

Review Article

3D Printing Technologies in Personalized Medicine

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3D printing technologies enable medicine customization adapted to patients' needs. There are several 3D printing techniques available, but majority of dosage forms and medical devices are printed using nozzle-based extrusion, laser-writing systems, and powder binder jetting. 3D printing has been demonstrated for a broad range of applications in development and targeting solid, semi-solid, and locally applied or implanted medicines. 3D-printed solid dosage forms allow the combination of one or more drugs within the same solid dosage form to improve patient compliance, facilitate deglutition, tailor the release profile, or fabricate new medicines for which no dosage form is available. Sustained-release 3D-printed implants, stents, and medical devices have been used mainly for joint replacement therapies, medical prostheses, and cardiovascular applications. The challenge is to select the 3D printing technique most suitable for each application and the type of pharmaceutical ink that should be developed that possesses the required physicochemical and biological performance. The integration of biopharmaceuticals and nanotechnology-based drugs along with 3D printing ("nanoprinting") brings printed personalized nanomedicines within the most innovative perspectives for the coming years. Continuous manufacturing through the use of 3D-printed microfluidic chips facilitates their translation into clinical practice. The integration of three-dimensional (3D) printing into biomedical research and personalized medicine reflects a significant paradigm shift in contemporary healthcare. This rapidly advancing technology offers substantial potential for breakthroughs in patient-specific therapeutic interventions and clinical innovation. This systematic review critically evaluates current literature to elucidate the status, challenges, and future prospects of 3D printing in enhancing biomedical applications and supporting tailored medical strategies.

Keywords: 3D-printed drugs, Personalized dosing, 3D printer, Polypills, Patient compliance, Drug release profile, Technologies of medicine pharmacogenomics, quality assurance, dosage forms, practicality.

INTRODUCTION

Three-dimensional printing (3DP) has been in existence for decades but has regained attention more recently due to the huge potential it holds to addressing several of the constraints associated with the current modality in therapeutic interventions. For example, conventionally manufactured dosage forms like tablets and capsules are regimented with a fit-for-all provision. Clinicians have limited options when gauging the required dose (based on the severity of the disease) from unit dose medicines like tablets or capsules. This situation is less acute with continuous dosage forms like syrups and suspensions. Limitations in calibrated dosing may pose constraints when prescribing/dispensing, which may

lead to sub-therapeutic levels or potentially toxic blood levels in patients. When we take into account the fact that patients express various levels of metabolizing enzymes such as CYP 450 and hence respond differently to the same treatment scheme, the preceding scenario is all the more crucial. As a result, pharmacogenomics, which deals with the interplay between genetic variations in individuals and their responses to medication, is recognized as key to ensuring safety in therapeutics. Several researchers have devoted their attention to unlocking many genetic codes that play a crucial role in drug metabolism. The emerging 3D printing technology signifies a ground-breaking evolution in the production of medicines, transitioning from conventional technological methods to additive

manufacturing. This advancement is particularly revolutionizing the pharmaceutical industry. For example, in hospital settings, 3D printing will facilitate the creation of personalized drug dosages, helping patients with specific medical needs. Similarly, in community pharmacies, this technology will enable on-demand drug production, ensuring medications are tailored to individual patients, thereby reducing wait times and enhancing treatment outcomes.

History

3D Printing posed as a possible platform for personalized medicine in the 1990s. There are major achievements in 3D printed medical device, FDA's Center for Device and Radiological Health (CDRH) has reviewed and cleared 3DP medical devices. The first 3D printing technique used in pharmaceuticals was achieved by inkjet printing a binder solution onto a powder bed, binding therefore the particles together. 3D printing is more advanced in the fields of automobile, aerospace, biomedical and tissue engineering than in the pharmaceutical industry where it is in its initial phase. FDA encourages the development of advanced manufacturing technologies, including 3D printing, using risk-based approaches [1,7]

Pros and Cons of 3D Pharmaceutical Printing:

The application of 3D printing in pharmaceuticals brings a range of benefits while also posing challenges, both of which play a crucial role in shaping its impact on drug [7,8]

development and patient care

One of the most significant transformative advantages of 3D printing in the pharmaceutical industry is the ability to customize medication. This technology enables the tailoring of drug combinations, release mechanisms, and dosages according to the specific requirements of each patient, thereby substantially improving treatment efficacy and adherence. In addition to facilitating customization, 3D printing enables the creation of intricate structures and geometries that cannot be achieved using conventional manufacturing techniques, thus facilitating the advancement of innovative medication

delivery systems. Sophisticated drug release profiles, including staggered or delayed release, are made possible by these novel structures, which effectively optimize therapeutic outcomes while reducing adverse effects. [1] The research and development phases of the pharmaceutical industry can be accelerated due to the streamlined design and production of prototype medications made possible by the rapid prototyping capabilities of 3D printing. Furthermore, the utilization of 3D printing technology enables hospitals and pharmacies to produce medications on demand. This is particularly significant when it comes to the development of orphan pharmaceuticals or treatments for rare conditions, which are not feasible to produce on a large scale. On-site manufacturing serves the dual purpose of reducing costs and waste related to drug overproduction and storage, while also accommodating the development of personalized medications that may have limited shelf lives. In addition, the possibility to modify the dimensions, form, taste, or pigmentation of pharmaceutical substances renders [2] them attractive and simpler to ingest, thereby enhancing adherence, especially among susceptible categories, including children and geriatric patients. These unique properties make 3D printing a key player in advancing medication discovery and improving patient-centered care. The integration of 3D printing in pharmaceuticals, while innovative, presents a range of challenges that slow down its broader applications. Regulatory issues are a significant concern due to the personalized nature of 3D-printed drugs; each new formulation might necessitate a full approval process, which can be both costly and time-consuming. The initial costs for setting up 3D printing technology are also substantial, encompassing expensive equipment, specialized training, and ongoing expenses such as software updates and maintenance. In terms of scalability, 3D printing does not yet match the efficiency of traditional manufacturing methods for large-scale production, limiting its use to specialized drugs or niche markets. Another obstacle is the limited range of materials suitable for 3D printing, as many active pharmaceutical ingredients and excipients used in traditional manufacturing are not compatible with current 3D printing technologies. The relatively limited availability of excipients is the major obstacle for designing specialized dosage forms.

Biodegradable, biocompatible, non-toxic, and stable excipients are essential for the wide application of 3D pharmaceutical printing. Furthermore, with the increase in the more complex structures of dosage forms, continuous updating of modelling software for its design and production is necessary. To avoid clogging or encourage consistency of the product, the control system, operating methods, and mechanical equipment must be updated and optimized. The efficacy of the printed products could also be influenced by physicochemical parameters, including the surface tension and viscosity of the adhesives, as well as the properties of the nozzle of the 3D printer. Furthermore, post-printing procedures such as drying methods, drying temperature, and drying time may influence the quality and appearance of the products. [6]

Principles of 3D Printing in Medicine

3D printing in medicine, also known as additive manufacturing, is a transformative technology that bridges the gap between digital medical imaging and physical reality. Its core principle is the creation of complex, patient-specific objects by depositing material layer-by-layer. [1]

1. The Workflow: From Image to Object

The primary principle of medical 3D printing is the digitization of anatomy. Unlike traditional manufacturing, which starts with a block of material (subtractive), 3D printing starts with nothing and adds material only where needed. [2]

1. **Image Acquisition:** High-resolution 3D data is captured using CT, MRI, or 3D ultrasound. The data is stored in DICOM (Digital Imaging and Communications in Medicine) format. [6]
2. **Segmentation:** Software is used to "isolate" specific tissues (e.g., a tumor or a specific bone) from the rest of the scan. [3–5]
3. **CAD Conversion:** The segmented data is converted into a 3D surface mesh, typically an STL file, which defines the geometry as a series of triangles. [7,8]

4. **Slicing:** The digital model is sliced into hundreds or thousands of horizontal layers. These layers become the "instructions" (G-code) for the printer. [1]
5. **Printing:** The printer follows these instructions to build the object from the bottom up. [2]

Advantages in medicine

- High precision and reproducibility
- Patient-specific customization
- Reduced material waste
- Rapid prototyping and production

3D Printing Technologies Used in Medicine (Methods in Detail)

1.1 Fused Deposition Modeling (FDM)

Fused Deposition Modeling (FDM), also known as Fused Filament Fabrication (FFF), is the most widely used 3D printing technology due to its cost-effectiveness and simplicity. In medicine, it serves as a critical tool for creating anatomical models, customized prosthetics, and even personalized drug delivery systems. [6]

1. The Core Mechanism

The fundamental principle of FDM is material extrusion. It operates like a highly precise, computer-controlled glue gun.

- **Feedstock:** The process begins with a solid thermoplastic filament (wound on a spool) being fed into the print head. [7,8]
- **Melting:** A "cold end" pulls the filament into a "hot end," where a heating element melts the plastic into a semi-liquid state. [1]
- **Deposition:** A motor pushes the molten material through a fine nozzle (typically in diameter) onto a build platform. [2]
- **Solidification:** As the plastic leaves the heated nozzle, it cools and hardens almost instantly, fusing to the layer beneath it through thermal bonding. [6]

2. Technical Parameters in Medicine

For medical applications, several technical factors must be tightly controlled to ensure safety and accuracy:

- **Layer Height:** Usually ranges from 0.1 to 0.2 mm. Smaller layers provide a smoother surface for surgical models but take longer to print. [7,8]

- **Infill Density:** The internal structure of the part. For a bone model, a "honeycomb" infill might be used to save material; for a functional prosthetic, density is required for strength. [1]
- **Shell Thickness:** The number of outer "walls." Thicker shells allow for post-processing like sanding or sterilization without compromising the part's integrity. [2]

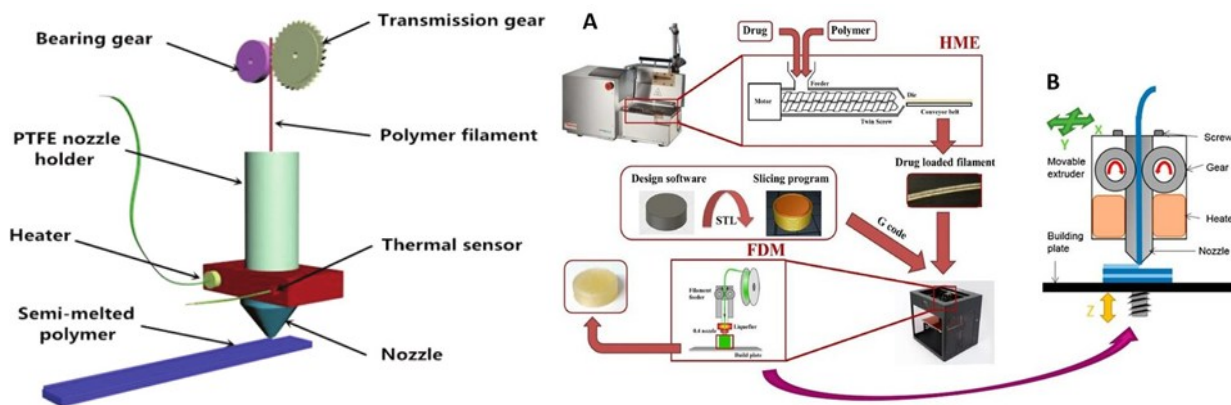


Figure 1. Workflow of medical 3D printing from medical imaging to final product fabrication.

3. Specialized Medical Materials

Unlike hobbyist printing, medical FDM requires materials that are either biocompatible or mechanically similar to human tissue.

Table 1. Specialized Medical Materials

Material	Key Property	Medical Use Case
PLA (Polylactic Acid)	Biocompatible, biodegradable	Anatomical training models, scaffolds for cell growth.
ABS	High strength, impact resistant	External prosthetic housings, durable tool handles.
PETG	Sterilizable, moisture resistant	Surgical templates, customized containers for medical tools.
PEEK / ULTEM	High-performance, heat resistant	Can be sterilized in autoclaves; used for high-end surgical guides.
PVA (Soluble)	Water-soluble	Used as "support material" for complex geometries, then dissolved away.

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6. Advanced Clinical Applications

Beyond simple models, FDM is pushing the boundaries of "Smart Medicine":

A. Personalized Pharmaceuticals ("Polypills")

Using a process called Hot-Melt Extrusion (HME), drugs are mixed directly into the polymer filament. The FDM printer then creates a tablet with a specific geometry. By changing the shape (e.g., a hollow cylinder vs. a solid cube), doctors can control exactly how fast the drug dissolves in the patient's stomach. [7,8]

B. Biocompatible Scaffolds

FDM is used to print porous scaffolds that act as a "template" for new bone or tissue growth. These structures have a specific porosity (often 20–80%) that allows blood vessels to grow through them as the material slowly biodegrades. [1]

C. Low-Cost Prosthetics

FDM's biggest impact is in global health. It allows for the production of custom-fitted prosthetic limbs for a fraction of the cost of traditional methods, which is particularly life-changing in developing regions or for growing children who need frequent replacements. [2]

1.2 Stereolithography (SLA)

1. The Core Principle: Photopolymerization

SLA belongs to a category called Vat Polymerization. Instead of melting plastic, it uses a chemical reaction triggered by light. [6]

- The Resin: The printer uses a vat of liquid photopolymer resin. This liquid contains "photo-initiators" that react to specific wavelengths of light. [3–5]
- The Light Source: A high-precision UV laser (or a digital projector in DLP/LCD variations) "draws" the cross-section of a medical model onto the resin surface. [7,8]
- The Reaction: When the UV light hits the liquid, it causes the molecules to chain together (polymerize), instantly turning the liquid into a solid plastic layer. [1]
- The Build: The build platform moves (up or down depending on the machine) by a fraction of a millimeter, and a "recoater blade" sweeps a fresh layer of liquid resin over the top to repeat the process. [2]

2.SLA is preferred over FDM for specific clinical needs due to three main factors:

- Extreme Precision: SLA can achieve layer thicknesses as small as 25 microns (). This is vital for dental applications (fitting a crown) or printing tiny hearing aid shells. [6]

- Isotropy: Unlike FDM parts, which are weaker "along the grain" (between layers), SLA parts are isotropic. This means they have equal strength in all directions (and), making them safer for surgical guides that might be under stress. [3–5]

3. Specialized Medical SLA Resins

SLA's versatility comes from the chemistry of the resins. Manufacturers have developed resins specifically for the human body: [1]

Table 2 Specialized Medical SLA Resins

Resin Type	Clinical Property	Primary Use Case
Biocompatible Clear	Non-toxic, USP Class VI certified.	Surgical Guides: Drilled directly into during surgery.
High-Temp Resin	Withstands the heat of an autoclave.	Tools that must be reused and sterilized.
Flexible/Elastic	Mimics soft tissue or cartilage.	Heart/Lung Models: Surgeons can cut and suture them for practice.
Radio-Opaque	Shows up on X-rays/CT scans.	Imaging Phantoms: Used to calibrate medical scanners.

4. The Critical Post-Processing Stage

An SLA print is not "finished" when it leaves the printer. To be medically safe, it must undergo three mandatory steps: [2]

1. Washing: The part is submerged in Isopropyl Alcohol (IPA) to dissolve any leftover liquid resin on the surface. [6]

2. Support Removal: Because the part is built in a liquid, it needs "scaffolding" (supports) which must be snipped off manually. [3–5]

3. Post-Curing: The part is placed in a UV oven. This ensures every molecule of resin has reacted, reaching its full strength and ensuring no toxic "uncured" liquid remains. [7,8]

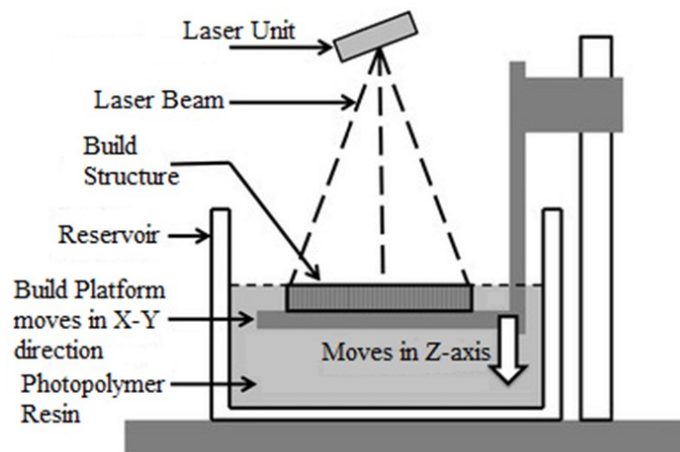


Figure 2. Layer-by-layer fabrication principle in additive manufacturing.

1.3 Selective Laser Sintering (SLS)

Selective Laser Sintering (SLS) is a powder-bed fusion technology that has revolutionized the production of permanent medical implants and complex orthopedic devices. Unlike FDM or SLA, it

uses a high-power laser to fuse small particles of plastic, ceramic, or metal powder into a solid structure. [1]

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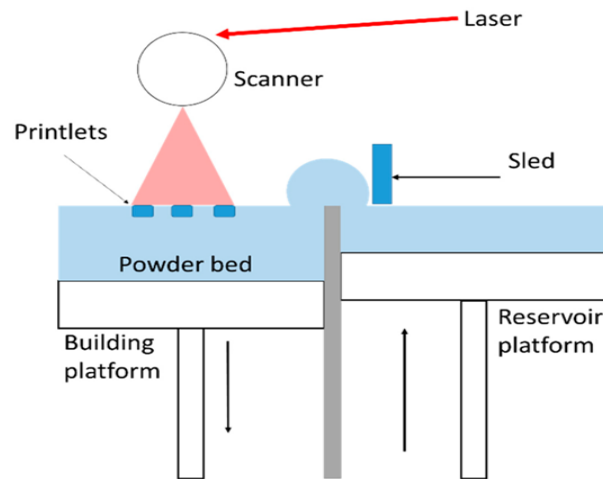


Figure 3. Comparison of major 3D printing technologies used in medicine.

1. The Core Principle: Sintering

The term "sintering" is key: the laser heats the powder to just below its melting point, causing the particles to fuse at a molecular level without fully turning into liquid. [2]

- **The Powder Bed:** The process takes place in a heated chamber filled with a fine powder. A "recoater" blade spreads an ultra-thin, even layer of powder across the build plate. [6]
- **The Laser Trace:** A CO₂ laser scans the surface, selectively fusing the powder according to the 3D model's cross-section. [3–5]
- **Self-Supporting Design:** One of the most significant principles of SLS is that it requires no support structures. The unsintered powder surrounding the part acts as a natural support. This allows for "impossible" geometries, such as a nested ball-and-socket joint printed as a single, moving piece. [7,8]
- **Cooling Phase:** Because the chamber is kept at high heat, the parts must cool slowly (often for several hours) to prevent warping and ensure mechanical strength. [1]

2. Why SLS is used for Implants

SLS is the preferred choice for "end-use" medical parts (parts that actually stay inside or on the body) for several technical reasons:

- **Porous Architectures:** SLS can print "trabecular" structures—metal or plastic lattices that look like the inside of a natural bone. This allows the patient's own bone cells to grow into the implant (osseointegration). [6]
- **Isotropic Strength:** Because the parts are fused in a heated environment, the bond between layers is nearly as strong as the material itself. This makes SLS parts much tougher than FDM parts. [3–5]
- **Material Bio-stability:** SLS can handle high-performance polymers like PEEK and metals like Titanium, which are highly resistant to the body's harsh internal environment. [7,8]

3. Key Medical Materials for SLS

While polymers are common, the medical field often uses a variation called DMLS (Direct Metal Laser Sintering) for permanent hardware. [1]

Table 3. Key Medical Materials for SLS

Material	Category	Medical Application
Nylon (PA 11/12)	Polymer	Orthotics: Custom leg braces and insoles that are lightweight but nearly indestructible.
Titanium (Ti64)	Metal	Cranial/Hip Implants: Used for custom skull plates or hip cups that fuse with bone.
Cobalt-Chrome	Metal	Dental Frameworks: Used for high-stress partial dentures and bridges.
TPU	Elastomer	Prosthetic Liners: Flexible, rubber-like parts that provide cushioning against a patient's skin.

4. Major Medical Applications

A. Orthopedic Implants

Traditional implants come in standard sizes (Small, Medium, Large). With SLS, a surgeon can take a CT scan of a patient's shattered pelvis and print a perfectly matching titanium replacement that fits only that specific patient. [2]

B. "Cake-Baking" Production (Batching)

Because SLS doesn't need supports, you can "stack" parts in 3D space. A hospital can print 50 different patient-specific dental guides or 10 different prosthetic hands in a single "cake" (the powder block), making it highly efficient for small-batch production. [6]

C. Complex Surgical Instruments

Engineers use SLS to create lightweight, ergonomic surgical handles that have internal cooling channels or hollow centers to reduce hand fatigue during long operations. [3–5]

1.4 Inkjet and Binder Jet Printing

1. Inkjet Printing (Material Jetting)

In medicine, Inkjet printing is often called Material Jetting. The core principle is the deposition of the actual "build material" in liquid form, which is then solidified. [7,8]

The Mechanism:

- **Droplet Deposition:** Hundreds of tiny nozzles on a printhead travel over the build tray, "jetting" droplets of liquid photopolymer (resin). [1]

- **Instant Curing:** A UV light source attached to the printhead follows the droplets, instantly curing (solidifying) them as they land. [2]

- **Multi-Material Printing:** This is the only technology that can jet multiple materials at once. It can print a hard "bone" material and a soft "vessel" material in the same layer. [6]

Medical Applications:

- **High-Fidelity Anatomical Models:** Because it can print in full color and varying textures (clear, rubbery, rigid), it is used to create incredibly realistic heart or brain models for surgical rehearsal. [3–5]
- **Bioprinting:** "Inkjet Bioprinting" uses the same principle but jets bio-inks (living cells in a nutrient medium). It is precise but can be stressful for cells due to the heat or pressure at the nozzle. [7,8]
- **Personalized Medicine:** Printing "ink" containing specific drug dosages onto edible films (like a Listerine strip) for precise oral delivery. [1]

2. Binder Jetting

Binder Jetting is a powder-bed process. Unlike Inkjet, the printhead does not spray the build material; it sprays a "glue" (the binder) onto a bed of powder. [2]

1. The Mechanism:

1. **Powder Spreading:** A roller spreads a thin layer of powder (metal, ceramic, or polymer) across the build platform. [6]

2. Selective Binding: The printhead moves across the bed, depositing liquid binder only where the part is being formed. [3–5]
 3. The "Green State": When the print finishes, the part is in a fragile "green state"—it is held together by glue, not fused. [7,8]
 4. Post-Processing (Mandatory): The part must be placed in a furnace (Sintering) to burn off the glue and fuse the powder particles together, or Infiltrated with another material (like bronze) to fill the gaps. [1]
- Bone Scaffolds: It is excellent for printing calcium phosphate or hydroxyapatite (the minerals found in bone). The natural porosity of the binder jetting process is actually an advantage, as it allows new bone to grow into the scaffold. [2]
 - Custom Implants: Used to create stainless steel or cobalt-chrome orthopedic tools and implants. [6]
 - Fast Dissolving Tablets: Binder jetting is the tech behind Spritam, the first FDA-approved 3D-printed drug. The "glue" binds the drug powder just enough so that it stays solid but dissolves instantly in the mouth with a sip of water. [3–5]

2. Medical Applications:

3. Key Comparison for Medicine

Table 4. Key Comparison for Medicine

Feature	Inkjet (Material Jetting)	Binder Jetting
Input Material	Liquid Photopolymer / Bio-ink	Powder (Metal, Ceramic, Drug)
Strength	High detail, multi-color/texture	Porous structures, metal strength
Support	Required (removable gel)	Self-supporting (in the powder)
Post-Processing	Low (Support removal)	High (Curing, Sintering, Infiltration)
Primary Med Use	Realistic surgical models	Bone scaffolds & fast-dissolve pills

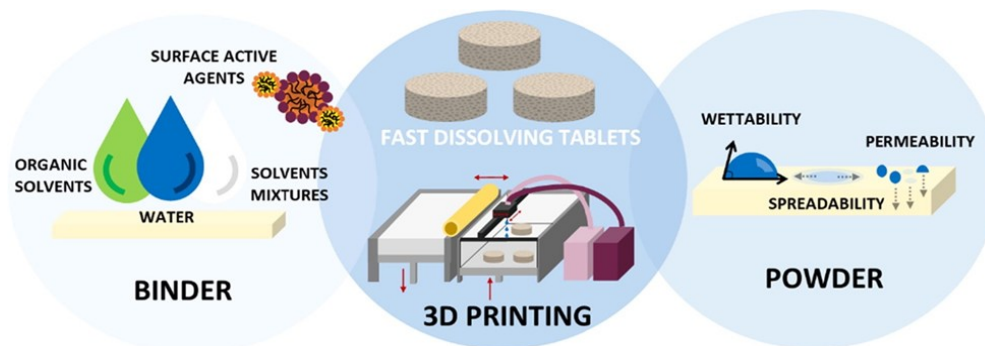


Figure 4. Bioprinting strategies for tissue engineering and regenerative medicine.

1.5 Bioprinting (Extrusion, Inkjet, Laser-Assisted)

Bioprinting is the precise spatial patterning of living cells and biomaterials (bio-inks) to fabricate functional 3D tissues. While it shares the "layer-by-layer" logic of standard 3D printing, the primary challenge is maintaining cell viability—keeping the cells alive and functional during and after the printing process. [7,8]

1. Extrusion-Based Bioprinting (EBB)

This is the most common bioprinting method. It uses mechanical or pneumatic pressure to push a continuous "spaghetti-like" filament of bio-ink through a nozzle. [1]

- Mechanism: A syringe is loaded with bio-ink (usually a hydrogel mixed with cells). It is then squeezed out using compressed air (pneumatic) or a piston/screw (mechanical). [2]
- Best for: Large, structural constructs like bone scaffolds, muscle, or skin.

- The Trade-off: * Pros: Can handle high-viscosity materials (thick gels) and high cell densities. It is the most affordable and versatile method. [6]
 - Cons: The pressure creates shear stress at the nozzle tip, which can damage or kill sensitive cells. Resolution is relatively low (). [3–5]

2. Inkjet Bioprinting

Often called "drop-on-demand," this method is highly similar to a desktop 2D printer but jets droplets of liquid bio-ink. [7,8]

- Mechanism: * Thermal: A heating element creates a tiny vapor bubble that pushes a droplet out. (The heat lasts only microseconds, so cells usually survive). [1]
 - Piezoelectric: An electric pulse changes the shape of a crystal, creating a pressure wave that ejects the drop. [2]
- Best for: Thin tissues, high-speed patterning, and "organ-on-a-chip" applications. [6]

LAB is a "nozzle-free" technology based on the principle of Laser-Induced Forward Transfer (LIFT). It is the most precise and gentle method available. [1]

- Mechanism: 1. A laser pulse hits a "donor ribbon" (a glass slide coated with a gold/titanium layer and a film of bio-ink). 2. The laser creates a high-pressure vapor bubble in the metal layer. 3. This bubble propels a tiny micro-droplet of bio-ink onto the "collector substrate" below. [2]
- Best for: High-resolution cellular patterning, such as creating hair follicles in skin or complex neural networks. [6]
- The Trade-off:
 - Pros: Zero shear stress (no nozzle), meaning cell viability is extremely high (). It can achieve single-cell resolution (). [3–5]
 - Cons: Extremely expensive and complex to set up. Preparing the "donor ribbons" for each layer is time-consuming. [7,8]

3. Laser-Assisted Bioprinting (LAB)

Comparison Table: Bioprinting Modalities

Table. 5 Laser-Assisted Bioprinting (LAB)

Feature	Extrusion (EBB)	Inkjet	Laser-Assisted (LAB)
Material Form	Continuous Filament	Discrete Droplets	Discrete Droplets
Viscosity Range	High (Thick gels)	Low (Watery)	Medium
Resolution	Moderate ()	High ()	Extreme ()
Cell Viability	(Shear stress)		
Common Use	Bones, Cartilage, Organs	Skin, Cornea	Single-cell research, Sensors

The Future: 4D Bioprinting

The newest principle is 4D Bioprinting, where the printed 3D tissue is designed to change shape or function over time in response to a stimulus (like

temperature or pH). This mimics how real human tissue grows and matures. [1]

Role of 3D Printing in Personalized Medicine

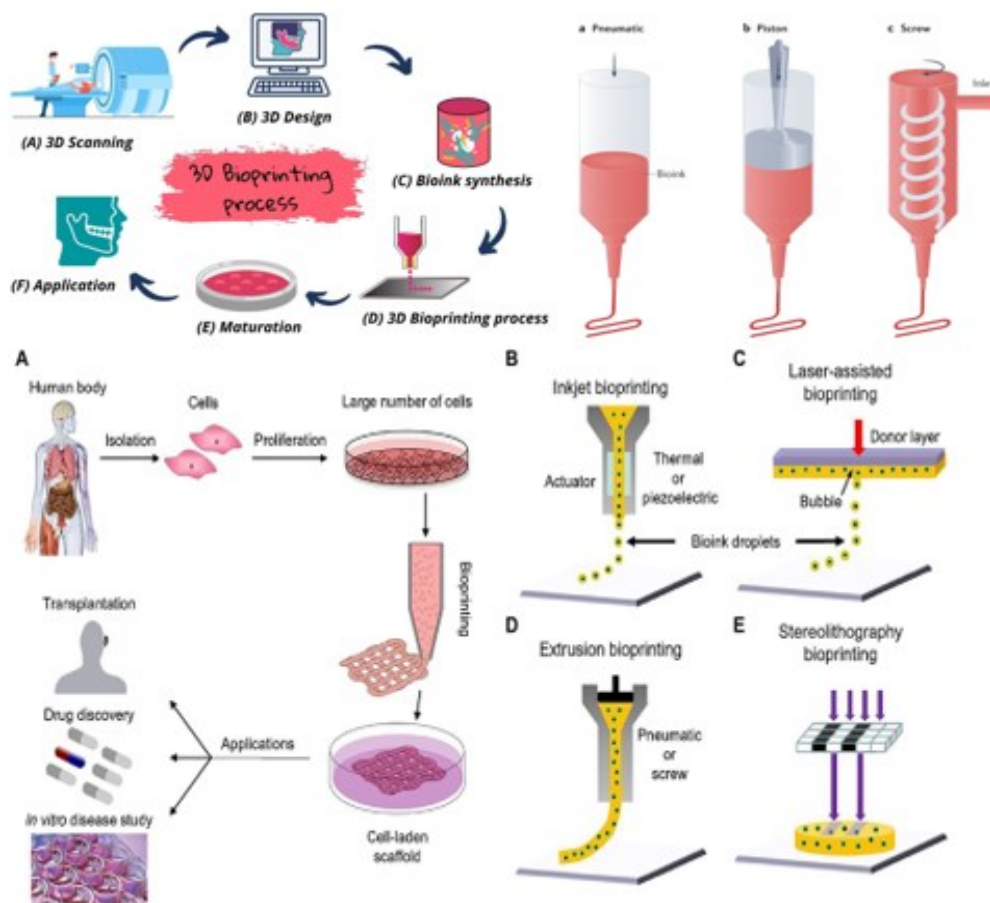


Figure 5. Role of 3D printing in personalized medicine.

3D printing is the technical engine behind Personalized Medicine, moving healthcare from a "one-size-fits-all" approach to treatments designed specifically for a single patient's unique anatomy, genetics, and lifestyle. [2] The role of 3D printing in this field can be categorized into four primary domains: [6]

1. Patient-Specific Anatomical Models

Before 3D printing, surgeons relied on 2D slices (CT/MRI) to visualize a 3D problem. Personalized medicine uses 3D printing to create physical replicas of a patient's exact organs. [3–5]

- **Surgical Rehearsal:** Surgeons can physically hold a replica of a patient's shattered pelvis or a heart with a congenital defect. They can cut, drill, and practice the procedure, reducing time in the operating room (OR) by up to 25–50%. [7,8]
- **Risk Mitigation:** By identifying a tumor's exact proximity to a major artery on a 3D model,

surgeons can avoid catastrophic errors that are not always obvious on a screen. [1]

- **Communication:** Doctors use these models to explain complex surgeries to patients, improving "informed consent" and patient anxiety. [2]

2. Personalized Drug Delivery (Pharmacology)

Traditional manufacturing creates millions of identical pills. 3D printing allows for the creation of bespoke medications at the point of care (the hospital or pharmacy). [6]

- **Custom Dosage:** Instead of a child taking half a "standard" adult pill, a 3D printer can produce a pill with exactly of an active ingredient. [3–5]
- **The "Polypill":** For elderly patients taking 10+ medications, 3D printing can combine multiple drugs into a single tablet. Each drug can be placed in a different "compartment" with a unique geometry to control its release (e.g., immediate

release for Drug A, 8-hour sustained release for Drug B). [7,8]

- **Fast-Dissolving Tablets:** Technologies like Binder Jetting create highly porous pills (like Spritam for epilepsy) that dissolve instantly with a sip of water, vital for patients with swallowing difficulties. [1]

3. Tailored Implants and Prosthetics

Standard implants come in sizes like "Small, Medium, Large." Personalized medicine uses 3D printing to create "Size: Patient." [2]

- **Osseointegration:** 3D printed titanium implants (using SLS) can be printed with a porous, "bone-like" texture. This encourages the patient's own bone to grow into the metal, creating a permanent, natural bond that standard smooth implants cannot achieve. [6]
- **Craniofacial Reconstruction:** For patients with severe facial trauma or cancer, 3D printing can recreate missing jawbones or skull plates that

perfectly restore the patient's original appearance. [3–5]

- **Dynamic Prosthetics:** 3D printing allows for lightweight, low-cost prosthetic limbs that are scanned to fit the patient's residual limb perfectly, preventing the sores and discomfort common with mass-produced versions. [7,8]

4. Bioprinting: The Future of Regeneration

The ultimate goal of personalized medicine is to replace a failing organ with one grown from the patient's own cells, eliminating the risk of transplant rejection. [1]

- **Organ-on-a-Chip:** Before giving a patient a new chemotherapy drug, doctors can print a "mini-version" of that patient's own tumor and test the drug on the 3D-printed tissue first to see if it works. [2]
- **Skin Grafting:** For burn victims, bioprinters can scan a wound and print skin cells directly onto the patient, using different cell types for different depths of the wound. [6]

Table 6. Comparison: Traditional vs. 3D Printed Personalized Medicine

Feature	Traditional Medicine	3D Printed Personalized Medicine
Manufacturing	Mass production (thousands of identical units)	On-demand (single, unique unit)
Fit/Accuracy	Standardized sizes; manual adjustment	Digital fit; exact anatomical match
Drug Dosage	Fixed (e.g.)	Infinite variability (e.g.)
Recovery Time	Longer (due to invasive adjustments)	Shorter (due to precision planning)

3D Printing in Nanomedicine

The intersection of 3D printing and Nanomedicine represents a leap from macroscopic surgical aids to microscopic therapeutic agents. This field focuses on two main principles: Top-Down Fabrication (using ultra-high-precision printing to create nanostructures) and Bottom-Up Material Enhancement (infusing traditional printing materials with nanoparticles). [7,8]

1. Nanoscale Printing Principles

While standard 3D printers have resolutions in the millimeter or micrometer range, nanomedicine requires precision at the nanoscale (). [1]

- **Two-Photon Polymerization (2PP):** This is the primary "nanoprinting" technology. It uses a femtosecond pulsed laser to solidify photosensitive resin only at the tiny focal point where two photons are absorbed simultaneously. This allows for the creation of structures like micro-needles or nano-scaffolds that are smaller than a single human cell. [2]
- **Nanofiller Integration:** Instead of printing at the nano-size, researchers add "nanofillers" (like

carbon nanotubes or silver nanoparticles) into standard filaments or resins. The printing process often helps align these nanoparticles, giving the final medical device specialized electrical or antimicrobial properties. [6]

2. Advanced Nanocomposite Materials

By embedding nanoparticles into 3D-printed matrices, scientists create "smart" medical devices that behave differently than standard plastic or metal. [3–5]

Table 7. Advanced Nanocomposite Materials

Nanofiller	Medical Benefit	Application
Silver Nanoparticles (AgNPs)	Potent antimicrobial effect.	Wound dressings and catheters that kill bacteria on contact.
Magnetic Nanoparticles	Responsive to external magnetic fields.	Micro-swimmers: Tiny 3D-printed robots that can be "steered" through the blood to deliver drugs to a tumor.
Carbon Nanotubes (CNTs)	High electrical conductivity.	Neural Scaffolds: Printing tissue that can transmit electrical signals for nerve or heart repair.
Hydroxyapatite (nHAp)	Bioactive bone mineral.	Bone Implants: Nanoscale surface textures that trick the body into growing bone faster.

3. Key Medical Applications

A. Precision Drug Delivery (The "Nanopill")

3D printing is used to create complex pill architectures where the "ink" itself is a nanosuspension of a drug. [7,8]

- **Controlled Release:** The 3D geometry can be printed with nanolayers that dissolve at different rates. [1]
- **Blood-Brain Barrier (BBB) Penetration:** 3D-printed scaffolds can be impregnated with lipid-based nanoparticles designed to carry medications across the BBB to treat neurological diseases like Parkinson's or Brain Tumors. [2]

B. Nano-Textured Implants

A major principle in orthopedics is Nano-topography. 3D printing (specifically SLS or DMLS) can create implants with surfaces covered in nanometer-sized "pillars" or "pores." [6]

- **Why it works:** These tiny features mimic the natural extracellular matrix, encouraging cells to adhere and grow much more effectively than a smooth, standard implant. [3–5]

C. Diagnostic "Lab-on-a-Chip"

Nanoscale 3D printing is used to manufacture microfluidic devices—tiny chips that can analyze a single drop of blood. [7,8]

- **Biosensors:** 3D-printed channels are coated with nanoparticles that change color or electrical state when they detect specific cancer biomarkers or viral particles. [1]

4. Challenges: The "Nano-Safety" Gap

Despite the potential, 3D printing in nanomedicine faces unique hurdles:

- **Toxicity:** Certain nanoparticles, if released from a 3D-printed device, could be toxic to the liver or kidneys. [2]
- **Scaling:** Printing at the nanoscale is currently very slow. Creating a large-scale organ with nanometer precision could take weeks with current technology. [6]
- **Regulation:** The FDA treats "nanomaterials" and "3D-printed devices" as separate complex categories; combining them creates a very difficult path for clinical approval. [3–5]

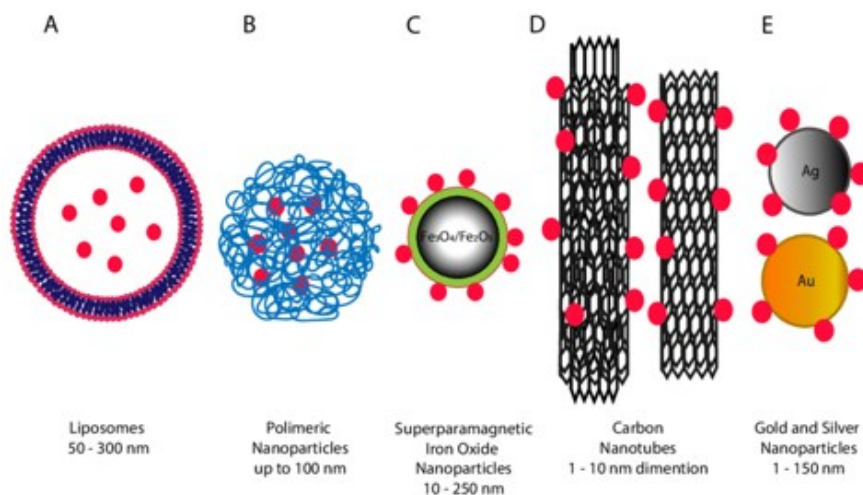


Figure 6. 3D printing in nanomedicine.

6. Applications in Biopharmaceuticals

3D printing is transforming biopharmaceutical development and manufacturing.

Key Areas

- Customized drug delivery devices
- Controlled-release biologics
- Organ-on-chip systems for drug testing

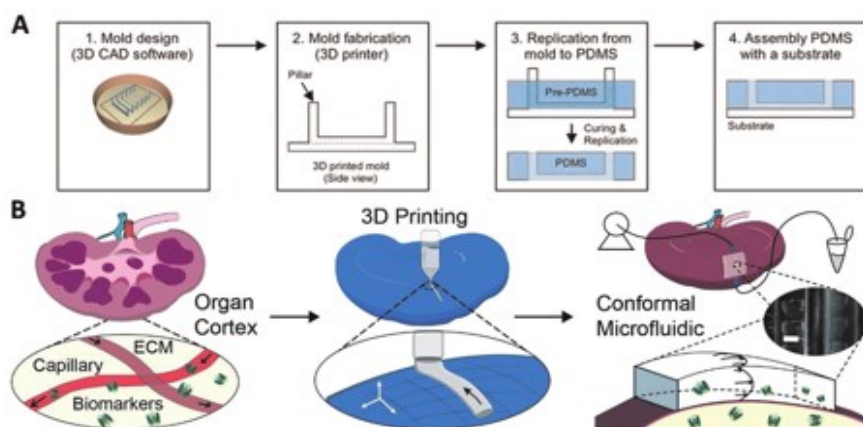


Figure 7. Regulatory framework for medical 3D printing (FDA, EU MDR, ISO).

Advantages

- Reduced development time
- Improved reproducibility
- Enhanced patient compliance

Regulatory and Quality Considerations

Regulatory and quality considerations are the most complex "principles" in medical 3D printing because they transform a technical innovation into a safe, legal clinical tool. Because 3D printing creates "mass-

customized" products, it challenges traditional laws designed for identical, mass-produced items. [7,8]

1. Regulatory Frameworks: FDA and EU MDR

Regulators do not regulate the 3D printer itself; they regulate the intended use of the final product. [1]

- **USA (FDA):** The FDA uses a risk-based classification (Class I, II, and III). Most 3D-printed guides are Class II (510(k) clearance required). The FDA issued specific guidance in 2017 focusing on Technical Considerations for

Additive Manufactured Medical Devices, requiring manufacturers to "lock down" their process so that every printed part is consistent. [2]

- European Union (EU MDR 2017/745): The MDR significantly tightened rules on "Custom-Made Devices. "Previously, many 3D-printed parts were exempt from strict oversight. Now, if a device is "mass-produced by industrial means" (which includes most 3D printing), it must meet nearly the same stringent standards as standard implants, including rigorous post-market surveillance. [6]

2. Quality Management Systems (ISO 13485)

For a hospital or company to legally 3D print medical devices, they must typically follow ISO 13485, the international standard for medical device quality management. Key principles include: [3–5]

- Traceability: You must be able to trace a finished implant back to the specific batch of powder or resin used, the specific printer used, and even the technician who operated it. [7,8]
- Software Validation: The software used to "segment" a CT scan (turning 2D slices into 3D models) must be FDA-cleared or CE-marked. Using unvalidated hobbyist software for surgical planning is a major regulatory violation. [1]
- Equipment Qualification:
 - IQ (Installation Qualification): Is the printer installed correctly?
 - OQ (Operational Qualification): Does it print within the specified tolerances?
 - PQ (Performance Qualification): Can it consistently produce safe medical parts over time? [2]

3. The "Point-of-Care" (PoC) Challenge

A major shift is occurring as hospitals set up their own 3D printing labs. This creates a "legal grey area": Is the hospital now a manufacturer? [6]

- Hospital as Manufacturer: If a hospital designs and prints its own surgical guide, it may be legally liable for the device's performance, similar to a company like Medtronic or Stryker. [3–5]
- The Exemption: Many jurisdictions allow a "Health Institute Exemption" for devices made and used within the same hospital, provided they have a mini-Quality Management System in place and can justify why a commercial alternative wasn't used. [7,8]

4. Quality Control (QC) and Validation

Because you cannot "test" a custom implant (since destroying it for testing would leave nothing to give the patient), you must validate the process instead. [1]

- Anisotropy: Unlike traditional parts, 3D prints have different strengths depending on which direction they were printed (or). Quality control must ensure the part is oriented in the printer to handle the specific stresses it will face in the body. [2]
- Cleaning and Sterility: 3D-printed parts (especially SLS/Powder) can have tiny pores that trap uncured resin or raw powder. Validation must prove that the cleaning process (ultrasonic baths, autoclaves) removes these toxic residues. [6]
- Dimensional Accuracy: Before use, the physical print is often compared back to the digital file (using calipers or a 3D scanner) to ensure it hasn't warped during the cooling or curing process. [3–5]

Future Perspectives

The future of 3D printing in medicine is moving toward a convergence of technologies: where the physical precision of nanotechnology, the biological complexity of bioprinting, and the intelligence of 4D responsive materials merge into a single healthcare ecosystem. [7,8]

1. 4D Printing: The Dimension of Time

The most significant evolution is the shift from 3D to 4D Printing. 4D printing uses "smart" materials that

change their shape, property, or function over time in response to external stimuli. [1]

- **Self-Adjusting Stents:** In pediatric cardiology, a 3D-printed stent is fixed in size. A 4D-printed stent can be designed to expand as the child's blood vessels grow, eliminating the need for repeat surgeries. [2]
- **Stimuli-Responsive Implants:** Implants that "activate" based on the body's environment. For example, a bone scaffold that releases growth factors only when it senses the specific pH level of an inflammatory healing phase. [6]
- **Shape-Memory Polymers:** Devices that can be folded or compressed for minimally invasive (keyhole) surgery and then "unfold" into their functional 3D shape once they reach body temperature. [3–5]

2. Convergence with Nanomedicine ("Nanoprinting")

The future lies in Two-Photon Polymerization (2PP) and other sub-micron printing techniques that allow us to manufacture at the scale of a single cell. [7,8]

- **Micro-swimmers & Nano-robots:** Printing tiny, magnetized "bots" that can be injected into the bloodstream and guided by a doctor using external magnets to deliver a high-dose "payload" directly into a tumor, bypassing healthy tissue. [1]
- **Surface Engineering:** Implants with nanoscale "topography" that can physically kill bacteria (by rupturing their cell walls) without the use of antibiotics, addressing the global crisis of antibiotic resistance. [2]

3. Biopharmaceuticals & Advanced Drug Delivery

3D printing is disrupting the traditional pharmaceutical supply chain, moving it from massive factories to Point-of-Care (PoC) manufacturing in hospitals. [6]

- **The "Digital Pharmacy":** Instead of shipping boxes of pills, pharmaceutical companies may one day ship "Digital Files." A hospital's 3D

printer will then produce the exact medication, dosage, and release profile required for a patient that very morning. [3–5]

- **On-Demand Biologics:** Printing complex biopharmaceuticals (proteins, antibodies) directly into stabilized hydrogels. This prevents the degradation of sensitive drugs that usually require a strict "cold chain" (constant refrigeration) during transport. [7,8]
- **Multi-Drug "Polypills":** Advanced printers will create single tablets containing up to 5-10 different drugs, each with its own "compartment" and release timer, drastically increasing medication adherence for elderly patients. [1]

4. Space-Based Bioprinting

One of the most radical frontiers in 2025 and beyond is Bio fabrication in Microgravity. [2]

- **The Gravity Problem:** On Earth, printing soft tissues (like a heart or lung) is difficult because they collapse under their own weight before the structure is finished. [6]
- **The Space Solution:** In the microgravity of the International Space Station (ISS), complex tissues can be printed without supports. This allows for the creation of finer, more intricate vascular networks (blood vessels) that are currently impossible to replicate on Earth. [3–5]

CONCLUSION

3D printing is reshaping the future of medicine by enabling precision, personalization, and innovation across medical devices, nanomedicine, and biopharmaceuticals. Although regulatory and technical challenges remain, continuous advancements in materials science, bioengineering, and digital health will drive widespread clinical adoption. 3D printing's journey into medicine is a shift from industrial mass production to individualized precision. As we integrate nanotechnology and biopharmaceuticals, the technology is moving beyond creating "static" objects to creating "living" and "intelligent" therapies.

1. The Death of the "One-Size-Fits-All" Model

The most profound conclusion is that 3D printing has finally made Personalized Medicine practical.

- **Clinical Efficacy:** By tailoring dosages to an individual's metabolism (genomics) rather than their weight, we can maximize therapeutic effects while nearly eliminating side effects.
- **Patient Centricity:** For populations like pediatrics and geriatrics, 3D printing solves the "unmet needs" of standard manufacturing, such as the ability to swallow large pills or the need for highly specific, small-increment doses.

2. The Nanomedicine Convergence

The future belongs to Nanoprinting. The ability to print at the nanoscale means we are no longer just making devices that sit in the body; we are making devices that interact with the body's cells.

- **Targeted Warfare:** 3D-printed micro-robots and nanocarriers represent the next generation of oncology, where medicine is delivered with surgical precision to a tumor, leaving healthy tissue untouched.
- **Antimicrobial Innovation:** Nano-textured surfaces on 3D prints offer a non-chemical way to fight the growing threat of superbugs.

3. Decentralized Healthcare (The "Pharmacy of the Future")

The logistical conclusion of this technology is Point-of-Care (PoC) manufacturing.

- **Digital Supply Chains:** Instead of massive warehouses and global shipping, medicine will become a digital file. This will revolutionize rural healthcare, disaster zones, and even space exploration, where medications can be "downloaded" and printed on-site.
- **Speed to Market:** 3D printing collapses the time between drug discovery and clinical application by allowing for rapid prototyping of complex biopharmaceuticals without the need for million-dollar molds or factory re-tooling.

4. Remaining Hurdles

While the technical future is bright, the regulatory and ethical future is still being written.

- **Liability:** If a hospital prints a device that fails, who is responsible? The software designer, the printer manufacturer, or the surgeon.
- **Equity:** There is a risk that "Personalized 3D Medicine" remains a luxury for wealthy nations. The final goal must be to use FDM and other low-cost methods to bring this precision to the global south.

Final Synthesis

3D printing in medicine is not just a "new way to make things"—it is a new way to think about healing. By merging the precision of the digital world with the complexity of biological systems, we are entering an era where medicine is no longer something a patient "takes," but something that is "designed" specifically for their unique biological signature.

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