HOSPITAL STERILIZATION OF 3D PRINTED DEVICES

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Outline

- **Introduction** to 3D printing in Healthcare
- **Path of a 3D printed device** from Patient Scan to Operating Theater
- **Sterilization** of 3D Printed Devices
- **Overview** of Hospital 3D Printing Process
- **3D Printed Materials** after VH2O2 sterilization

Introduction to 3D Printing in Healthcare

- **3D printing/additive manufacturing (AM)** is the process of making three dimensional solid objects from a digital file
- **Applications in patient and healthcare professional education, training, pre-surgical and surgical use, and as a personalized implant**
  - Better patient experience: less pain, shorter hospital stays and quicker recoveries
- **In healthcare, 3D printing is not new**
  - GE™ Additive Arcam™ has made over 100,000 3D printed hips since 2007*
  - What is new is the Point-of-Care, in-hospital printing of patient-specific devices
  - Is MDR appropriate for hospital produced devices?
    - Chapter II, Article 5: regulation shall not apply to devices manufactured and used in a hospital so long as certain conditions are met

* https://www.ge.com/additive/stories/3d-printed-joints-implants-100000-patients-later-3d-printed-hip-decade-old-and-going-strong

3D Printing Techniques

Fused Deposition Modeling (FDM)

A strand of material is heated and deposited in layers to create a 3D printed object

Direct Metal Laser Sintering

Creates objects by fusing a metal powder with a laser

Stereo-Lithography Apparatus (SLA)

A curable photopolymer (typically a liquid resin) is hardened by applying focused light or UV light

Material Jetting (MJ)

Droplets of material are selectively deposited and cured on a build plate

Selective Laser Sintering (SLS)

A laser is used to fuse a thermoplastic powder to build parts

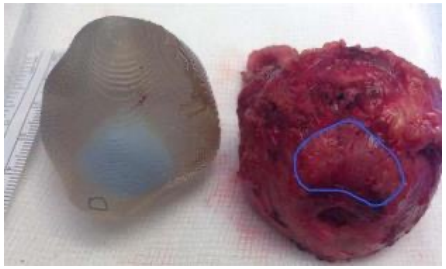
Electron Beam Melting (EBM)

An electron beam is used to fuse metal powder together to build parts

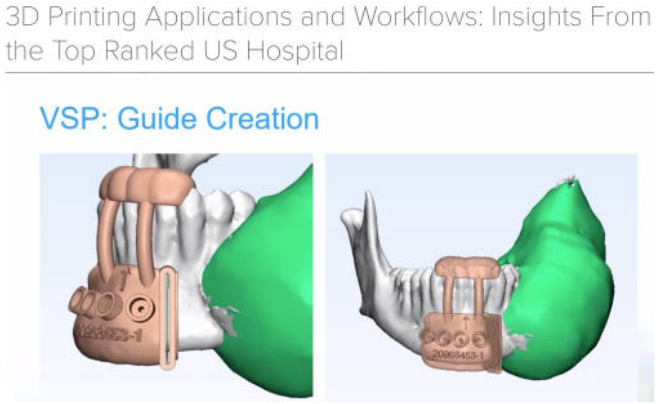
Why 3D Print in Healthcare?

Splint/Prosthetics
Patient specific, quick production

Hearing Aid
Complex design, quick production



Training/Patient Education



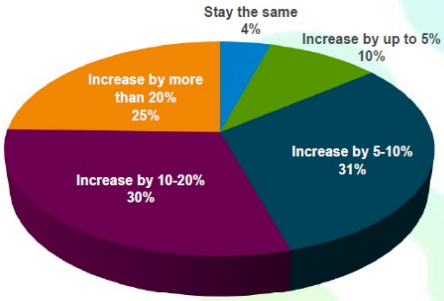
Surgical Guide
Patient specific, surgical use

https://www.3ders.org/articles/20160304-london-doctor-uses-3d-printed-model-to-successfully-remove-prostate-tumor.html

Expected Growth in 3D Device Use

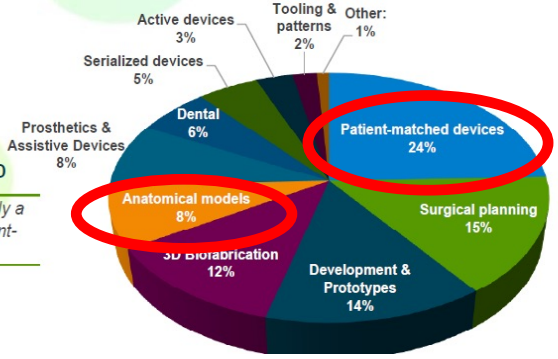
Community Survey

During the first quarter of 2020, the medical additive manufacturing/3D printing community was surveyed to better understand how the technology is being used, what challenges exist, and expectations for growth. A total of 308 responded from diverse application areas.



GROWTH IS EXPECTED WIHTIN 1 YEAR

80% expect the applications of medical and dental additive manufacturing to increase more than 5% and nearly half (48%) expect more than 10% in the next year. Although "decrease" was a survey option, no one responded that they expect to see a decrease in use.

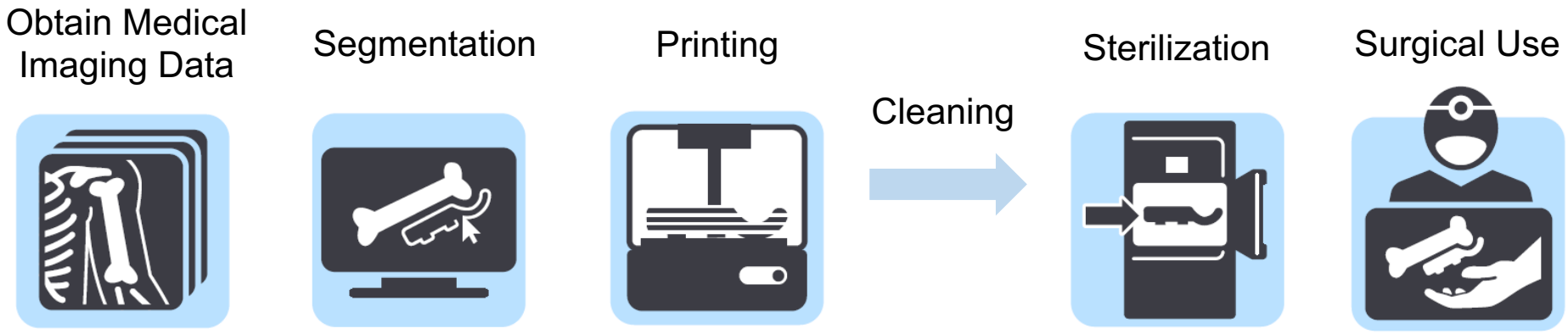


WHERE THE GREATEST GROWTH IS EXPECTED

Growth is expected in all application areas with nearly a quarter (24%) expecting the greatest growth in patient-matched devices.

https://resources.asme.org/hubfs/AM%20Summit/Medical%20AM3DP%20Year%20In%20Review%2019-20.pdf

Path of a 3D/AM Device from Patient Scan to Operating Theater



Regulatory Challenge: Lack of standards or guidance for in-hospital 3D printing in hospital

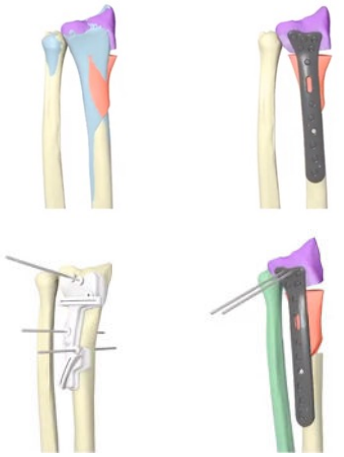
Path of a 3D/AM Device from Patient Scan to Operating Theater

Obtain Medical Imaging Data

- **Radiology and image acquisition processes**
  - Computed Tomography (CT)
  - Magnetic Resonance Imaging (MRI)
  - Ultrasound (US)

Segmentation

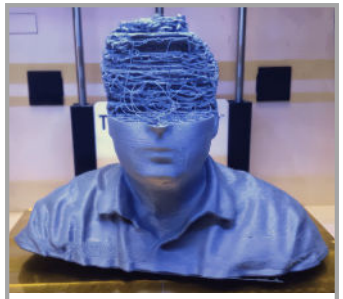
- **Segmentation software manufacturer** is responsible for providing validated, cleared software with clear instructions for use
- **3D lab performs segmentation and conversion** of patient data to 3D printer readable files
- **Clinicians review segmentation data** and generate surgical plan



Path of a 3D/AM Device from Patient Scan to Operating Theater

Printing

- **3D lab prints device** with an approved printer and material
- **Radiology and hospital 3D print lab** are responsible for following the printer manufacturer's instructions for use (including the post-processing steps), the process validation and quality control procedures



A Quality Management System is Needed!

Cleaning

Sterilization

- Wash, clean, dry and package for sterilization
- Sterilize as directed for the material

Surgical Use

Sterilization of 3D Printed Devices

- **Industrial Sterilization Methods for 3D printed items**
  - Radiation
  - Ethylene Oxide
  - Vaporized Hydrogen Peroxide
- **Hospital Sterilization Methods for 3D printed items**
  - Steam
  - Ethylene Oxide
  - Vaporized Hydrogen Peroxide

Sterilization of 3D Printed Devices

- **A 3D print sterilization process should demonstrate**
  - Sterile efficacy
  - Biocompatibility (pre- and post-sterilization)
    - ISO 10993 series
    - Level of testing is based on device application
  - Material compatibility
    - Material properties
    - Geometric stability

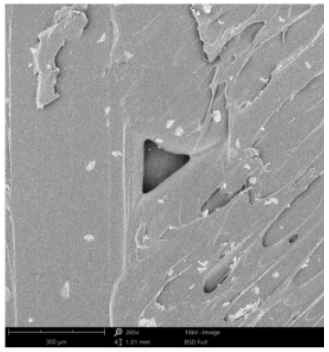
Biocompatible

(adj.) compatible with living cells, tissues, organs, or systems, and posing no risk of injury, toxicity, or rejection by the immune system.

3D Printing Special Interest Group (rsna.org)

Sterilization of 3D Printed Devices

- **Print in a clean, controlled environment**
- 3D devices should be **printed in a way that allows for sterilization**
  - Popescu *et al* noted that FDM printed ABS showed formation of air gaps within layers
- **US FDA and Australian TGA have identified voids or bubbles within a 3D printed material** as a potential concern for sterilization
- Some processes may be more likely to create voids in printing



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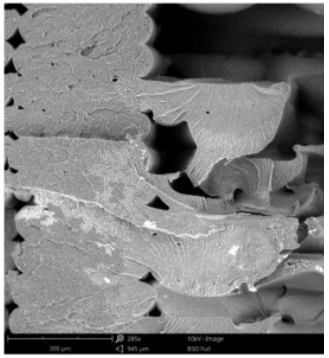


(d)

Popescu D_Effect Disinfect Absorption Med Decontam of 3D ABS parts_Polymers_2021 13 4249
2017, FDA, "Technical Considerations for Additive Manufactured Medical Devices Guidance for Industry and Food and Drug Administration Staff"
https://www.tga.gov.au/resources/resource/guidance/3-d-printing-additive-manufacturing-medical-devices

Sterilization of 3D Printed Devices

- Just as with traditional surgical guides, **surgeons can damage surgical guide**s during use with drills or sagittal saws
- **Potential for plastic debris and potential for contamination from voids** that are opened with the damage
- As with traditional medical device manufacturing, part production under a QMS with a **fully validated process mitigates the contamination risk**

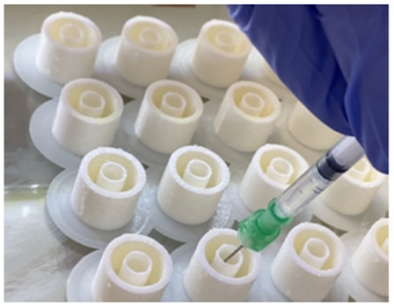
Shea G et al; A review of the manufacturing process and infection rate of 3D-printed models and guides sterilized by hydrogen peroxide plasma and utilized intra-operatively. 3D Printing in Medicine, 2020 6:7.

Sterilization of 3D Printed Devices

Does the 3D printing process sterilize devices?

- Neches evaluated FDM printed items for their intrinsic sterility
  - FDM printer with thermal contact time of 16s at 220°C
    - *Staphylococcus epidermidis* and *Propionibacterium acnes* observed (common to skin)
  - SLA printer: UV light cure is part of process

- Aguado-Maestro *et al* evaluated FDM printed cylinders, halting the manufacturing process halfway and inoculating with E8 *S. epidermis*
  - Printing was resumed and sealing of cylinders completed
  - Cylinders sterilized with EO, steam and VH2O2
  - No growth in EO or steam; 1-12 CFU in unsterilized and VH2O2



Neches RY, Flynn KJ, Zaman L, Tung E, Pudlo N. 2016. On the intrinsic sterility of 3D printing., PeerJ, 4:e2661

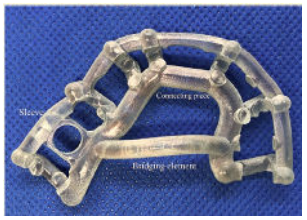
Aguado-Maestro, M. De Frutos-Serna, A. González-Nava et al., Are the common sterilization methods completely effective for our in-house 3D printed biomodels and surgical guides? Injury, VOLUME 52, ISSUE 6, P1341-1345, JUNE 01, 2021

Sterilization of 3D Printed Devices

- **VH2O2 is used industrially** to sterilize 3D printed items
- **Vaporized hydrogen peroxide sterilizers** already in hospital are being used to sterilize 3D printed devices
- **Multiple publications from around the world**
  - Studies do not evaluate all aspects of sterilization verification (efficacy, biocompatibility and material compatibility)
- **The hospital sterilizer's current cycles do not have claims for 3D printed devices**

VH2O2 Sterilization of 3D Printed Devices

Author (year)	Result
Török (2020)	• Disinfection and sterilization effect on dimensional changes and mechanical properties of 3D printed surgical guides • The guides were not changed by the VH2O2 sterilization or steam sterilization at 121 °C.
Shaheen (2018)	• Evaluated after steam and VH2O2 sterilization for material changes, specifically volume of the test article • Steam was noted to have an effect, VH2O2 did not
Shea (2020)	• Clinically used devices infection rate for VH2O2 sterilized 3D-printed models and guide • Infection rate (7%, 8/114) not different traditional surgical methods. • Of the 114 cases, there were 59 anatomical models & 55 surgical guides
Toro (2021)	3D printed parts maintained dimensional stability after VH2O2 sterilization



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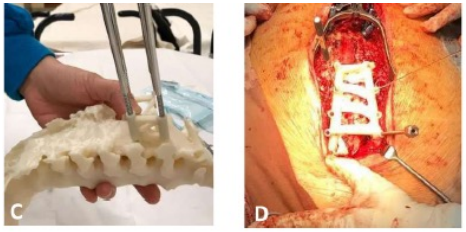
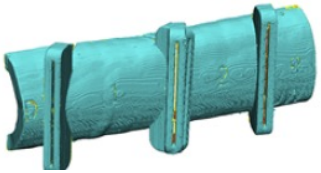


Shea



Toro

Török, G, et al; Effects of disinfection and sterilization on the dimensional changes and mechanical properties of 3D printed surgical guides for implant therapy – pilot study., BMC Oral Health (2020) 20:19.

Shaheen E, et al; Evaluation of dimensional changes of 3d printed models after sterilization: a pilot study. Open Dent J 2018;12:72–9.

Shea G; et al, A review of the manufacturing process and infection rate of 3D-printed models and guides sterilized by hydrogen peroxide plasma and utilized intra-operatively, 3D printing in medicine, (2020 Mar 30) Vol. 6, No. 1, pp. 7.

Toro M; et al, Does vaporized hydrogen peroxide sterilization affect the geometrical properties of anatomic models and guides 3D printed from computed tomography images?., 3D printing in medicine, (2021 Sep 14) Vol. 7, No. 1, pp. 29.

Sterilizer Indications for Use

The Specialty Cycle Can Sterilize:

Patient-specific surgical guides (e.g. osteotomy, shoulder, hip, knee, spine) or anatomical models fabricated via additive manufacturing (3D printing) processes and intended for single-use during operative procedures**

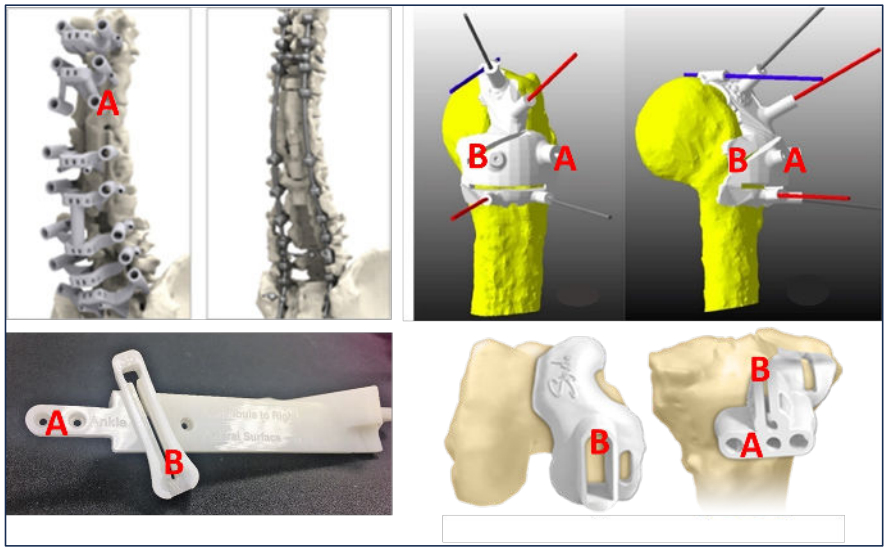
** The validation studies were conducted using a validation load consisting of pouched guide(s)/model(s) (with or without tray) for a total weight of 5 lbs (2.3 kg) 3D printed material. Devices used in validation studies were prepared in accordance with printer manufacturers' instructions for use, to include printing, curing, removal of support material and cleaning

Material	Printer(s)	Manufacturer	Specialty Cycle	Lumen Inner Diameter (ID) x Length (L)
BioMed Amber Resin	Form 3B, Form 3B+, Form 3BL	Formlabs™	F	≥3 mm ID x ≤30 mm L
BioMed Clear Resin	Form 3B, Form 3B+, Form 3BL	Formlabs™	D	≥3 mm ID x ≤30 mm L
Biocompatible Clear MED610	J720™ Dental, J750™ 3D, J750™ Digital Anatomy, J850™ Digital Anatomy	Stratasys™	E	≥3 mm ID x ≤20 mm L
Biocompatible Opaque MED615RGD	J750™ 3D, J750™ Digital Anatomy, J850™ Digital Anatomy	Stratasys™	E	≥3 mm ID x ≤20 mm L
VeroGlaze™ MED620	J720™ Dental, J750™ 3D	Stratasys™	E	≥3 mm ID x ≤20 mm L

K223476 at FDA 510(k) Premarket Notification website.

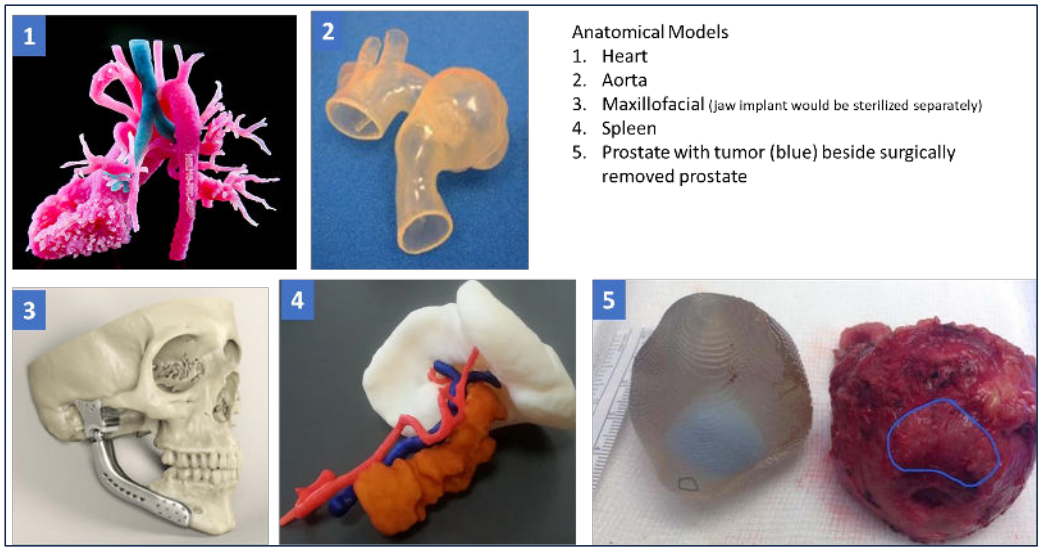
Surgical Guides and Anatomical Models

Surgical Guides



*Pin guides/penetrations (A), Surgical guide slits (B)

Anatomical Models



Specialty Cycle Design

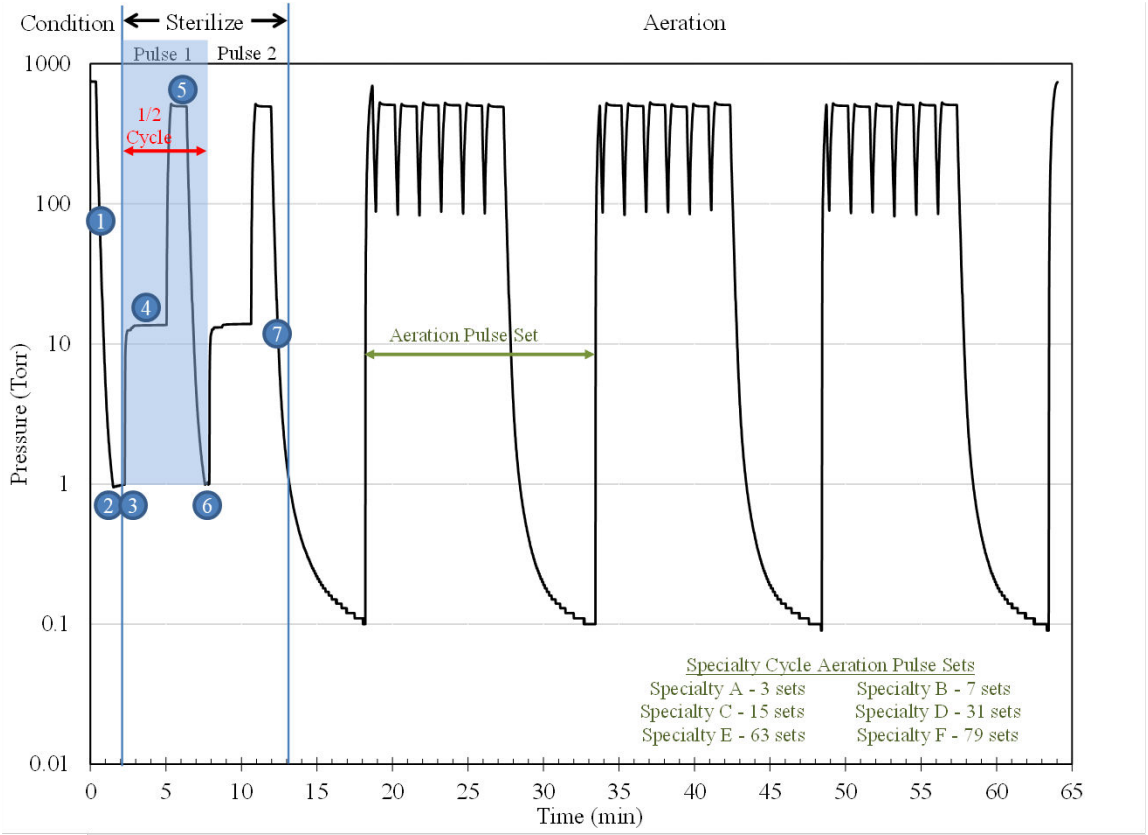
Condition Phase

Sterilize Phase

- 7.5 minutes

Aeration

- Different aeration time based on material
- Aeration time set to ensure device is biocompatible after processing
- Observation: 3D printed materials more difficult to aerate than reusable medical devices (aerated in 6 minutes or less)



Specialty Cycle Design

- **Hydrogen peroxide** release from a material can be fast or slow
- **Aeration design** is based upon applying heat with air flushes and vacuum to remove H_2O_2
  - Evaporation is endothermic and will cool a material
  - Heat can be applied to provide a driving force for vaporization
  - Heat transfer is poor under vacuum. Further, heat transfer is limited to surfaces and the subsequent thermal transfer within an object
  - Expectation is that device will be at chamber temperature (50C) in about 60 minutes. At this point, hypotheses is that residual removal governed by diffusion of H_2O_2 to outer surfaces where vaporized

US Patent 11,541,139

Specialty Cycle Microbicidal Efficacy

Sterilization

- A proprietary designed test article was used to evaluate for surface and lumen sterilization
- 3D printed test articles of each material were used for evaluations in three Specialty Cycles per material
- 10^6 *Geobacillus stearothermophilus* spores per test site (most resistant organism to VHP sterilant)
- Exposed to a one-pulse cycle with 59% hydrogen peroxide
- Incubated in growth media then evaluated for growth
- All sterile results verifies sterilization efficacy

Material	Specialty Cycle	Lumen Sites		Surface Sites
		Lumen Dimension	# Sterile/# Tested	# Sterile/# Tested
Formlabs BioMed Amber	F	3 mm ID x 30 mm length	6/6	18/18
Formlabs BioMed Clear	D	3 mm ID x 30 mm length	6/6	18/18
Stratasys MED610	E	3 mm ID x 20 mm length	6/6	18/18
Stratasys MED615	E	3 mm ID x 20 mm length	6/6	18/18
Stratasys MED620	E	3 mm ID x 20 mm length	6/6	18/18

Specialty Cycle Biocompatibility

- All materials are identified by their manufacturer (Formlabs or Stratasys) as Biocompatible
- In accordance with ISO 10993-1, 3X processed Specialty Cycle processed materials were categorized for use as a limited contact (< 24 hour) patient contact via mucosal membrane, breached or compromised surface, blood path (indirect), circulating blood, or tissue/bone/dentin

Material	Evaluation					
	Cytotoxicity* ISO 10993-5	**Sensitization ISO 10993-10****	**Intracutaneous testing ISO 10993-10****	**Systemic Toxicity ISO 10993-11****	**Material Mediated Pyrogenicity ISO 10993-11****	**Hemocompatibility ISO 10993-4****
Formlabs BioMed Amber	Not cytotoxic	Not sensitizing	Not an irritant	Not a systemic toxin	Not pyrogenic	Hemo-compatible
Formlabs BioMed Clear						
Stratasys MED610						
Stratasys MED615						
Stratasys MED620						

* Testing conducted at STERIS in accordance with ISO 10993-5 standard under Good Laboratory Practice (GLP) regulations as provided in 21 CFR § 58.

** Testing conducted at NAMSA in accordance with the identified ISO 10993 standards. NAMSA is certified to ISO 9001:2015 and is accredited to ISO/IEC 17025:2017.

Specialty Cycle Sterilant Residue

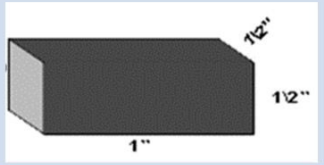
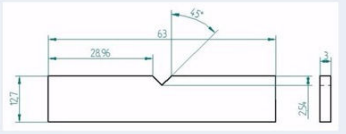
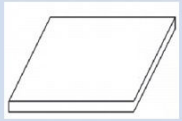
- Materials were processed for three Specialty Cycles
- Extracted and evaluated for hydrogen peroxide residual for 72 hours

Hydrogen Peroxide Sterilant Residue After 3x Specialty Cycle Exposure and 72-hour Extraction

Material	Specialty Cycle	mg H_2O_2/g Device
Formlabs BioMed Amber	F	0.27
Formlabs BioMed Clear	D	0.22
Stratasys MED610	E	0.13
Stratasys MED615	E	0.12
Stratasys MED620	E	0.12

Specialty Cycle Material Evaluations

- **Mechanical Properties Evaluations**
  - Based on ISO/ASTM 52910:2018(E) *Additive Manufacturing – Design – Requirements, guidelines and recommendations*
  - Coupons printed for each method
  - Worst-case chemical exposure (15x Specialty Cycle sterilant dose)
  - Simulated Use, single Specialty Cycle exposure (select tests)

Test Method	Standard Number	Test Specimen
Tensile Properties	ASTM D638	
Flexural Properties	ASTM D790	
Compressive	ASTM D695	
Izod Notched Impact	ASTM D256	
Shore Hardness	ASTM D2240	

Material Compatibility

Mechanical Property Evaluations after Worst-Case Chemical Exposure

Test Name	ASTM	Result
Tensile Strength	D638	Results showed either: • No statistical difference from unexposed control • Greater strength after exposure • Non-significant loss in strength
Flexural Strength	D790	
Compressive Strength	D695	
Izod notched impact	D256	
Shore Hardness	D2240	

Mechanical Property Evaluations after Simulated Use Exposure

Test Name	ASTM	Result
Tensile Strength	D638	Results showed: • Simulated Use exposure is less aggressive than worst-case chemical exposure
Compressive Strength	D695	
Shore Hardness	D2240	

Material Compatibility

- Comparison of published data to VH2O2 Sterilizer processed material

Stratasys MED610 Test Name	Sterilization Method / % Change after sterilization					
	Steam 4 min 132°C % change[1]	Gamma % change[1]	EtO (after 1 cycle) % change[1]	Steam 20 min 121°C % change[2]	Steam 10 min 134°C % change[2]	VH2O2 Exposure % change
Tensile strength	-6%	19%	11%	-3%	15%	-7.5%
Flexural Strength	-4%	42%	41%	0 to -7%	-44 to 14%	11.6%
Impact, Xy, cut notch	-1%	-5%	-7%	---	---	9.7%
Dimensional Changes	0 to < 0.35 mm	0 to < 0.1 mm	0 to < 0.3 mm	---	---	0 to ≤ 0.2 mm

1. Stratasys "Creating full color medical models that can be sterilized." Technical application guide, 2021
2. Török, G, et al; Effects of disinfection and sterilization on the dimensional changes and mechanical properties of 3D printed surgical guides for implant therapy – pilot study., BMC Oral Health (2020) 20:19.

Structural deformation seen with steam at 134 °C.

Specialty Cycle Dimensional Analysis

- **Dimensions evaluated pre- and post-sterilization**
  - physical measurements (calipers)
  - Scanning with a Faro inspection arm/digital scanner
- **Twenty to twenty-seven** physical measurements were made for each model

Dimensional Analysis Pre- and Post-Sterilization Differences

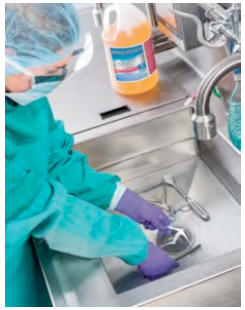
Material	3D Scan Differences	Measured Differences
Formlabs BioMed Amber	≤ 0.5 mm	≤ 0.01 mm
Formlabs BioMed Clear	≤ 0.1 mm	≤ 0.01 mm
Stratasys MED610	≤ 0.2 mm	≤ 0.1 mm
Stratasys MED615	≤ 0.5 mm	≤ 0.1 mm
Stratasys MED620	≤ 0.5 mm	≤ 0.1 mm

New Path of a 3D/AM Device from Printing to Surgical Use

- **Sterilizer IFU with validated process provides value to sterile processing department**

Printing

Cleaning



Packaging

Sterilization

Surgical Use

Conclusion

- **3D printing medical devices** at the Point of Care (POC) **is growing**
- **Radiological and medical community is engaged**
- **VH2O2 is a fully compatible sterilization method** for select 3D printed medical devices
- **V-PRO™ maX 2 Sterilizer Specialty Cycle is a validated sterilization process** for specified materials, printers, and device designs

Additional Resources

Questions

- Journal of 3D Printing in Medicine
- RSNA (Radiological Society of North America) 3D Printing Special Interest Group (SIG) (https://www.rsna.org/membership/involvement-opportunities/3d-printing-special-interest-group)
- US FDA (https://www.fda.gov/medical-devices/products-and-medical-procedures/3d-printing-medical-devices)
- American Society of Mechanical Engineers (ASME). https://www.asme.org/topics-resources/content/additive-manufacturing
- YouTube