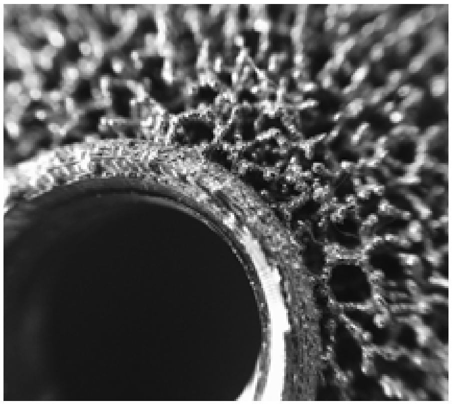
Medical Additive Manufacturing/ 3D Printing



Improving Public Health

Each year, healthcare needs and costs grow due to an aging population, the rise in chronic diseases, and more. In fact, global healthcare spending is projected to reach nearly $9 trillion by 2020[1].

To address this, practitioners in the healthcare industry continue to look for innovations that can provide quality care to patients at a reasonable cost. But they can't do it alone. Today, the manufacturing industry is an important partner, with one particularly bright opportunity focused on Medical Additive Manufacturing/3D Printing (AM3DP).

From anatomical models to early bioprinting applications, the use of AM3DP is providing benefits for patients and physicians/institutions including:

- Better patient outcomes
- Less time in the operating room
- Reduced costs

In 2017, as outlined in this Annual Report, collaboration between hospitals, device manufacturers, U.S. Food and Drug Administration (FDA), and partners such as SME, led to extraordinary strides in identifying industry trends, opportunities, challenges and solutions.

These partnerships drive efficiency through best practice sharing as well as accelerate innovation for applications such as bioprinting and tissue fabrication. They also lay the groundwork for 3D printing of organs and scaling up production of tissues which are still decades away.

With millions of patients already directly impacted by the technology, this momentum continues into 2018 and beyond where AM3DP will continue to positively impact public health and drive strong business results.

This 2017 Annual Report covers:

- Industry Overview
- SME's 2017 Medical AM/3DP Survey Results
- 017 Highlights
- Expectations for the Future

By the Numbers

FUTURE OF GLOBAL HEALTHCARE

$8.7 TRILLION

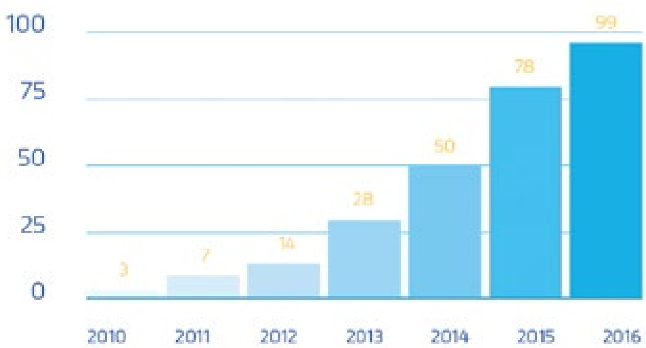
Global healthcare spend projected by 2020[2]

11.5%

Percent of total population over 65 years of age.[3]

HOSPITALS IN THE US WITH A CENTRALIZED 3D PRINTING FACILITY

Using Materialise Mimics technology



OVERALL 3D PRINTING/AM GROWTH[4]

21% Compound annual growth rate (CAGR) of AM industry in 2017

$7.3 BILLION 2017 AM market size

11% Approximate revenues from medical/dental pieces

97% AM professionals who expect an increase in Medical AM/3DP applications[5]

3D PRINTING IN HEALTHCARE

3200%

Increase in the number of hospitals in the U.S. with a centralized 3D printing facility between 2010 and 2016 *(using Materialise Mimics technology)*[5]

16

Number of hospitals out of the top 20 as ranked by U.S. News and World Report that have implemented a medical 3D printing strategy *(using Materialise Mimics technology)*[6]

A Look Back

Dramatic news headlines imply that the use of additive manufacturing/3D printing in medicine is a new way to save and improve lives. The truth is, it's not so new. Twenty years ago anatomical models were beginning to be used for planning complicated surgeries. In 2000, hearing aid cases were being 3D-printed and within a few years became industry standard. Medical applications have been a leader in taking 3D printing technology far beyond a product development tool. The combination of using medical imaging data to create patient-matched devices and the ability to manufacture structures difficult to produce with traditional technologies is compelling to an industry always looking for ways to innovate.[6]

FACTORS CONTRIBUTING TO MEDICAL 3D PRINTING INCREASES

3D printing applications in medicine are increasing due to many factors:

- **Precision medicine: Better patient outcomes and lower costs from developing treatment plans and devices specifically for the patient**
- **3D printing processes: More accessible technology becomes mainstream**
- **Materials: Workable materials from polymers to metals allow for varied applications**
- **Software: Improved software allows for faster and more accurate segmentation of medical imaging files**
- **Resources: Industry rallying behind potential and sharing body of knowledge**
- **Studies: Growing evidence of patient outcomes and cost-effectiveness**

Medical 3D Printing Applications[7]

According to SME's 2017 Medical Additive Manufacturing/3D Printing Survey[8], 97 percent said they are expecting an increase in Medical AM3DP applications like those below. Underway are exciting innovations that are changing patient treatments such as 3D printed microbots made to "swim" through a patient's body and deliver drugs to cancer cells and 3D-printed specialized contact lenses developed to help epileptic wearers avoid seizures.

General (non-personalized instruments or prototypes). Examples: Specialized metal instrument for hospital/surgical use (e.g., plate bending); prototypes for iterative design process

Photo courtesy EOS

Prototype clamp produced with the EOS StainlessSteel 17-4 PH IndustryLine parameter set. Only the internal springs were not 3D printed.

Anatomical Modeling (patient-matched anatomical models from medical imaging studies like CT/MRI). Examples: Cranial conjoined twins model for training and simulation; scoliosis model; simulation/demo model (e.g., stent deployment, implant sizing)

Photo courtesy Stratasys

Printed with resin, this anatomical hand features clear sections of skin, revealing veins, muscles, and bones, thus making it useful for training medical students and educating patients.

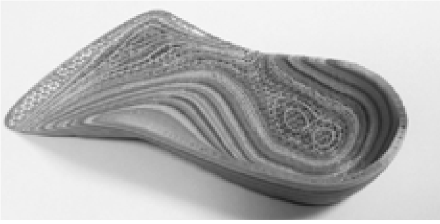
Surgical Planning (templates, guides and models after preparing a patient-specific surgical plan in a software environment/3D printed items brought into operating room). Examples: Surgical marking guide; implant placement guide; radiation shield; surgical saw guide.

Photo courtesy 3D Systems Healthcare

Anatomical model of conjoined McDonald twins with guides developed via virtual planning for separation and the 3D-printed.

Precision Prosthetics (patient-matched implants, prosthetics, or orthotics). Examples: Small quantity cases (e.g., oncology case); knee replacement; nasal stent; hearing aid cases

Photo courtesy Arkema Inc.



An orthopedic shoe insert designed to provide comfort, pain relief, and orthopedic correction.

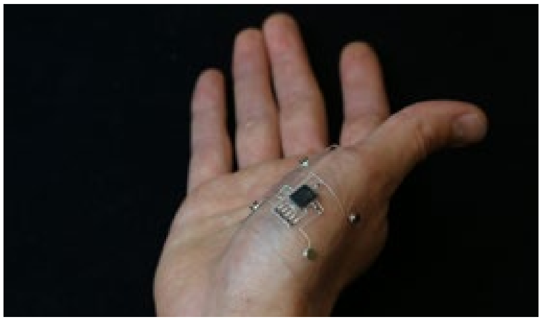
Permanent Implants ("off-the-shelf" implants). Examples: Metallic implants (e.g., titanium, cobalt chrome alloy); tracheal splint; cranial implants.

Photo courtesy GE Additive/Arcam

Cobalt Chromium Orthopedic Knee implant

Active & Wearable Devices (devices that include electronics or other active elements). Examples: Wearable sensors; lab on a chip; microfluidics.

Photo courtesy Alex Valentine, Lori K. Sanders, and Jennifer Lewis/ Harvard University



Potential application of 3D printing flexible sensors include custom strain and pressure sensors to track post-surgery rehab progress with direct measurement of joint angles, body position, and extremity deflection.

Bioprinting/Tissue Fabrication (materials that incorporate living cells). Example: Tissues or scaffolds used for regenerative engineering, drug delivery, drug discovery, etc.; organ on a chip.

Photo courtesy SME

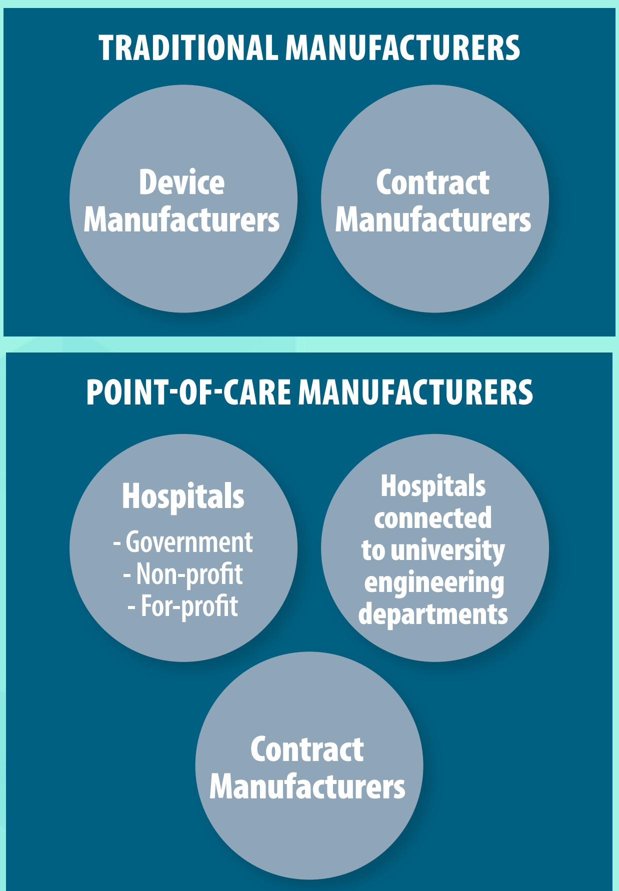
Bioprinted gelatin for tissue repair and regeneration including bioprosthetic ovary developed at Northwestern University.

The Players

Traditional manufacturers such as device manufacturers make up the bulk of the industry, often partnering with contract manufacturers. Smaller hospitals may also work with contract manufacturers for segmentation and to prepare files for 3D printing.

Larger research hospitals may have their own in-house 3D printing laboratories (see POC Manufacturing Sidebar).

Another important group are the bioengineers doing research as industry looks at continuing innovation for applications such as bioprinting and tissue fabrication. While 3D printing of organs and scaling up production of tissues are decades away, research can be accelerated with additional focus.



> "Forward-looking hospitals are implementing on-demand 3D printing service lines and, in turn, are reaping benefits of an improved patient experience, better training of physicians and growth in innovation which can drive non-traditional revenue streams in addition to the inherent cost saving that can be realized."
>
> —Todd Pietila, Global Business Development, 3D Printing for Hospitals, Materialise

Point-of-Care Manufacturing

Point-of-Care (POC) is a non-traditional form of manufacturing referring to the just-in-time creation of anatomical models, surgical instruments, prosthetics, scaffolds, and other 3D printed applications at the place of patient care, based on their personal medical imaging data (MRI, CT, or surface scans). Larger research hospitals may have their own in-house 3D printing laboratories while smaller hospitals may work with contract manufacturers. Medical "hubs," such as the 150 hospitals and over 800 outreach centers run by the U.S. Department of Veterans Affairs (VA), are standardizing 3D printing best practices across its locations.

With more successes and precedents for this model, there will be a greater shift to POC. Already, in the last decade, hospitals with a centralized 3D printing facility have increased significantly, according to Materialise. Traditional manufacturers, which often supplement hospital POC projects, are a valuable part of the partnership. Whether providing anatomical models for use in the operating room, a sterile field, or handling overflow projects, these partners work closely with surgeon groups and clinicians, bringing years of industry experience to the table.

The POC trend is forecast to strengthen as software and hardware/materials continue to improve, and regulatory guidelines become clearer.Further industry collaboration, additional clinical studies, and regulatory guidance will help encourage innovation and ensure in-hospital manufacturing becomes the standard of care.

INDUSTRY COLLABORATION

Activities from regulatory agencies, industry, and clinical groups, and technology providers are helping to expand the impact of Medical AM3DP. These include:

- **The U.S. Food and Drug Administration (FDA)**
- **SME Medical Additive Manufacturing/3D Printing Workgroup**
- **RSNA 3D Printing Special Interest Group**
- **DICOM Workgroup-17 3D Manufacturing**
- **Additive Manufacturing Standardization Collaborative (AMSC)**

Benefits of POC

While POC may not be for every hospital due to the investment in equipment and staff, for those that are considering this business avenue, there are a number of benefits:

- Quicker Turnaround: Traditionally, models, prosthesis, instruments and more were 3D printed at remote production facilities and sent back to the hospital. POC manufacturing significantly improves turnaround time by the eliminating shipping step.
- Team Approach: Clinicians and engineers can collaborate onsite. Radiology is most often the home of 3D printing within the hospital. Providing needed anatomy and imaging knowledge, radiologists are the facilitators, leaders, and champions of POC.
- Onsite Quality Control: High quality standards at an internal lab are easily monitored.
- Improves Patient Consultation: Patient-matched anatomical models allow better patient communication and education.
- Pre-surgical Planning, Intraoperative Planning: Clinician involvement through each step helps with planning. On-site printing allows for quicker adjustments if needed. This preparation also saves time in the operating room, lowering costs.
- Improved Outcomes: Surgeons and engineers pool knowledge and skills to address issues and create innovative patient solutions.
- Potential to Impact More Patients: Ultimately, 3D-printed POC applications will be nearly as common as off-the-shelf and available to a wide range of patients.

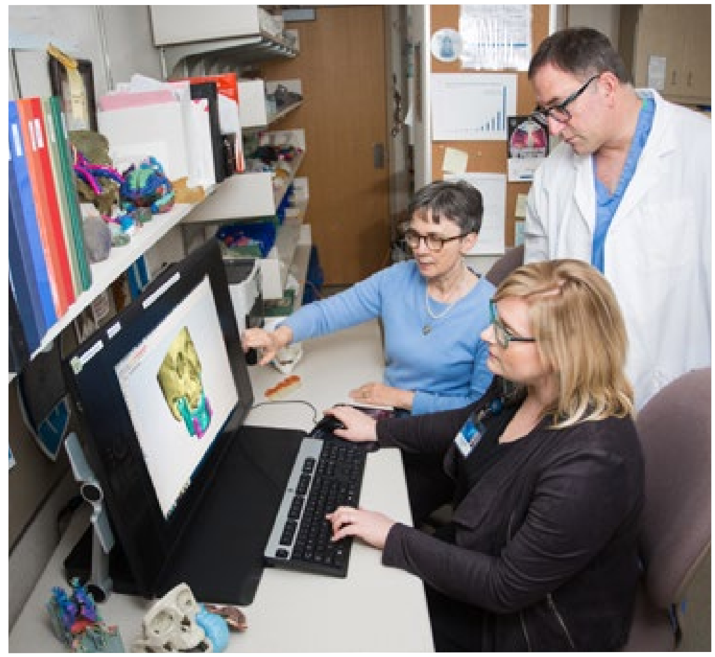
Medical AM3DP in Action

From point-of-care manufacturers to device manufacturers, the industry is successfully exploring — and investing in — the potential of Medical AM3DP. The following are examples:

Mayo Clinic Committed to POC Manufacturing

Mayo Clinic in Rochester, Minn. has fully embraced its role as a POC manufacturer for anatomical modeling, virtual surgical planning, and some Class 2 medical devices. The institution has invested more than $1 million for a lab and equipment to cover the entire enterprise. Staffing is robust with one full time radiologist, two engineers, full time segmenters and others onsite which leads to valuable collaboration. Jonathan M. Morris, MD, Associate Professor of Radiology/ Co-director of the 3D Anatomic Modeling Lab, Mayo Clinic, said that the major benefit to in-hospital 3D printing is allowing the clinical teams, engineering, and radiology to interact where the medical care is being delivered. This close relationship helps them "innovate on the fly" and collaboratively solve complex medical and surgical problems in a way not possible if they worked in silos. Mayo surgeons across multiple specialties regularly use accurate 3D printed models based on patient CT or MRI scans to plan complex surgeries. This has led to improved care and better outcomes through innovative approaches, less time under anesthesia and in the operating room (OR), shorter hospital stays, smaller incisions, and a more efficient use of overall resources.

Photo courtesy Mayo Clinic



Dr. Jane Matsumoto and Dr. Jonathan Morris, co-directors of Mayo Clinic's 3D Printing Lab, work with biomedical engineer, Amy Alexander, to prepare files for 3D printing.

> **"At Mayo, we're a destination medical center committed to giving our patients the highest level of care and one of the ways we are doing that is with 3D printing."**
>
> — Jonathan M. Morris, MD, Associate Professor of Radiology/Co-director of the 3D Anatomic Modeling Lab, Mayo Clinic

Device Manufacturers Help Transform Healthcare Delivery

The use of medical 3D printing technology has the potential to transform healthcare delivery, resulting in truly personalized healthcare solutions for patients and consumers, according to Dan Fritzinger, manager, Global Instrument Innovation for DePuy Synthes, part of the Johnson & Johnson family of companies. To better serve patients and consumers, J&J established the 3D Printing Center of Excellence to pursue and rapidly advance this new avenue of technology, which offers benefits over traditional manufacturing, including customization, efficiency, personalization and globalization. "3D printing was once an innovation of the future and is now an exciting reality," said Fritzinger. "This technology presents enhanced career growth opportunities for each new generation of engineers and manufacturers entering the workforce."

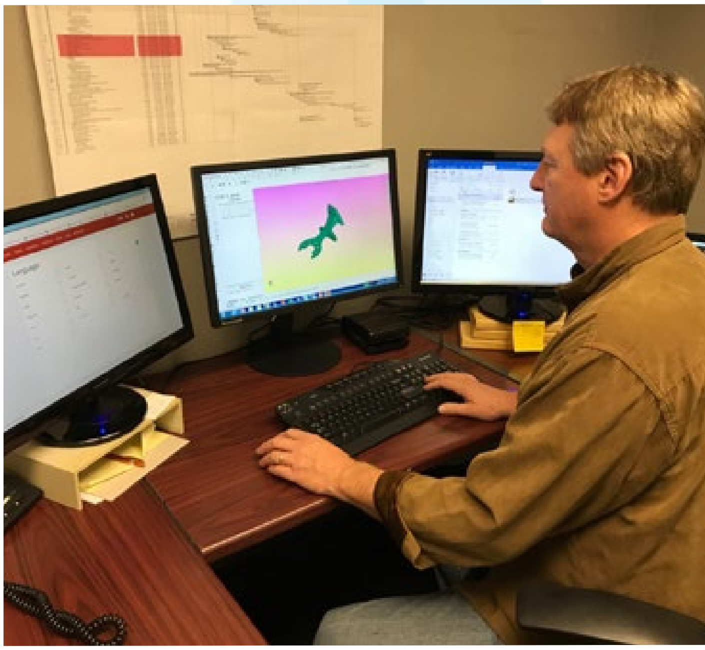


Photo courtesy DeputSynthes

Dan Fritzinger designs a cutting tool to be produced with additive manufacturing

Bioengineers Wanted

With rapid growth and potentially life-saving benefit, there is urgency around recruiting and training bioengineers who can handle what is, in theory, a new occupation with unique skillsets.

These bioengineers will have the exciting challenge of not just addressing current medical application needs — but of developing innovations that propel us into a future of enhanced healthcare. There is a challenge, however, to meeting this potential: a lack of skilled professionals who combine the diverse expertise in biology and engineering that is needed to imagine, design and produce complex anatomical models and other medical innovations using 3D printing.

Competency Model

To build a common language among employers and job candidates, the SME Medical Additive Manufacturing/3D Printing Workgroup, comprised of medical device manufacturers, clinicians, technology providers, and educators, has developed a Competency Model that covers these three main job roles:

- **Medical 3D Printing Engineer**
- **Medical AM Engineer**
- **Medical AM/3D Printing Technologist**

The Competency Model helps with the development of job descriptions as well as curriculums and job training programs, and is part of the process for ensuring consistency for engineers and technologists pursuing careers in medical 3D printing. Another resource is SME's Additive Manufacturing Body of Knowledge that serves as the basis for the Additive Manufacturing Fundamentals Certification program.

"3D printing in the medical field demonstrates the fascinating intersection of medical imaging, surgical insight, engineering, and human artwork. There is a big demand for this kind of medical design at hospitals, universities and device manufacturers."

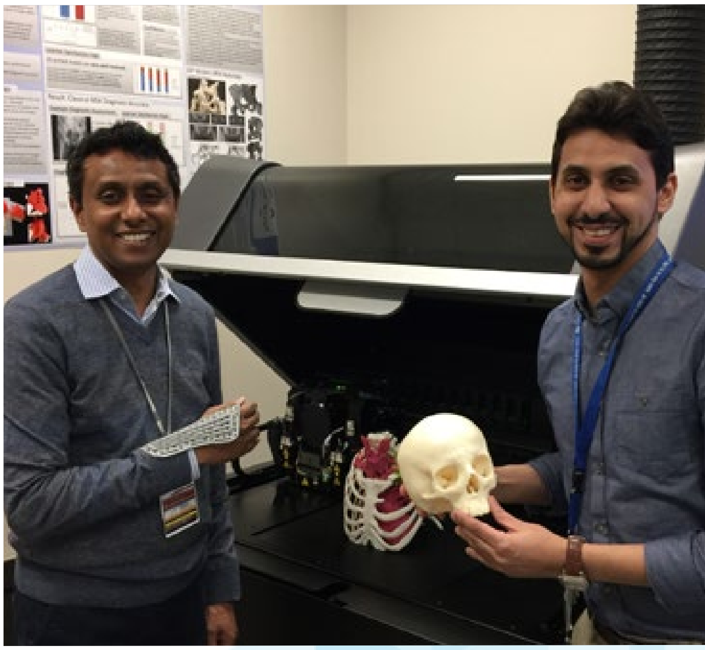
— Amy Alexander, biomedical engineer in the Mayo Clinic Department of Radiology's Anatomic Modeling Lab, Rochester, Minn.

Challenges for Medical 3D Printing Growth

From a stringent regulatory environment to funding, this burgeoning industry is seeing challenges (see survey results), which the industry is actively addressing:

- **Regulatory environment:** With little history of medical 3D printing applications, regulations are still being formulated. In December 2017, the FDA released guidance on 3D printed medical devices, [9]"preparing for a significant wave of new technologies that are nearly certain to transform medical practice," according to a statement.
- **Reimbursement:** Costs are not reimbursed through health insurance. Typically, hospitals will cover the cost as it saves time/ costs later. For surgical planning, for instance, it's cheaper in the long run since it saves time in the operating room. Device manufacturers may include a patient-matched device as part of an implant kit without separate reimbursement because it adds value to their implant, providing them with an edge over other device manufacturers.
- **Technology:** Materials, processes and software for 3D printing for medical applications are evolving. Manufacturers are continually learning more about interaction between materials and the 3D printer, biocompatibility, validation processes, creating standards for raw material suppliers, and more. Segmentation is complicated and requires specialized expertise. The segmentation software is costly.
- **Qualified workforce, recruiting, talent:** The blending of biology and engineering is a relatively new need and there is a strong demand. Educators, industry, and medical institutions are working together to make recruiting and training a priority.

Photo courtesy Frank Rybicki



Adnan Sheikh, MD and Waleed Althobaity, MD with some of the anatomical models produced at the University of Ottawa, The Ottawa Hospital

Moving Forward

By bringing together the industry to collaborate, share information, and work together to address the challenges beyond technology, stakeholders will be able to quickly leverage new technology developments. This emerging technology will improve patient outcomes and create more efficient and cost-effective practices.

Collaboration will also encourage innovation, by moving Medical AM3DP beyond anatomical models and surgical guides to bioprinting, tissue fabrication and, perhaps one day, even 3D printed organs.

Photo courtesy Stratasys

Patient holding her heart model used by physicians at Nicklaus Children's Hospital to aid in planning for a double aortic arch surgery.

Photo courtesy 3D Systems

Katie Weimer, 3D Systems with twins after separation surgery performed with support from 3D-printed anatomical models and surgical guides along with virtual surgical planning.

Thank you to the members of the SME Medical AM3DP Workgroup who have contributed to this report AND for all their efforts to impact more patients with the benefits of AM3DP.

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- Travis Bellicchi, Maxillofacial Prosthodontist, Indiana University School of Dentistry
- Danielle Beski, Application Engineer, Materialise
- Matthew Bramlet, Director, Jump trading Simulation & Education Center at OSF
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- Brent Chanin, CEO, CTO, Mediprint.us
- Andy Christensen, Somaden
- Kenneth Church, Research Scientist, nScrypt
- Meghan Coakley PhD, Project lead, NIH 3D Print Exchange, NIH
- James Coburn, Sr. Research Engineer, FDA
- Michael Coleman, Development Engineer, HCL America
- Daniel Crawford, CEO and Founder, axial3D
- Brent Cross, Simulation Engineer II, OSF HealthCare Systems
- Ayanna-Rene De Noon, Mechanical Engineer/Instructor, The University of the West Indies
- David Dean PhD, Associate Professor, The Ohio State University
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- Quo Tuan Duong, Sales Representative, Miller 3D
- Dima Elissa, CEO, Founder, VisMed3D
- Alejandro Espinoza Ph.D., Assistant Professor, Rush University Medical Center
- Randy Favot, Intern, SME
- Davis Fay, Core Manager, University of Minnesota-Twin Cities
- Dan Fritzinger, Engineering Team Lead-TruMatch, Depuy Synthes
- Michael Gaisford, Director of Marketing, Stratasys
- Laura Gilmour, Medical Account Manager & Business Development, EOS of North America
- Chuck Hansford, Director Advanced material processing, Tecomet
- Ola Harryson PhD, Professor, North Carolina State University
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- Jennifer Herron, Emerging Technologies Librarian, Indiana University School of Medicine
- Evan Hochstein, Applications Engineer, Stratays
- Peyton Hopson, Engineering Fellow, Johnson & Johnson
- Adam Jakus, Hartwell Postdoctoral Fellow, Northwestern University
- Joseph Johnnie, Design Engineer, Medivators
- Benjamin Johnson, Director Product Development, 3DSystems
- Sumanas Jordan MD, PhD, Plastic Surgery Fellow,
- Shay Kilby, Anaplastologist, NYU Langone
- Mukesh Kumar PhD, Director, Advanced Process Technology Group, Zimmer Biomet
- Geoff Lai, Sr. Product Development Engineer, Mighty Oak Medical
- Shuai Leng PhD, Associate Professor of Medical Physics, Mayo Clinic
- Chris Letrong, 3D Technologist, Stanford School of Medicine
- Peter Liacouras PhD, Director of Services, 3DMAC, Walter Reed national Military Medical Center
- Dave MacCutcheon, VP Product Management, TeraRecon
- Gaurav Manchanda, Strategy + Partnerships Lead, Healthcare, Formlabs
- Marcelo Martinez, Manager, Grado Cuatro SRL
- Jane Matsumoto MD,, Mayo Clinic
- Angie Mines, Product Development Engineer, Smith & Nephew
- Robert Morrison MD, Clinical Instructor and Fellow in Laryngology, Vanderbilt University Medical Center
- Reese Myers, Vice President of Product Development, WishBone Medical
- Roger Narayan, Professor, UNC/NCSU Joint Department of Biomedical Engineering
- Allan Noordvyk, Executive Director of Research, Change Healthcare
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- Godfrey Onwuboli PhD, President, Delta Additive Manufacturing
- Ibrahim Ozbolat PhD, Associate Professor, Penn State University
- Jayanthi Parthasarathy PhD, Director Biomedical Engineering, MedCAD
- Martin Petrak, President and CEO, Orthopaedic Innovation Centre
- Peter Piechocniski, Engineering Manager, Memorial Sloan Kettering Cancer Center
- Todd Pietila, Sr. Business Development Manager-Hospital 3D Printing, Materialise
- John Procter,, JMPro Innovation
- Michael Raphael, CEO, Direct Dimensions
- Justin Ryan, Research Scientist, Phoenix Children's Hospital
- Frank Rybicki MD, PhD, Professor, Chair and Chief, Department of Radiology, The Ottawa Hospital, General Campus
- Ben Salatin, Clinical Rehabilitation Engineer, US Department of Veterans Affairs / Albuquerque Veterans Hospital
- Janelle Schrot, Biomedical Engineering Business Development Manager, Materialise USA
- Victoria Sears, Graduate Student, University of Michigan-Dearborn
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- Rami Shorti PhD, Biomechanical Scientist, Intermountain Healthcare
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- Katie Weimer, Vice President, Medical Device Healthcare, 3D Systems
- Robert Wesley, 3D Printing Engineer, St. Louis Children's Hospital
- Neil Willner, Attorney, Wilson Elser Moskowitz Edelman & Dicker, LLP
- Kyu Won Shim MD, PhD, Professor, Severance Children's Hospital, Yonsei university, College of medicine
- Atif Yardimci Ph.D.,, Exponent
- Steven Yoon, Graduate Student, Columbia University

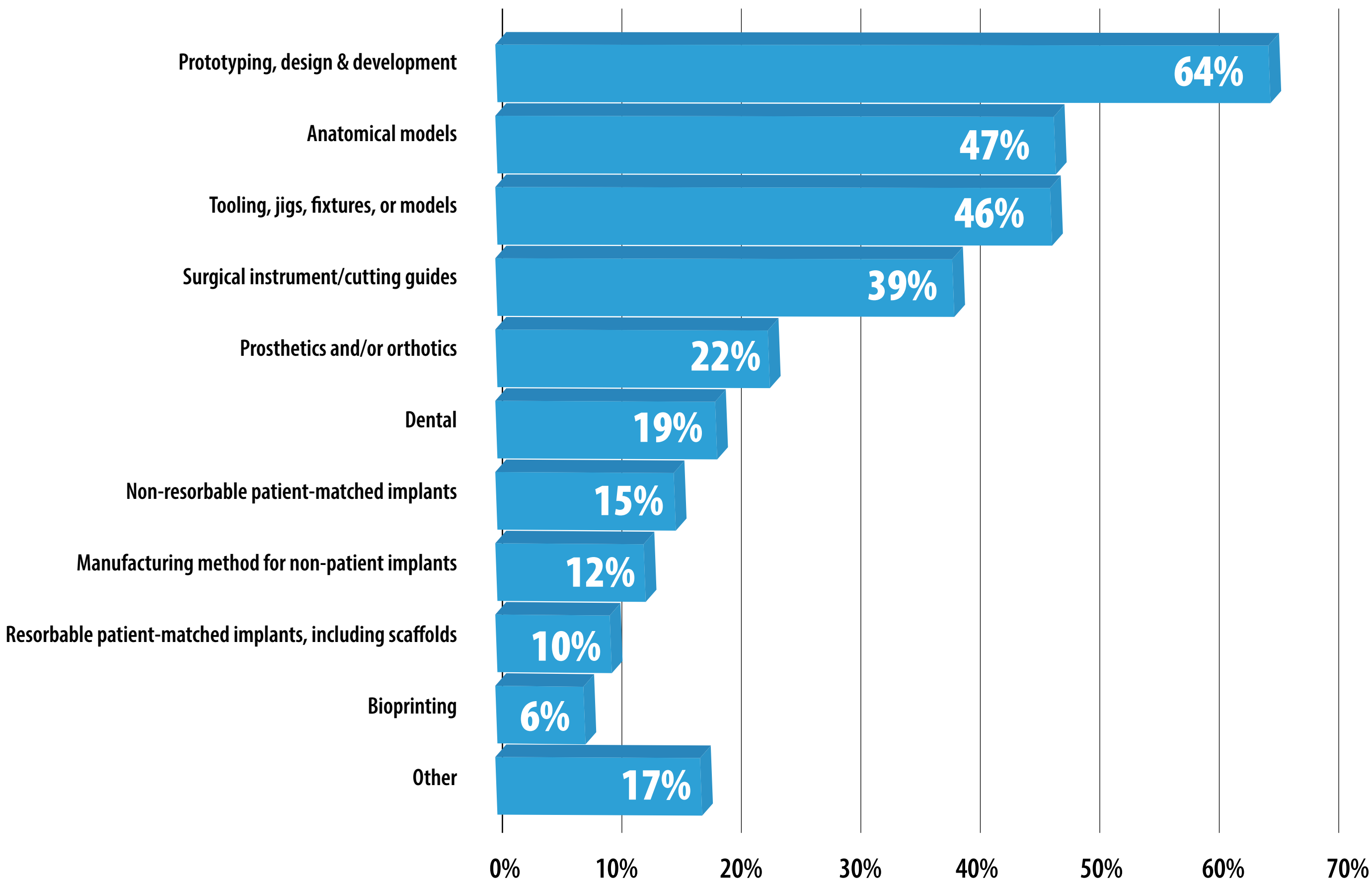
2017 Overview

During the fourth quarter of 2017, a diverse group using AM3DP for medical applications completed a survey sent by SME. Questions focused on their current applications and technology, as well as expectations of future use. Respondents represent medical device manufacturers, point-of-care (hospitals) manufacturers, researchers, and more. (See Appendix for respondent profile.) The results provide a snapshot of how AM3DP is being used for medical applications along with the challenges to impacting more patients with the benefits of the technology.

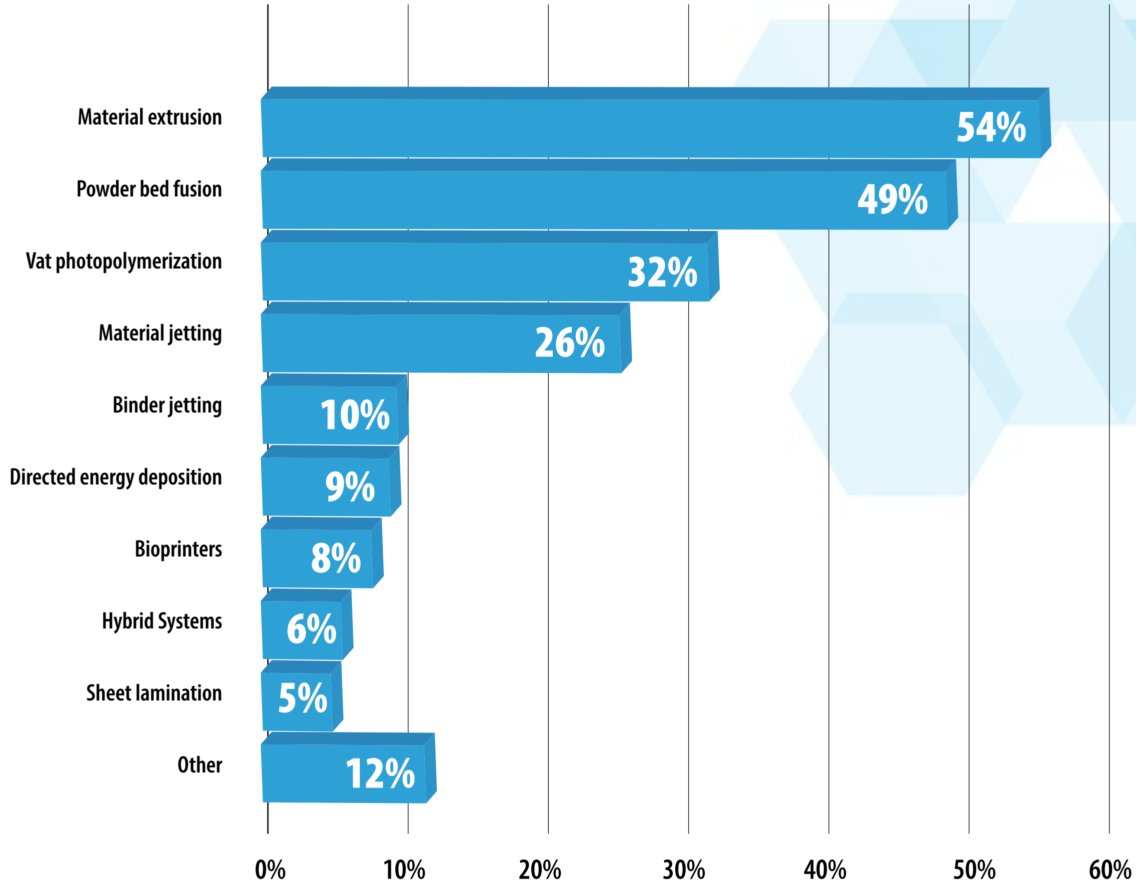
Applications, Technology, Process, & Impact

How AM3DP is being used

While prototyping remains the top use, anatomical models and surgical instruments are significant application areas. Other applications include microfluidics, education, management support, and packaging.



Technologies Used

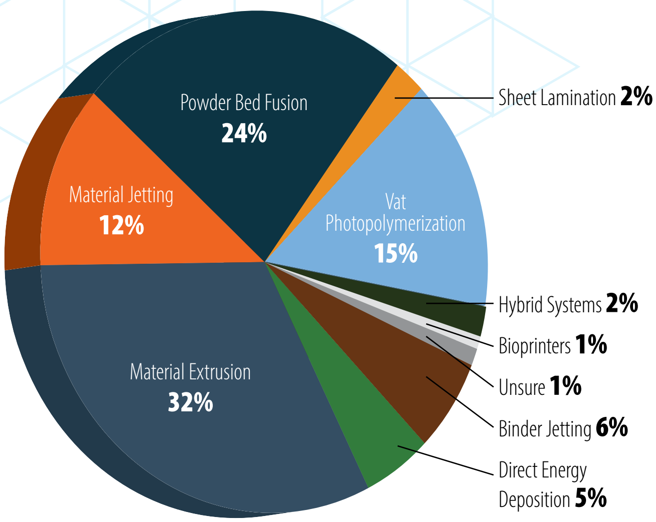


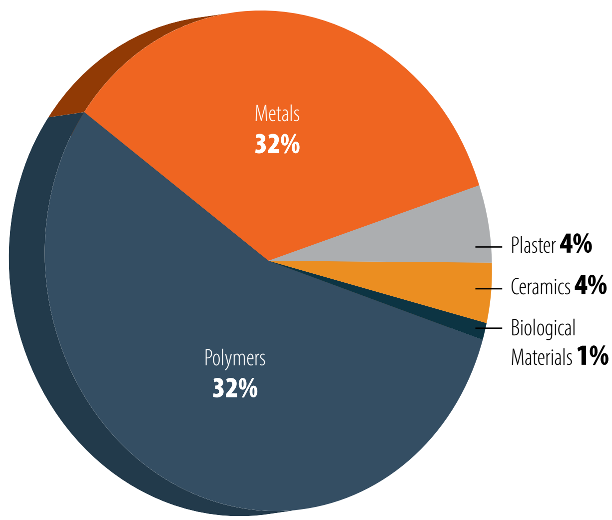
QUICK GUIDE TO AM3DP Processes: http://www.sme.org/uploadedFiles/AMtechnologies.pdf

- Sheet Lamination (includes CBAM, SDL, LOM)
- Hybrid Systems (deposition with CNC)
- Bioprinters
- Directed Energy Deposition (includes LMD, EBAM, LENS, DMD)
- Binder jetting (includes CJP, CBJ, ExOne)
- Material Jetting (includes MJM, MJP, SCP, Polyjet)
- Vat Photopolymerization (includes SL (A), DLP, CLIP)
- Powder Bed Fusion (includes LS, SLS, DMLS, EBM)
- Material Extrusion (includes FDM, FFF, MEM)

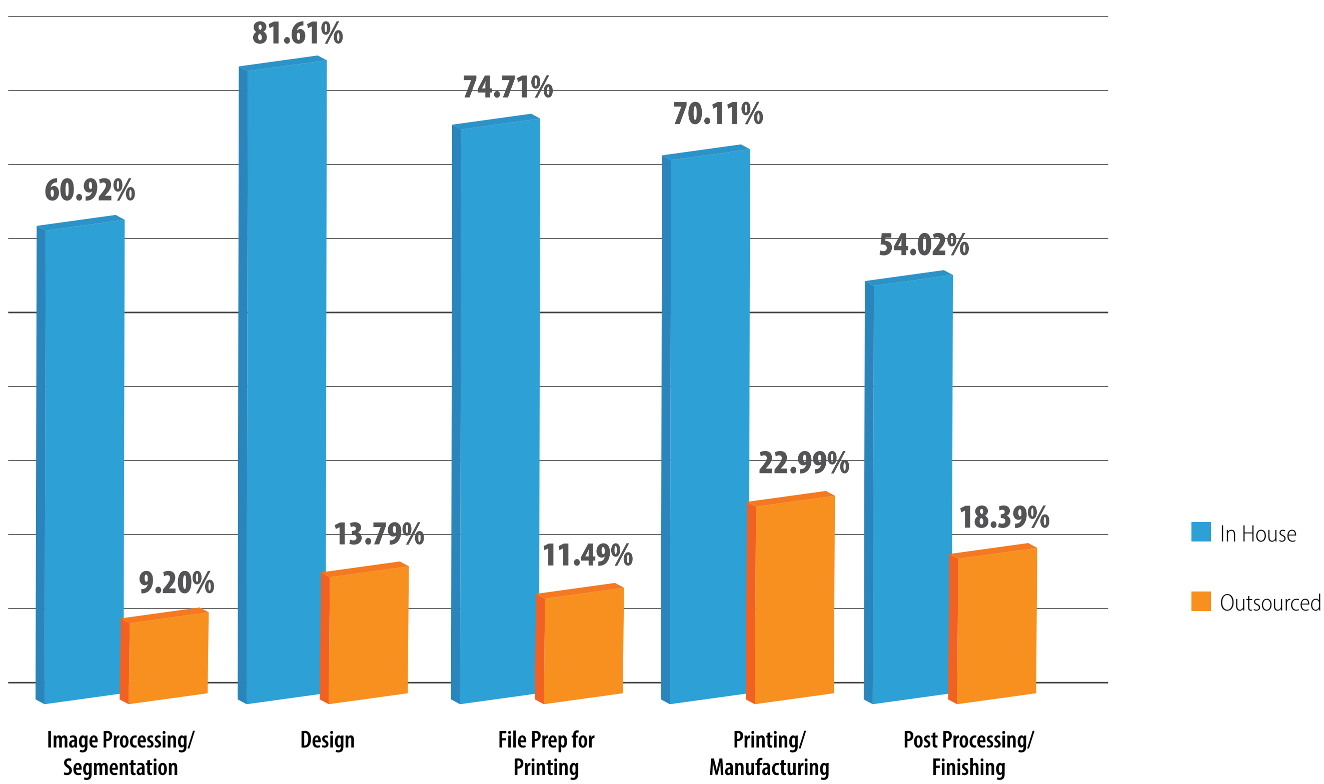
Application Areas: Technology, Materials, & Outsourcing

Prototyping, Design, & Development





Process Steps



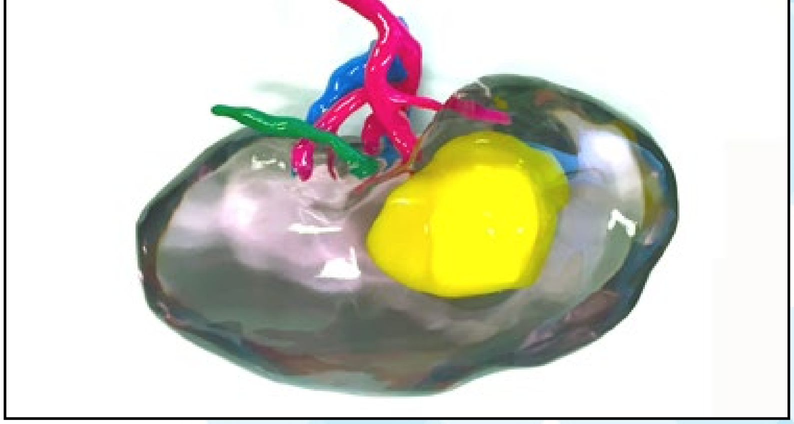
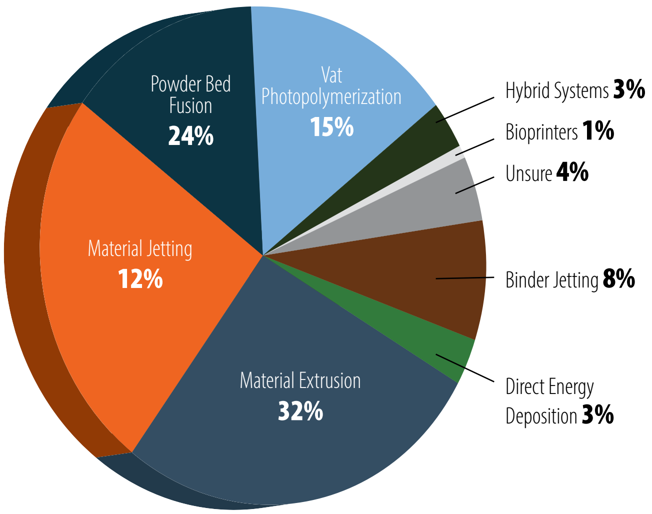
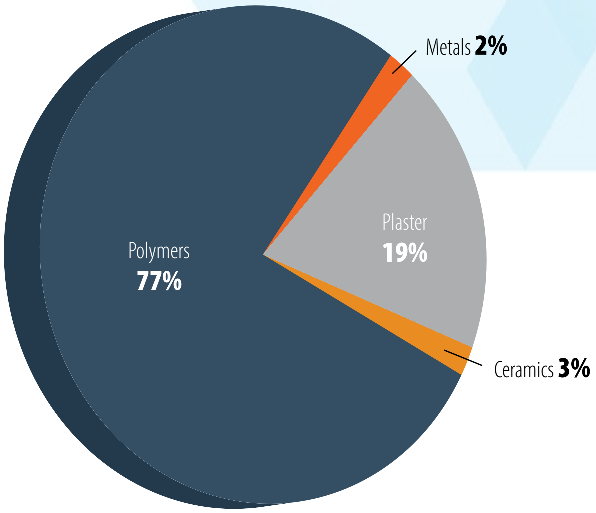


Photo courtesy Nicole Wake

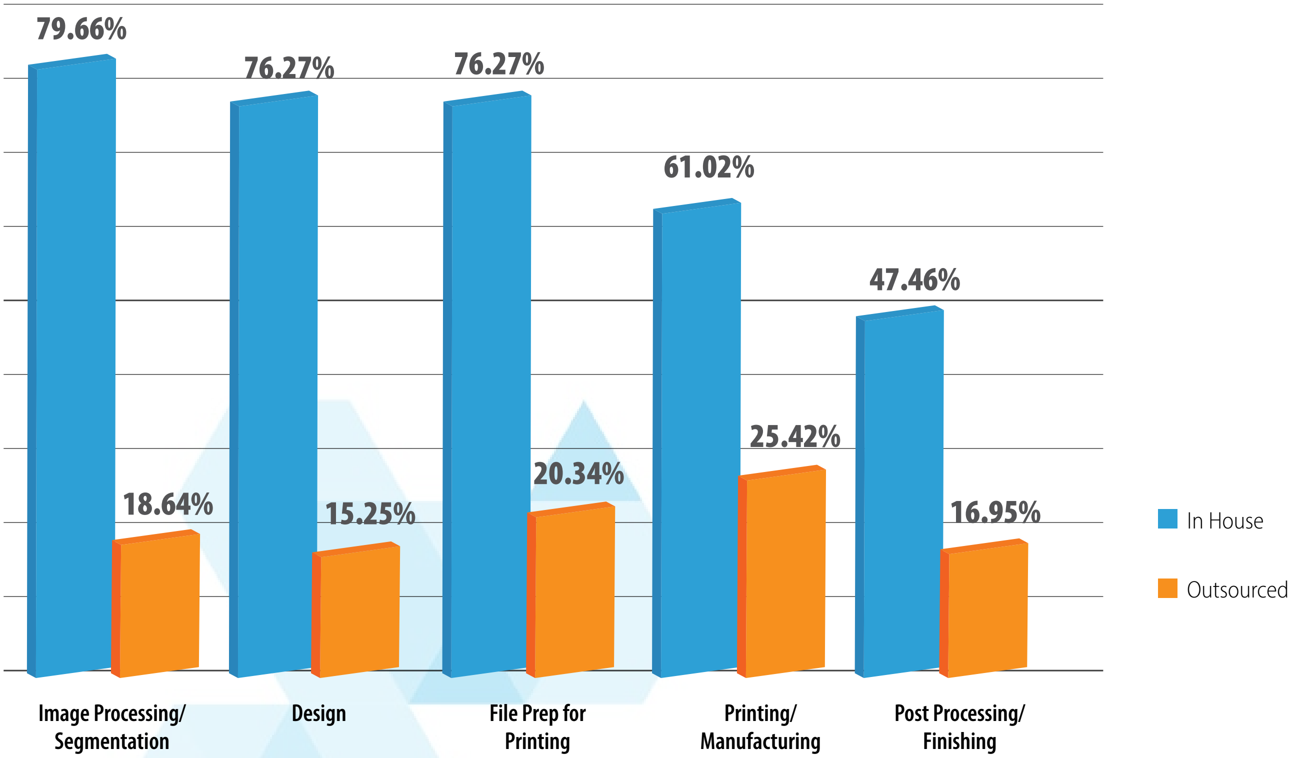
Patient-specific kidney tumor model generated from MRI data and used for surgical planning at NYU School of Medicine as part of an ongoing clinical trial.

Anatomical Models

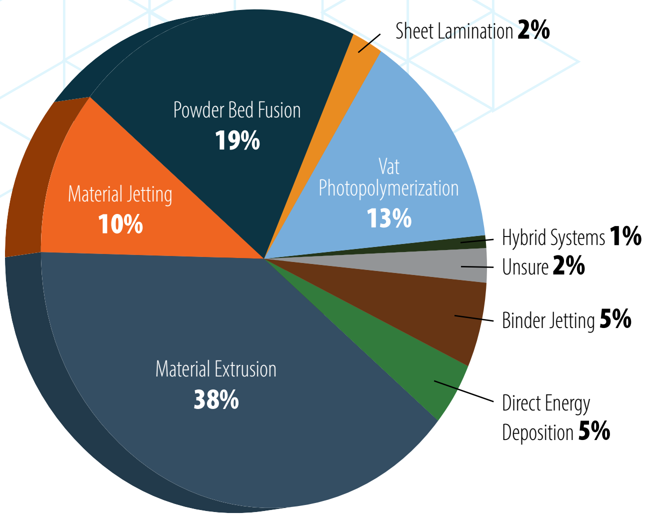


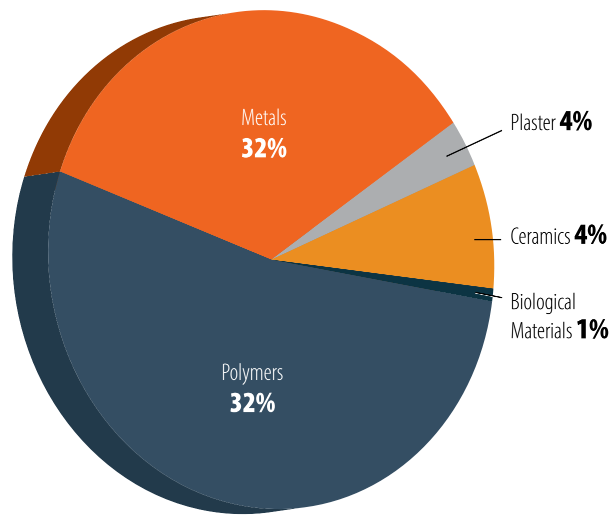


In-house or Outsourced: Process Steps



Tooling Jigs, Fixtures, or Molds





Process Steps

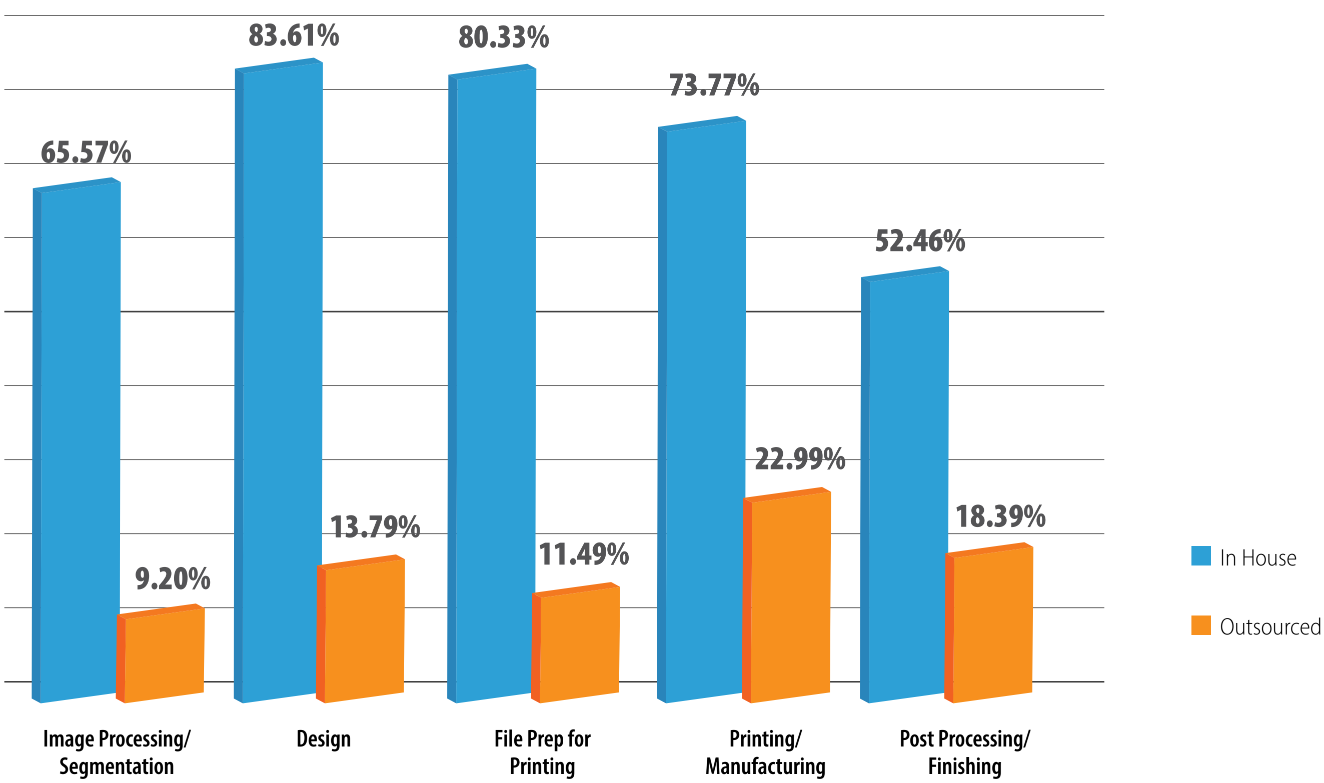
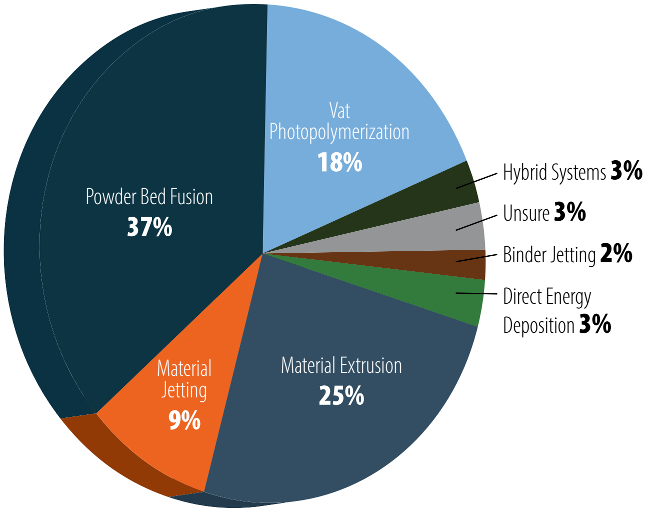
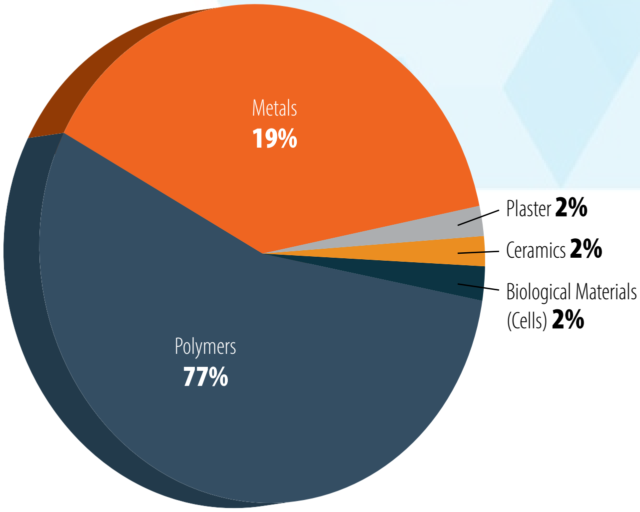


Photo courtesy Materialise

3D-printed osteotomy guide to correct a double forearm malunion; shown on patent's anatomical model.

Surgical Instruments/Cutting Guides





Process Steps

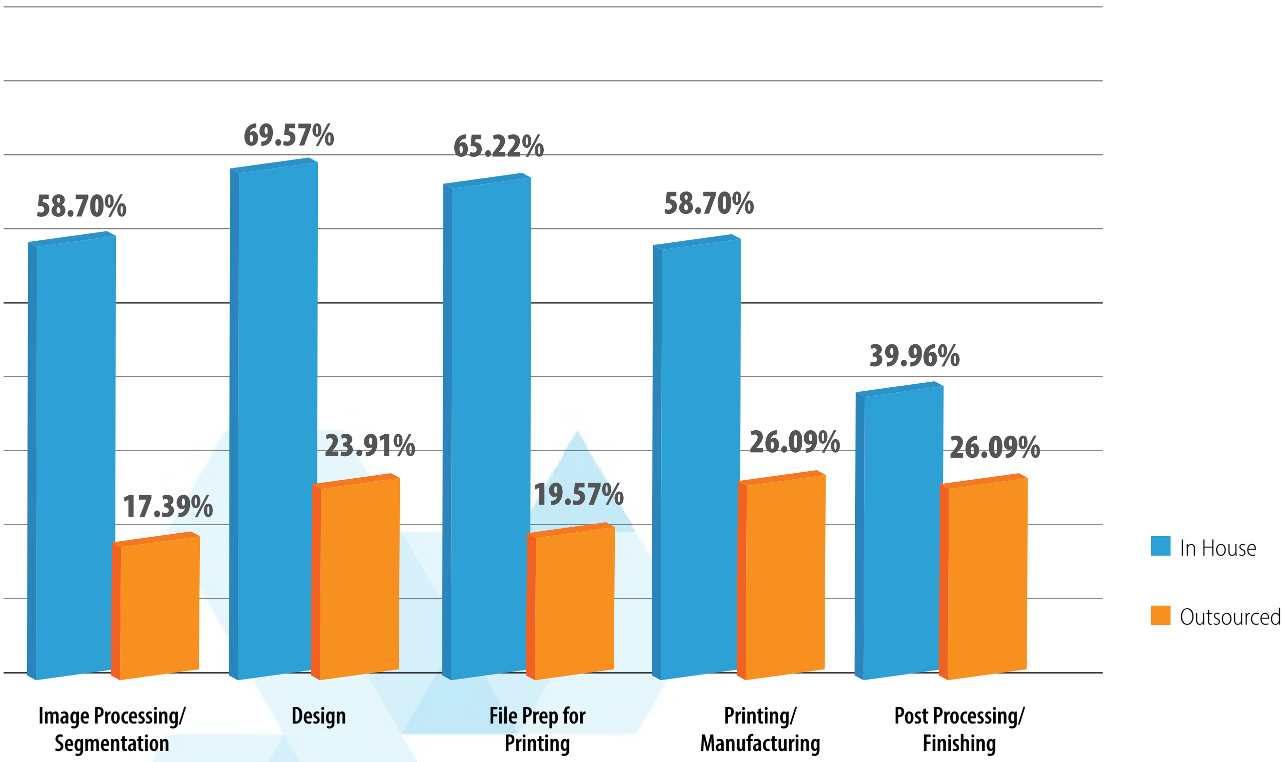
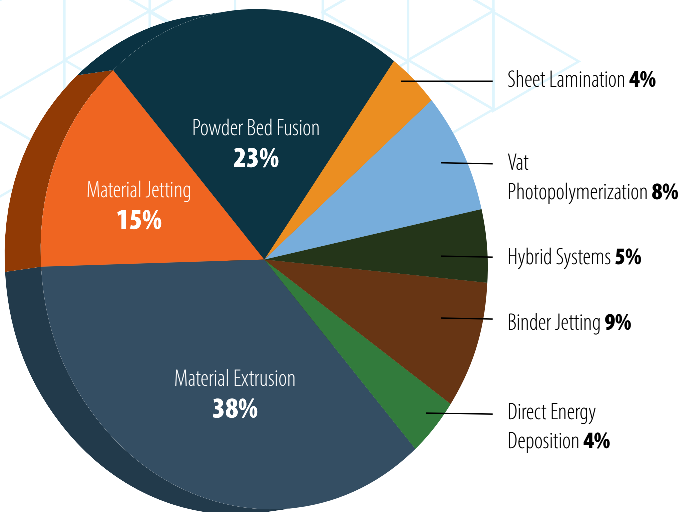
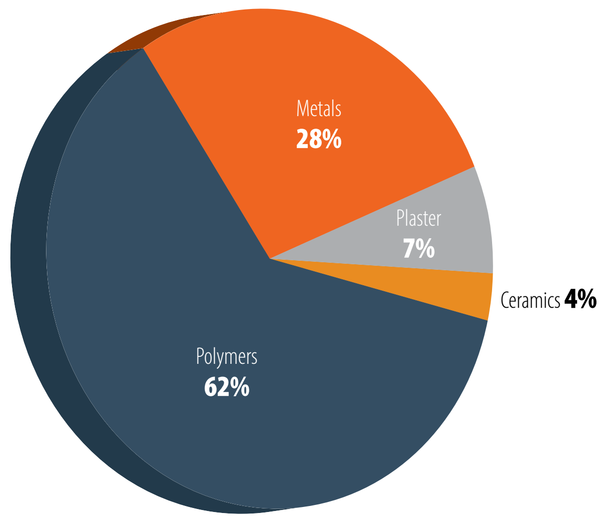


Photo courtesy New Attitude Prosthetic Design

Titanium thumb prosthesis to restore function after an amputation of the thumb with no residual amputation stump to support a conventional prosthesis.

Prosthetics and/or Orthotics





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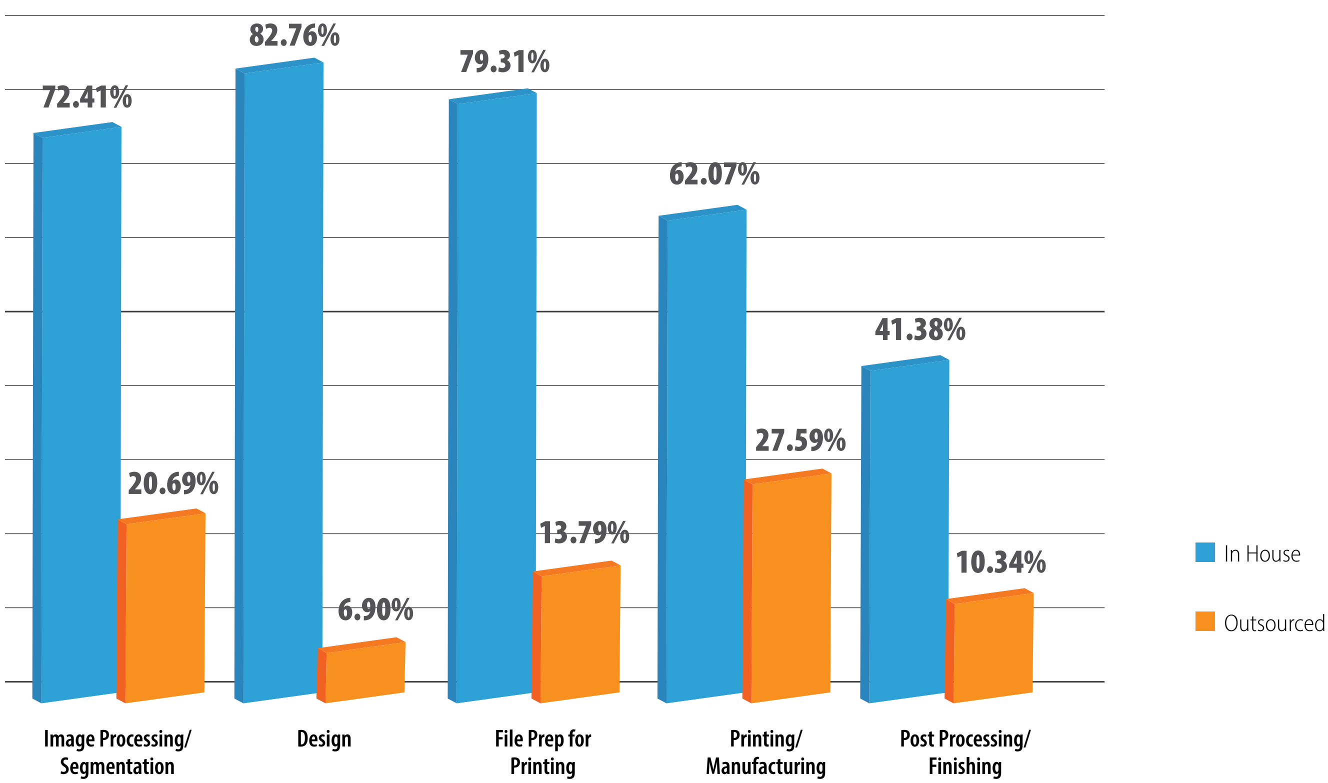
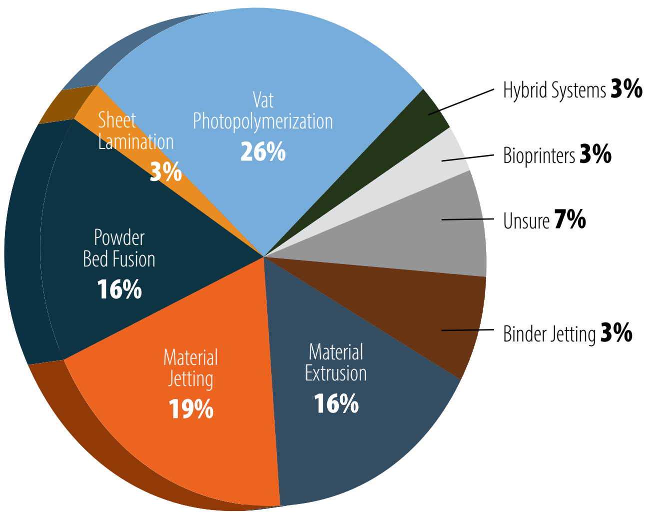


Dental



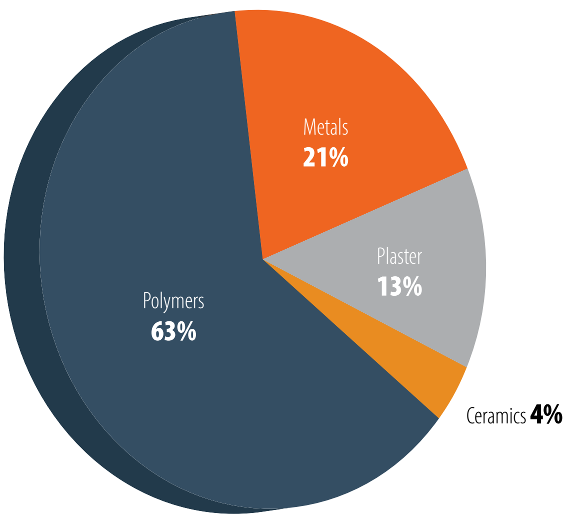
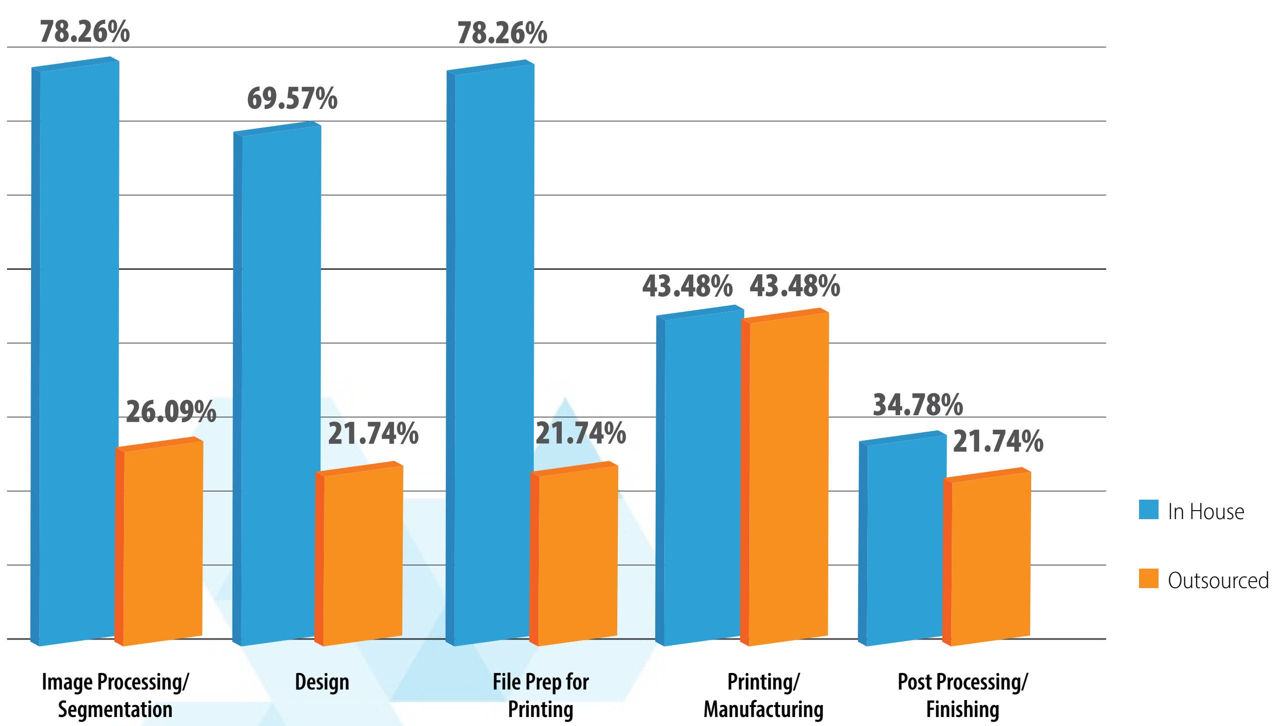



Photo courtesy GE Additive\Concept Laser

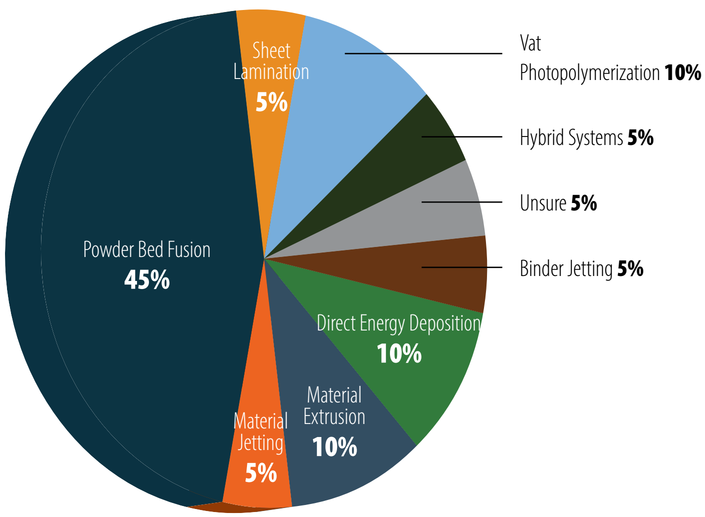
Cobalt Chrome dental bridge

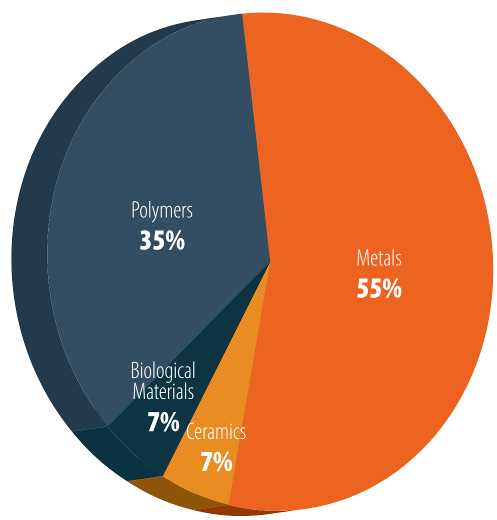
Process Steps



Metal hip implant attached to the pelvic girdle.

Non-resorbable Patient-matched Implants





Process Steps

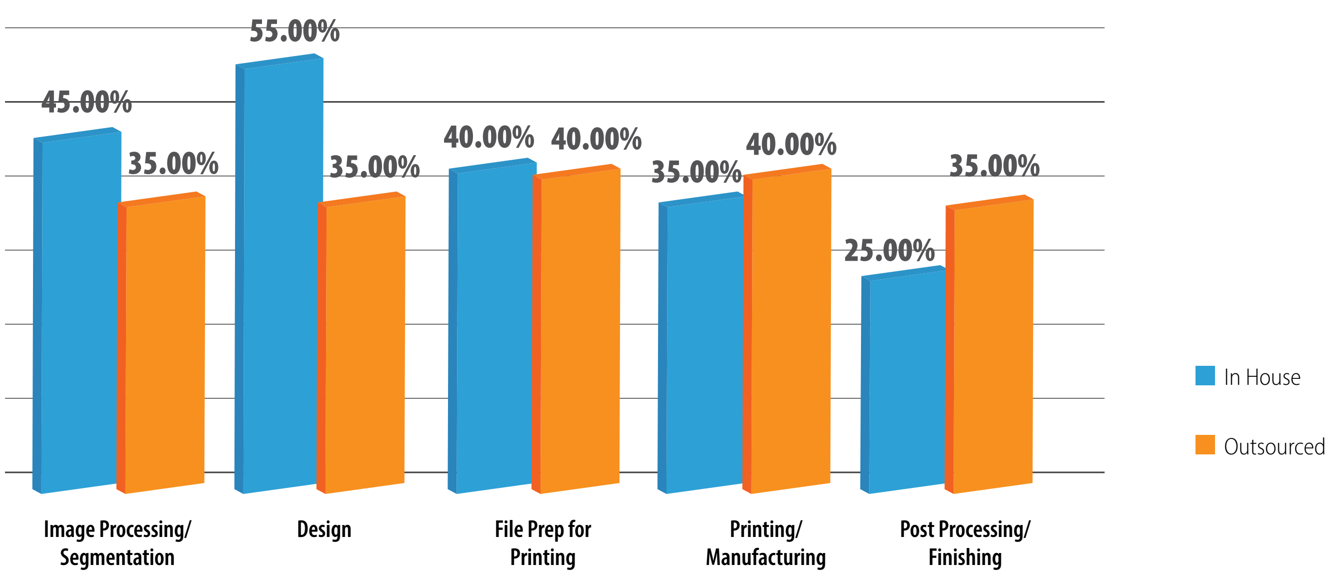
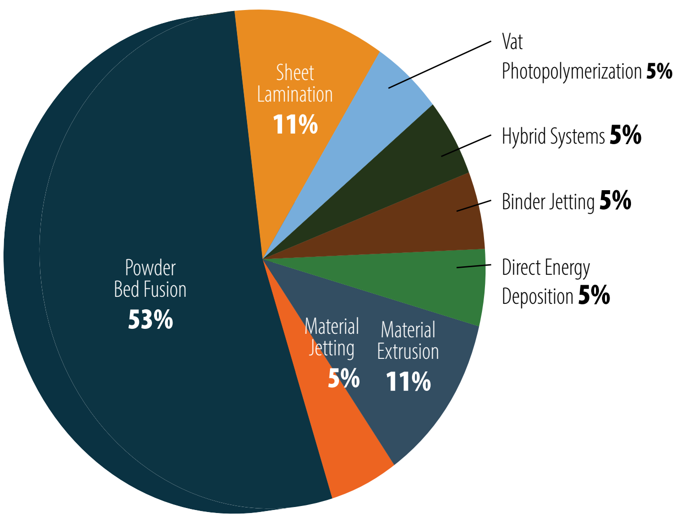
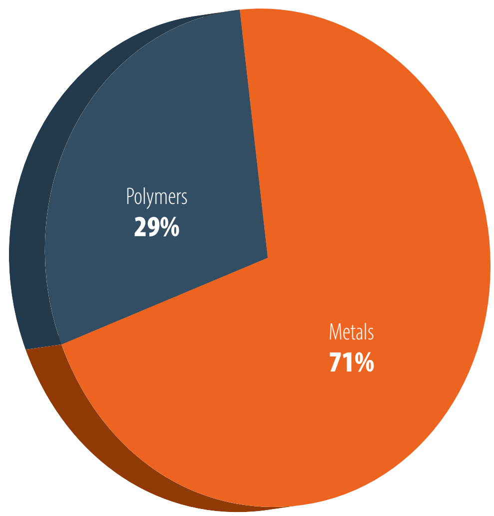


Photo courtesy SME

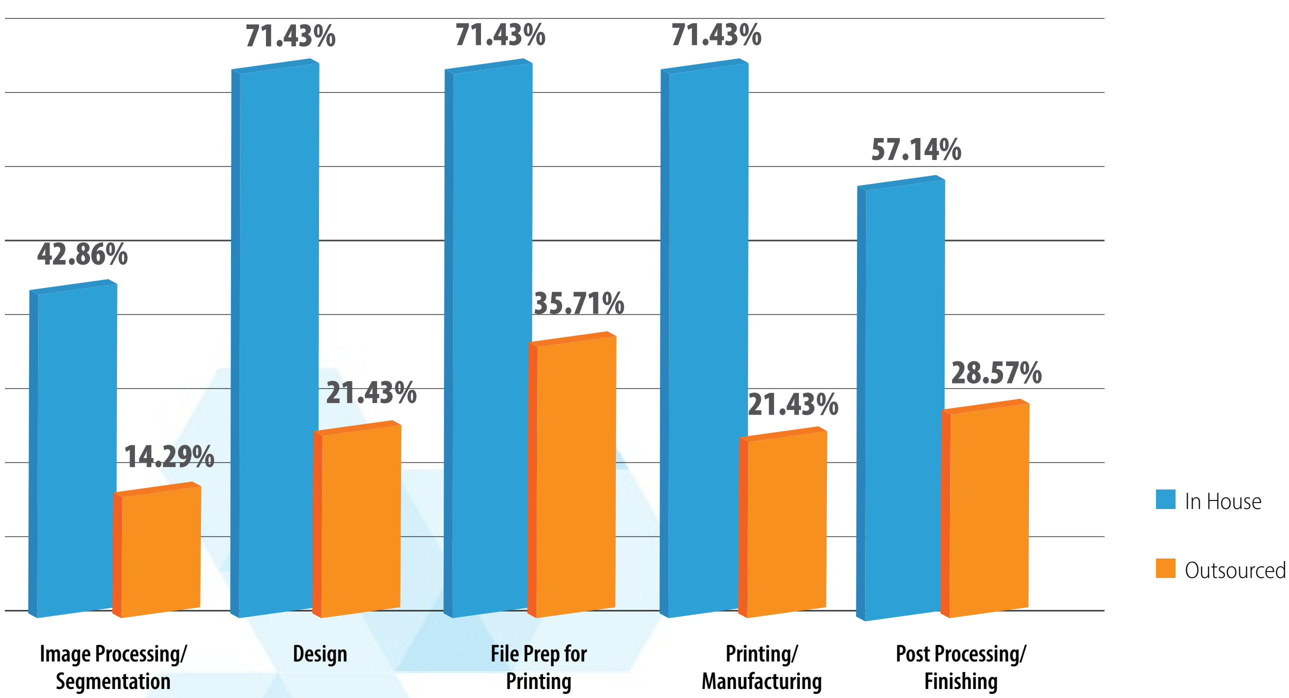
Titanium acetabular cup for hip replacement.

Manufacturing Method for Non-patient-matched Implants

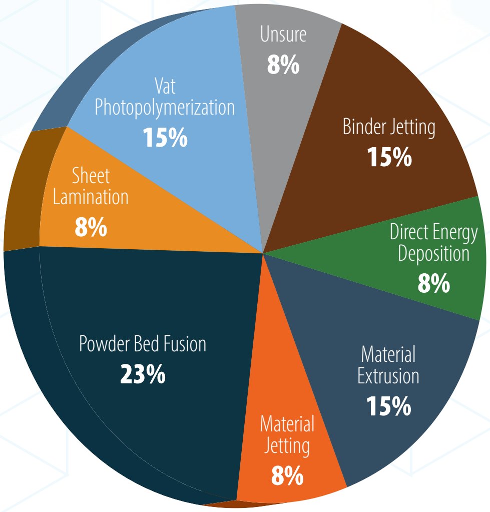




Process Steps



Resorbable Patient-matched Implants, Including Scaffolds



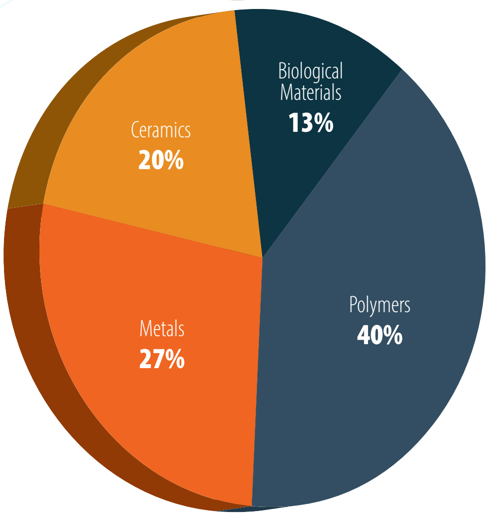
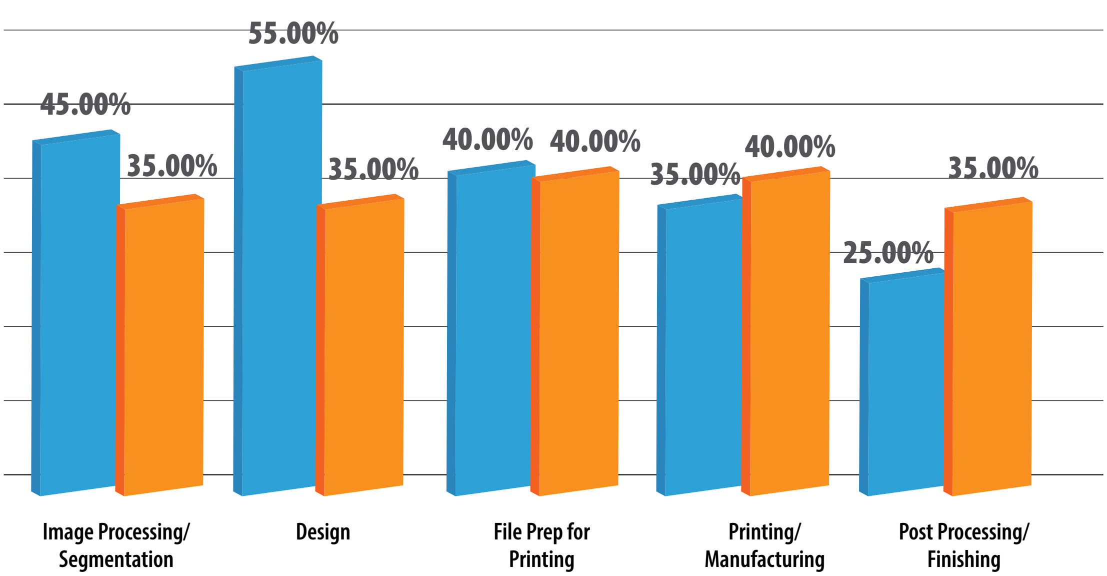


Photo courtesy SME

Patient-matched tracheal splint to treat TBM developed at the University of Michigan.

Process Steps



NOTE: Bioprinting is an emerging area. Breakout of bioprinting by process, material, and process did not achieve a 95% confidence level and has not been shared in this section.

Photo courtesy Nicole Wake

Nicole Wake holds a 3D printed full color model of a prostate tumor.

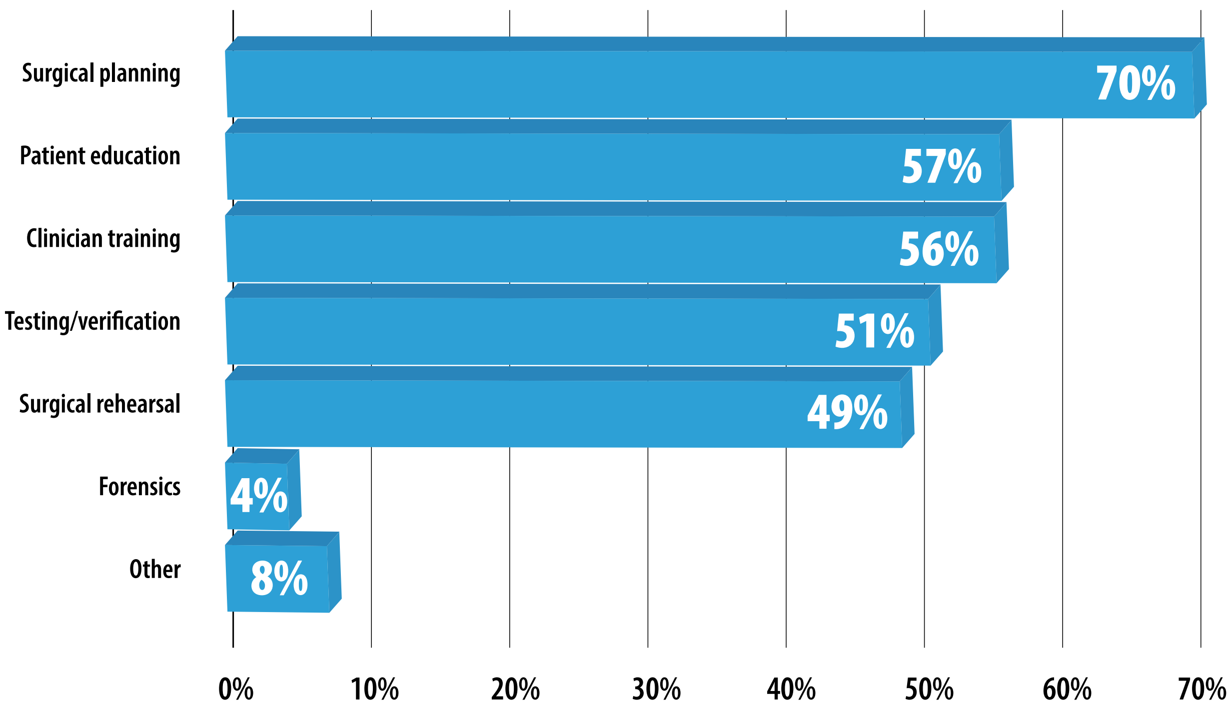
Photo courtesy Stratasys

A model of a normal, healthy human spine segment created with BIOMIMICS technology, making it useful for practice procedures.

Anatomical Models

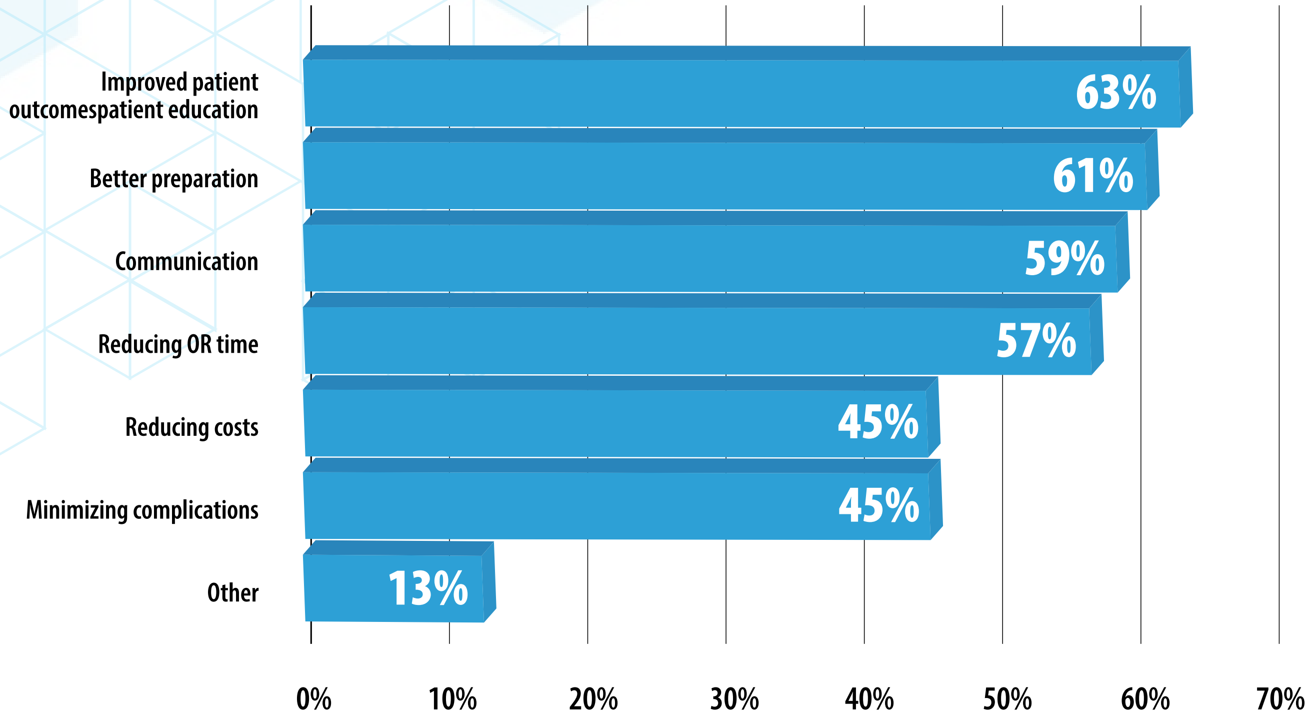
HOW anatomical models are usedbeing used

Anatomical have been one of the most visible applications of AM3DP in medicine and the primary driver of radiology-centered point-of-care manufacturing within a clinical setting. To better understand the benefits and the process, several survey questions focused on those using anatomical models.



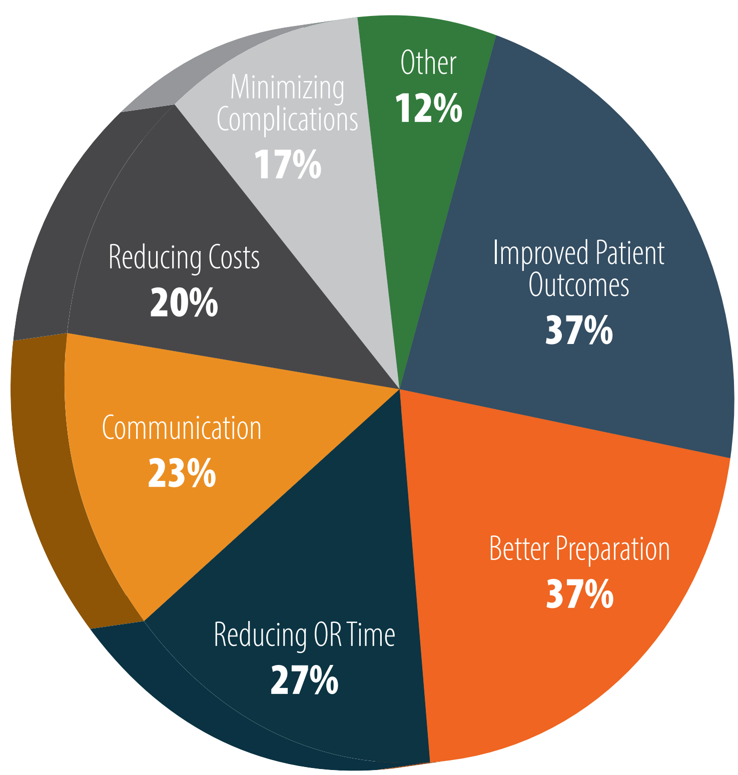
Other includes demonstrations, pre-bending, and research.

Anatomical Model Use Drivers



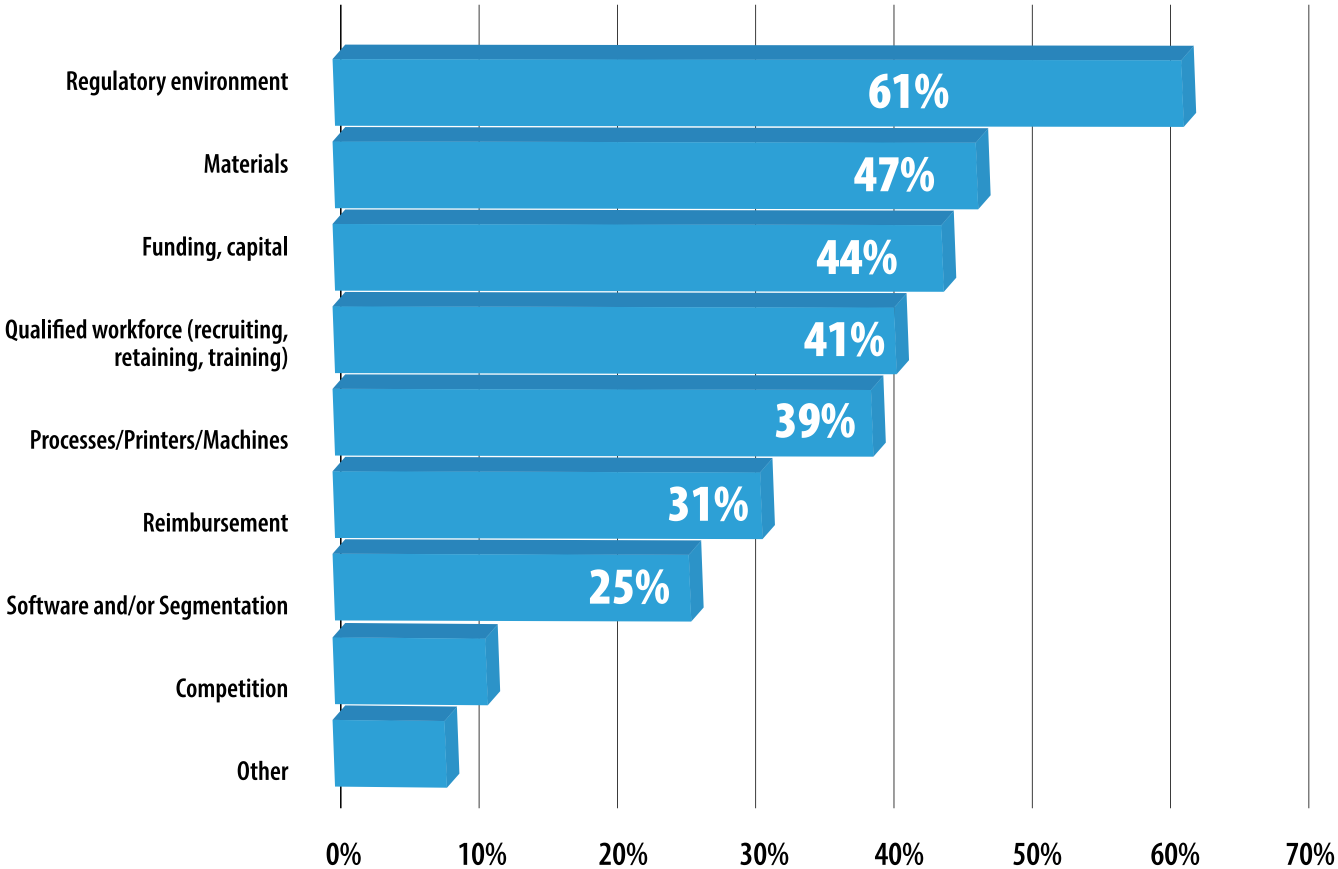
Other includes demonstrations, pre-bending, and research.

Greatest Value Provided By Anatomical Models



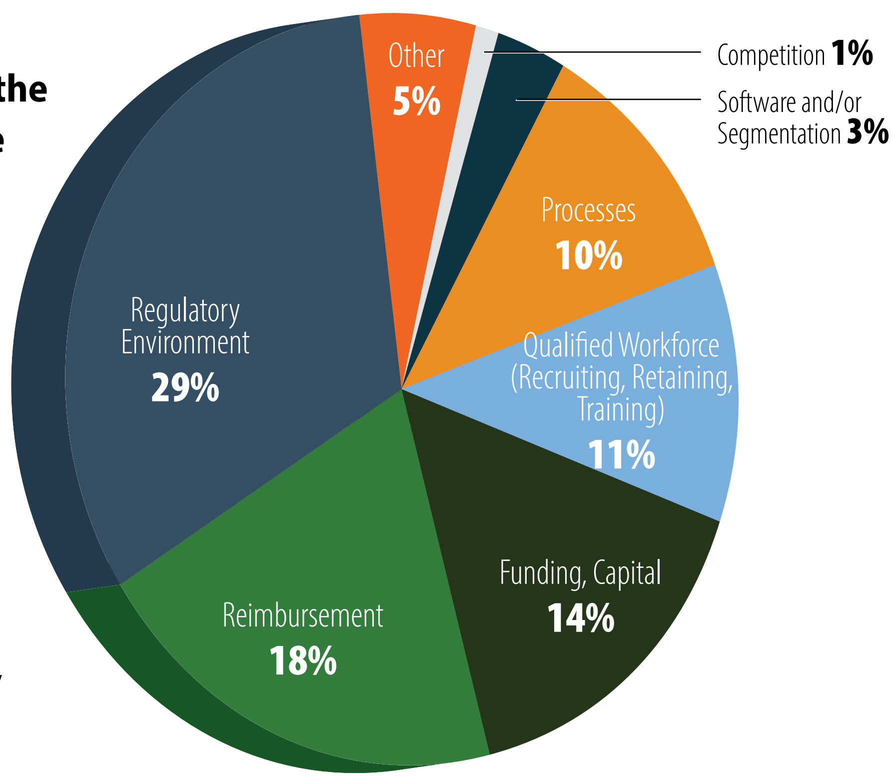
Challenges

Which of These are Challenges to Increasing Medical AM3DP Applications?



Other includes materials, process, attitude, awareness, and standards.

Of These, Which is the Greatest Challenge



Other includes accuracy, cost, and repeatabilty.

2017 Highlights

Activities from regulatory agencies, industry and clinical groups, and technology providers covered a wide variety of applications and helped to expand the impact of AM3DP in medicine.

Regulatory Activities

The U.S. Food and Drug Administration (FDA) has reviewed more than 100 devices currently on the market that were manufactured on 3D printers. These include patient-matched devices tailored to fit a patient's anatomy including knee replacements and cranial implants. Devices cleared in 2017 include HD Life Sciences' HD Lumbar Interbody System, a spinal fusion device; and Materialise's TruMatch CMF titanium 3D printed implant system, a bone plate. In 2017, the FDA also approved the first drug produced on a 3D printer, which is used to treat seizures and has a more porous matrix than the drug manufactured in the traditional way, enabling the drug to dissolve more rapidly in the mouth to work faster.

Preparing for a significant wave of new technologies enabled by AM, the FDA has been actively involved in understanding the technology to provide a more comprehensive regulatory pathway that keeps pace with technology advances and helps facilitate efficient access to safe and effective innovations enabled by AM. This commitment was demonstrated in 2017 through several activities.

Technical Guidance

Device Manufacturers: On December 5, 2017 the FDA released Technical Considerations for Additive Manufactured Medical Devices. The document clarifies what the FDA recommends manufacturers include on submissions for AM3DP produced medical devices including device design, testing of products for function and durability, and quality system requirements. The technical guidance — categorized as a "leap-frog" guidance because it helps bridge where the FDA is today with innovations of tomorrow — is only intended to provide the FDA's initial thoughts on an emerging technology with the understanding that recommendations are likely to evolve as the technology develops in unexpected ways.

Point-of-care Manufacturers: The FDA is also working to establish a regulatory framework for how to apply existing laws and regulations that govern device manufacturing to point-of-care manufacturers that create patient-matched devices for patients they are treating. Consistent with these goals, the FDA held a joint meeting with the RSNA 3D Printing SIG in August 2017. The meeting focused on clinically used 3D-printed anatomical models to identify current best practices, levels of benefit versus risk for different intended uses, and gaps in clinical evidence needed to perform effective regulatory review of anatomical models. A white paper is expected to be published as a result of the joint meeting. More information on the meeting including recorded webcasts from the meeting, can be accessed here.

Tissue Fabrication: The FDA is also reviewing the regulatory issues related to the bioprinting of biological, cellular and tissue-based products in order to determine whether additional guidance is needed beyond the regulatory framework on regenerative medicine medical products released on November 17, 2017. The framework – outlined in a suite of four guidance documents – builds upon the FDA's existing risk-based regulatory approach to more clearly describe what products are regulated as drugs, devices, and/or biological products. The documents most relevant to the use of 3D printing or bioprinting are:

- Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use clarifies how the agency interprets the existing regulatory definitions "minimal manipulation" and "homologous use." As this field advances, the FDA has noted that there are a growing number of regenerative medicine products subject to FDA premarket authorization. These guidance documents will help explain how the FDA will provide a risk-based framework for its oversight. The policy framework defines how we intend to take action against unsafe products while facilitating continued innovation of promising technologies.
- DRAFT: Evaluation of Devices Used with Regenerative Medicine Advanced Therapies addresses how the FDA intends to simplify and streamline its application of the regulatory requirements for devices used in the recovery, isolation, and delivery of regenerative medicine advanced therapies (RMATs).
- DRAFT: Expedited Programs for Regenerative Medicine Therapies for Serious Conditions describes the expedited programs that may be available to sponsors of regenerative medicine therapies, including the new Regenerative Medicine Advanced Therapy (RMAT) designation. The guidance also describes the regenerative medicine therapies that may be eligible for RMAT designation – including cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products, as well as gene therapies that lead to a durable modification of cells or tissues (including genetically modified cells).

Research

To keep pace with evolving AM3DP technology as well as encourage and support innovation, the FDA is involved in several research activities. The FDA has a core facility and agency-wide working group takes an interdisciplinary approach to better use and evaluate AM3DP across regulated product areas. Some FDA researchers use the AM technologies as tools to advance their own research. Others investigate the technology itself to develop and validate quality metrics and measurement techniques that can be applied to medical product evaluation.

- Research projects use a multidisciplinary approach to develop metrics, test methods, and a framework to evaluate accuracy and reproducibility with several popular printing methods. These include:
- Developing AM optical and radiographic phantoms to provide anatomic, reproducible, and complex geometries to test the capabilities of advanced imaging systems
- Creating a test artifact to reliably measure the amount of residual material left in parts with complex lattice structures, aiding the evaluation of post-processing and cleaning steps of AM medical product production
- Comparing the static and dynamic mechanical properties of machined, laser, and electron beam sintered parts to produce baseline knowledge and process quality information for AM Medical device review
- Developing a model polymer system to explore how structure-property relationships are affected by AM parameters, allowing appropriate evaluation of new materials used for AM medical devices and combination products
- Develop process control knowledge and critical to quality features of AM drug formulations, using several processing techniques, to allow transparent and appropriate regulation of AM drug products.
- Evaluating the effects of 3D printing a drug delivery device, such as a metered dose inhaler, on the efficacy of the drug delivery compared to standard drug delivery devices

Other research projects use AM as a tool to augment their research methods and facilitate meeting research goals. These projects include:

- Developing an anatomically realistic nasal cavity model to measure regional distribution fractions of nasally insufflated drugs
- Using miniature AM saddles and brackets to stabilize rodent neural electrodes to improve signal quality
- Iterating designs of field test equipment that can be used during inspection of imported medical products
- Testing designs for feasibility of focusing or diffusing ultrasound, radiographic energy
- Create miniature fluidic sensors and diagnostic tools

For more information on the FDA's research efforts, visit: Additive Manufacturing of Medical Products

Groups & Organizations

Several organizations are working to support the application of AM3DP in medicine. Below are some of the most active groups.

SME Medical Additive Manufacturing/ 3D Printing Workgroup

The SME Medical Additive Manufacturing/3D Printing Workgroup collaborates to identify challenges, develop resources, and to facilitate changes to support anyone using the technologies for medical/biomedical applications. The workgroup members represent medical device manufacturers, clinicians, technology providers and more to provide a multi-perspective approach to all projects and discussions. In addition to all of the organizations represented by workgroup members, cooperative relationships are maintained with several groups including DICOM WG-17 3D Manufacturing, RSNA 3D Printing Special Interest Group, Additive Manufacturing Standardization Collaborative (AMSC), ARMI/ BioFabUSA, and the FDA/CDRH Additive Manufacturing team.

In 2017, the SME AM3DP Workgroup prioritized several challenges for projects including understanding biocompatibility, workforce development, and keeping track of developments within the industry.

The SME Medical AM3DP Workgroup meeting was hosted by 3D Systems in Littleton, Colorado in June 2017

Bicompatability: With biocompatibility being a complex concern, the group continues to work to develop a tool that combines a list of potential materials along with a tool to assist in assuring biocompatablity. The list and tools are anticipated to be available in 2018.

Workforce Development: Addressing the unique combination of medicine and engineering needed for those using AM3DP for medical applications, the SME workgroup developed and published job description templates and competency models. Covering technicians and engineers for both medical device manufacturers and point-of-care manufacturers, these tools are available for download at www.sme.org/am3dpjobmodel. The release of the tools was accompanied by a white paper describing the need and opportunities. Download the paper here. The group also began work on the next step to support curriculum development and training, developing a detailed Body of Knowledge (BOK) expected to be available in 2018.

Annual Report: To help understand developments in all areas of medical applications of AM3DP, the group committed to publishing this annual report. Their work has included collaborating on the survey design, selection of 2017 highlights to include, and insight on what might be seen.

For more information on the SME Medical AM/3DP Workgroup and information on how to get involved, visit: www.sme.org/medical-am3dp-workgroup

Photo courtesy Mayo Clinic

Dr. Morris discusses a surgical planning model with Amy Alexander, biomedical engineer, and Dr. Kevin Arce, maxillofacial surgeon.

RSNA 3D Printing Special Interest Group

The 3D Printing Special Interest Group (SIG) of the Radiological Society of North America (RSNA) officially launched at the RSNA Annual Meeting in late 2016. Recognizing the importance of collaboration, the SIG leaders worked with RSNA to allow non-traditional RSNA members to join the SIG. This included those working outside a clinical setting like technology developers and device manufacturers. With a goal to support radiology-centered, hospital-based, point-of-care 3D printing to impact more patients, 2017 was a very active year for the SIG led by Chair, Jonathan Morris, MD, Mayo Clinic, Vice Chair, Jane Matsumoto, MD, Mayo Clinic, and Emeritus President, Frank Rybicki, MD, The Ottawa Hospital.

- The SIG has focused much of their effort on anatomical models, the most prevalent use of 3D printing within a hospital setting. This has included:
- Drafting quality imaging protocols designed for 3D printing
- Developing appropriateness criteria for the use of anatomical models. The criteria indicates whether a model is usually appropriate, sometimes appropriate, or usually not appropriate and is separated by conditions in areas like craniomaxillofacial, vascular, breast, and congenital heart
- Building support for the development of the CPT code process and evidence needed to reach reimbursement
- Held a joint meeting with the FDA in August 2017 to better understand how regulations might impact those working within a clinical setting. While the FDA technical guidance expressly does not address the most common anatomical models, a white paper is in development. Based on discussions during the joint meeting, the paper will provide more information on the role regulations have in their operations
- Assigned an official liaison with the DICOM committee to engage the SIG in updates and encourage discussion

Photo courtesy Nicole Wake

SIG leadership at Scottsdale meeting, March 2017.

During the SIG meeting at the 2018 RSNA Annual Meeting, they set out goals for continued activities by setting up several committees to work in different areas. These included:

- Education-Residents
- Education-Engineers & Technologists
- Research
- Regulatory and Compliance
- Reimbursement Strategies
- Simulation
- Prosthetics/Orthotics/Molding/Anaplastology/Surface Scanning

For more information, visit: http://www.rsna.org/3D-Printing-SIG/

DICOM Workgroup-17 3D manufacturing

In late 2016, Allan Noordvyk, Change Healthcare presented a proposal developed with support from the SME Medical AM3DP workgroup, to the DICOM Standards Committee to update the DICOM standard to facilitate the AM3DP process based on medical imaging data. The result was the reactivation of Workgroup 17 renamed 3D Manufacturing, co-chaired by Noordvyk and Justin Ryan, Phoenix Children's Hospital. WG-17's mandate is to extend and promote the use of DICOM for the creation, storage and management of 3D printing models in a healthcare setting, where the model is either (a) derived from medical images, or (b) expected to be compared/composited with medical images.

The first conference call of the group was held on January 25, 2017 with a diverse group of professionals representing hospitals, device manufacturers, researchers, technology developers, government agencies, and more. Since that first conference call, WG-17 has been very active. After much discussion, a survey was conducted in April 2017 to understand which 3D model file formats should be encapsulated. Formats included in the survey were GCODE, STL, X3D, AMF, 3MF, OBJ, PLY, and VRML. The results showed that STL is the format most frequently used, followed by X3D/VRML, OBJ, and 3MF. Other formats were rejected for encapsulation based on the survey results. The survey was followed by a ballot in July to determine supplement development priority after STL.

With STL being the clear leader, work began to draft a supplement 205 to the DICOM standard, "DICOM Encapsulation of STL Models for 3D Manufacturing." Sup205 was posted for public comment on December 8, 2017 with a deadline of January 22, 2018. For anyone involved in the often long standards development process, the dedication of WG-17 to propose a thorough supplement draft in less than a year, is extraordinary. The final DICOM supplement for STL files is expected to be released in 2018. Key aspects of the draft supplement include:

- Allowing straightforward extension of institutions' existing extensive DICOM-based infrastructure to receive and manage the STL model data as part of the persistent medical record
- Providing a straightforward extension of 3D modeling software to store data to this DICOM infrastructure
- Avoiding potential data translation errors by maintaining the STL data in its original format within the DICOM object
- Adapting existing, well-tested approaches to preserving patient identification, laterality, creation date/time and other metadata
- Allowing intended purpose of the model to be included in metadata, as an aid to later searches
- Ensuring units of scale used in the model are unambiguous
- Allowing optional spatially-mapped, references back to the source images used to construct the STL model
- Allowing optional inclusion of a preview image for visual selection
- Helping protect patient privacy by indicating the presence of protected health information (PHI) in the STL model itself

The survey conducted during the Spring was followed by a ballot in July to determine supplement development work after STL. The ballot indicated (in order) OBJ, VRML/X3D, and 3MF as the next file formats to encapsulate. Proceeding with encapsulating these formats now does not exclude other formats from being discussed in the future.

For more information on the DICOM standard the efforts of WG-17, visit: www.dicomstandard.org/

Additive Manufacturing Standardization Collaborative (AMSC)

The Additive Manufacturing Standardization Collaborative (AMSC) is working to accelerate the development of cross-sector industry standards. Led by America Makes and ANSI, more than 200 AM/3DP experts and several Standards Development Organizations (SDOs) including ASTM, ASME, SAE, AWS, MITA, and AAMI, are working together to identify needed standards and priorities for development. With the support of the SME Medical AM/3DP Workgroup, the standards roadmap addresses many needs of the medical community.

In February 2017, the AMSC published a standardization roadmap identifying existing standards and specifications, those in development, and existing gaps along with recommendations for priority and potential SDOs for development. The roadmap identified 89 total gaps with 17 gaps specific to medical applications, four of which were rated as high priority.

In September 2017, AMSC launched development of the second version of the roadmap with a focus to add standards for polymers and review industry sector needs. The medical group is co-chaired by Lauralyn McDaniel, SME, and Dan Fritzinger, DepuySynthes. Standardization Roadmap for Additive Manufacturing 2.0 is expected to be published in June 2018.

For more information, visit: www.ansi.org/amsc

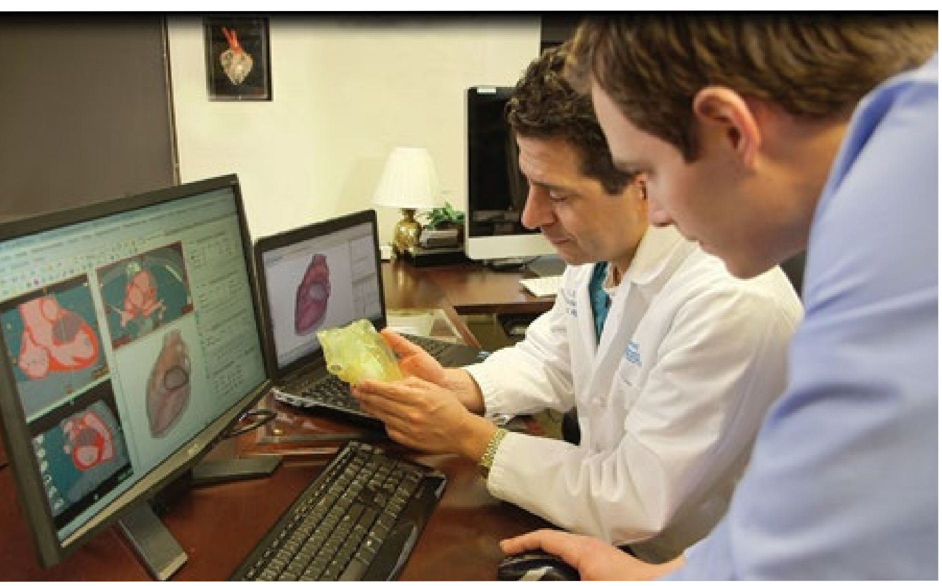


Photo courtesy Materialise

Todd Pietila, Materialise, works with Dr. David Morales, Chief Pediatric Cardiothoracic Surgery, Cincinnati Children's Hospital to review digital images and a patient's cardiac model before surgery

Technology, Materials, Research, Collaborations & More

With collaboration needed to advance medical AM3DP applications, much of developments in 2017 reflected cross-organization, cross-technology efforts.

Partnerships

Anatomical Models: Materialise and Formlabs announced a collaboration to deliver a complete, cost-effective and easy-to-use solution for hospitals who are looking to start an in-house 3D print lab. The new offering combines the Materialise Mimics inPrint medical imaging software with Formlabs' Form 2 printers. This complete 3D printing package will facilitate the implementation of patient-specific solutions at an affordable price-per-print. As the use of 3D anatomical models rapidly progresses in the medical field, it has become a standard procedure and valuable tool for communicating complex surgical plans with patients. Once hospitals have adopted on-site 3D printing, they are able to easily scale their operations as demand for anatomical models grows. For more information, visit www.materialise.com/en/medical/mimics-inprint-formlabs

Dental Guides: Formlabs announced a partnership with 3Shape to introduce software integration solutions that enable seamless dental 3D printing workflows. The partnership offers the first complete digital solution for dental professionals, streamlining surgical guide design and manufacturing workflow, making it easier and more affordable to produce surgical guides. Using 3Shape TRIOS intraoral scanners, completing design in 3Shape Implant Studio software and then clicking "Print" in Formlabs' PreForm software, guides can be manufactured using Formlabs' biocompatible Dental SG resin. While printing surgical guides used to take weeks, integration creates a workflow that makes even same-day guided surgery possible. For more information, visit: https://formlabs.com/blog/new-formlabs-3shape-integration-to-simplify-dental-surgical-guide-workflow/

Photo courtesy Formlabs & 3Shape

Surgical guide design in 3Shape Implant Studio with options to toggle display settings so doctors have as many viewpoints as possible.

Tissue Fabrication: 3D Systems and United Therapeutics Corporation announced plans for a multi-year collaboration and development agreement to develop solid-organ scaffolds for human transplants. 3D Systems will collaborate with United Therapeutics and its organ manufacturing and transplantation-focused subsidiary, Lung Biotechnology PBC. The agreement focuses on development of 3D printing systems for solid-organ scaffolds, beginning with lung scaffolds. The printing system will target collagen and other building block proteins as scaffold raw materials. United Therapeutics will cellularize the scaffolds with patient-specific biological material, including re-differentiated stem cells. For more information, visit: https://www.3dsystems.com/press-releases/3d-systems-and-united-therapeutics-announce-bioprinting-agreement

Medical Imaging Software: Materialise and Siemens Healthineers announced a partnership to bring Materialise Mimics inPrint software to the Siemens Healthineers syngo.via open app platform. 3D printing technology is growing rapidly in the medical field, and soon it will be even more mainstream as 3D printing software becomes more accessible in hospitals. Adopting virtual 3D anatomical models facilitates surgical planning and collaboration between radiologists and surgical teams. 3D-printed anatomical models improve patient communication, training and education surrounding anatomically complex pathologies.For more information, visit: http://www.materialise.com/en/press-releases/materialise-and-siemens-healthineers-syngovia-partner-to-bring-3d-printing-to

Bone Implants for Tumor Treatment: A five-year project, "Just in time implants," brings together the Australian Government, RMIT University in Melbourne, the University of Technology Sydney (UTS), St Vincent's Hospital Melbourne and global medical technology company Stryker. The Australian research project using 3D implants and robotic surgery is set to advance the way physicians surgically treat tumors and bone cancer and expected to improve patient and healthcare outcomes. Combining specialized imaging techniques, 3D printing and the accuracy of robotic assisted surgery, the aim is to deliver a patient-matched implant in time for the surgeon to remove the cancer and repair the patient's bone in the one operation. For more information, visit: https://www.rmit.edu.au/news/all-news/2017/oct/just-in-time-3d-implants-set-to-transform-tumour-surgery-

Photo courtesy RMIT University

An adult femur with the "Just in time implant" in the place of a cancerous section of the bone.

Anatomical Models Workflow: Philips announced agreements with 3D Systems and Stratasys to help progress patient care and improve the clinician experience. IntelliSpace Portal 10 features an embedded 3D modeling application for creating and exporting 3D models intuitively into the clinical workflow. Through interfacing with IntelliSpace Portal 10, clinicians will now have a virtually seamless connection to 3D Systems and Stratasys solutions to expedite 3D printing to create anatomical models. Users can create the model in IntelliSpace Portal 10, save the data and easily transfer the data to the 3D vendors' solutions without leaving the clinical environment. For more information, visit: https://www.usa.philips.com/a-w/about/news/archive/standard/news/press/2017/20171127-philips-teams-with-3d-printing-industry-leaders-3d-systems-and-stratasys.html

Applications & Methods

Anti-seizure Contact Lenses: 3D-printed polarised contact lenses have provided sufferers of photosensitive epilepsy – where flashing light can cause epileptic seizure – with a tool to overcome the threat of the condition. The inventor, a University of Canterbury Master of Science psychology student and entrepreneur, Logan Williams says he was inspired by a close friend who suffers from photosensitive epilepsy to address the condition with special contact lenses he calls Polar Optics. For more information, visit: http://www.canterbury.ac.nz/news/2017/uc-student-develops-revolutionary-polarised-contact-lenses.html

Photo courtesy University of Canterbury

UC Master of Science psychology student and entrepreneur Logan Williams says he was inspired by a friend with epilepsy to address the condition with Polar Optics contact lenses.

Hydrogel 3D Printing Method: A new method and material system capable of 3D-printing hydrogel inks with programmed bacterial cells as responsive components into large-scale (3 cm), high-resolution (30 μm) living materials, where the cells can communicate and process signals in a programmable manner, has been developed. The structures produced are tougher than articular cartilage yet capable of encapsulating cells. The method developed at MIT, could be used to 3D print logic gates, spatiotemporally responsive patterning, and wearable devices.

Upper Extremity Osteotomy Guides: Materialise has expanded its 3D printed orthopaedic solutions to include osteotomy guides for adults in the United States with metacarpal/phalange and clavicle bone deformities. These guides, developed in collaboration with surgical teams, are designed specifically for each individual patient to help orthopaedic surgeons understand and execute even the most complex cases with confidence. For more information, visit: http://www.materialise.com/en/press-releases/materialises-upper-extremity-osteotomy-guides-aid-surgeons

Photo courtesy Materialise

Upper extremity osteotomy guides allow surgeons to plan procedures and view anatomical structures from different angles.

Multi-silicone 3D Printing: ACEO has developed a technology to 3D print multiple materials at the same time. Silicones of different colors, hardness or even chemical or physical properties can now be placed independent from each other at any given point throughout the process, which allows sharp as well as merging gradients. The result is even more freedom of design in the construction of objects with multiple materials, in particular those with both soft and hard segments. For more information, visit: https://www.aceo3d.com/wp-content/uploads/2017/10/ACEO-Press-Release-Multi-Material3D-Printing.pdf

Photo courtesy ACEO

Blood vessels made of 3D printed silicone, using data taken from an MRI or CT scan.

Software & Hardware

Workflow Software: 3D Systems announced a new D2P™ (DICOM to PRINT) technology that helps clinicians and radiologists quickly create accurate, digital 3D anatomical models from medical imaging data. D2P is a stand-alone modular software package that is designed to address and consolidate all 3D model preparation steps. It relies on automatic segmentation tools that minimize the effort and time associated with the creation of a digital patient-specific model. The software is intended to be used by medical staff for preoperative surgical planning and allows for the export of 3D digital models in various file formats that can be used by numerous applications. For more information, visit: https://www.3dsystems.com/dicom-to-print

Dental Printer: Stratasys debuted the Stratasys J700 Dental™ 3D Printing solution – a PolyJet-based 3D printer for production of clear aligner molds. Providing production rates of more than 400 clear aligner molds per day, the system uses VeroDent™ material with greater accuracy and minimal post-processing. For more information, visit: http://investors.stratasys.com/news-releases/news-release-details/stratasys-debuts-new-dental-3d-printer-orthodontics-offering

Photo courtesy Stratasys Ltd.

Mold for clear aligner, produced on the J700 Dental 3D Printing Solution, and the resulting clear aligner.

Materials

Dental LT Clear: Formlabs released a new dental materials: Dental LT Clear for orthodontic applications. Dental LT Clear can be used to print splints and retainers in less than 50 minutes for a single unit. Full build platforms, with up to seven splints, can be completed in under two hours. For more information, visit: https://formlabs.com/materials/dentistry/#dental-lt-clear-overview

Hyperelastic Bone: DimensionInx released a 3D-printable synthetic osteoregenerative biomaterial, hyperelastic "bone" (HB). HB, which is composed of hydroxyapatite and polycaprolactone or poly(lacticco- glycolic acid), can be rapidly 3D printed (up to 275 cm3/hour) from room temperature extruded liquid inks. The resulting 3D-printed HB exhibits elastic mechanical properties (32 to 67% strain to failure, ~4 to 11 MPa elastic modulus), is highly absorbent (50% material porosity), supports cell viability and proliferation, and induces osteogenic differentiation of bone marrow-derived stem cells. For more information, visit: https://www.dimensioninx.com/

Stainless Steel: EOS released StainlessSteel 17-4PH IndustryLine. The product consists of an iron-based metal alloy powder and a specially developed process parameter for manufacturing on the EOS M 290 metal system. EOS StainlessSteel 17-4PH IndustryLine is a high-strength, easily curable, highly corrosion- and acid-resistant material which is ideal for surgical and orthopedic instruments. Material data sheets and batch-specific material test certificates include the tests used as well as the material standards. For more information, visit: https://www.eos.info/press/eos-sets-industry-wide-quality-standard-for-metal-based-additive-manufacturing

Photo courtesy EOS

Prototype clamp produced with the EOS StainlessSteel 17-4 PH IndustryLine parameter set. Only the internal springs were not 3D printed.

Dental Model: Formlabs released Dental Model, a high accuracy resin for crown and bridge models with removable dies. The material can achieve crisp margins and contacts within ± 35 microns, and removable dies with consistently tight fit. A smooth, matte surface finish and color similar to gypsum make it easy to switch from analog to digital model production. For more information, visit: https://formlabs.com/materials/dentistry/

E-Denture: EnvisionTEC received FDA clearance for its new E-Denture material for the 3D printing of lifelike dentures and can be combined with E-Dent 100 and 400 materials for the direct printing of restorations that simulate teeth. Dental labs and dentists can now combine a pink 3D printed denture base and tooth restoration into a denture that patients can wear for long-term use.

Photo courtesy EOS

Prototype clamp produced with the EOS StainlessSteel 17-4 PH IndustryLine parameter set. Only the internal springs were not 3D printed.

Clinical trials, Workforce Development & More

BioFabUSA: The Advanced Regenerative Manufacturing Institute(ARMI)/BioFabUSA, headquartered in Manchester, NH launched in 2017. A Department of Defense (DOD)-sponsored initiative in the Manufacturing USA network is the first to address biomanufacturing. The BioFabUSA program looks to bridge the gap between early scientific research and later-stage product development by advancing critical technologies to enable large-scale biological manufacturing efforts. The DOD awarded $80 million in funding to ARMI through BioFabUSA; industry partners pledged an additional $214M. The purpose of BioFabUSA is to bring together industry, academia and government to work on problems that are more difficult than any one institution alone can solve. For more information, visit: https://www.armiusa.org/

Photo courtesy Steve Lipofsky

Members of BiofabUSA gathered for a ribbon-cutting ceremony during the grand opening of the Advanced Regenerative Manufacturing Institute's research facility.

Clinical Trial: Nicole Wake, a Ph.D. candidate in Biomedical Imaging at the Scalar Institute of Biomedical Science at the New York University School of Medicine began a two-year clinical trial to study how multi-material, multi-color 3D printed models can change and improve patient care. Working with surgeons in NYU's urology department, Wake will print patient-specific, multi-material kidney and prostate tumor models as part of a randomized prospective study at NYUSOM. Wake aims to measure the impact these patient-specific 3D models can have on pre-surgical planning versus using traditional 2D models. Ultimately, Wake hopes her application of 3D medical models will help lay the groundwork for a new standard of patient care, and help to establish reimbursement for these models. For more information, visit: http://www.stratasys.com/resources/search/case-studies/new-york-university

Photo courtesy NYU School of Medicine

Nicole Wake holds a 3D printed full color model of a prostate tumor.

Workforce Development: Recognizing the importance of engineering within point-of-care manufacturing, the British National Health Service (NHS) appointed its first ever biomedical 3D technician in 2017 at Morriston Hospital in Swansea, Wales. Heather Goodrum works with surgeons to 3D print anatomical models, surgical guides, and implants for facial reconstruction. Since her appointment, other medical centers in the NHS have contacted Morriston Hospital to learn more to create a similar position within their hospital. For more information, visit: https://www.walesonline.co.uk/news/wales-news/woman-designing-3d-printing-implants-13322959

Photo courtesy Abertawe Bro Morgannwg University Health Board

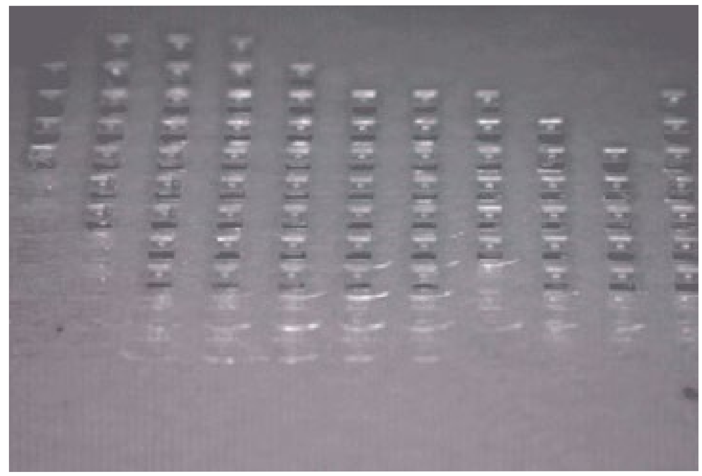
Heather Goodrum, the new biomedical 3D technician at Morriston Hospital in Swansea, Wales.

Life Science Award: For the first time, MilliporeSigma awarded one of its annual grand prize life science awards for bioprinting innovation and research. Alexandra Rutz, University of Cambridge received a $10,000 grand prize for her work on Hydrogel Inks for 3D Tissue and Organ Printing. For more information, visit: https://www.emdmillipore.com/US/en/20171020_174445

Developments & Research to Watch

Drug Delivery System: A targeted drug delivery system has been developed utilizing a 3D-printed magnetic tubular microstructure (tetrapod), which could be used to treat diseases in the female reproductive tract. The system first loads a motile sperm cell with an anticancer drug (doxorubicin hydrochloride), guiding it magnetically, to an in vitro cultured tumor spheroid, and finally freeing the sperm cell to deliver the drug locally. The sperm release mechanism is designed to liberate the sperm when the biohybrid micromotor hits the tumor walls. This system combines several intriguing features, namely, high drug loading capacity, self-propulsion, in situ mechanical trigger release of the drug-loaded sperm, sperm penetration ability, and improved drug availability. For more information, visit: https://pubs.acs.org/doi/10.1021/acsnano.7b06398

Tissue Fabrication: Scientists at the University of Oxford have developed a new method to 3D-print laboratory-grown cells to form living structures. The approach enable the production of complex tissues and cartilage that would potentially support, repair or augment diseased and damaged areas of the body. The team devised a way to produce tissues in nanolitre droplets wrapped in a lipid coating that support the structures to keep their shape. The method enables the fabrication of patterned cellular constructs, which, once fully grown, mimic or potentially enhance natural tissues. For more information, visit: http://www.ox.ac.uk/news/2017-08-15-new-method-3d-printing-living-tissues



MIT Langer Lab

An automated dispensing system being used to load drugs into the 3D printed microparticles

Time-release Drug Delivery: MIT engineers have invented a new 3-D fabrication method that can generate a novel type of drug-carrying particle that could allow multiple doses of a drug or vaccine to be delivered over an extended time period with just one injection. The new microparticles resemble tiny coffee cups that can be filled with a drug or vaccine and then sealed with a lid. The particles are made of a PLGA (already used in FDA-cleared devices) that can be designed to degrade at specific times, spilling out the contents of the "cup." The method has the potential to create a library of tiny, encased vaccine particles, each programmed to release at a precise, predictable time, so that people could receive a single injection that, in effect, would have multiple boosters already built into it. For more information, visit: http://news.mit.edu/2017/one-vaccine-injection-could-carry-many-doses-0914

Ceramic Bone Scaffolds: 3D-printed ceramic implants that gradually disappear and become actual bone have been developed by Hala Reigat at the University of Sydney. The implanted scaffold holds fractured bones together to heal, fusing with the bone, and eventually dissolving in the body after the bone is healed. The scaffold is made of calcium silicate, mineral gahnite, and small amounts of strontium and zinc which are trace elements in natural bone. Some animal testing and more will be needed for human use. For more information, visit: https://futurism.com/new-implant-heals-broken-legs-transforming-real-bone/

Photo courtesy University of Sydney

Hala Zreiqat in her lab examining a piece of a 3D printed ceramic implant

Anatomical Models Directly from Imaging Software: GE announced research into developing a CT scanner that prints anatomical models directly from the files that derived from the imaging software. The team at GE's Advanced Manufacturing & Engineering Center in Wisconsin is currently researching ways to efficiently translate images from CT scanners and other machines into 3D printable files. The goal is to make 3D-printed anatomical models that can be produced quickly with a push of a button. For more information, visit: https://www.ge.com/reports/heart-new-software-3d-print-organ-replicas-demand/

Hologram 3D Printing: The ability to use holograms to 3D print all at once rather than layer by layer has been demonstrated by Daqri. Using photo curable resins, the holograms are created by a holographic chip developed by Daqri that doesn't need complex optics. The process has the potential to greatly increase the speed of build. Currently, small objects like a paper clip can be printed in about five seconds. The process also eliminates structural weaknesses that can be created during the layering process and support structures needed by other additive manufacturing methods. For more information, visit: https://www.technologyreview.com/s/603605/this-super-fast-3-d-printer-is-powered-by-holograms/

3D Printed Ovaries: Bioprosthetic ovaries constructed of 3-D printed scaffolds that house immature eggs have successfully restored fertility in mice. Developed as a collaboration between the Northwestern University Feinberg School of Medicine and McCormick School of Engineering, the mouse was able to not only ovulate but also give birth to healthy pups. The ovary was constructed of a biological hydrogel made from broken-down collagen that is safe to use in humans and rigid enough to be handled during surgery and porous enough to naturally interact with tissues. For more information, visit: https://news.northwestern.edu/stories/2017/may/3-d-printed-ovaries-offspring/

Photo courtesy Adam Jakus

Adam Jakus, Dimension Inx, working on the next generation of 3D-printable materials.

3D Printed Wound Care and Monitoring: osteVTT Technical Research Centre of Finland is developing a 3D wound care product using nanocellulose for monitoring wound condition in hospital care. The purpose is to have the healed wound area remain flexible instead of it developing stiff scar tissue. In collaboration with the University of Tampere, VTT's wound care prototype combines nanocellulose, a protein used in wound care, and printed electronics measuring wound healing into a single product. Nanocellulose has not yet been approved for medical use, which means that it will take several years before this application is used in hospitals. For more information, visit: http://www.vttresearch.com/media/news/vtt-is-developing-3d-printing-materials-for-wound-care-and-decorative-elements

Photo courtesy VTT Technical Centre of Finland

A spoonful of nanocellulose material, which can be used to improve the rigidity of 3D structures.

Electric-eel Inspired 3D-printed Power Source: Inspired by the electric-eel, a 3D printed soft power source has been developed in work supported by U.S. Air Force Office of Scientific Research and National Institutes of Health. The system uses gradients of ions between miniature polyacrylamide hydrogel compartments bounded by a repeating sequence of cation- and anion-selective hydrogel membranes. A scalable stacking geometry can generate 110 volts at open circuit or 27 milliwatts per square metre per gel cell. Unlike typical batteries, these systems are soft, flexible, transparent, and potentially biocompatible. These characteristics suggest that artificial electric organs could be used to power next-generation implant materials such as pacemakers, implantable sensors, or prosthetic devices in hybrids of living and non-living systems. https://www.youtube.com/watch?v=5tSDPQrgTWM

3D Printed Vascular Structures: In advances toward 3D printable vascular structures, the Symbiolab has produced a complex geometrical network of vessels, shaped as the vasculature of an earlobe, using hydrogels. With vascularization being a major challenge for bioprinting tissues, new protocols to fabricate vessel systems will be needed. For more information, visit: http://irnas.eu/bio-lab-symbiolab/2017/11/29/making-earlobe-shaped-channels-using-vitaprint

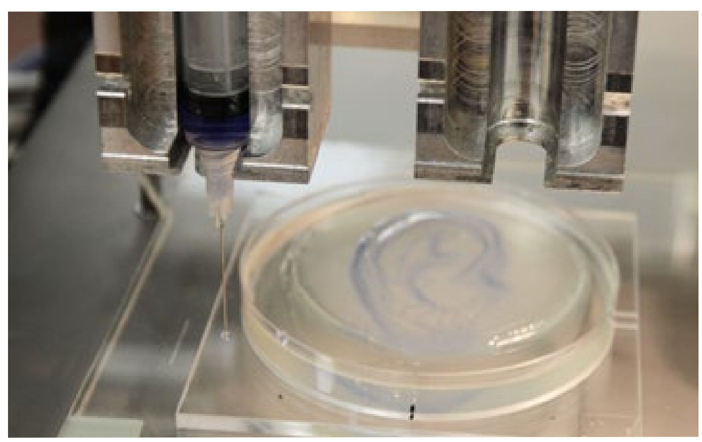


Photo courtesy Institute IRANS

Vitaprint having completed the ear vasculature print in the gel matrix, before dye insert.

Printable Bacteria Inks: ETH Zurich researchers have developed a biocompatible ink for 3D printing using living bacteria and hydrogels. This makes it possible to produce biological materials capable of breaking down toxic substances or producing high-purity cellulose for biomedical applications. The development enables the printing of mini biochemical factories with certain properties, depending on which species of bacteria put in the ink. For example, one type of bacteria that relieves pain, retains moisture, and is stable, opens up potential applications in the treatment of burns. The scientists have named their new printing material "Flink", which stands for "functional living ink."

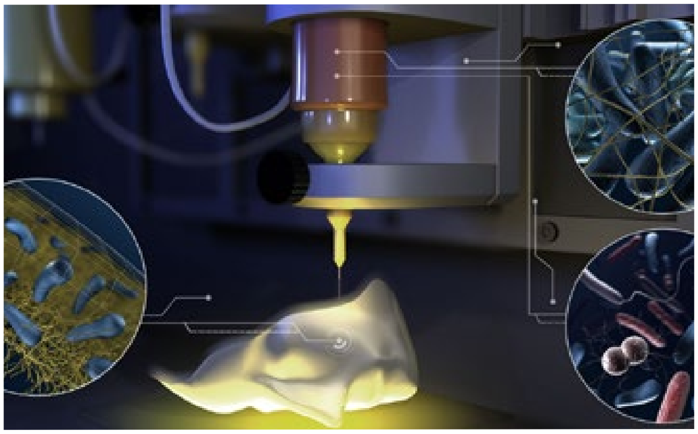


Photo courtesy ETH Zurich

3D Printing with ink that contains live bacteria which can break down toxic substances or produce high-purity cellulose.

What's Next?

Looking to the Future

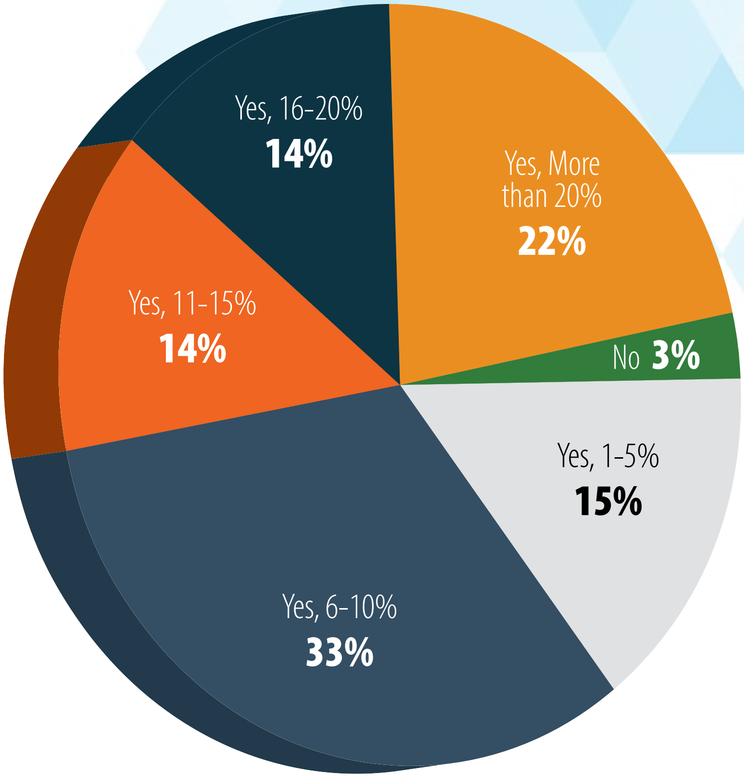
The SME Medical AM/3DP Workgroup discussed what will be seen for medical applications. Below is a summary of this diverse, experienced group's thoughts on what's next along with results from the SME Medical AM3DP survey.

San Antonio VA staff are actively exploring opportunities for 3D printing. While 3D printed, weight-bearing prosthetics are not in routine clinical use within the VHA system, this is an area of active research focused on quality, safety, comfort, and durability of 3D printed prosthetics.

What will be the next big application for medical AM/3DP? What technologies, materials, or services do you expect to see?

- New materials including printing different silicone with different physical properties
- Building devices specific to the biomechanics of a patient which will be a broad application for orthopedic device including joint replacement
- Patient-matched instruments will continue to grow
- Point-of-care (hospital-based) manufacturing will continue to grow with some sort of oversight or standards to be set
- Faster printing and higher volume
- Better integration between tools; particularly between imaging, software, and hardware which will be enabled by more collaboration between companies and industry groups
- Apps that can take images to create 3D models
- Gesture capturing will increase ease of software use
- Participation from medical societies and regulatory agencies will continue to grow
- New payment models
- Better understanding of how to print drugs
- Growth in bioprinting and printing electronics, including the integration of electronics into medical devices
- More veterinarian usage
- For point-of-care (hospital-based) manufacturing
  - Increased use for education and surgical planning
  - Increased prediction and verification of outcomes including the ability to measure a procedure or skill so that it can be tracked
  - May be recognized as a device manufacturer with some sort of oversight for manufacturing, cleaning, and sterilization
  - Point-of-car still limited to anatomical models, no big change in the near future, new hospitals adopting the technology
  - Developments in software will allow better integration within the hospital setting
  - Outside of hospital, orthotics and prosthetics will continue to grow
  - Efforts to minimize misinformation and expectations—not everyone with a 3D printer can work in medicine
- For medical device manufacturers
  - Small, innovative companies using AM3DP for final products will be targets for purchase by large device manufacturers
  - Device manufacturers will continue to work through the additive process, understanding what it can and can't do, and adopting where it makes sense within existing business.
  - Strong evaluation of AM as final production method for new devices

Expecting an Increase of Medical AM3DP Applications



What challenges beyond those in the survey that need to be addressed to expand medical AM3DP?

- Need a certifiable supply of polymers from established materials so that the supply chain can be verified
- Integration into the point-of-care will require continued effort in education to address the skills gap
- Better understanding and development of in situ monitoring for process verification
- Combatting the hype of what AM3DP, unrealistic expectations
- Low cost isn't necessarily the case
- Inventory carrying cost will still exist; will still have to carry some instruments inventory
- Transferring the knowledge of verifying and validating processes with traditional machines to AM3DP

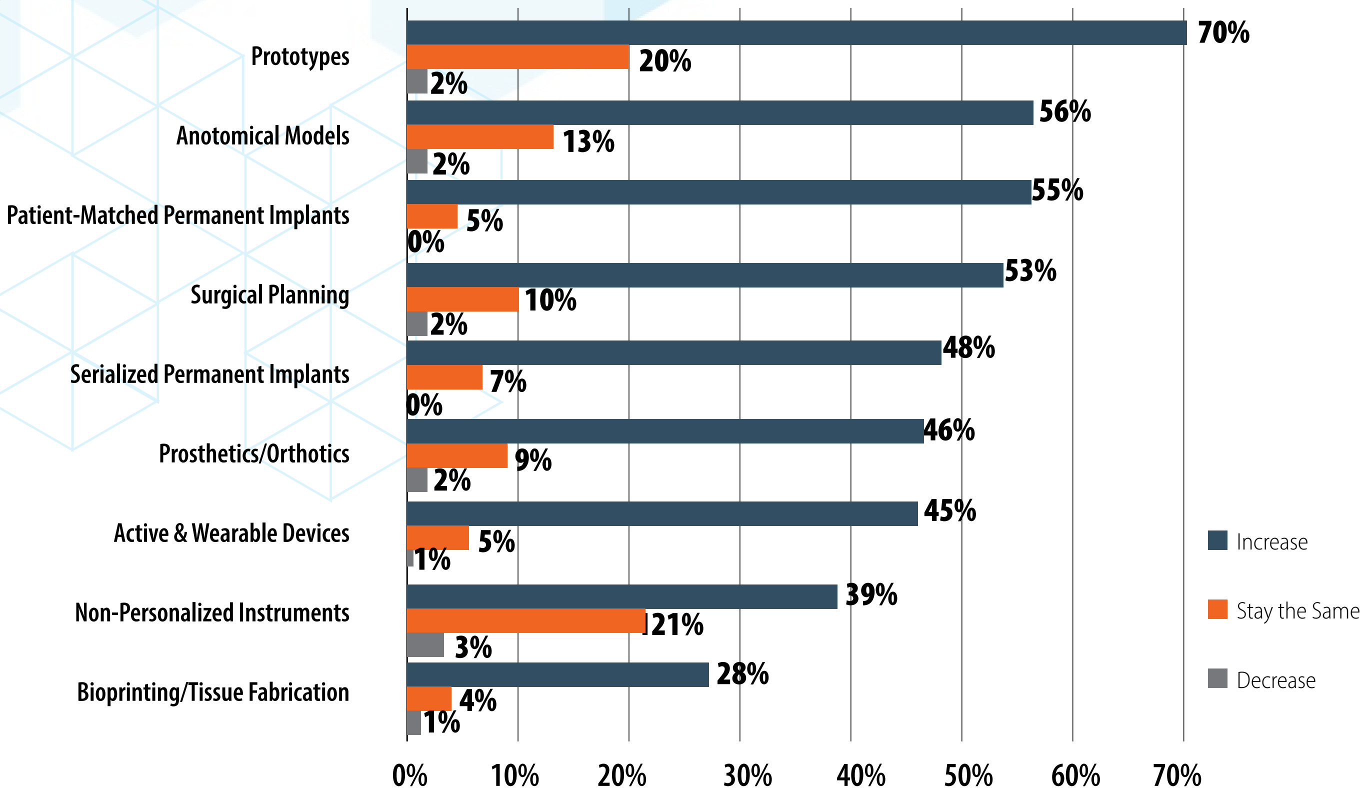
What questions are you expecting to have answered in the next 1-2 years?

- Will directed energy deposition use growing in aerospace transfer to medical applications? From aerospace?
- What will be the impact of software development that supports iterative process and topology optimization?
- How will the biocompatibility issues be addressed?

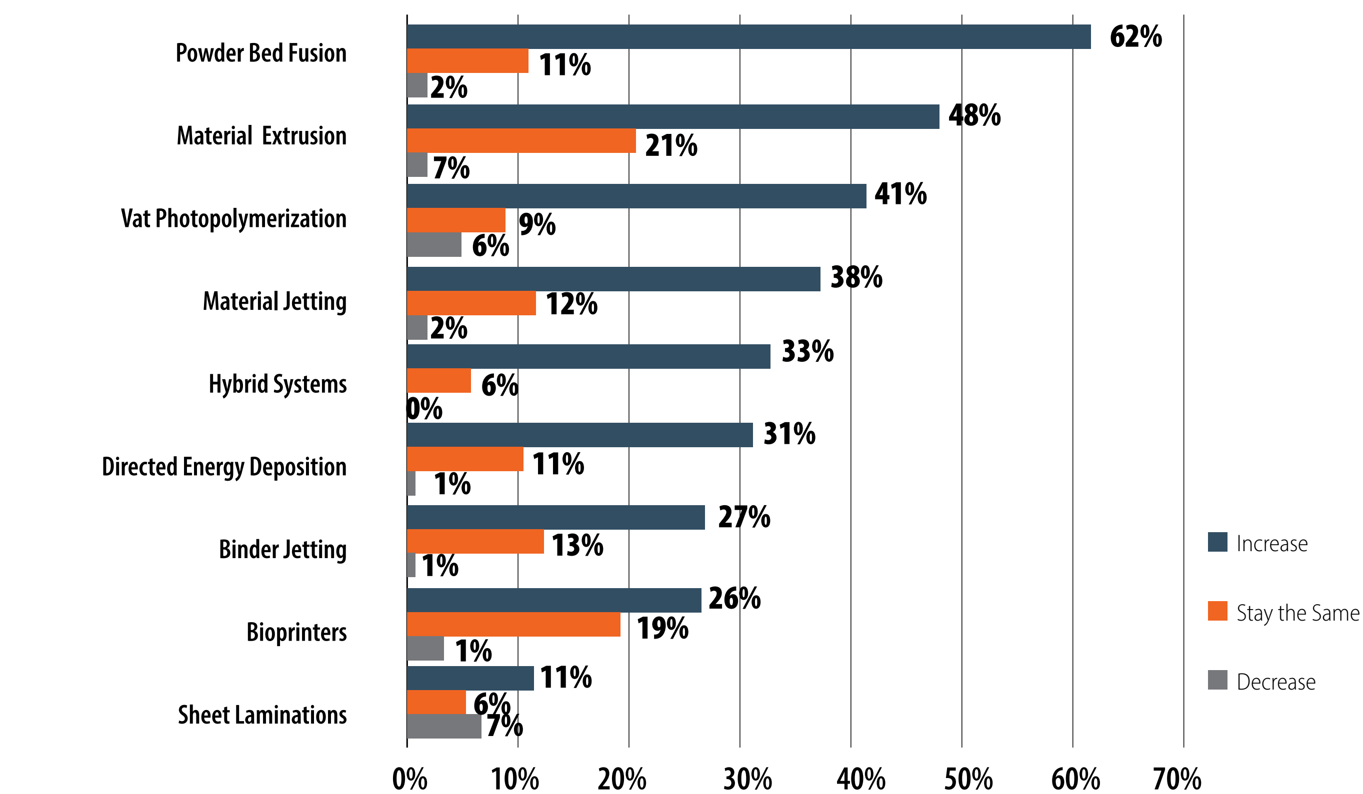
Photo courtesy 3D Systems Healthcare

Katie Weimer, 3D Systems Healthcare, works with the surgical team in the operating room with both digital and 3D-printed anatomical models for the McDonald twins' separation surgery.

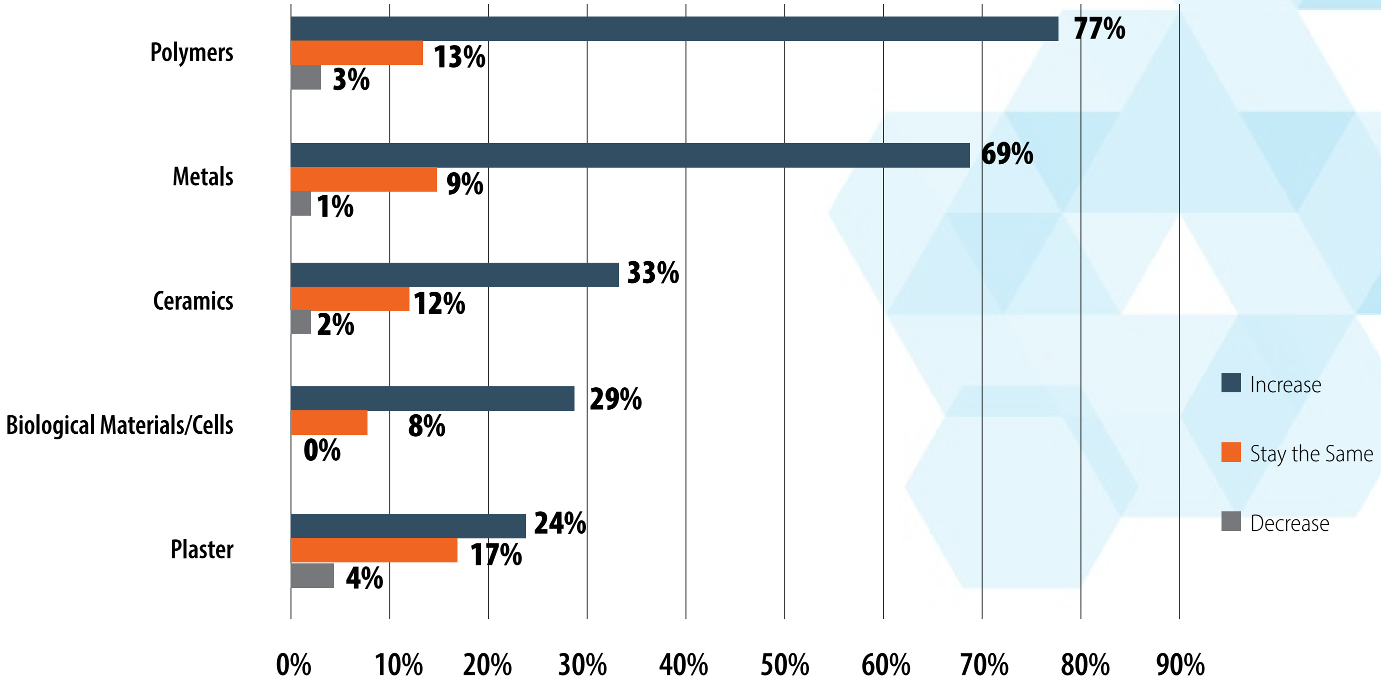
Expectations By Application Area



Expectations By Technology



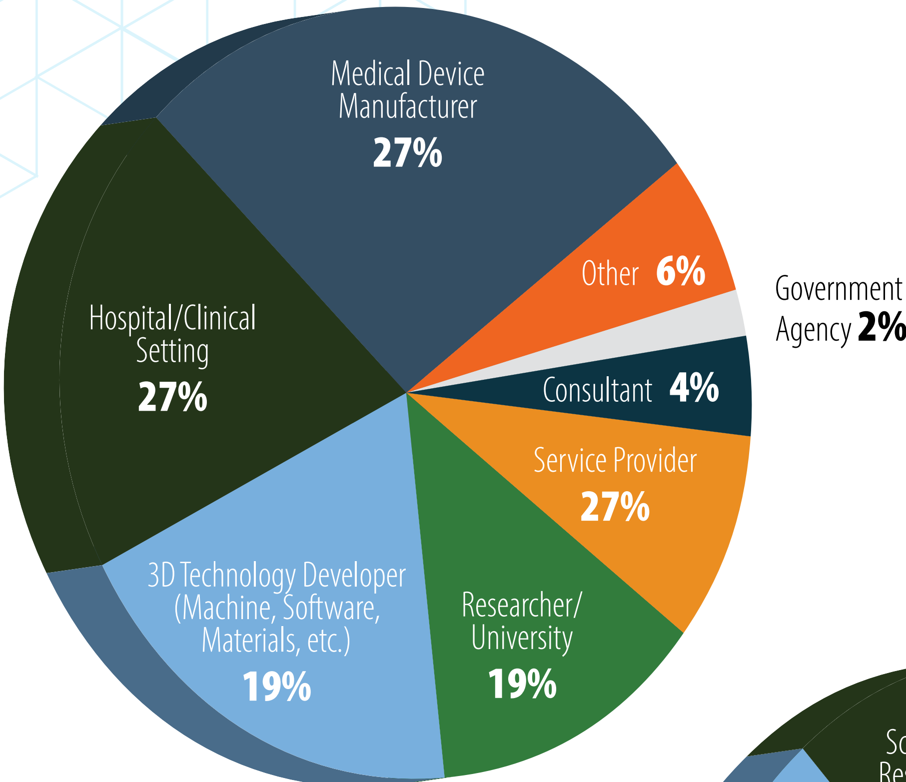
Expectations By Material



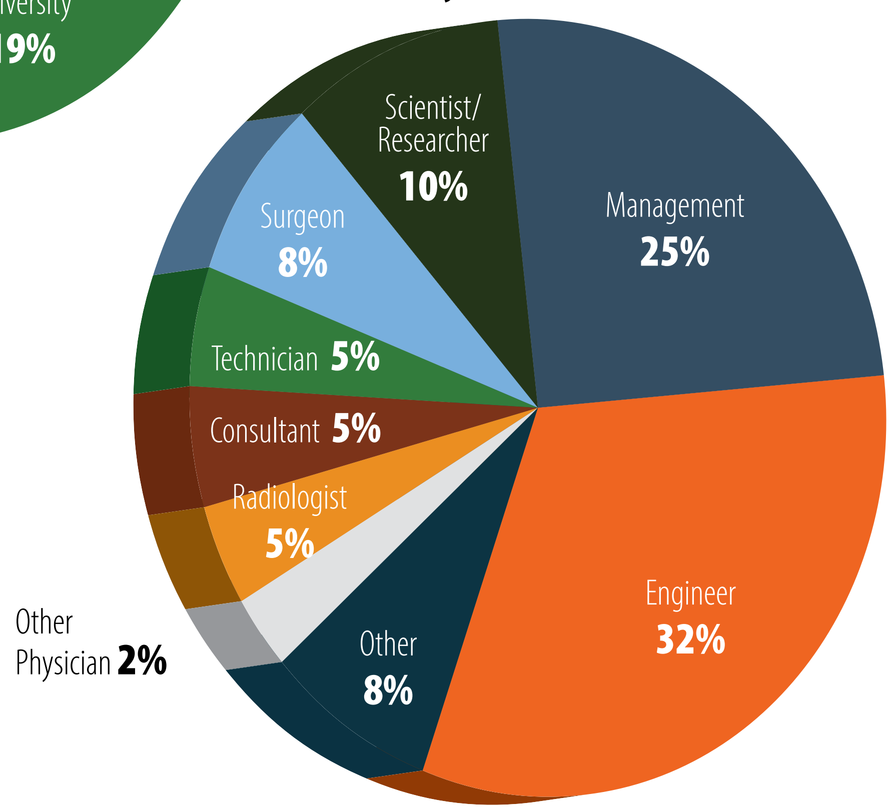
APPENDIX A: Profile of survey responders

sample size = 181; 95% confidence level

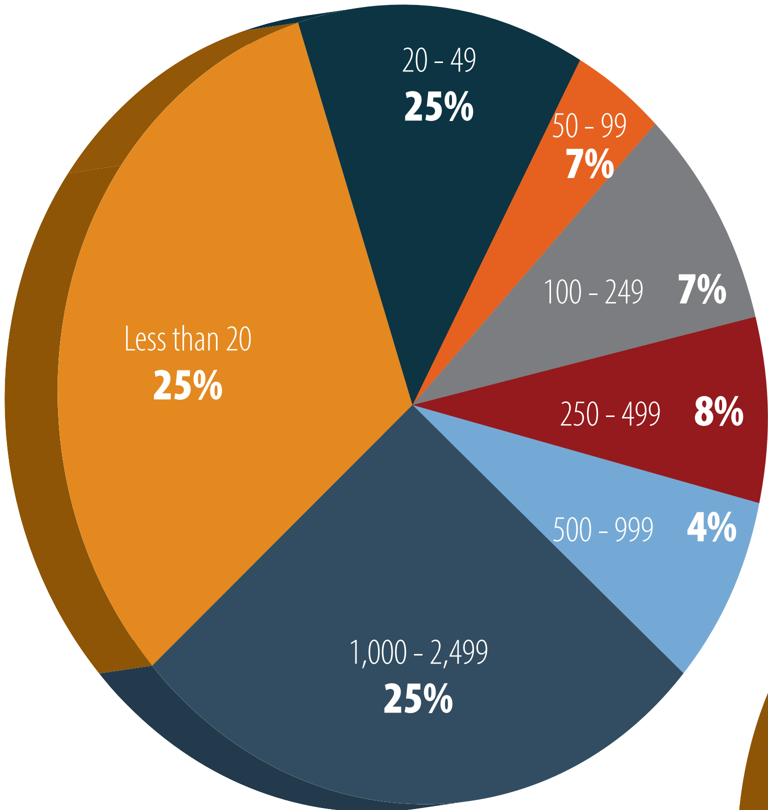
By Organization Type



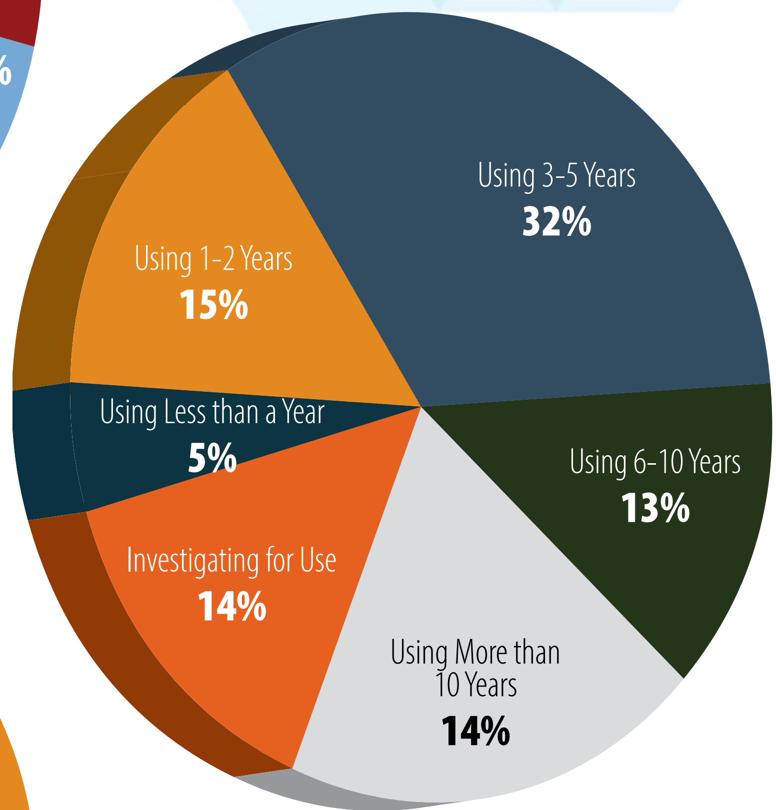
By Role



By Size (Number of Employees)



Experience Using AM3DP for Medical Applications



By Region