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