3D-Printed Metallic Medical Devices: Increasing Interest from Medical Device Manufacturers, Opportunities & Challenges

Ming Tang, Ph.D., P.E.; Lawrence Eiselstein, Ph.D., P.E.
Exponent

Have you ever imagined an implantable medical device, manufactured specifically for your needs and available exactly when you need it? What once sounded like science fiction is now becoming reality, thanks to the revolutionary technology of 3-dimensional (3D) printing.

3D-printing, also known as additive manufacturing (AM), is the process of joining materials to make objects from 3D model data, usually layer upon layer [1]. AM is generating significant attention in manufacturing, given the diversity of its potential applications across the medical and aerospace industries, including to develop prototypes and customized product designs [2-4]. AM also enables the creation and manufacture of design geometries that otherwise would be difficult, if not impossible, to produce through subtractive techniques, such as machining or other standard techniques, such as casting, or extrusion. AM enables the creation of highly complex and intricate designs, offering significant advantages for unique structural configurations and fluid flow applications, including nozzles, microfluidic systems, and cellular ingrowth structures.

In this article, we will focus on a specific and important aspect of the use of AM in the medical industry: the intersection between biomaterials, medical devices, and 3D-printing — and the growing promise, as well as challenges, associated with manufacturing implantable medical materials or devices through selective laser melting (SLM) of metals and alloys. This includes discussing the benefits and uses of SLM in 3D-printing of metals/alloys for medical devices and exploring the growing number of 510(k) submissions and patents for these devices. We will also cover some of the potential disadvantages, risks, and hurdles associated with obtaining regulatory approval for bringing 3D-printed medical devices to market [5-9].

1 What is 3D-printing and how does it work?

Milestones in 3D-printing

The first major milestone in 3D-printing is widely recognized as the creation of solid objects using photopolymerized resins through the use of a laser at Battelle Memorial Institute in the late 1960s [10]. Then came the development of stereolithography or standard tessellation (STL) language: the first fully-fledged 3D printer, which is usually credited to Charles Hull, the founder of 3D Systems Corp., in 1986. Hull developed the STL file format, the most commonly used format in 3D-printing, which is still in use today [3, 11]. In 1992, powder bed fusion systems were introduced to the market by DTM Corporation (now 3D Systems). Early research funded by DARPA, Dr. Carl Deckard and his advisor, Dr. Joe Beaman at the University of Texas at Austin, in 1986 addressed issues such as why it takes so long to make a part for the first time. The pair patented the process for selective laser sintering (SLS) of plastic powders, metals, and ceramics for use in AM [4, 12].

Over the past three decades, 3D-printing has fulfilled its promise of revolutionizing industries and it continues to create new opportunities in materials, design, and manufacturing across a wide range of applications. For instance, 3D-printing of metal powders (in this context, referring to both pure metals and metallic alloys) has been used to manufacture rocket engine parts, turbine blades for jet engines, and race car components [13]. One success example in using 3D-printing to develop a highly reliable mass-produced part was GE Aviation's CFM LEAP (Leading Edge Aviation Propulsion) engine fuel nozzles, manufactured

from cobalt chromium powders; see Figure 2 [10, 14]. To accomplish this, GE invested $1.1 billion to acquire AM companies Concept Laser GmbH from Germany (laser machines) and Arcam AB from Sweden (electron beam melting system) to accelerate its efforts in metal-based 3D-printing [15-17]. By August 2021, GE had produced 100,000 3D-printed fuel nozzles [14], marking one of the most significant developments in the metal AM industry.

Figure 1. GE Aviation's 3D-printed fuel nozzle tip. [14]

Materials and processes used in AM

A wide range of materials can be used in AM or 3D printing, including plastics and metals. In the case of plastics, SLS commonly uses polyamide polymers such as Nylon 11 and 12, as well as polystyrene (PS) [3]. High-performance polymers like polyetheretherketone (PEEK), polyetherketoneketone (PEKK), polyetherketone (PEK), and polyetherketoneetherketoneketone (PEKEKK) are also suited for SLS, along with thermoplastic elastomers and other thermoplastics, which are widely available as powders for this process [18-20]. For metals, AM technologies are often categorized by their feedstock material and energy source. Powder bed fusion (PBF) and directed energy deposition are the most prevalent AM techniques using metal powders [21]. PBF processes typically employ either a laser or electron beam to melt and fuse metal powders during fabrication.

The figure below illustrates how SLM works, a common method in metal 3D-printing often referred to as "mini welding" [22]. In this process, a laser beam heats and melts a bed of fine metal powder — spheroidal, with diameters smaller than strands of human hair. After one layer of powder is melted, the build platform shifts down by the thickness of one layer, and a new layer of powder is added. This step-by-step process continues until the entire three-dimensional object is completed.

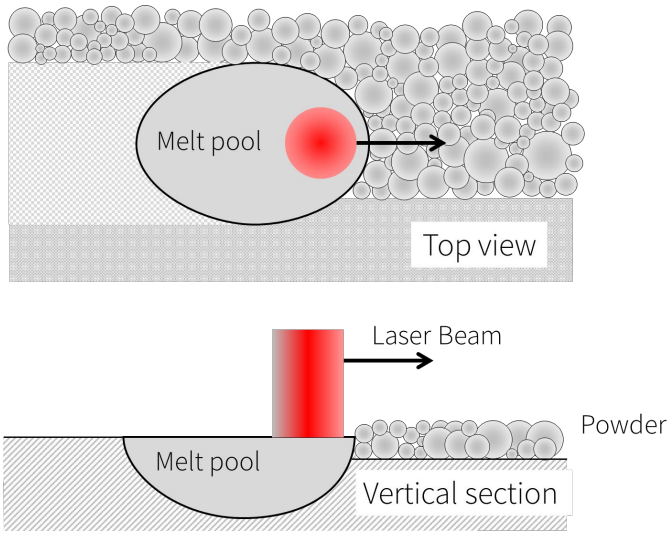

Figure 2. Schematic of 3D-printing through SLM of powder metal layers [22].

2 Applications in medical device manufacturing

Biomaterials and devices

AM has been used to develop implantable biomaterials or devices. These biomaterials and devices are manufactured from both metal and non-metals, including polymers as well as biological cells [23-26].

Distinguishing a biomaterial from a medical device involves understanding how these terms are used in the healthcare industry. A biomaterial is a substance (natural or synthetic) that is engineered to interact with biological systems for medical purposes, either as part of a medical device or to replace or repair tissue. Biomaterials can be used in applications that include medical implants (artificial joints, heart valves, stents), tissue engineering (scaffolds to help cells grow into functional tissues), drug delivery systems (materials that release medication at a controlled rate), and wound healing (materials that promote tissue regeneration). Notably, 3D-printed scaffolds combined with tissue engineering have been given the name 4D-printing to encompass the growth stage of cells on the scaffolds [23, 27]. A review of this concept is available from Wang et al [27] in, "Emerging 4D Printing Strategies for Next-Generation Tissue Regeneration and Medical Devices."

In addition to establishing common definitions for biomaterials and their distinction from medical devices, it is also important to delineate what we mean by medical devices: A medical device is any instrument, apparatus, or machine, used to diagnose or treat a medical condition. A medical device can contain multiple components, including electronics, biomaterials, and mechanical parts, and generally performs a mechanical or electrical function. Biomaterials are often evaluated based on their biocompatibility, but medical devices are regulated not only for their biocompatibility but also for their mechanical safety and functionality. Regulatory bodies such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA) ensure that medical devices meet strict criteria for safety and effectiveness.

3D-printing in medical devices: a growing field

The use of 3D-printing in the medical device industry has been growing rapidly. In 2016, FDA shared some novel examples of 3D-printed medical devices [28]: a 3D-printed splint that helped save a child's life; a 3D-printed plate that replaced part of a patient's skull; a knee joint custom-made to fit a patient perfectly; and a first-of-its-kind spinal device with a complex design, all showing new possibilities for what 3D-

printing might be used to accomplish. In 2023, FDA provided a descriptive graphic (see Figure 3) showing the percentages of the different types of AM technologies used for medical devices, where they are used in the body, the type of material employed, and whether porous materials were used, from 2010-2020 [29]. Additional data on the rapid growth of AM in medical applications can be found in some review papers [2, 3], highlighting the same trend of device development using AM increasing from 2010 to 2020.

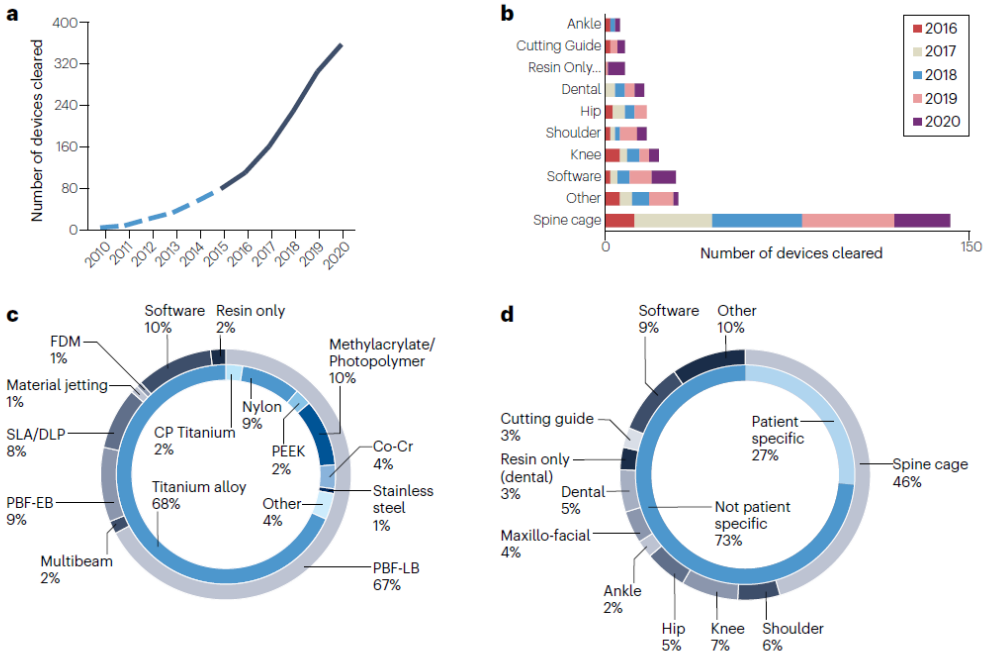

Fig. 1 | Breakdown of FDA 510(k)-cleared additively manufactured medical devices. a, Timeline of medical devices cleared from 2010 to 2020. Dashed line indicates previously reported data (2010–2015)[3]. **b**, Breakdown of device types cleared by year, from 2016 to 2020. **c**,**d**, Concentric pie charts showing printing technologies and materials (**c**) and device type and patient specificity (**d**). This dataset contains only additively manufactured medical devices declared substantially equivalent through FDA's 510(k) pathway and does not include additively manufactured products cleared through other pathways and in other centres. CP, commercially pure; FDA, US Food and Drug administration; FDM, fuse deposition modelling; PBF-EB, electron beam powder bed fusion; PBF-LB, laser beam powder bed fusion; PEEK, poly-ether-ether-ketone; SLA/DLP, steriolithography/digital light project.

Figure 3. Graphic from FDA showing the types of 510(k) medical devices cleared between 2010 and 2020 [29].

The graph below (Figure 4) is developed from Exponent's own literature review and research on 510(k) and patent submissions. It adds to FDA's figure, expanding the agency's analysis through 2022 and showing the continued increase in 510(k) submissions for Class II devices with summaries that reference "additive manufacturing" or "3D-printing."

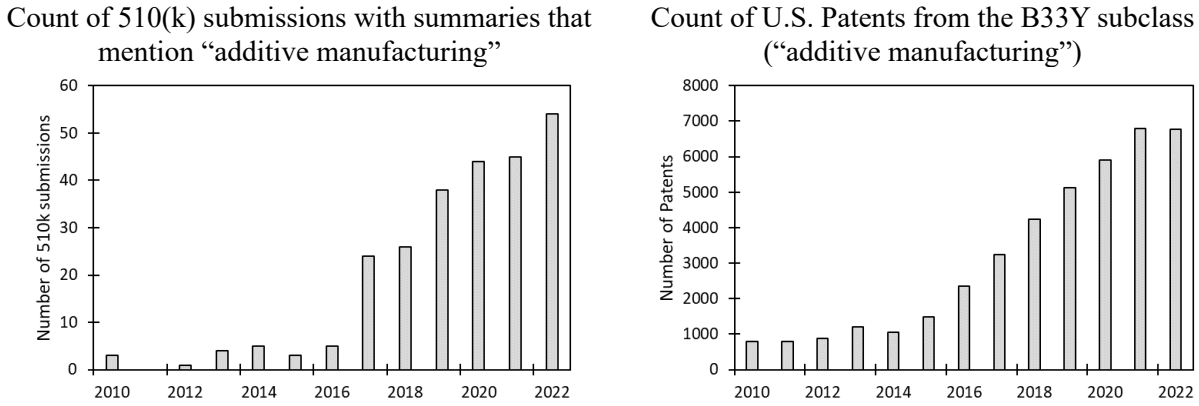

Figure 4. History of the number of 510(k) submissions and U.S. Patents related to "additive manufacturing" per year through 2022. Data source: https://open.fda.gov/apis/device/510k/download/, and app.innography.com. The raw data was last retrieved on September 30, 2024.

Challenges and risks of AM for medical devices

One of the earliest 3D-printed metal medical devices submitted to FDA for approval was a device called Exactech® Novation® Empire™ Acetabular Augments with lnteGrip™ in 2010, which used a 3D-printed titanium alloy to create a porous structure for bone ingrowth [30]. As an example of legal and regulatory issues associated with AM of medical devices, there was a recall for this product that was initiated because of an employee error "due to an out-of-range condition for an in-vitro biological evaluation standard" [31].

Following such early development in 2010, the surge of 510(k) submissions from 2016 to 2017 (as seen in Figure 4) reflects growing interest, acceptance, and use of AM technology. Notable examples include legal discussions [9], a white paper on 3D-printing technology and legal principles [7], the release of FDA's first guidelines on 3D-printing medical devices in 2017 [32], and a lawsuit related to intellectual property between two flagship metal 3D-printing companies of Desktop Metal Inc and Markforged Inc. in 2018 [33].

As with aerospace structures, medical devices and implantable materials developed through AM need to be highly reliable [34], but also biocompatible. One of the key challenges in developing and manufacturing these devices is thoroughly characterizing additive manufacturing (AM) materials and components to ensure consistent properties and verify that they meet the reliability and safety standards required by regulatory bodies.

As previously mentioned, FDA provides guidelines with respect to AM [32] medical devices. Further, the American Society for Testing and Materials (ASTM) has also provided guidance and guidelines. ASTM Committee F42 on Additive Manufacturing Technologies was formed in 2009 [35] and provides over 57 ASTM standards and papers covering AM devices [1, 35, 36]. Among these ASTM standards, two are specifically related to medical applications: ASTM F3456-22 ("Standard Guide for Powder Reuse Schema in Powder Bed Fusion Processes for Medical Applications for Additive Manufacturing Feedstock Materials") and ASTM F3604-23 ("Standard Practice for Validating the Additive Manufacturing Production Process for Medical Devices Produced Using Laser Powder Bed Fusion").

(See *Appendix 1: Literature Review* for a selected summary of recent technical papers, FDA publications, and industrial standards.)

How can materials science research enhance 3D-printed parts?

Currently, metallic AM is mostly used in medical devices to develop custom or personalized devices or porous structure development for cell ingrowth or to design complex micromechanical structures (honeycombs) and other cellular structures that would be difficult to machine, cast, or forge. However, recent advances in metallurgy have opened innovative opportunities for enhancing the properties of 3D-printed metallic alloys. Some of these opportunities include the development of new metal alloys using metallic powder additions to pre-alloyed powders, amorphous alloy compositions for AM devices, or high entropy alloys (HEA) to develop new biomaterials. These potential applications for AM metals for medical devices are currently underrepresented in AM devices, likely because of development costs.

As an example of one of these methods, Zhang et al explored microalloying (adding nanoparticle alloying additions) to readily available metal powders for 3D-printing to achieve titanium alloy with more uniform mechanical properties, the results of which were published in *Science* in 2024 [37]. 3D-printed metallic alloys often form coarse, heterogeneously distributed phases, resulting in anisotropic and inconsistent properties. The researchers aimed to address the formation of coarse columnar grains and uneven phases in 3D-printed alloys, which weaken the material. Using pre-alloyed Ti-5Al-5Mo-5V-3Cr (Ti-5553) powder mixed with molybdenum (Mo) nanoparticles, Zhang et al refined the grains and improved phase distribution during the heating and cooling process in AM through SLM. Figure 5 shows how this change leads to more consistent mechanical properties and improves both the strength and flexibility of the material. Zhang et al's approach demonstrates the possibility of tweaking the alloy with just one element to overcome the usual problems (unfavorable microstructures) and achieve desired mechanical qualities directly from 3D-printing.

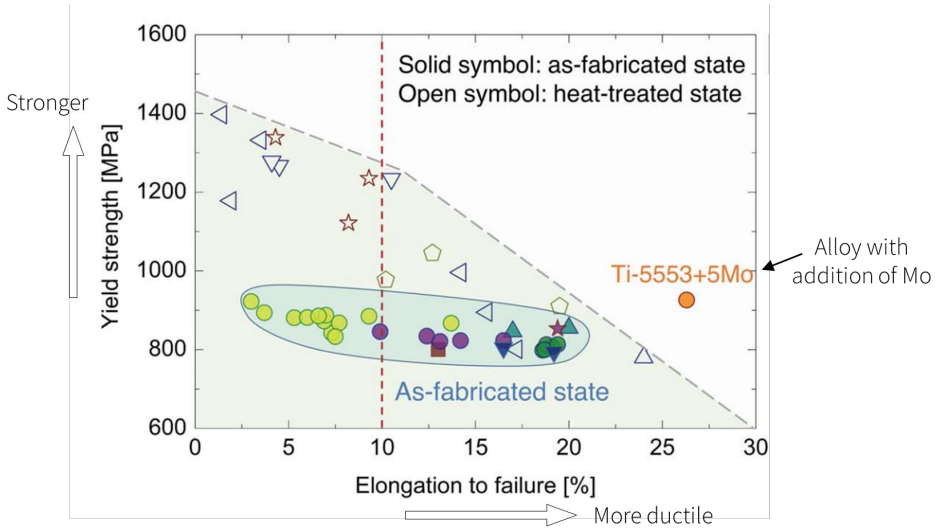

Figure 5. A new design method to improve the mechanical properties of 3D-printed material, with an example of adding Mo to Ti-5Al-5Mo-5V-3Cr, taken from Zhang et al [37]. Annotations are added by Exponent.

In addition to the use of microalloying described by Zhang et al, SLM techniques offer the possibility of high solidification rates for exceedingly small grain sizes or even amorphous microstructure, and the potential to use HEAs for devices.

(Examples for these two topics are summarized in *Appendix 2: Materials Science Research on 3D-Printing.* Along with biocompatibilities and the potential for machine learning to develop new biocompatible metallurgies.)

3 Are 3D-printed parts reliable?

Metallurgical fatigue and fracture

Although AM is revolutionizing the development of intricate medical device designs, these new products must be reliable over the device's design life. This is especially important in healthcare applications, where device failure can lead to serious problems. Fatigue — a major reason metal parts fail — represents approximately 90% of all mechanical service failures. Imagine bending a paper clip repeatedly until it breaks. This is a specific type of failure called fatigue that occurs when metals are subjected to repeated stress. Such fatigue can occur (infrequently) in medical devices from in vivo loadings.

Mechanical fatigue and fracture are a particular concern that can be addressed through assessing manufacturing and design defects. For example, we tested 3D-printed rod-shaped aluminum alloy samples to see how long they could withstand repeated use before breaking [38]. Then, the fractured surface was examined under a microscope (optical and scanning electron microscopes) as shown in the figure below, to determine the "culprit" defect: where this crack initiated, how the crack spread, and where the fracture transitioned from fatigue to fast crack growth failure. We found that tiny imperfections, such as pores, were often the starting point for these breaks.

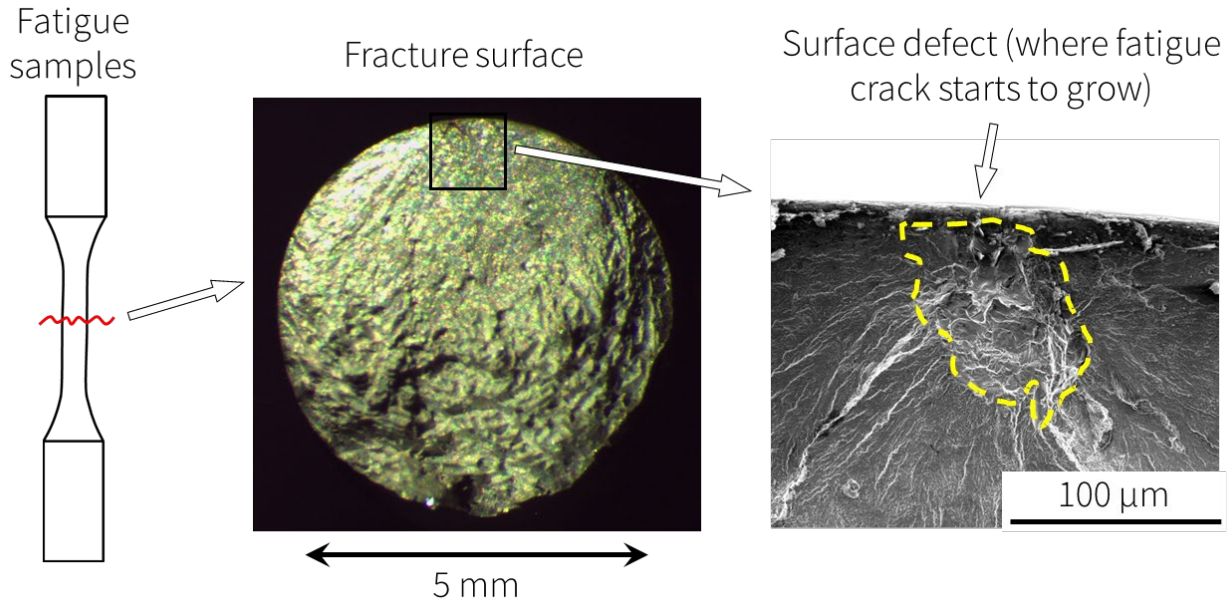

Figure 6. Fracture surface of 3D-printed aluminum alloy sample. [38]

Finding out that small pores in 3D-printed metal parts can cause big issues like fatigue failure is unsurprising; however, selecting 3D-printing processing parameters to reduce these defect sizes to less than a critical dimension, given specific loading conditions, is crucial for the development of reliable medical devices.

Device makers must use appropriate materials and printing parameters and apply surface finishes to strengthen their products against overload and fatigue failures. Mr. Lindenfeld's article on legal considerations for 3D-printing covers some of the issues that may surface if a device fails in service [39]. Both design and manufacturing defects can occur, but from an engineering perspective, these two types of

defects often overlap. For instance, understanding the worst-case scenario for in vivo loading conditions and selecting the appropriate size and shape of the device and required material (accounting for strength and corrosion resistance) can enable further analysis to determine what "critical defect size" is permitted. If the 3D-printing parameters cannot reliably produce parts with pores or other defects that are smaller than this critical defect size, the following changes may be required:

- The material may need to be changed (strength, fatigue resistance, or fracture toughness)
- 3D-printing parameters modified to reduce the size of printing defect size and frequency.
- Part dimension changed to reduce the stress/cyclic stresses when in service.

What affects 3D-printed product quality?

In 3D-printing, many factors such as powder quality, laser power, and post-heat treatment can affect quality, and interestingly, the orientation of the laser scan direction really matters with respect to where the maximum principal stress direction will be applied to the material in service. Figure 6 illustrates that a 3D-printed object with the laser scan consolidated in the x-y plane will result in pores with their ellipsoidal axis also orientated in this plane. If the part is primarily loaded in the x-y plane, it will be stronger and last longer under fatigue conditions than a part that is loaded perpendicular to this plane. That is, it will be weaker if the principal axis of the pore is perpendicular to the maximum principal stress. This is because the tiny pores inside the material, formed during printing, stretch horizontally in the direction of the laser scan. When stress is applied perpendicular to the scan direction, these elongated pores can become an Achilles' heel, making the material less durable.

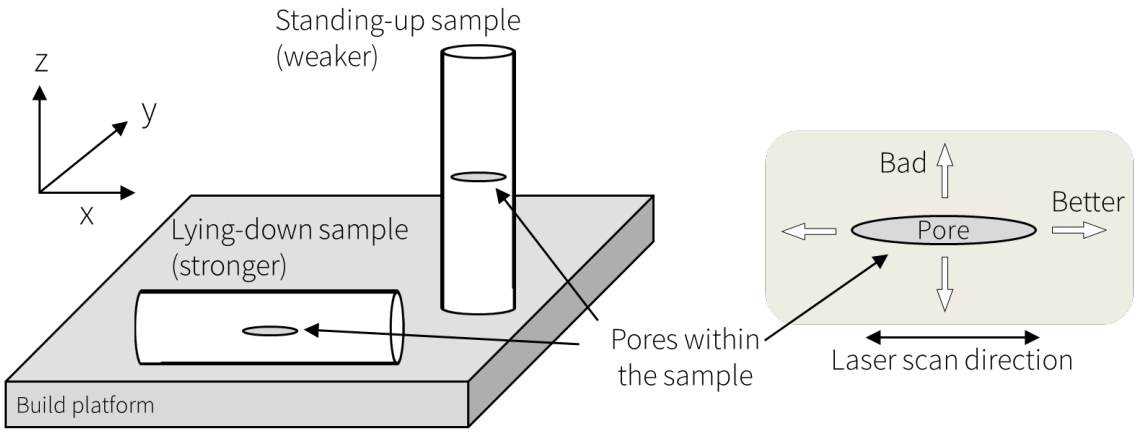

Figure 7. Orientations of samples during 3D-printing and inherent lack-of-fusion defects/pores.

This concept can be explained with a simple analogy: just like cutting steak is easier in certain directions (cutting against the grain), the strength of a 3D-printed material changes depending on how it is printed.

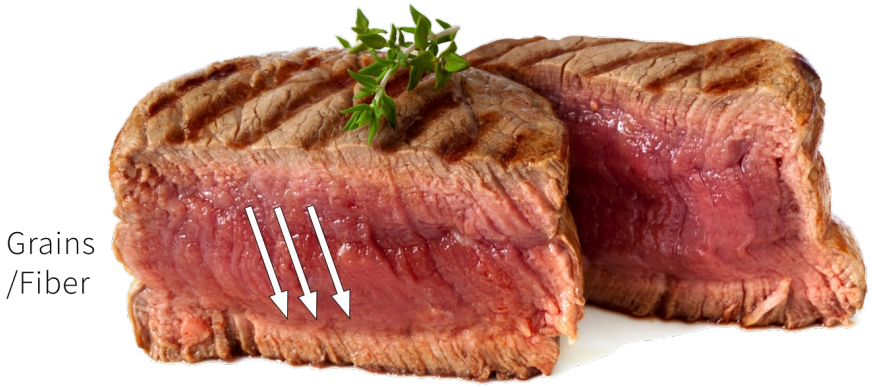

Figure 8. Using a steak analogy to explain the anisotropy in 3D-printed materials. Image source: [40].

4 How can Exponent help?

At Exponent, we provide technical engineering and scientific consulting services to medical device manufacturers to help make safer, more reliable equipment and devices. Exponent has decades of experience across a wide spectrum of products, from medical devices to consumer electronics, buildings, structures, and more. We perform corrosion testing, fatigue, and other accelerated life testing, as well as conduct computational studies of mechanical and thermal analysis (finite element analysis) for medical device stakeholders in support of product development, quality assurance, regulatory submissions, and post-market surveillance.

Over the past several decades, Exponent has developed extensive experience in 3D-printing of metals, polymers, cells, and related research and business applications, through the contributions of our multidisciplinary experts to peer-reviewed research. This includes Manuel Garcia-Leiner, Ph.D. [18, 20, 41]; Scott Lovald, Ph.D., MBA, P.E. [42]; Cameron Morley [24], Ehsan Mostaed, Ph.D. [26]; Sean Murray, Ph.D., P.E. [13, 43, 44]; Tim Myers, Ph.D., P.E., CFEI [8], Kevin L. Ong, Ph.D., P.E. [45]; Arthur Racot [46], Maureen Reitman, Sc.E., P.E., NAE, FSPE [5, 6, 47]; Alexis Sauer-Budge, Ph.D. [25]; Ryan Siskey, M.S. [48]; Connor Slone, Ph.D., P.E. [49]; Lonnie Smith, Ph.D. [50]; Collin Stabler, Ph.D., P.E. [51]; and Nevin Taylor, Ph.D. [52].

About the Authors

Dr. Ming Tang specializes in mechanical metallurgy, with an emphasis on defect characterization, root cause analysis, and lifetime prediction of metals. He has 10 years of research experience in metals, including aluminum, iron and steel, titanium, and nickel. He has expertise in the application of microscopy techniques in various areas, particularly in quantifying defects for a broad range of metallic materials and examining their effect on mechanical performance.

Dr. Lawrence Eiselstein's medical device expertise includes aerosol delivery devices, anastomosis devices, catheters, cochlear implants, delivery systems, electrosurgical tools, feeding tubes, fertility control devices, guidewires, heart valves, heart valve repair devices, aneurysm repair devices, orthopedic devices, hypodermic needles, batteries, intra-aortic balloon pumps, pacemakers, stents and stent-grafts, syringes, trocars, as well as other medical devices [53]. He consults clients on design analysis and testing for FDA approval of implantable devices manufactured from plastics, ceramics, stainless steel, superelastic nitinol (NiTi), Elgiloy, and MP35N; 510(k) and PMA submissions to FDA as well as failure modes and effect

analysis for medical devices; failure analysis of implantable medical devices; and intellectual property issues.

5 Appendix 1: Literature review

Recent publications on 3D-printed medical devices and biomaterials include technical review papers by researchers [21, 54-63], FDA publications [28, 29, 64, 65], ASTM, and ISO standards [1, 66-68], as summarized below.

Technical review papers

Singh's paper discloses the various metals (as well as polymers and ceramics) used for 3D-printed medical devices that FDA had cleared as of 2017 [62]. These materials include but are not limited to pure Ti, Ti alloys including nitinol (shape memory metal), stainless steel and cobalt-chromium alloys, PMMA, PEEK, zirconia, and hydroxyapatite.

Culmone et al paper discusses a literature survey of the use of 3D-printed medical instruments for surgical and diagnostics [54]. They noted that although most of these instruments were manufactured from polymeric materials, polymer-printed instruments can have problems with sterilization due to their low softening temperature, which3D-printed metals do not have.

Shahrubudin et al paper discusses some of the challenges of 3D-printing of biomedical products and notes that SLM can produce precise porous titanium implants with a pore size of 400 to 1000 microns and a porosity of 60 to 95%. These implants can bond well with bone inside the body; if an implant is too stiff, it reduces the pressure on the bone needed to encourage bone growth [61].

Da Silva et al note that AM allows for fine-tuning of the microstructure to produce purposeful anisotropy, porosity, and varying chemical composition, which may be desired in many medical devices. They further note that commercial implants are already manufactured by SLM, SLS, and EBM, such as acetabular components for hip arthroplasty, dental abutments, and knee implants, in which porosity is to be beneficial for osseointegration.[55]. Their article highlights some of the limitations of using EBR versus laser consolidation.

Vafadar et al discuss AM and its usage in various industries, including the medical industry, and provide a list of 40 ASTM and ISO current and standards under development for AM [63].

Salmi provides a table that summarizes the advantages of AM producing various implants and medical devices for dental and orthopedic and pharmaceutical applications [60]. The benefits include cost and time savings, personalization, incorporation of antibiotics, "surgeon as designer" with innovation potential, and the ability to develop complex geometries.

Davoodi et al provide a summary table that lists the advantages, limitations, and applications of various types of metals used or considered for additive manufacturing [56]. These metals include Ti alloys, Ta alloys, stainless steel, Co-Cr, Mg alloys (controlled dissolution), and shape memory alloys like nitinol.

In the Kumar et al article, a summary is provided on how AM has grown over the last four decades with an emphasis on drug/pharmaceutical products [57].

Pesode and Barve note that although 3D-printed Ti and its alloy Ti-6Al-4V have been studied and used in clinical applications for several years, they believe further research is needed for porous AM titanium implants to evaluate their long-term reliability [59].

Mobarak et al have noted, as have others, that the emergence of AM and advancements in computerized tomography (CT) scanning techniques and CAD modeling have brought about significant changes in the medical implant industry in recent decades. While 3D-imaging data was initially utilized for visualization and diagnosis, it has now been integrated with AM to create medical devices personalized to an individual patient's physiology [58]. They also report on a surge in recent years for the production of implants made from biodegradable metals such as magnesium, zinc, iron, and calcium [21].

FDA publications

A 2016 paper by researchers from FDA [28] summarized FDA's perspectives based on different departments, including the Center for Device and Radiological Health (CDRH) for reviewing and clearing AM medical devices, the Center for Drug Evaluation and Research (CDER) for 3D-printed drug, and Center for Biologics Evaluation and Research (CBER) on 3D-printed biologics. Their paper mentions AM devices that have caught the world's attention such as a 3D-printed bronchial splint that saved a child's life, a 3D-printed cranial plate that replaced a large portion of a patient's skull, a new artificial knee that was personalized to fit the patient's own anatomy, and a spinal device made with complex internal architecture.

Ricles et al from FDA summarized common FDA pathways for regulating AM medical products; presented a graphic showing how FDA-approved AM medical devices through the 510(k) process have grown between 2010-2015; and provided a table that lists resources available to medical device manufacturers regarding 3D-printing and interacting with FDA [65]. They also analyzed the Manufacturer and User Facility Device Experience (MAUDE) database for the most recent year (2014) and reviewed complete medical device reports on adverse events for AM-developed devices. They found 836 reports but only 59 were product related. The primary reasons for these 59 reports were (in rank order): improper size or incompatibility with other components of the device; device fracture or shaving; inadequate or incorrect device sizes for the patient; implant wear: and use error where the incorrect device was implanted. FDA noted that these adverse events (AEs) were consistent with AEs found for traditionally manufactured devices and that given the limitations of the MAUDE Medical Device Reports (MDRs), they could not conclude that any were related to the manufacturing process or workflow.

Researchers from ASTM and FDA [64] published a review on the regulations and standards for additive manufacturing in healthcare. In this paper, the authors compare steps to bringing medical devices to market in the U.S. and EU markets, as well as highlight FDA-recognized AM consensus standards. They note that AM metal medical implants have been cleared by FDA since 2010 and that the complex nature of AM technology and the lack of AM standards for medical device production is a leading cause for the lack of clarity on meeting existing regulatory requirements. They also note that currently, FDA guidance does not cover the use or incorporation of biological, cellular, or tissue-based products in AM.

Another paper published by authors from FDA [29] shows analysis based on FDA's internal database indicating that since 2010, there has been near-exponential growth in AM medical devices, with over 357 devices using various methods and materials added from 2010 to 2020. FDA believes that this exponential growth was driven by FDA's development of guidance for industry and AM standards, reducing regulatory and technical uncertainty in 510(k) clearance. FDA notes that as technology advances, AM applications in medical device production are expected to continue expanding.

ASTM and ISO standards

ASTM and ISO have worked together globally to develop and promote standards for the AM community by using expert knowledge. A few fundamental standards (from ISO and ASTM [67, 68] [1]) define key terminology and classification for AM technologies, providing a standardized framework for industry. The importance of these developments lies in defining consistent language and processes, helping ensure quality and safety across AM applications globally. These standards are essential for guiding manufacturers and regulators in developing AM products.

Finally, there are an increasing number of articles being published on regulations and legal issues, like regulatory systems [69-72], legal concerns [6, 47], risk management [5], product liability [73], data protection [74], intellectual properties [75, 76], etc. For example, Beck and Jacobson [73] highlighted that since all 3D-printed medical devices currently on the market have been cleared by FDA as "substantially equivalent" to existing non-3D-printed devices, they have not impacted product liability preemption. Once 3D-printed devices receive pre-market approval from FDA, preemption will depend on whether FDA has imposed any specific "requirements" on 3D printing.

6 Appendix 2: Materials Science Research on 3D-Printing

AM of medical devices with amorphous metals (metallic glasses)

Researchers have also explored using AM to create metallic glasses with a unique amorphous structure [77-81]. TRUMPF, a laser melting system provider, showed that amorphous metals are perfect for making long-lasting scalpels and medical tools, and they could also be used for implants inside the body [77, 78]. TRUMPF made an amorphous metal radius plate implant (Figure 9) that they state is versatile, extraordinarily hard, yet also highly elastic, resistant to corrosion and wear, and as biocompatible as the current material of choice, titanium or its alloy Ti6Al4V [78]. As an example of academic research, Liu et al [79] presented a review on this topic by highlighting a 2009 pioneering trial of the fabrication of a Fe-based alloy, where the amorphous phase was only obtained in the deposited layer near the substrate. Recently, new AM methods, like laser-foil printing, ultrasonic AM, and pneumatic-injection 3D-printing, offer additional ways to produce fully amorphous metallic glasses (MGs). Instead of melting MG powders, these methods involve welding or bonding larger amorphous foils, strips, ribbons, or powder slurry, which provide benefits like avoiding pores, trapped gas, and achieving higher cooling rates without using high-energy beams. However, these techniques may have downsides, such as uneven structures between the foils, strips, or ribbons, and weaker mechanical properties.

Figure 9. 3D-printed radius plate implants produced with amorphous metals, which adapt to the movement of bones and encourage the healing process. [77, 78]

AM of medical devices with HEAs

Another example is the potential for using HEAs in AM 3D-printed medical devices. Although some amorphous alloys can be considered HEAs, particularly if they contain multiple principal alloying elements in significant amounts leading to high configurational entropy, not all amorphous alloys are high entropy because many traditional amorphous alloys have fewer elements and typically tend to crystallize into FCC or BCC solid solutions. HEAs can be made amorphous by high cooling rates or by choosing element combinations that favor glass formation, such as choosing alloying elements with significant differences in atomic size that form deep eutectics (low melting point liquid).

HEA research took off in the early 2000s through research by J.W. Yeh [82] and B. Cantor [83]. HEAs have been considered for use in AM 3D-printing for their good corrosion resistance and mechanical properties but there are few examples of AM 3D-printed medical devices or implants [84-89]. Whereas normal engineering alloys are alloys of three or four metals of different concentrations, HEAs are mostly equiatomic mixtures of five or more metals. Their high configurational entropy, which is a result of the near-equal concentration of multiple elements (entropy of mixing), stabilizes the formation of simple solid solution phases such as face-centered cubic (FCC), or body-centered cubic (BCC) phases. This phased stabilization and homogeneous microstructure improves the mechanical properties and thermal stability of these alloys. Although thermal stability is not so much of an issue for medical implants, the increase in strength is an advantage, as well as the single-phase improving corrosion resistance.

While many papers discuss using HEAs in 3D-printing, there are far fewer examples of 3D-printing HEAs specifically for medical devices. An example of a review paper titled “Medical high-entropy alloy: Outstanding mechanical properties and superb biological compatibility” on HEA for medical devices is from Liu et al [90].

Biocompatibility of 3D-printed medical devices

Additionally, 3D-printing can be used to explore new, potentially biocompatible alloys. For instance, Ti-6Al-4V (Ti64) is widely used in biomedical applications for its robust mechanical properties, yet there are concerns regarding its vanadium content posing a health risk. A recent research article [91] indicates that AM, leveraging its rapid cooling rate, can enhance pure titanium to achieve the benefits of Ti64, such as improved strength and corrosion resistance. This potentially makes AM 3D-printing of pure titanium potentially a better option for medical applications such as dental and orthopedic devices.

Machine learning for alloy development for 3D-printing

Material science has made great progress in the computational design of new material over the last 20 years using density functional theory (DFT). However, despite recent progress, current generative models often fall short of producing stable materials [92, 93].

Recently, the machine learning process has been used for the discovery of novel alloys [92, 93]. Traditional testing and validation by experiments is time-consuming whereas 3D-printing offers a potentially cost-effective, versatile method to quickly test and validate materials that have been selected by DFT, AI, or ML processes. This technology accelerates development by enabling rapid prototyping and iterative testing, streamlining the path from discovery to application. For example, applications of new AM materials include smart materials, ceramics, electronics, biomaterials, and composites, with 3D-printing being an integral part of a multi-process system for designing novel materials [94]. As another example, in 3D-printing metals, ML is used to model and optimize the complex process of building metal components layer by layer [95].

These techniques help reduce time and costs, drawing on methods already used in materials science to improve 3D-printing technology.

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