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22nd Asian Harmonization Working Party Annual Meeting

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Considerations in Quality Management of 3D printed Medical Devices

Dr. Jang-yong Choi

Ministry of Food and Drug Safety

Dr. Jangyong Choi

Deputy Director
Medical Device Safety Evaluation Division
Korea MFDS

- Main expertise: Medical device policy, inspection & QMS
- AHWP WG member

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1. QMS and its Operation of Korea MFDS

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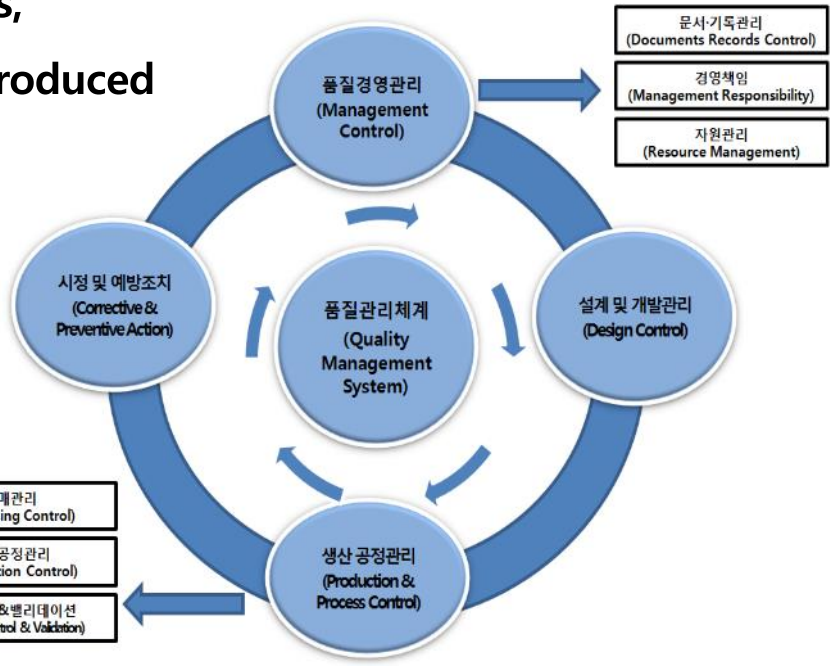
QMS (Quality Management System)

ensures **safety** and **effectiveness of** medical devices,

and guarantees that the devices are **consistently** produced

with appropriate quality to its **intended use.**



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QMS (Quality Management System)

1. Based on International Standard, ISO 13485

2. Audit types :
   - ① Initial audit : An initial audit to approve QMS conformity assurance
   - ② Renewal audit : At least one audit that will be conducted in 3 years after the initial audit
   - ③ Audit of approval changes : Audits to be conducted again if manufacturers notify changes of manufacturing sites.
   - ④ Supplementary audit : Audits to be conducted if a product is added from a different product group

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QMS (Quality Management System)

3. Audit method : Conducting on-site audits and document review for each product group of manufacturing sites

※ Product group : Products whose raw materials, manufacturing process and quality management system are similar to those of which have been classified into 26 groups

4. Certification period : 3 years

5. Miscellaneous information :

① Low-risk class 1 medical devices excluded

② 6 regional offices and 4 medical device quality audit institutions are conducting on-site audit and document review together

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2. 4th Industrial Revolution and 3D Printing

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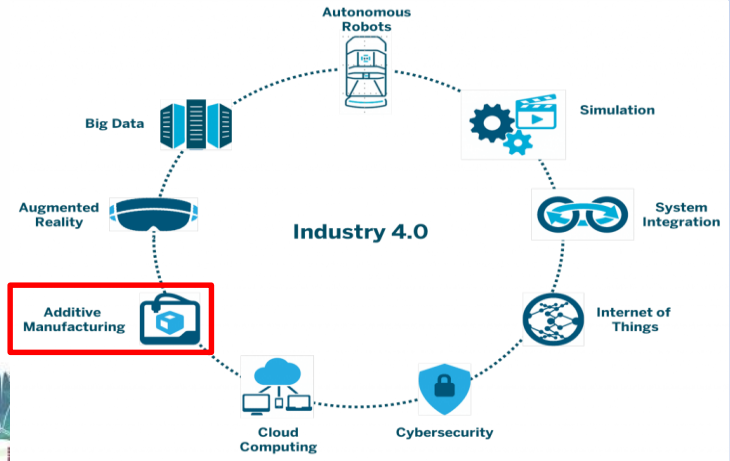
Industry 4.0

- A new era of converged technologies without any digital, physical and biological boundaries
- Paradigm shift focusing on prediction, prevention and consumer participation
- 3D printing technology is one of the best emerging technologies selected in the era of 4th industrial revolution at the World Economic Forum (WEF)

* Artificial Intelligence (AI) & Robotics were selected to Top List of Technologies in Need if Better Governance('16.11)



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The Pros and Cons

PROs

Amazing medical and design possibilities

Can reduce labor time and cost

Can allow for more customization

Can reduce risk of danger associated with some manual prototyping processes

CONs

3D printing tech has a long way to go

Print speed

Limited material offering

Not always easy to use

The possibility for unnecessary overproduction

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3D Printing Technologies

Process (ASTM)	Description	Materials	Pros	Cons
Material extrusion	Material extruded through nozzle	ABS, PC, PLA, ULTEM	Parts are relatively strong and can be good for some functional testing. Can make complex geometries.	Poorer surface finish than SLA and SLS
Material Jetting	Droplets of material deposited	Acrylic-based photopolymers, elastomeric photopolymers, wax-like materials, "digital" materials	Yields best surface finish of additive processes and is the best choice for complex parts with undercuts.	Poor strength compared to SLA
Binder Jetting	Liquid bonding agent is deposited to join powder materials	Plaster, metal, sand	Fastest time of any additive process. Can print in multiple color combinations and is one of the least expensive options for prototyping.	Parts are rough and less durable.
Sheet Lamination	Sheets of material are bonded and cut	Plastic, metal, paper	Inexpensive, full color prints using paper. Strong metal parts with composite materials.	Paper models are not durable. Few ultrasonic machines.
Vat Photopolymerization	Liquid photopolymer in a vat is cured by light-activated polymerization	Photopolymers	Can produce parts with complex geometries and excellent surface finishes compared to other additive processes.	Parts are weaker than those made from engineering grade resins; typically unsuitable for functional testing.
Powder Bed Fusion	Thermal energy fuses regions of a powder bed	Metal, plastic	Fully dense (~99.5%). Extremely durable. No post thermal treatment required. Strong parts. Most are fully functional.	Poor surface finish combined with expensive materials.
Directed Energy Deposition	focused thermal energy fuses and melts material as it is being deposited	Metal	Ideal for adding material to existing parts for repair or hybrid manufacturing.	Worst surface finish of all additive processes. Usually requires post-operations.

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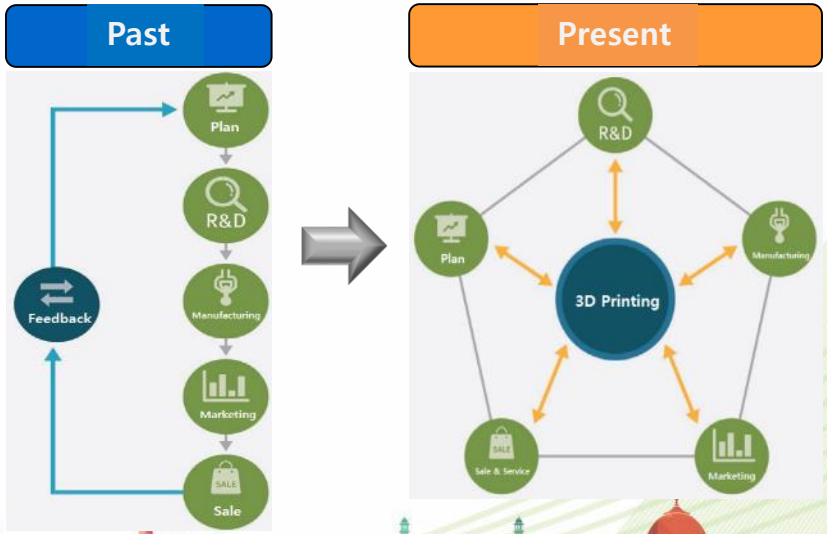
Paradigm Shift (Patient-specific medical devices using 3D printing)

- Changes to production and consumption processes

  ** mass production and conventional & uniform services*

  → customized production service

- Streamlining manufacturing process and reducing time and costs (revolution in manufacturing)



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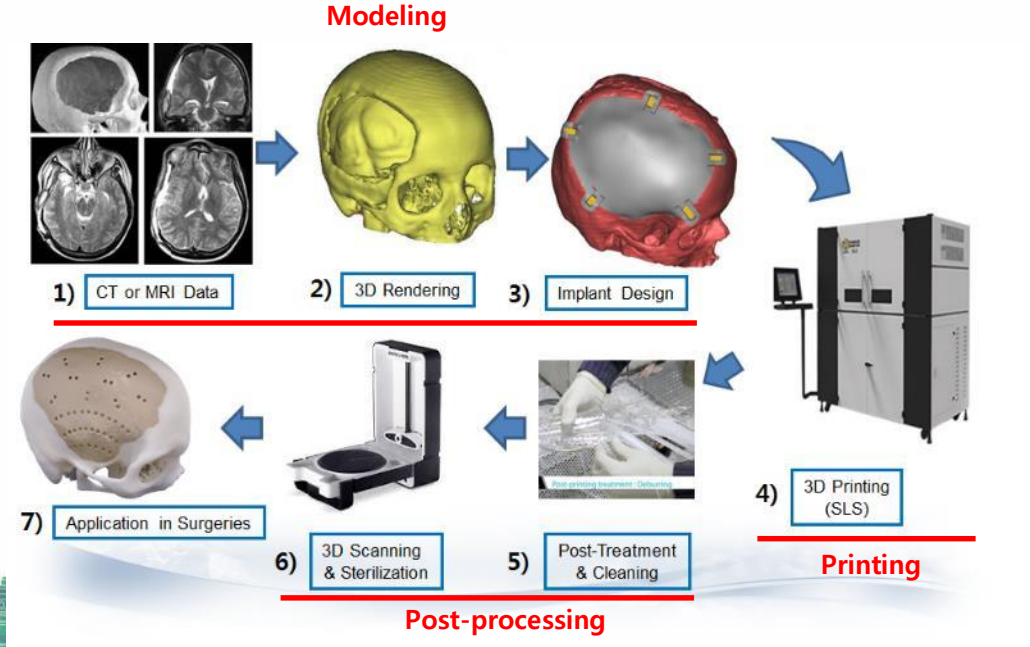
3D printing

- Manufacturing 3-dimensional medical devices by laminating materials based on 3D data
- Manufacturing process : Modeling → Printing → Post-processing



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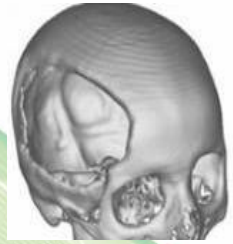
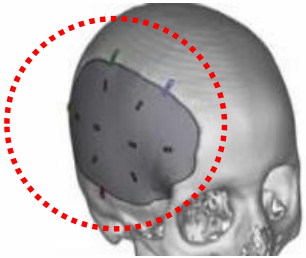
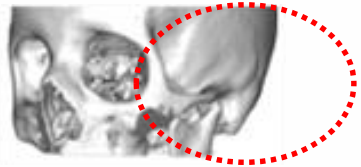
Current development status of 3D printed medical devices in Korea

- Cranioplasty plate : an implant to restore defects of cranial bone

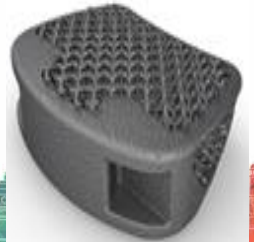




- Zygomatic Prosthesis : an implant to replace or restore zygomatic bone



- Spinal Cage : an implant to treat structural abnormality due to degenerativeintervertebral disks



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3. Considerations when implementing QMS

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Interactive Order Process

- **Effective communication procedure to reflect user requests into product realization**

1) Use separate identification number to protect confidential information regarding the patient including medical images

2) Need informed consent form for release of patients' personal information to manufacturers

3) Ensure bi-directional communication between manufacturers and users

4) Designated persons for every step (placing an order, design, review, shipping and delivery, etc.)

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Documentation Requirements (ISO 13485 4.)

- Identify, document, and record user's requests related to medical device designs
- Verification procedure of 3D design that is matched to a patient's medical images and user's requests
- Management and documentation of total life cycle of design files including revisions
- Storage and disposal management of patients' medical images
- Tracking and management procedure of products from manufacturing to distribution

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Resource Management (ISO 13485 6.)

- Documentation on specific information of raw materials, additives and cross linking agents
  * laminating process using 3D printing technology involves significant physical and chemical changes in accordance with raw materials

- Specification and testing methods of raw materials based on the corresponding 3D printing technology
  * (raw material) The available raw materials differ depending on the facilities powder, liquid, hardening, etc.
  * (testing method) Testing methods are different depending on the raw material types - solid, liquid, polymer, metal, ceramic and animal tissues

- Considerations on recycling of raw materials (residual power after injection)
  * verify the recycling of raw material that does not impact on the finished product
  * monitoring for changes on chemical characteristics and oxygen and water content of the recycling of raw materials

※ Technical Consideration for Additive Manufactured Devices, FDA, 2016

(2) Material Recycling

Some additive manufacturing approaches (e.g., powder bed fusion, stereolithography) allow efficient use of raw material by recycling the material that is not incorporated into the device (e.g., unsintered powder or uncured resin). However, the reused material could be exposed to conditions (e.g., heat, oxygen, humidity, ultraviolet energy) that may alter it from the virgin state. Therefore, we recommend that you describe the material recycling process, which may include, but is not limited to, a description of recycling processes such as filtering recycled material, or monitoring for changes in chemistry, oxygen, or water content. We also recommend that you document evidence that material recycling does not adversely affect the final device. This may include an assessment of the recycling protocol by conducting studies on the effect of material recycling on the properties of the final finished device (see section V.E.1 Process Validation).

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Human Resources (ISO 13485 6.2)

- **Setting a qualification standard to evaluate eligibility in each position**
  - * (modeling) understanding of anatomical images of patients, experience in basic design of modeling, education and qualifications, etc.
  - * (3D printing) understanding of 3D printing technology, experience in quality management and qualifications, etc.
- **Establishing specialized training for employees in each position**
  - * providing periodic training in phases for employees involved in managing quality system
- **Considering having a certificate for appropriate qualification (modeler)**
  - * for example, a license for design management using 3D printing software

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Work Environment and Contamination Control (ISO 13485 6.4)

- **Prevention of flowing- in pollutants**
  * Clean room or the corresponding environment is needed in case of exposure to external environment for its laminated manufacturing method
  * Validation of products or facilities is needed including door opening & closing process and initial setting process when the 3D printer itself is sealed such as vacuum chamber from the external environment

- **Consideration of environmental factors related to 3D printer methods**
  * establishing management standard which can control temperature, humidity, electromagnetic waves, magnetic field, dust and gas supply, etc.

- **Establishment of appropriate facilities and space for post- processing after printing**
  * air jetting, water pressure jetting, polishing, ultrasonic wave cleaning and sterilization, etc.

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Customer-related Processes (ISO 13485 7.2)

- **Essential contents to review**
  - * delivery schedule, modifiable and unmodifiable ranges if existing products are modified, response and procedure for changes in requirements, range of warranties, unit cost, delivery methods, performance, and stability, etc.
- **Essential contents to maintain**
  - * information on the user who placed an order, intended use, scope of design and design modifications, Unique Number(traceable) and vendors, etc.
  - * materials such as medical images that are needed for designing and modeling to manufacture the product (personal information of patients excluded)
- **Final verification to confirm user requests before printing**
  - * including verification and confirmation process before the printed product is used for clinical trials

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Design and Development (ISO 13485 7.3)

- Establishment of responsibilities and authorities for tasks among different groups and departments
  * internal review process between the relevant groups and departments
  * Preparation of documentation format for user's requests when placing a direct order in person
  * Interactive communication between designer and user for good design transfer activities

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Production and Service Provision (ISO 13485 7.5)

- For porous structure in patient-specific medical devices, validation of cleaning and sterilization of residual materials should be confirmed.
  * Verification of cleaning and sterilization of the internal structure residues (geometric structure)
  * For residue materials that are removed during the manufacturing process (ex. Metal powder), there should be a label placed on the product to avoid confusion or error
  * Separate maintenance procedure for pre-cleaning, cleaning and post-cleaning processes

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Identification and Traceability (ISO 13485 7.5.3)

- **Identification and traceability management through Unique Number:**
  - * Use of UN since a patient-specific medical device is produced only one lot
  - * Traceability of all processes including raw material of products, modified design and inspection
  - * Continuous recording of activities by manufacturers if maintenance is needed after delivering products

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Monitoring and Measuring of Processes
(ISO 13485 8.2.5)

- Identifying necessary 3D imaging equipment that can verify the products' conformity
  * Rapid Prototyping model, 3D scanner, 3D Jig, etc.
- Establishing test parameters for different types of patient-specific devices
  * elasticity, solidity, viscoelasticity, fatigue and abrasion, etc.
- Monitoring and management for any negative influence due to false manufacturing method

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4. Other Considerations

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Quality Management System(QMS) of Medical Devices is to ensure safety and effectiveness of medical devices and to guarantee that the devices are consistently produced with appropriate quality to its intended use.

In order to meet the requirements of QMS for patient-specific medical devices using 3D printing technology, there exists additional matters to consider as we went over, including “interactive order process”, “documentation requirements”, “resource management of raw materials, human resources and environment”, “design and development”, “identification and traceability” and “monitoring and measurement”

However, it does not imply that the goal of QMS for patient-specific medical devices was achieved; therefore, continuous efforts and improvements are needed.

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Thank you

- Jangyong Choi
- E-mail: navante1@korea.kr