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3D PRINTING TECHNOLOGIES - AN OVERVIEW

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ABSTRACT: 3D printing is an emerging technological advancement that could be applied in several medical fields, the educational arena, and preoperative planning. 3D printing technology, also known as additive manufacturing, is significant as it is cost-effective compared to traditional cadaveric models. The purpose of writing the current review on 3D printing techniques was to compile the recent literature with a special focus on the methods, principles, and fabrication mechanisms to generate 3D printed models. The novel technology is reliable and appropriate for analyzing congenital heart diseases, but 3D printing has limitations and potential bias about subjectivity in the modernization of treatment for congestive heart diseases. 3D models can serve as a summary of diagnosis and a reliable tool for the choice of disease treatment. Albeit, high-resolution 3D printing methods are still in the initial stage of development with limitations, they demonstrate a huge potential to manufacture multi-functional materials. The present review briefly explains the applications, limitations, and regulatory challenges to be overcome in the fabrication of 3D printed models.

INTRODUCTION: 3D printing technology, also known as additive manufacturing, is an advanced technology that produces three-dimensional structures by constructing successive layers of the material utilized by computerized software [1]. 3D printed structure for the first time reported in the year 1982 by Hideo Kodama. Later, 3D printing technologies have undergone major development. Various multinational companies and even individuals with their printers may construct different types of 3D. Structures variable in quality and cost based on their intended application.

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3D printing is an emerging technological advancement in several medical fields, like medical education and preoperative planning. 3D printing technology is significant as it is cost-effective compared to traditional cadaveric models.

In addition, applications of additive manufacturing technologies in tissue engineering have been recently highlighted with promising results. They are evident by the vivid growth of sales reported by 3D printer producers, who claim a rise of 17.4 % in worldwide revenues, in 2016, compared to the previous years. A significant amount of research is contributed, *i.e.*, $ 6 billion in 2016 to $ 21 billion worldwide by 2021 [2, 3].

Methods of 3D Printing:

- ✓ Stereolithography
- ✓ Inkjet printing technology

- ✓ Selective laser sintering
- ✓ Direct ink writing
- ✓ Shape deposition modeling
- ✓ Fused deposition modeling
- ✓ Semisolid extrusion-based 3D printing
- ✓ Sheet lamination method
- ✓ Powder-based 3D printing technology
- ✓ ZipDose® technology
- ✓ Digital light processing
- ✓ Bioplotting

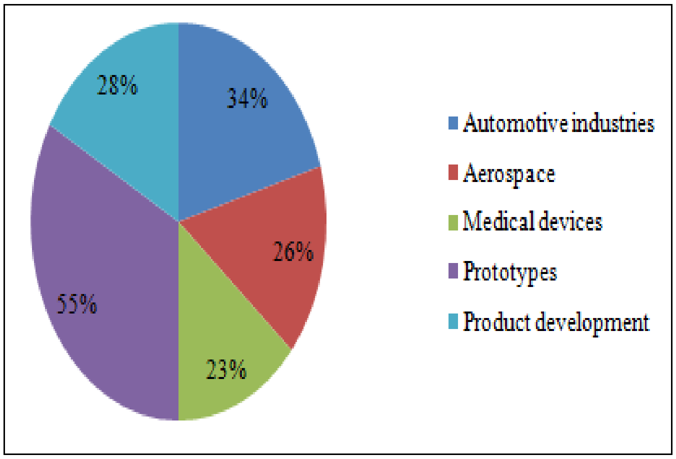

FIG. 1: PERCENTAGE OF 3D PRINTING USAGE IN VARIOUS FIELDS

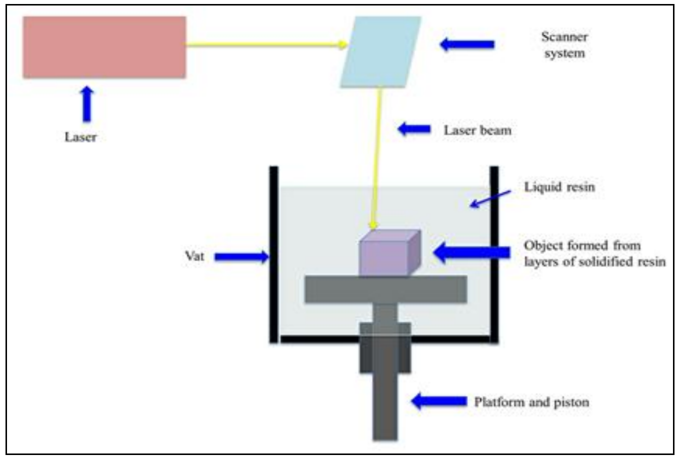

FIG. 2: STEREOLITHOGRAPHY TECHNIQUE

Stereolithography: It is one of the most common 3D printing techniques. The process consists of a container with a photopolymerizable resinous liquid and UV laser retained by galvanometers controlled through a CAD program. The laser beam traces a particular design onto the resin producing a hardened layer. The sequence of steps is reiterated with new resin layers until the design is finished [5].

Advantages [6, 7]:

- ✓ High speed, resolution, and cell viability
- ✓ Cost-effective and no shear stress.

Disadvantages:

- ✓ High cost of laser unit used in stereolithography
- ✓ Poor hollow-structure capabilities and cell toxicity due to UV rays
- ✓ Requirement of the photocurable bio link

Inkjet Printing Technology: In the inkjet 3D printing technique, 1-100 μL droplets of a cell-laden bio-ink is dispensed in a defined way to create a design. Piezoelectric, thermal heating, or pressure wave technique dispenses the droplets. In the thermal heating method, an external thermal element is placed on the nozzle, attaining temperatures in the range of 100-300 °C to produce an internal vapor bubble that drives a droplet *via* the orifice.

Advantages: Easily available, minimum cost, higher speed, and resolution

Disadvantages: Decreased cell viability, not suitable for viscous bioink due to non-complex architecture [5].

Selective Laser Sintering: The deposition material in the case of additive manufacturing is metal and SLS to form required 3D objects. Post-processing steps like sintering infiltration and finishing are desirable for carrying out device fabrication [9].

Advantages: Fully automatic and greater resolution.

Limitations: Powder precursor remains in small cavities Non-transparent.

Shape Deposition Modeling: Shape deposition modeling is used to fabricate complex geometries with different types of materials, majorly for rapid prototyping applications. It is a cyclic process that consists of many steps such as deposition [10, 11].

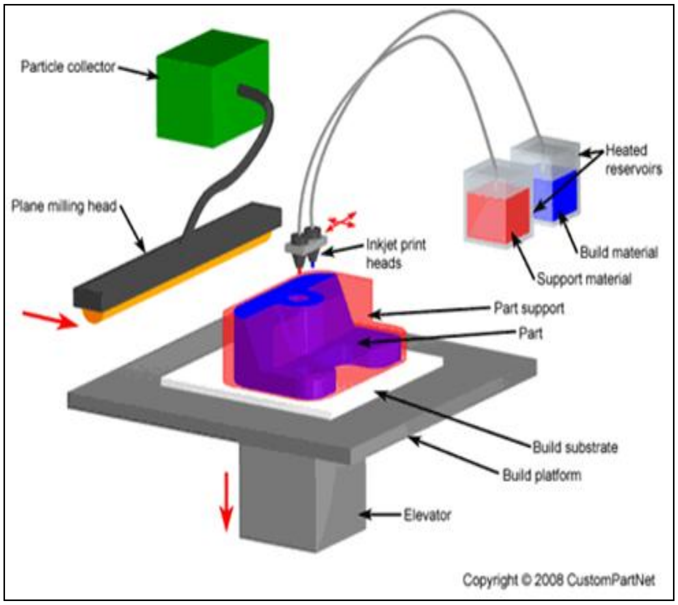

FIG. 3: INKJET PRINTING TECHNOLOGY

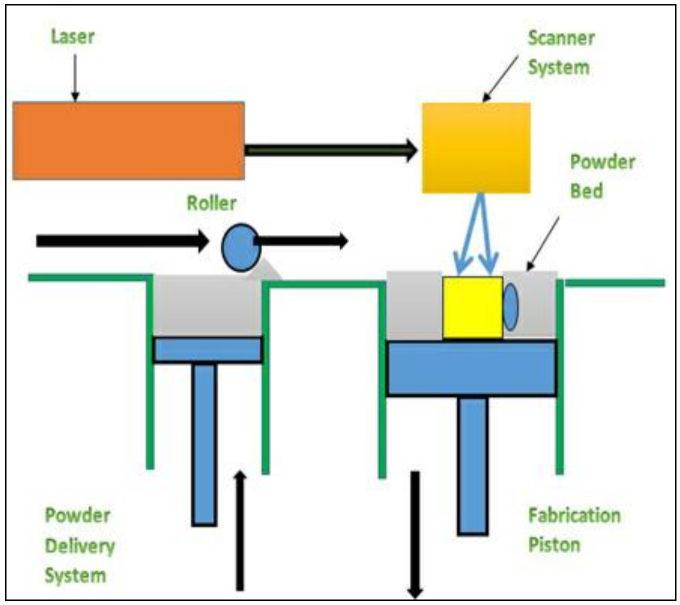

FIG. 4: SELECTIVE LASER SINTERING TECHNOLOGY

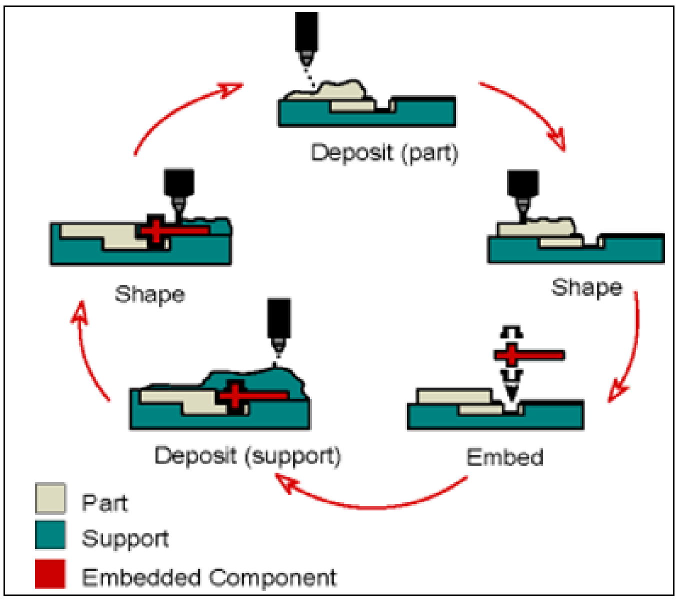

FIG. 5: SHAPE DEPOSITION MODELING TECHNOLOGY

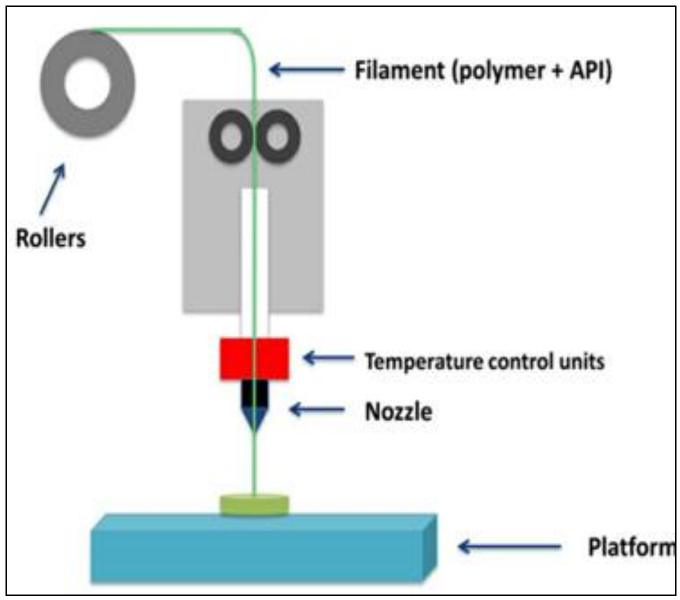

FIG. 6: FUSED DEPOSITION MODELING TECHNIQUE

Applications: Biomimetic robotic mechanism and components.

Limitations: Irregular bonding among the materials used and machines of plastic cause fatigue failure due to surface imperfections. Requires precise control [12].

Fused Deposition Modeling In fused deposition modeling, the extrusion principle is utilized to print 3D structures. 3D printers are used heat to extrude thermoplastic material.

Polylactic acid or acrylonitrile butadiene styrene) in layers from a nozzle onto a base. Such deposited layers fuse and further harden into the final object [13].

Advantages: High accuracy, durability, and low material cost [14].

Limitations: Enlargement of printed materials occur. The material requires processing into filaments.

Uses: Used to produce commercial plastics**.** It allows the printing of cell suspension into scaffold support [15].

Powder-Based 3D Printing Technology:

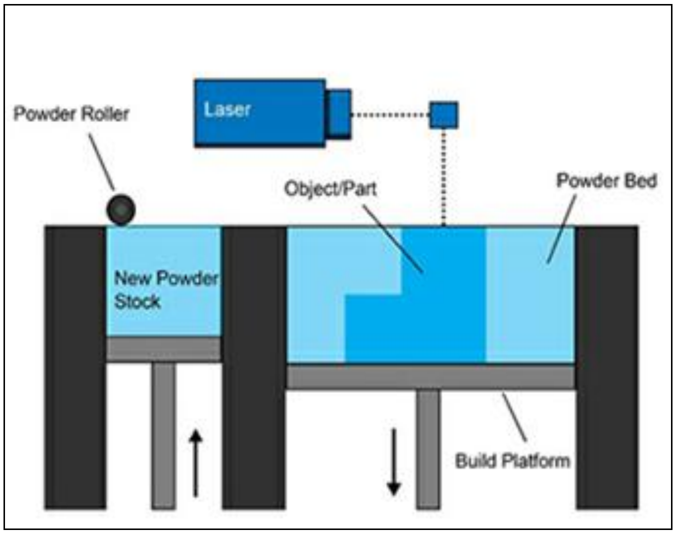

FIG. 7: POWDER-BASED 3D PRINTING TECHNOLOGY

Powder-Based 3d Printing Technology [16] was developed by the Massachusetts Institute of Technology in 1980 [17]. It involves the spreading of thin layers of powder selectively held by adding drops of liquid binder through piezoelectric or inkjet printer head. In another alternative approach, the binder solutions are jetted onto layers of powder [18]. 3D printing technology has been explored in wide areas such as pharmaceutical and tissue engineering applications between 1993 and 2003 to its advantages in manufacturing oral dosage forms [19] and implants.

Advantages: Greater resolution. It is capable of creating multifaceted formulation designs consisting of loose powders in inner regions [20].

Disadvantages: Greater porosity, Poor mechanical strength.

Semisolid Extrusion 3D Printing: It involves layer by layer accumulation of semisolid (initial materials) using a syringe-based tool head. Semisolids (gels or pastes) are prepared by blending appropriate ratios of polymers and solvents to obtain a proper viscosity for printing. It has broad applications and the accessibility of a benchtop platform to promote its creative use in faster prototyping of several objects [21, 22].

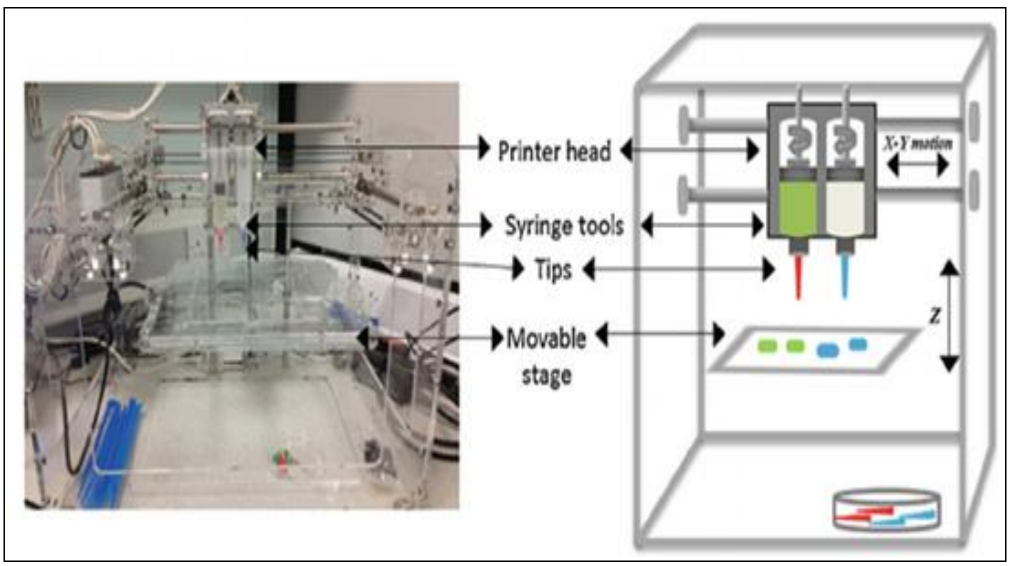

FIG. 8: SEMISOLID EXTRUSION 3D PRINTING TECHNOLOGY

Semisolid Extrusion 3D Printing Technology [23]**:**
Advantages: Minimal costs of the entry-level. Wide variety of raw materials availability and ease of customization.

Disadvantages: Low precision level, Long construction time [24].

Sheet Lamination Technology [25]**:** It is the first laminated object manufacturing system shipped in 1991. The technology was developed by Helisy's of Torrance; the main parts include a feed mechanism, a heated roller for applying pressure to join the sheet with the layer below, and laser to cut the contour of the part in each sheet layer.

Applications: Less number of detailed parts**,** Firm testing, quick tooling patterns.

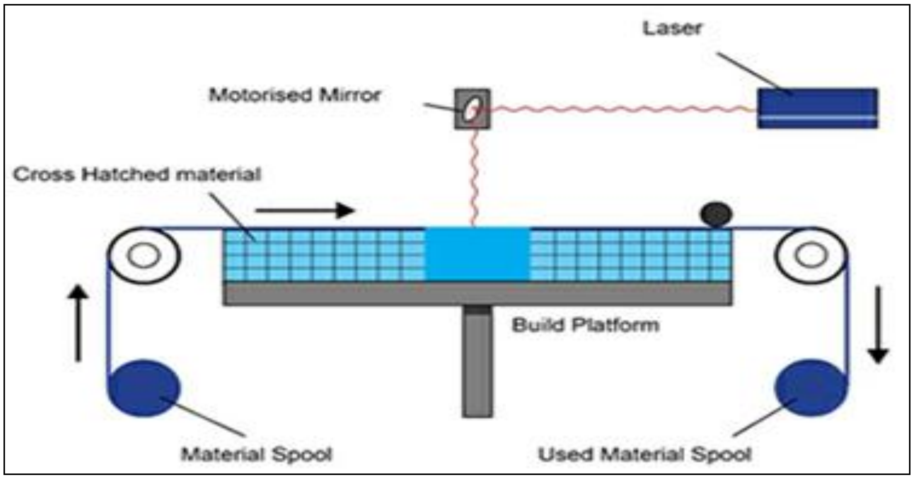

FIG. 9: SHEET LAMINATION TECHNOLOGY

Sheet Lamination Technology:

Zipdose® Technology [26]: It is the first 3D pharmaceutical dosage form globally made with Aprecia's proprietary method. ZipDose® technology is beneficial for designing the dosage forms with ease of administration by providing less potent medications in a rapidly disintegrating form. The technology surmounts swallowing difficulty and patient adherence challenges. The technology can hold high drug doses due to its unique digitally coded layering and zero-compression methods yet, still maintain faster disintegration with just a sip of water. It can help patients with high pill burden or swallowing difficulty administer medications easily.

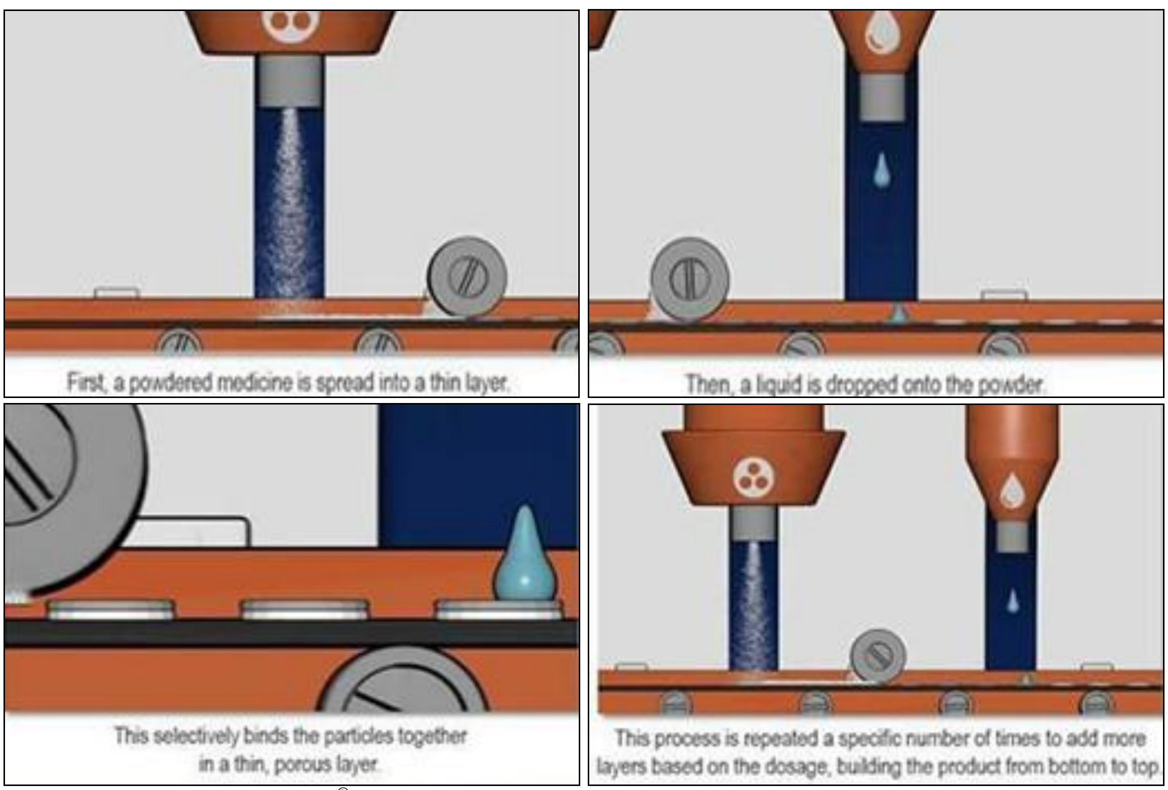

FIG. 10: ZIPDOSE® TECHNOLOGY USING 3D PRINTING: HOW IT'S MADE

Zipdose® Technology using 3D Printing: How it's made:

Digital Light Processing [27]: The technology works with photopolymers and utilizes a more Conventional light source (arc lamp) along with a liquid crystal display panel, making it faster than stereolithography. It provides highly accurate components with excellent resolution.

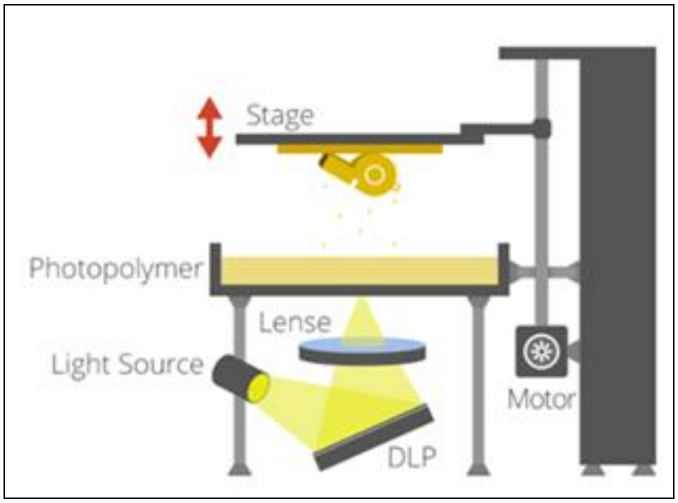

FIG. 11: DIGITAL LIGHT PROCESSING TECHNOLOGY

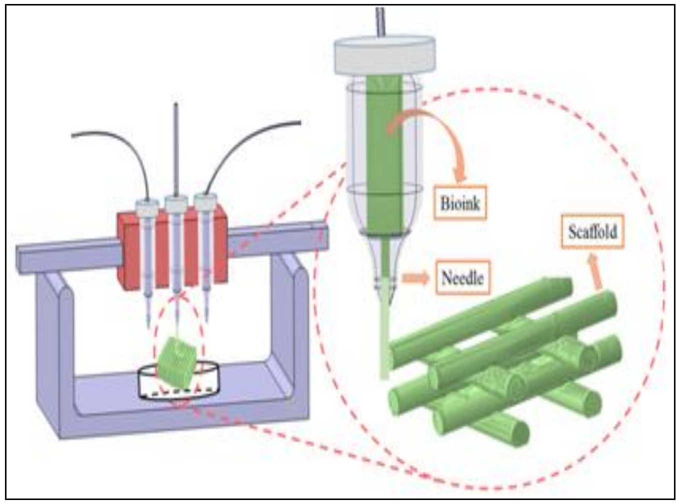

FIG. 12: BIO PLOTTER

Digital Light Processing Technology:
Advantages

- ✓ Lesser operating costs
- ✓ Requires a shallow vat of resin only
- ✓ Less wastage

Applications:

- ✓ Prototype testing
- ✓ Visual prototypes
- ✓ Dental sectors which require high detailed finishing.

Bio Plotting [28]: 3D bio plotter enables rapid prototyping of biomaterials for computer-aided tissue engineering from 3D CAD models. It is also suitable for processing patient CT.

Data to physical 3D scaffold with a well designed and defined outer form and an open inner structure. It can be used to extrude paste and gel materials with up to 100 layer micron resolution.

Bio Plotter:
Advantages: Use of several materials in single point, greater resolution for an extrusion system.

Disadvantages: Less build volume, expensive and limited part geometry.

APPLICATIONS:

- ✓ Fabrication of comfortable, customized prosthetics for amputees in the field of biomedicine.
- ✓ Applicability of technology for small–batch custom production.
- ✓ 3D printing technology has recently emerged as a novel technique in liver-related surgical fields [29, 30].
- ✓ Both 3D modelling and 3D printing technologies are reliable and appropriate for the analysis of congenital heart diseases.
- ✓ The novel applications of 3D printing for user-specific and customizable hardware have advanced to open–source does it yourself "DIY" fabrication of assistive devices, encompassing a profound impact worldwide for consumers with little choice [31, 32].

Limitations:

- ✓ 3D printing technologies (FDM, EXT) depend on nozzle mechanisms in order to construct sequenced layers during the fabrication of the printed object. This initiate the most important challenge of sustaining a consistent and reproducible flow during printing a single or multiple objects.
- ✓ Binder migration, blocking of the nozzles printer head and, uneven powder feeding, scrapping are limitations in powder-based 3D printing technology that must be addressed as it necessitates special laboratories to carry out printing [33, 34].

- ✓ Surface imperfections in the finished products may occur due to piles up of plastic beads or coarser powder on top of each other.
- ✓ Further, post-operative treatment methods like drying rate and method can influence the appearance and characteristics of the final product, which are of significance in extrusion-based inkjet as well as powder-based 3D printing.
- ✓ The mechanical resistance of 3D printed tablets is based on its product technology. Extrusion and powder-based 3D printing generate weaker structures with higher friability values (3.55%) than conventional tablets [35, 36].

Regulatory Challenge

- ✓ Expensive
- ✓ Change in the approach of designers to the use of 3D printing technology.
- ✓ Post-operative treatment is needed due to incrementally placing one layer on top of finishing layers.
- ✓ Challenges for the approval of 3D printed products are significant as nearly 85 3D printed implantables and medical devices have gained FDA clearance.
- ✓ Standardization and development of new materials.
- ✓ Despite regulatory obstacles related to 3D printing medicines, the FDA approved the first 3D printed pill, Spritam (Levetirace), in August 2015 [37, 38, 39].

CONCLUSION: 3D printing technology has advanced extensively since its introduction, with broad applications across various fields. Albeit, high-resolution 3D printing methods are still in the initial stage of development with limitations, they demonstrate a huge potential to manufacture multi-functional materials [40]. Significant research progress has been made at the interface between tissue engineering, biology, and materials science over the past decade in the fabrication of complex *in-vitro* models and in vivo therapeutics using novel designs of objects, equipment, methods and even working principles [41]. HME, together with 3D printing technology, led to the development of cost-effective, customized drug dosage forms for achieving personalized pharmacotherapy. On the other hand, challenges associated with the fabrication of dosage forms using FDM 3D printing technology in terms of regulatory aspects must be overcome [42]. 3D printing has applications in various surgical conditions, such as preoperative planning and education. 3D printing is also being utilized for cosmetic surgeries [43]. Since, limited research work has been reported so far, continuing efforts must be put forth to validate and assess clinical performance. Therefore, the translation of technology and design methods can be improved. The novel technology is reliable and appropriate for the analysis of congenital heart diseases, but 3D printing has its limitations & potential bias about subjectivity in the modernization of treatment for congestive heart diseases. 3D models can serve as a summary of diagnosis and a reliable tool for choosing disease treatment [44].

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REFERENCES:

1. Bangeas P: Role of innovative 3D printing models in the management of hepatobiliary malignancies. World Journal of Hepatolology 2019; 11(7): 574-85.
2. Chiulan I, Frone AN, Brandabur C and Panaitescu DM: Recent advances in 3D printing of aliphatic polyesters. Bioengineering 2018; 5(1): 1-18.
3. Wohler’s T: Wohlers report wohlers associates fort collins co. USA 2016.
4. https://jcadusa.com/3d-printing-trends-statistics-2018-2019.
5. Cleversey C, Robinson M and Willerth SM: 3D printing breast tissue models: a review of past work and directions for future work. Micromachines 2019; 10: 1-18.
6. Melchels FP, Feijen J and Grijpma DW: A review on stereolithography and its applications in biomedical engineering. Biomaterials 2010; 31: 6121-30.
7. Zhang X, Jiang X and Sun C: Micro-stereolithography of polymeric and ceramic microstructures. ELSEVIER 1999; 77: 149-56.
8. https://www.custompartnet.com/wu/ink-jet-printing
9. https://manufactur3dmag.com/all-about-sls-technology/

10. Gul JZ: 3D printing for soft robotics - a review. Science and Technology of Advanced Materials 2018; 19(1): 243-62.
11. http://www-cdr.stanford.edu/biomimetics/sdm.html
12. Xu X, Cheng W and Dudek D: Material modeling for shape deposition manufacturing of biomimetic components. American Society of Mechanical Engineers 2000; 1-10.
13. Ahn SH, Montero M, Odell D, Roundy S and Wright PK: Anisotropic material properties of fused deposition modeling ABS. Rapid Prototype Journal 2002; 8: 248-57.
14. Kalita SJ, Bose S, Hosick HL and Bandyopadhyay A: Development of controlled porosity polymer-ceramic composite scaffolds *via* fused deposition modeling. Materials Science and Engineering C 2003; 23: 611-20.
15. Liu C, Huang N, Xu F, Tong J, Chen Z and Gui X: 3D printing technologies for flexible tactile sensors toward wearable electronics and electronic skin. Polymers Basel 2018; 10(6): 1-31.
16. https://www.lboro.ac.uk/research/amrg/about/the7categoriesofadditivemanufacturing/powderbedfusion/
17. https://aprecia.com/zipdose-platform/zipdose-technology.php
18. Prasad LK and Smyth H: 3D printing technologies for drug delivery: a review. Drug Development and Industrial Pharmacy 2016; 42(7): 1019-31.
19. Wang J, Goyanes A, Gaisford S and Basit AW: Stereolithographic (SLA) 3D printing of oral modified-release dosage forms. International Journal of Pharmaceutics 2016; 503(12): 207-12.
20. Katstra WE, Palazzolo RD, Rowe CW, Giritlioglu B, Teung P and Cima MJ: Oral dosage forms fabricated by three dimensional printing TM. Journal of Controlled Release 2000; 66(1): 1-9.
21. Alhnan MA, Okwuosa TC, Sadia M, Wan KW, Ahmed W and Arafat B: Emergence of 3D printed dosage forms: opportunities and challenges. Pharmaceutical Research 2016; 33(8): 1817-32.
22. Rattanakit P, Moulton SE, Santiago KS, Liawruangrath S and Wallace GG: Extrusion printed polymer structures: a facile and versatile approach to tailored drug delivery platforms. International Journal of Pharmaceutics 2012; 422(12): 254-63.
23. https://link.springer.com/chapter/10.1007/978-3-319-90755-07
24. https://3dprint.com/230168/advantages-disadvantages-of-food-3d-printing-methods/
25. https://www.lboro.ac.uk/research/amrg/about/the7categoriesofadditivemanufacturing/sheetlamination/
26. https://www.kurzweilai.net/fda-approves-the-first-3d-printed-drug-product
27. https://www.think3d.in/digital-light-processing-dlp-3d-printing-service-india/
28. https://www.3dprintingmedia.network/additive-manufacturing/am-technologies/what-is-3d-bioplotter-technology/
29. Norman J, Madurawe R, Moore C, Khan MA and Khairuzzaman A: A new chapter in pharmaceutical manufacturing: 3d-printed drug products. Advanced Drug Delivery Reviews 2017; 108: 39-50.
30. Diogo JH: 3D printing of pharmaceutical drug delivery systems. Archives of Organic and Inorganic Chemical Sciences 2018; 1(2): 65-69.
31. Andrea AK, Marta GP and Dolores RS: Personalized 3D printed medicines: which techniques and polymers are more successful. Journal of Bioengineering 2017; 4(79): 1-16.
32. Akoury E, Weber MH and Rosenzweig DH: 3D-printed nanoporous scaffolds impregnated with zoledronate for the treatment of spinal bone metastases. MRS Advances 2019; 156: 1-7.
33. Wang M, Wu Y, Lu S, Chen T and Zhao Y: Fabrication and characterization of selective laser melting printed Ti–6Al–4V alloys subjected to heat treatment for customized implants design. Progress in Natural Science-Materials International 2016; 26(6): 671-77.
34. Khan A, Nag MV, Mirt G and Dhiman S: Dental image analysis approach integrates dental image diagnosis. IJCCR 2020; 12(16): 47-52.
35. Leist SK and Zhou J: Current status of 4D printing technology and the potential of light-reactive smart materials as 4D printable materials. Virtual Physical Prototyping 2016; 11(4): 249-62.
36. Dumpa NR, Bandari S and Repka MA: Novel gastroretentive floating pulsatile drug delivery system produced via hot-melt extrusion and fused deposition modeling 3D printing. Pharmaceutics 2020; 12(1): 52.
37. Finnegan, Henderson, Farabow and John Hornick: 3D printing in healthcare. Journal of 3D Printing in Medicine 2017; 1(1): 13-17.
38. Albert Manero: Implementation of 3D printing technology in the field of prosthetics: past, present and future. International Journal of Environmental Sciences Public Health 2019; 16: 1609-41.
39. Mao M, He J, Li X, Zhang B, Lei Q and Liu Y: The emerging frontiers and applications of high-resolution 3D printing. Micromachines 2017; 8(4): 1-20.
40. https://aprecia.com/zipdose-platform/zipdose-technology.php
41. Ford S and Minshall T: 3D printing in education : a literature review 3D printing in education : a literature review. Additive Manufacturing 2018.
42. Bateaux: 3D-printed models for surgical planning in complex congenital heart diseases: a systematic review. Frontiers in Pediatrics 2019; 7(23): 1-8.
43. https://jcadusa.com/3d-printing-trends-statistics-2018-2019/
44. Qian Y, Hanhua D, Jin S, Jianhua H, Bo S and Qingsong W: A Review of 3D printing technology for medical applications. Engineering Journal 2018; 4(5): 729-42.

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