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Review

3D printing prostheses using additive manufacturing and regenerative engineering

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Abstract

Additive manufacturing is a manufacturing process utilized to make prosthetics. It offers an affordable means to create custom-made prostheses. Yet, the number of studies exploring the domain of 3D printing and bioprinting of prosthetics remains limited. In this paper, we provide a comprehensive review of the current research in additive manufacturing to produce prosthetic limbs, bionic eyes, temporomandibular joints (TMJ), cardiac valves, and skin. We concluded that the research gap lies in the long-term, periodic assessment of 3D-printed prosthetic limbs for durability. 3D-printed prosthetic sockets' reinforcement materials are a particularly underexplored topic and the main shortcoming of 3D-printed prostheses is their failure under shear stresses. In bioprinting, research must focus on developing tissue-specific bioinks and hydrogels to overcome their existing scarcity. Bioprinting techniques like extrusion, inkjet, and laser-assisted bioprinting subject bioinks to conditions of high temperature and pressure. Bioinks must withstand the printing process and simultaneously retain their rheological properties and cell viability. Moreover, some bioprinting techniques are still quite expensive. However, 3D printing and bioprinting offer the prospect of customization to the patient's unique anatomy, increasing the wear time of prostheses and offering unique benefits like improved tissue regeneration and adaptability to changing patient anatomy. 3D printing specifically reduces costs, and production time and improves accessibility in war-stricken areas with more amputees.

Keywords

3D printing, biomaterials, prosthetics, additive manufacturing, tissue engineering, regenerative medicine, precision medicine

1. Introduction

Global violence significantly affected traumatic amputations, reported at 13.23 million incidences and 552.45 million prevalence in 2019 alone [1, 2]. Such amputations, in addition to having a physical disbarment on individuals, have also been associated with depression, anxiety, deteriorating mental health, and other psychological states [3]. All these conditions combined lead to amputees facing unfair employment practices [4]. Prosthetics have played a key role in improving

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the quality of life of amputees, allowing them to perform everyday tasks that would otherwise be difficult or impossible. A study performed at Harborview Medical Center and the Department of Veterans Affairs (VA) Puget Sound Health Care System indicated that prosthetic rehabilitation even increased the likelihood of amputees returning to work by wearing prosthetics for 10-12 hours per day [5]. To further cement the advantages of prosthetic use, researchers have also studied the consequences of not using or abandoning these devices. The effects include compensatory motions that result in harmful secondary musculoskeletal conditions [6]. Despite these benefits, prosthesis use remains low worldwide [7], especially in developing countries [8], where the World Health Organization estimates that only 5% of the 40 million amputees have access to prosthetic care due to prohibitive costs [9]. Retinal degeneration leading to blindness has shown a similar outlook. The estimated global prevalence of age-related macular degeneration was projected at 196 million in 2020, with an anticipated increase to 288 million by 2040 [10]. Conditions such as macular degeneration and retinitis pigmentosa can benefit from the use of bionic eyes, which restore spatial detail, a fundamental aspect of vision [11]. Even so, the accessibility challenge extends to bionic eyes, where high costs have similarly restricted access to bionic eyes for many individuals [12]. However, advances in 3D printing are substantially lowering costs, making both prosthetic limbs [13] and bionic devices, like compound eyes, more affordable [14]. Figure 1 showcases the key differences between 3D printing and 3D bioprinting.

3D-printed prosthetics also improved patient satisfaction [15]. This is in stark contrast to the reviews of conventional upper limb prosthetics. Based on an analytical survey of studies spanning 25 years [16], and a questionnaire of 70 Australian upper limb amputees [17] it was concluded that 52.3% of prosthetic owners used their prostheses for less than 6 hours a day which suggests either dissatisfaction (poor design, functionality, and fit with the prostheses or the perception that their use does not bring considerable positive change in the users' daily lives. 3D printing technology offered a promising solution. This method provided greater accuracy, reduced production time, and ensured better fit and comfort. Notable examples are the 3D printing of coloured silicone-based prosthetic fingers [18], the use of Artificial Intelligence to improve transtibial prosthetic sockets' fit to the amputee's residual limb [19] or 3D printed hemispherical photodetector arrays used to make the first 3D printed prototype bionic eye [20]. In this review we dive into some of the most commonly and widely used prosthesis in various anatomical parts of the human body. Moreover, we also look at how 3D printing has, in recent years, played a vital role in helping achieve personalization fits for individuals.

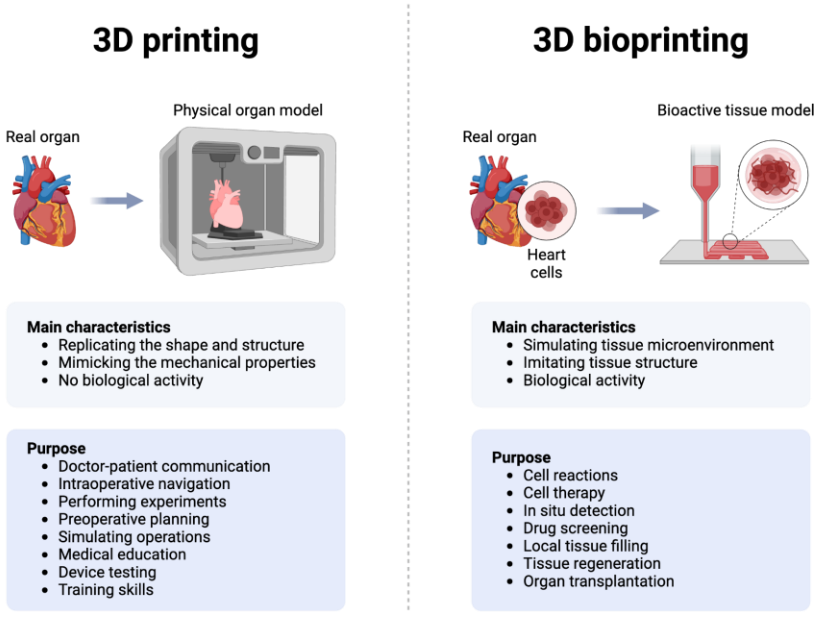

Figure 1. 3D Printing vs. 3D Bioprinting in Healthcare, by BioRender.com (2024). Retrieved from https://app.biorender.com/biorender-templates

2. Methodology

2.1. Bionic Eyes

Various non-congenital eye diseases like retinitis pigmentosa and macular degeneration have been shown to cause visual impairment and blindness [21]. This is where bionic eyes played the role of fully or partially restoring vision [12]. Visual neuroprostheses replaced the working of neuronal systems that constituted the anatomical pathway from the retina to the brain [11]. A major component of bionic eyes embedded inside the eye was a chip implanted behind the retina during a microsurgery. This chip functioned as the damaged part of the retina [22]. It contained an array of microelectrodes that provide micro-electrical stimulation, which was perceived as organized patterns of light by the patient [11]. Other components of bionic eyes included cameras (usually mounted inside glasses) that processed visual information into digital signals received by a visual processing unit, which in turn, converted these into stimulation patterns for the microelectrodes to deliver [23]. While these were the common elements of bionic eyes, 3-D printing has also been employed in bionic compound eye lenses. This was done by 3-D printing a hemispherical surface with a 100+ lens array. An optical relay system converted the curved image formed by the compound eye into a flat, planar image recognized by the CMOS image sensor. This helped form a compound bionic eye camera [24]. In another study carried out in China, spherical lenses were 3D-printed to make the compound eye using photosensitive resin. Mask photocuring was carried out after 3D printing [14]. Though the paper discussed the application of such bionic compound eyes in medical fields, it did not specifically shed light on biocompatibility. However, it is important to note that biocompatible photosensitive resins did exist and have been widely tested for use in the medical arena [25].

2.2. Biocompatible Hydrogel Skin

Skin is the human body's barrier, the first layer of defence [26], and the largest organ [27]. The most common treatment for skin defects was autologous skin transplantation [28]. However, this treatment was compromised by issues like donor-site shortage, infections, secondary injuries, etc. Adding to this, autologous skin transplants were not feasible at times with large-scale skin injuries like third-degree burns and extensive irradiation therapy which may exhaust supplies of healthy autologous skin tissues [29].

Much attention was being shed on creating bioprinted cell-laden constructs to serve as skin [30]. This was because bioprinting allowed the production of heterogeneous cell populations, soluble factors, and biomaterials in pre-determined locations, increasing the potential for automation and replication of such products [31]. 3D bioprinted skin also provides accurate placement of relevant cells and tissues which helps reconstruct the damaged skin [32]. Hydrogels (networks of crosslinked hydrophilic polymers) [33] had the ability to absorb water equalling 90% of their initial weight [34]. This moisture-laden environment made hydrogels a great carrier for cells and improved wound healing [35]. In doing so, hydrogels also replicated the hydrated nature of the extracellular matrix of native skin [36, 37]. This made hydrogels a popular biomaterial in skin bioprinting [38]. The cells most used in bioinks for skin were fibroblasts and keratinocytes [39]. The use of such living skin cells in the bioprinted constructs promoted the proliferation of such cells, hence improving skin regeneration [40].

2.3. Artificial Cardiac Valves

Valvular heart disease is an increasing healthcare concern, with projections showing it could take 23.6 million lives till 2030 [41]. For this growing dilemma, replacement with prosthetics was the usual recommendation [42, 43]. However, conventional prosthetics were not suited to functioning optimally in adolescents and children in their growing years and 3D-printed cardiac valves were thought to overcome this issue. Both organic and synthetic polymers were used in 3D-printed cardiac valves [44]. Natural polymers needed certain structural features to promote tissue regeneration [45]. These qualities were present in collagen, fibrin, and chitosan [46]. Encapsulated aortic root sinus smooth muscle cells (SMC) and aortic valve leaflet interstitial cells (VIC) had been successfully printed into aortic valves. They were viable within alginate/gelatin hydrogels and underwent cell viability assays over a 7-day period [47]. This particular aortic valve was 3D printed using extrusion-based bioprinting technique as shown in Table 1. Customization to the patient's anatomy was a rising trend in the 3D printing of heart valves. CT scans and MRIs were done to ensure the 3D-printed valves fit into the unique anatomy of each patient [48, 49]. The results showed that better compatibility is achieved when this process of personalization is followed [50].

3D bioprinted heart valves have involved the 3D printing of scaffolds out of biocompatible materials [51]. These scaffolds were then seeded with stem cells [52, 53]. These functional valve constructs have been expected to bypass the need for artificial valves entirely. This was because they overcame the major issues faced with mechanical valves like calcification, thrombogenicity, and non-adaptability to young, growing patients [54].

2.3.1. Bioprinting Techniques

Extrusion, laser-assisted, and inkjet bioprinting are the three most popular bioprinting technologies. Extrusion bioprinting was the most important, second to inkjet printing [55]. Most of the other examples of prosthetics studied in this paper are also printed through these three 3D bioprinting techniques. Extrusion bioprinting involves filling a syringe with bioink and extruding it through a nozzle [56]. The dispensing force is created by pneumatic, screw-based, or piston-based systems [57]. The movement of the syringe (and sometimes the printing stage) is automated. It controls the shape and 3D location where bioink is placed on the printing stage [58] or, in some cases, suspended in a support bath material that helps print fidelity [59]. Inkjet bioprinting is based on the working of desktop inkjet printers and was developed in 2003 [60, 61, 62]. In this type of bioprinting, dilute solution droplets are jetted through a nozzle, in pre-determined patterns through computer-aided design (CAD) software [63]. The dispensation systems are driven by thermal, piezoelectric, or microvalve processes [64, 65]. Laser-assisted bioprinting uses pulses of a laser beam passed through a ribbon [66]. A ribbon is a thin, flexible layer made of metal, usually gold or titanium. The ribbon is coated with biomaterials such as alginate bioink, collagen bioink, keratinocytes, fibroblasts, and human mesenchymal stem cells [67, 68]. When laser pulses land on the ribbon, the metal heats up, causing the liquid biomaterials to evaporate and turn into droplets deposited on the receiving substrate [69]. The receiving substrate also contains a biopolymer or cell culture medium to promote cell viability, cellular adhesion [70], and growth after droplet deposition [64]. Table 1 compares these 3D bioprinting techniques in detail, in terms of the key parameters, target applications, advantages, and challenges with each of these three techniques.

Reference	Bioprinting technique	Key parameters	Target Prosthetic Application	Advantages	Challenges
[71]	Extrusion Bioprinting	feed rate, pressure, path design, nozzle height, temperature	articular cartilage, muscle, ears, skin	multiple print heads to allow multi-printing in the same bioprinted tissue; can allow printing with bioinks of higher cell concentrations; can be used with more biomaterials than other printing techniques	cells are subjected to shear stress when passing through the nozzle; cells experience pressure in the syringe before extrusion; most bioinks require one or more types of crosslinking
[55]	Inkjet Based Bioprinting	Size of droplets, ejection rate, deposition rate	Skin, cartilage	low cost, high cell viability, high resolution, high throughput, non-contact printing	limited bioinks, low strength, nozzle blockages, risk of mechanical and thermal stress on cells, chances of cell agglomeration
[72]	Laser-Assisted Bioprinting	UV wavelength, pulse energy deposition, pulse duration	DNA, cells, tissue, and organ printing	high cell viability, noncontact, nozzle-free, high precision, high resolution	low scalability, low flow rate caused by fast gelation, and time-consuming

Table 1. *Comparison between three popular 3D-bioprinting techniques.*

2.4. Temporomandibular Joint Replacement Prostheses

The mandible (lower jaw) and the mandibular fossa of the temporal bone are joined by the ginglymoarthrodial Temporomandibular Joint (TMJ) [73, 74]. This joint is an integral part of the anatomy of the human skull, and it had been noted that joint replacement implants yield reasonable outcomes when personalized to the patient to ensure a result that closely resembled native anatomy whilst preserving range of motion and joint function [75]. Due to the patient-specific nature of this prosthesis, testing was needed to analyze the prosthetic's biomechanical behaviour and load distribution. This was usually done using FEA/FEM (finite element analyses/methods) [76, 77]. 3D printing of the TMJ prostheses had been implemented for a patient with end-stage osteoarthritis of the TMJ. The patient needed a total joint replacement surgery of the TMJ [78]. A personalized 3D print model was created after analysis of X-rays, MRI, and CT scans [79]. Bionic joint discs have been developed using a combination of Ultra High Molecular Weight Polyethylene (UHMWPE) and High-Density Polyethylene (HDPE). This material was printed using Fused Deposition Modeling (FDM) [80]. Using this hybrid material improved the elasticity of the prosthetic as proven by biomechanical tests. This elasticity allowed the prosthetic to closely mimic the functional behaviour of natural articular disks. Natural articular disks use these elastic properties to distribute stress evenly [81 82]. This elasticity was lacking in conventional TMJ prostheses made of metal alloys.

2.5. Upper Limb Prosthesis

The human hands allow for dexterity and detailed sensory input. These are some of the features that prostheses for this part of the body should emulate. Intuitive control of hand prostheses has been identified as an essential requirement to fulfill the motor requirements of the human upper limbs [83]. Intuitive control of a neuroprosthesis required the application of surface electrodes that responded to the innervation of residual limb muscles [84]. Their effectiveness was contingent upon sufficient signals being received through the skin barrier. Higher-level amputations often lacked residual muscle, which made it more challenging to provide the dexterity and control required of hand prostheses with skin electrodes [85]. To bypass this issue, Targeted Muscle Reinnervation (TMR) was developed [86]. This surgical technique involved the transplantation of nerves from the residual limb into nearby muscles that had been deprived of nerve supply. This amplified neural signals [87] and enhanced the myoelectric control of the prostheses [88]. Regenerative Peripheral Nerve Interface (RPNI) is another technique that was less affected by the amputation level. For RPNI, a peripheral nerve was implanted into a free muscle graft, causing reinnervation of this muscle graft [89]. In doing so, RPNI made it possible for muscles to record signals that actuated individual finger movements. This peripheral nerve amplifier could be utilized in neuroprostheses [90]. However, RPNI required harvesting muscle and nerve tissue from healthy areas in patients who had already lost a limb. This pushed researchers to look into the area of tissue-engineered peripheral nerve or muscle grafts [91]. Scientists have studied the novel idea of combining bioprinting hydrogels with neural progenitors to create living electrodes [92]. Haptic sensors have also been 3D printed [93]. Their soft sensor has been printed using TPU (PALMIGA PI-ETPU 95-250 Carbon Black; Creative Tools, Sweden) whereas the structural component-the soft case printed using soft TPU type known as NinjaFlex (NinjaTek, Lititz, PA, USA) [94]. These and other sensors have been embedded in 3D-printed hand prostheses [95].

2.6. Lower Limb Prosthesis

Prosthetic leg sockets were an area where AM has shown much potential to outshine conventional manufacturing processes [96]. This was because 3D printed models allow the creation of complex geometrical arrangements in the final product [97]. It was especially useful for patients with varying limb volumes who needed multiple socket re-fittings (e.g. children in their growing age) [98, 99] because 3D printing poses reduced fabrication times as compared to conventional approaches [100]. 3D printed sockets strength assessment was done as laid out by the International Organization for Standardization (ISO) 10,328: Prosthetics–Structural testing of lower-limb prostheses. Failures were mostly observed in the distal end of the socket or the pyramid attachment [101]. To alleviate these issues, researchers proposed a composite infill approach. The layer-by-layer filament deposition in 3D printing was held responsible for the shear failure of the socket [102]. To address this, printing parameters like infill density and pattern were modified [103].

Additionally, material selection was identified as a major contributor to socket strength. Historically, polylactic acid (PLA), polypropylene (PP), and polycaprolactone (PCL) have been recognized as reliable print materials for Fused Filament Fabrication (FFF) [104]. However, to enhance strength, scientists have also used carbon-reinforced and glass-reinforced composite polymer filaments [103]. Specifically for layer-on-layer adhesion, using carbon fiber composite while 3D printing has been shown to help [105].

3. Discussion

We currently have limited options for biomaterials, specifically hydrogels, used in bioprinting [106]. Most were crosslinked hydrogels because they can absorb moisture and remain insoluble, providing an environment similar to the extracellular matrix (ECM) [107, 108]. The criteria for bioink selection was a stringent process. High temperature and pressure during printing led to decreased cell viability in bioinks. The bioink had to retain a suitable environment for cell viability whilst possessing rheological properties that allowed it to be printed [109]. These strict standards were only met by a small number of bioinks. There should be an emphasis on the production of bioinks and hydrogels for various body tissues, that can offer both structural integrity and cellular compatibility.

A cell's microenvironment is partly determined by the extracellular matrix which varies in stiffness depending upon cell phenotype [110]. A diverse variety of hydrogels would have allowed a range of viscoelastic properties which would in turn help us mimic the microenvironment of cells provided by different extracellular matrices. This progress would also help us explore the possibility of having dynamic hydrogels that change depending on whether tissues would be in development or healing stages, similar to the adaptable nature of extracellular matrices [111, 112].

Another pressing issue was the control of degradation rates of various hydrogels. Studies suggest that future research should focus on producing a library of bioinks with various degradation rates while controlling for factors like rigidity and stress relaxation [113].

Vascularization and innervation were other important aspects that needed attention in order to realize regenerative tissues that can assimilate with the human body. Vascularization of bioprinted tissues and the printing of tubular constructs is only possible if we can have high-precision, micropatterned bioprinting [114]. Laser-induced forward transfer (LIFT) bioprinting technique is a kind of laser-assisted bioprinting; it offers the ability to print at single-cell resolution [115]. LIFT and other single-cell bioprinters like high-definition single-cell printing (HD-SCP) [116] that integrate the field of microfluidics and offer high spatiotemporal control over cells in bioprinting should be explored to enable the production of more well-integrated bioprinted tissues. In particular, progress is needed to make LIFT more affordable [117].

Other than printing vessels to vascularize tissue, tissue-regenerative scaffolds can induce innervation [118]. This is done by incorporating electroactive materials in 3D bioprinting scaffolds of tissues. It has been tested in bioprinted skin tissues along with the implantation of a 3D coaxial-printed self-adaptive delivery chip to release biochemical and bioelectrical substances to restore skin nerves. Results have shown recovery of excitation function within 23 days [119]. Further understanding of cell-cell and cell-material interfaces is needed to understand their role in the innervation process. Advances in the functionality of human and 3D-printed tissues will also help progress their use in drug screening and disease modelling [120].

In addition to improving printing resolution, work is required to enhance printing speed. Stereolithography (SLA) based bioprinting is known for its high printing speed [121]. This is important because printing time represents the duration for which cells in bioink are exposed to conditions that can decrease their viability [122]. Another motivation for improving printing speed is to aid the industry-scale translation of bioprinting [106].

While it is imperative to focus on improving individual factors affecting the success of bioprinting, reviews should collectively evaluate factors too. Cost and benefit analyses should be conducted for various bioprinting techniques evaluating all possible factors affecting the feasibility of producing bioprinted tissues: printing speed, resolution, cell viability, etc. This would help determine the best approach towards industrializing bioprinting and improving accessibility.

Furthermore, there was a lack of clinical testing of 3D bioprinted tissues in animals and humans. There were a few examples like transplanting hydrogel scaffolds to damaged penis corpus cavernosum in rabbits which helped them regain erectile function and fertility [123]. However, the model has yet to be used in human clinical transplants to treat erectile dysfunction.

While 3D bioprinted tissues have been tested and implanted in humans sporadically, 3D printed organs are yet to be approved or standardized for clinical use because of the lack of unified global directives guiding the human testing of these organs [124].

Ethical and moral considerations were important in the 3D bioprinting of tissues. Sources of cells for bioinks sometimes included embryonic stem cells [125]. This involved the destruction of human embryos which raised religious concerns as well as questions regarding the sanctity of life and whether to categorize this as murder [126]. The ethical issues surrounding this field were variegated and multifaceted. The moral status of 3D-printed tissues was under question too [127]. This was because of the puzzle of whether they should be treated as purely functional tools or whether their significance increased as the level of biofabrication progressed towards organs and tissues that interacted with human neural and reproductive systems. Assigning moral significance to bioprinted tissues also had implications on the perceived value and price of these tissues, increasing the inequities that already permeate the healthcare system. This even endangered the very purpose of 3D printing in some cases, i.e. to alleviate issues of donor shortages and lack of access.

In 2020, a Russian study shed light on the ethical and regulatory concerns that impede the legalization of 3D-bioprinting technologies for reproductive organs, particularly the ovaries (for patients having undergone ovariectomy after developing ovarian cancer) [128]. It discussed the issue of informed consent. Firstly, ovary printing and the conception of an offspring through that ovary directly affected the offspring. Secondly, manipulation of ovarian follicles in the process would lead to genetic and epigenetic changes that would affect the offspring in ways not well-understood. Moreover, the 3D bioprinting of an ovary took several years. During this time the intended receiver of the ovary could change their mind about whether they wanted to conceive a child. However, the weight of the expense and effort already spent in the process of making an artificial ovary would taint their decision and could incline them toward motherhood they did not freely consent to. Even if the intended receiver decided not to undergo the ovary transplant, the question of who then possessed ownership of the bioprinted ovaries still stood.

These and other ethical dilemmas necessitate legal preparations and regulatory bodies to set the standards for the approval and use of printed tissues in humans. In the realm of 3D printing prosthetic limbs, research had focused on the pre-printing aspects like printing techniques, design, and material. There was a dearth of research on the post-printing advancements that can be made to 3D-printed limbs and leg prosthetic sockets in particular [103]. Complaints regarding 3D-printed limbs arose due to their inability to withstand frictional forces that act on the body of the limb [129]. Even so, there were very few papers studying the long-term durability of 3D-printed prosthetics. Consequently, research should focus on periodic assessments of the robustness of limbs and how they can withstand wear and tear during everyday use. Specifically, reinforcement using fiberglass, carbon fiber, and cement is an under-studied topic that could improve the mechanical stability of prosthetic sockets. Studies should investigate materials best suited for layering on sockets and bodies of 3D-printed bionic limbs to provide strength whilst preserving functionality, movement, and user compatibility.

Accessibility was a factor that set 3D-printed prosthetics apart from conventional prostheses. It was not only cheaper [130] but also required fewer visits for fittings [131] and had a shorter production time [132]. A research study performed in Qatar in 2022 inspected 3D-printed hands for war-wounded children [133]. While 'The American Orthotic & Prosthetic Association' reported that traditional upper extremity prostheses costs lie between 1,500-5,000 USD [134], this study in Qatar produced prosthetic hands for a minimum of 19 USD. The use of CAD files from open-source communities like E-nable [135], helped cut down costs. The accompanying Table 2 provides a comparative analysis of accessibility parameters, including regional availability, costs of 3D-printed versus non-3D-printed prosthetics, and the average number of patient visits required for production and fitting.

Reference	Type of 3D printed prosthetic	Cost (USD)	Cost of Non-3D Printed Counterpart (USD)	Production Time of 3D-printed prosthesis	Production Time of Conventional Prosthesis	Number of visits to the clinic required
[136, 137, 138]	Leg prosthetics	87.00	3,000.00 to 10,000.00 (simple transfemoral prosthetic limb)	17 hours	4-8 weeks	2
[139, 140 130] [141]	Upper limb prosthetics	509.66	1,2741.50 (functional prosthetic hand)	4-7 hours	4-5 days	2
[142]	Ocular Prosthetics	0.32	1,500.00 to 8,000.00 (handmade ocular prosthetics)	85 minutes	4-6 weeks	1

Table 2. *3D bio-printed prosthesis vs counterparts, a cost analysis.*

3. Conclusion

AI and machine learning holds a lot of promise for the field of 3D printing prosthetics. It should be used to analyze scans and images of amputees' stumps to 3D print a prosthetic of the best fit for them. This model can also be translated to non-functional cosmetic prosthetics like ocular prosthetics. In the area of 3D bioprinting, stem cells have been incorporated in bioinks. Still, in the future, we see bioinks that can produce biological cues that induce differentiation of the stem cells into the required lineages for the specific tissue being printed [143]. With the existence of technology like 3D echocardiography, it can be taken to the next level through 3D modeling which can help design personalised cardiac valves and other cardiac prostheses. Moreover, it is expected that we might see handheld bioprinting devices become part of surgical tools. These will be operated by the surgeon and will bioprint personalised structures that will reduce patients' recovery times. One area that could be explored in bioprinting is the development of and printing using smart materials that can respond to various external stimuli by changing shape or function to adapt to changing environments [144]. This field also expands the customizability of 3D bioprinted constructs, further catering to each patient's unique physiology and potentially accelerating patient recovery. Multimaterial and multicellular bioprinting is another field with a positive outlook. It can help enable anastomosing with patients' existing blood vessels. This technique can then also be applied to the nervous and lymphatic systems.

Author Contributions

S.M.H. formal analysis, methodology, validation, writing – original draft, reviewing & editing. K.D., S.V., conceptualization, writing - review & editing.

Conflicts of Interest

The authors declare no competing financial interests or conflicts of interest.

References

[1] Yuan, B.; Dong, H.; Gu, S.; Xiao, S.; Song, F. The Global Burden of Traumatic Amputation in 204 Countries and Territories. Frontiers in Public Health 2023, 11. https://doi.org/10.3389/fpubh.2023.1258853.

[2] Rivera, J. A.; Churovich, K.; Anderson, A. B.; Potter, B. K. Estimating Recent US Limb Loss Prevalence and Updating Future Projections. Archives of Rehabilitation Research and Clinical Translation 2024, 100376. https://doi.org/10.1016/j.arrct.2024.100376.

[3] Pundlik, A.; Verma, S.; Dhingra, K. Neural Pathways Involved in Emotional Regulation and Emotional Intelligence. J. Knowl. Learn. Sci. Technol. 2024, 3 (3), 165-192. https://doi.org/10.60087/jklst.vol3.n3.p.165-192.

[4] Lee, C.; Engdahl, S.; Riegger, A.; Davis, A.; Kelly, B. M.; Gates, D. H. Employment Status in Individuals with Upper-Limb Amputation. JPO Journal of Prosthetics and Orthotics 2021, Publish Ahead of Print. https://doi.org/10.1097/jpo.0000000000000366.

[5] Raichle, K. A. Prosthesis Use in Persons with Lower- and Upper-Limb Amputation. The Journal of Rehabilitation Research and Development 2008, 45 (7), 961–972. https://doi.org/10.1682/jrrd.2007.09.0151.

[6] Kulkarni S, Dhingra K, Verma S., "Applications of CMUT Technology in Medical Diagnostics: From Photoacoustic to Ultrasonic Imaging", International Journal of Science and Research (IJSR), Volume 13 Issue 6, June 2024, pp. 1264-1269, https://www.ijsr.net/archive/v13i6/SR24619062609.pdf.

[7] Wyss, D.; Lindsay, S.; Cleghorn, W. L.; Andrysek, J. Priorities in Lower Limb Prosthetic Service Delivery Based on an International Survey of Prosthetists in Low- and High-Income Countries. Prosthetics and Orthotics International 2013, 39 (2), 102–111. https://doi.org/10.1177/0309364613513824.

[8] Sreenivasan, N.; Ulloa Gutierrez, D. F.; Bifulco, P.; Cesarelli, M.; Gunawardana, U.; Gargiulo, G. D. Towards Ultra Low-Cost Myoactivated Prostheses. BioMed Research International 2018, 2018, 1–14. https://doi.org/10.1155/2018/9634184.

[9] Marino, M.; Pattni, S.; Greenberg, M.; Miller, A.; Hocker, E.; Ritter, S.; Mehta, K. Access to prosthetic devices in developing countries: Pathways and challenges. IEEE Xplore. https://doi.org/10.1109/GHTC.2015.7343953.

[10] Wong, W. L.; Su, X.; Li, X.; Cheung, C. M. G.; Klein, R.; Cheng, C.-Y.; Wong, T. Y. Global Prevalence of Age-Related Macular Degeneration and Disease Burden Projection for 2020 and 2040: A Systematic Review and Meta-Analysis. The Lancet Global Health 2014, 2 (2), e106–e116. https://doi.org/10.1016/s2214-109x(13)70145-1.

[11] Merabet, L. B. Building the Bionic Eye: An Emerging Reality and Opportunity. Progress in Brain Research 2011, 192, 3–15. https://doi.org/10.1016/b978-0-444-53355-5.00001-4.

[12] Suvvari, T.; Madhu, M.; Nagendra, S. Bionic Eye: An Iconic Innovation. TNOA Journal of Ophthalmic Science and Research 2021, 59 (1), 52. https://doi.org/10.4103/tjosr.tjosr_168_20.

[13] Goshe, M. T.; Kassegne, S. K. 3D Printing: Cost-Effective Solution for Increased Access to Prosthesis of Lower Extremity. https://doi.org/10.13140/RG.2.2.31137.28001.

[14] Wang, S.; Li, T.; Liu, T.; Xu, Y.; Liu, Z.; Chen, Y.; Weng, Z.; Wang, Z. Fabrication of Bionic Compound Eye Lens by 3D Printing and UV Mask Curing. 2022 IEEE International Conference on Manipulation, Manufacturing and Measurement on the Nanoscale (3M-NANO) 2022, 439–442. https://doi.org/10.1109/3m-nano56083.2022.9941590.

[15] Srija Vennam; Vijayasankar KN; Pati, F. 3D Printed Personalized Assistive Devices: A Material, Technique, and Medical Condition Perspective. Applied Materials Today 2024, 40, 102403–102403. https://doi.org/10.1016/j.apmt.2024.102403.

[16] Biddiss, E. A.; Chau, T. T. Upper Limb Prosthesis Use and Abandonment: A Survey of the Last 25 Years. Prosthetics and Orthotics International 2007, 31 (3), 236–257. https://doi.org/10.1080/03093640600994581.

[17] Davidson, J. A Survey of the Satisfaction of Upper Limb Amputees with Their Prostheses, Their Lifestyles, and Their Abilities. Journal of Hand Therapy 2002, 15 (1), 62–70. https://doi.org/10.1053/hanthe.2002.v15.01562.

[18] S. Odinotski et al., "A Conductive Hydrogel-Based Microneedle Platform for Real-Time pH Measurement in Live Animals," Small, vol. 18, no. 45, Sep. 2022, doi: https://doi.org/10.1002/smll.202200201.

[19] Raina, D.; Dawange, A.; Bandha, T.; Kaur, A.; Wasekar, R.; Verma, K.; Verma, S.; Dhingra, K. Convoluted Neural Network and Transfer Learning Algorithm for Improved Brain Tumor Classifications in MRI. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 200-212. https://doi.org/10.60087/jklst.v3.n4.p200.

[20] Tsui, J. K. S.; Bell, S.; Cruz, L. da; Dick, A. D.; Sagoo, M. S. Applications of Three-Dimensional Printing in Ophthalmology. Survey of Ophthalmology 2022, 67 (4), 1287–1310. https://doi.org/10.1016/j.survophthal.2022.01.004.

[21] Baarah, B.; Shatnawi, R.; Khatatbeh, A. Causes of Permanent Severe Visual Impairment and Blindness among Jordanian Population. Middle East African Journal of Ophthalmology 2018, 25 (1), 25. https://doi.org/10.4103/meajo.meajo_202_16.

[22] Suthar, A.; Suthar, T. The Bionic Eye…a New Vision of the Future. International Journal of Science and Research (IJSR) ResearchGate Impact Factor 2018. https://doi.org/10.21275/SR20607185604.

[23] George, D. A. S.; George, A. S. H.; Shahul, A. Insightful Innovation: Exploring the Efficacy of Bionic Eyes in Restoring Vision Impairment. Partners Universal International Innovation Journal 2023, 1 (3), 276–291. https://doi.org/10.5281/zenodo.8085602.

[24] Wang, Y.; Shi, C.; Xu, H.; Zhang, Y.; Yu, W. A Compact Bionic Compound Eye Camera for Imaging in a Large Field of View. Optics & Laser Technology 2021, 135, 106705. https://doi.org/10.1016/j.optlastec.2020.106705.

[25] Guttridge, C.; Shannon, A.; O'Sullivan, A.; O'Sullivan, K. J.; O'Sullivan, L. W. Biocompatible 3D Printing Resins for Medical Applications: A Review of Marketed Intended Use, Biocompatibility Certification, and Post-Processing Guidance. Annals of 3D Printed Medicine 2022, 5, 100044. https://doi.org/10.1016/j.stlm.2021.100044.

[26] Kabashima, K.; Honda, T.; Ginhoux, F.; Egawa, G. The Immunological Anatomy of the Skin. Nature Reviews Immunology 2018, 19 (1), 19–30. https://doi.org/10.1038/s41577-018-0084-5.

[27] Walker, M. Human Skin through the Ages. International Journal of Pharmaceutics 2022, 622, 121850. https://doi.org/10.1016/j.ijpharm.2022.121850.

[28] Weng, T.; Zhang, W.; Xia, Y.; Wu, P.; Yang, M.; Jin, R.; Xia, S.; Wang, J.; You, C.; Han, C.; Wang, X. 3D Bioprinting for Skin Tissue Engineering: Current Status and Perspectives. Journal of Tissue Engineering 2021, 12, 204173142110285. https://doi.org/10.1177/20417314211028574.

[29] Sörgel, C. A.; Cai, A.; Schmid, R.; Horch, R. E. Perspectives on the Current State of Bioprinted Skin Substitutes for Wound Healing. Biomedicines 2023, 11 (10), 2678–2678. https://doi.org/10.3390/biomedicines11102678.

[30] Teng, F.; Wang, W.; Wang, Z.-Q.; Wang, G.-X. Analysis of Bioprinting Strategies for Skin Diseases and Injuries through Structural and Temporal Dynamics: Historical Perspectives, Research Hotspots, and Emerging Trends. Biofabrication 2024, 16 (2). https://doi.org/10.1088/1758-5090/ad28f0.

[31] H. J. Pandya et al., "A microfluidic platform for drug screening in a 3D cancer microenvironment," Biosensors and Bioelectronics, vol. 94, pp. 632–642, Aug. 2017, doi: https://doi.org/10.1016/j.bios.2017.03.054.

[32] M. Safavieh et al., "Paper microchip with a graphene-modified silver nano-composite electrode for electrical sensing of microbial pathogens," Nanoscale, vol. 9, no. 5, pp. 1852–1861, 2017, doi: https://doi.org/10.1039/c6nr06417e.

[33] GhavamiNejad P, GhavamiNejad A, Zheng H, Dhingra K, Samarikhalaj M, Poudineh M., "A Conductive Hydrogel Microneedle-Based Assay Integrating PEDOT:PSS and Ag-Pt Nanoparticles for Real-Time, Enzyme-Less, and Electro-chemical Sensing of Glucose," Advanced Healthcare Materials, vol. 12, no. 1, Oct. 2022, doi: https://doi.org/10.1002/adhm.202202362.

[34] Waseeq Ur Rehman; Asim, M.; Hussain, S.; Khan, S. A.; Khan, S. B. Hydrogel: A Promising Material in Pharmaceutics. Current Pharmaceutical Design 2020, 26.

https://doi.org/10.2174/1381612826666201118095523.

[35] Barcena, A. J. R.; Dhal, K.; Patel, P.; Ravi, P.; Kundu, S.; Tappa, K. Current Biomedical Applications of 3D-Printed Hydrogels. Gels 2024, 10 (1), 8. https://doi.org/10.3390/gels10010008.

[36] H. J. Pandya et al., “Label-free electrical sensing of bacteria in eye wash samples: A step towards point-of-care detection of pathogens in patients with infectious keratitis,” Biosensors and Bioelectronics, vol. 91, pp. 32–39, May 2017, doi: https://doi.org/10.1016/j.bios.2016.12.035.

[37] Barreiro Carpio, M.; Dabaghi, M.; Ungureanu, J.; Kolb, M. R.; Hirota, J. A.; Moran-Mirabal, J. M. 3D Bioprinting Strategies, Challenges, and Opportunities to Model the Lung Tissue Microenvironment and Its Function. Frontiers in Bioengineering and Biotechnology 2021, 9. https://doi.org/10.3389/fbioe.2021.773511.

[38] Deptuła, M.; Zawrzykraj, M.; Sawicka, J.; Banach-Kopeć, A.; Tylingo, R.; Pikuła, M. Application of 3D- Printed Hydrogels in Wound Healing and Regenerative Medicine. Biomedicine & Pharmacotherapy 2023, 167, 115416. https://doi.org/10.1016/j.biopha.2023.115416.

[39] Manita, P. G.; Garcia-Orue, I.; Santos-Vizcaino, E.; Hernandez, R. M.; Igartua, M. 3D Bioprinting of Functional Skin Substitutes: From Current Achievements to Future Goals. Pharmaceuticals 2021, 14 (4), 362. https://doi.org/10.3390/ph14040362.

[40] Persaud, A.; Maus, A.; Strait, L.; Zhu, D. 3D Bioprinting with Live Cells. Engineered Regeneration 2022, 3 (3), 292–309. https://doi.org/10.1016/j.engreg.2022.07.002.

[41] Sun, Z.; Zhao, J.; Leung, E.; Flandes-Iparraguirre, M.; Vernon, M.; Silberstein, J.; De-Juan-Pardo, E. M.; Jansen, S. Three-Dimensional Bioprinting in Cardiovascular Disease: Current Status and Future Directions. Biomolecules 2023, 13 (8), 1180. https://doi.org/10.3390/biom13081180.

[42] Gourlay, T.; M. Rozeik. Improving the Hemocompatibility of Heart Valves. Elsevier eBooks 2017, 395–429. https://doi.org/10.1016/b978-0-08-100497-5.00012-4.

[43] Kellar, R. S.; Lancaster, J. J.; Goldman, S.; McAllister, T. N.; L’Heureux, N. Cardiovascular Tissue Engineering. 2011. https://doi.org/10.1016/b978-0-08-055294-1.00177-x.

[44] Bhandari, S.; Yadav, V.; Ishaq, A.; Sailakshmn Sanipini; Chukwuyem Ekhator; Rafeef Khleif; Alee Beheshtaein; Jhajj, L. K.; Aimen Waqar Khan; Khalifa, A. A.; Muhammad Arsal Naseem; Bellegarde, S. B.; Muhammad Ather Nadeem. Trends and Challenges in the Development of 3D-Printed Heart Valves and Other Cardiac Implants: A Review of Current Advances. Cureus 2023. https://doi.org/10.7759/cureus.43204.

[45] Sell, S. A.; Wolfe, P. S.; Garg, K.; McCool, J. M.; Rodriguez, I. A.; Bowlin, G. L. The Use of Natural Polymers in Tissue Engineering: A Focus on Electrospun Extracellular Matrix Analogues. Polymers 2010, 2 (4), 522–553. https://doi.org/10.3390/polym2040522.

[46] Bhandari, S.; Yadav, V.; Ishaq, A.; Sailakshmn Sanipini; Chukwuyem Ekhator; Rafeef Khleif; Alee Beheshtaein; Jhajj, L. K.; Aimen Waqar Khan; Khalifa, A. A.; Muhammad Arsal Naseem; Bellegarde, S. B.; Muhammad Ather Nadeem. Trends and Challenges in the Development of 3D-Printed Heart Valves and Other Cardiac Implants: A Review of Current Advances. Cureus 2023. https://doi.org/10.7759/cureus.43204.

[47] Duan, B.; Hockaday, L. A.; Kang, K. H.; Butcher, J. T. 3D Bioprinting of Heterogeneous Aortic Valve Conduits with Alginate/Gelatin Hydrogels. Journal of Biomedical Materials Research Part A 2012, 101A (5), 1255–1264. https://doi.org/10.1002/jbm.a.34420.

[48] Gupte, P.; Dhingra, K.; Saloni , V. Precision Gene Editing Strategies With CRISPR-Cas9 for Advancing Cancer Immunotherapy and Alzheimer’s Disease. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 11-21. https://doi.org/10.60087/jklst.v3.n4.p11.

[49] Maxson, E. L.; Young, M. D.; Noble, C.; Go, J. L.; Heidari, B.; Khorramirouz, R.; Morse, D. W.; Lerman, A. In Vivo Remodeling of a 3D-Bioprinted Tissue Engineered Heart Valve Scaffold. Bioprinting 2019, 16, e00059. https://doi.org/10.1016/j.bprint.2019.e00059.

[50] Vashistha, R.; Kumar, P.; Dangi, A. K.; Sharma, N.; Chhabra, D.; Shukla, P. Quest for Cardiovascular Interventions: Precise Modeling and 3D Printing of Heart Valves. Journal of Biological Engineering 2019, 13 (1). https://doi.org/10.1186/s13036-018-0132-5.

[51] Piva, H. L.; Leite, V. O.; Tedesco, A. C. 3D Printed Collagen Scaffold for Heart Valve Repair. Annals of 3D Printed Medicine 2024, 16, 100181. https://doi.org/10.1016/j.stlm.2024.100181.

[52] Alonzo, M.; AnilKumar, S.; Roman, B.; Tasnim, N.; Joddar, B. 3D Bioprinting of Cardiac Tissue and Cardiac Stem Cell Therapy. Translational Research 2019, 211, 64–83. https://doi.org/10.1016/j.trsl.2019.04.004.

[53] Barreiro Carpio, M.; Dabaghi, M.; Ungureanu, J.; Kolb, M. R.; Hirota, J. A.; Moran-Mirabal, J. M. 3D Bioprinting Strategies, Challenges, and Opportunities to Model the Lung Tissue Microenvironment and Its Function. Frontiers in Bioengineering and Biotechnology 2021, 9. https://doi.org/10.3389/fbioe.2021.773511.

[54] Jana, S.; Lerman, A. Bioprinting a Cardiac Valve. Biotechnology Advances 2015, 33 (8), 1503–1521. https://doi.org/10.1016/j.biotechadv.2015.07.006.

[55] Tripathi, S.; Mandal, S. S.; Bauri, S.; Maiti, P. 3D Bioprinting and Its Innovative Approach for Biomedical Applications. MedComm 2022, 4 (1). https://doi.org/10.1002/mco2.194.

[56] Tripathi, S.; Verma, S.; Dhingra, K. Microfluidics and Personalized Medicine towards Diagnostic Precision and Treatment Efficacy. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 213-223. https://doi.org/10.60087/jklst.v3.n4.p213.

[57] Sharma, A.; Verma, S.; Dhingra, K. Microneedles-Mediated Transdermal Drug Delivery Techniques in Modern Medicine. J. Knowl. Learn. Sci. Technol. 2024, 4 (1), 20-31. https://doi.org/10.60087/jklst.v4.n1.003.

[58] Boularaoui, S.; Al Hussein, G.; Khan, K. A.; Christoforou, N.; Stefanini, C. An Overview of Extrusion-Based Bioprinting with a Focus on Induced Shear Stress and Its Effect on Cell Viability. Bioprinting 2020, 20, e00093. https://doi.org/10.1016/j.bprint.2020.e00093.

[59] Brunel, L. G.; Hull, S. M.; Heilshorn, S. C. Engineered Assistive Materials for 3D Bioprinting: Support Baths and Sacrificial Inks. Biofabrication 2022, 14 (3). https://doi.org/10.1088/1758-5090/ac6bbe.

[60] Park, J. A.; Lee, Y.; Jung, S. Inkjet-Based Bioprinting for Tissue Engineering. Organoid 2023, 3, e12–e12. https://doi.org/10.51335/organoid.2023.3.e12.

[61] Li, X.; Chen, J.; Liu, B.; Wang, X.; Ren, D.; Xu, T. Inkjet Printing for Biofabrication. 3D Printing and Biofabrication 2018, 283–301. https://doi.org/10.1007/978-3-319-45444-3_26.

[62] Chowdhury, S. R.; Yogeswaran Lokanathan; Xian, L. J.; Fauzi Mh Busra; Hoque, M. E. 3D Printed Bioscaffolds for Developing Tissue-Engineered Constructs. https://doi.org/10.5772/intechopen.92418.

[63] Kumar, P.; Ebbens, S.; Zhao, X. Inkjet Printing of Mammalian Cells – Theory and Applications. Bioprinting 2021, 23, e00157. https://doi.org/10.1016/j.bprint.2021.e00157.

[64] Rider, P.; Kačarević, Ž. P.; Alkildani, S.; Retnasingh, S.; Barbeck, M. Bioprinting of Tissue Engineering Scaffolds. Journal of Tissue Engineering 2018, 9, 204173141880209. https://doi.org/10.1177/2041731418802090.

[65] Ng, W. L.; Lee, J. M.; Yeong, W. Y.; Win Naing, M. Microvalve-Based Bioprinting – Process, Bio-Inks and Applications. Biomaterials Science 2017, 5 (4), 632–647. https://doi.org/10.1039/c6bm00861e.

[66] Keriquel, V.; Oliveira, H.; Rémy, M.; Ziane, S.; Delmond, S.; Rousseau, B.; Rey, S.; Catros, S.; Amédée, J.; Guillemot, F.; Fricain, J.-C. In Situ Printing of Mesenchymal Stromal Cells, by Laser-Assisted Bioprinting, for in Vivo Bone Regeneration Applications. Scientific Reports 2017, 7 (1), 1–10. https://doi.org/10.1038/s41598-017-01914-x.

[67] Ventura, R. D. An Overview of Laser-Assisted Bioprinting (LAB) in Tissue Engineering Applications. Medical Lasers 2021, 10 (2), 76–81. https://doi.org/10.25289/ml.2021.10.2.76.

[68] Jamee, R.; Araf, Y.; Naser, I. B.; Promon, S. K. The Promising Rise of Bioprinting in Revolutionalizing Medical Science: Advances and Possibilities. Regenerative Therapy 2021, 18, 133–145. https://doi.org/10.1016/j.reth.2021.05.006.

[69] Xie, Z.; Gao, M.; Lobo, A. O.; Webster, T. J. 3D Bioprinting in Tissue Engineering for Medical Applications: The Classic and the Hybrid. Polymers 2020, 12 (8), 1717. https://doi.org/10.3390/polym12081717.

[70] Riggs, B. C.; Dias, A. D.; Schiele, N. R.; Cristescu, R.; Huang, Y.; Corr, D. T.; Chrisey, D. B. Matrix-Assisted Pulsed Laser Methods for Biofabrication. MRS Bulletin 2011, 36 (12), 1043–1050. https://doi.org/10.1557/mrs.2011.276.

[71] Gillispie, G.; Prim, P.; Copus, J.; Fisher, J.; Mikos, A. G.; Yoo, J. J.; Atala, A.; Lee, S. J. Assessment Methodologies for Extrusion-Based Bioink Printability. Biofabrication 2020, 12 (2), 022003. https://doi.org/10.1088/1758-5090/ab6f0d.

[72] Olejnik, A.; Semba, J. A.; Kulpa, A.; Dańczak-Pazdrowska, A.; Rybka, J. D.; Gornowicz-Porowska, J. 3D Bioprinting in Skin Related Research: Recent Achievements and Application Perspectives. ACS Synthetic Biology 2021, 11 (1), 26–38. https://doi.org/10.1021/acssynbio.1c00547.

[73] Helland, M. M. Anatomy and Function of the Temporomandibular Joint. The Journal of orthopaedic and sports physical therapy 1980, 1 (3), 145–152. https://doi.org/10.2519/jospt.1980.1.3.145.

[74] Alomar, X.; Medrano, J.; Cabratosa, J.; Clavero, J. A.; Lorente, M.; Serra, I.; Monill, J. M.; Salvador, A. Anatomy of the Temporomandibular Joint. Seminars in ultrasound, CT, and MR 2007, 28 (3), 170–183. https://doi.org/10.1053/j.sult.2007.02.002.

[75] Pascal-André Vendittoli; Riviere, C.; Hirschmann, M. T.; Bini, S. Why Personalized Surgery Is the Future of Hip and Knee Arthroplasty: A Statement from the Personalized Arthroplasty Society. EFORT open reviews 2023, 8 (12), 874–882. https://doi.org/10.1530/eor-22-0096.

[76] Ramos, A. M.; Mesnard, M. The Stock Alloplastic Temporomandibular Joint Implant Can Influence the Behavior of the Opposite Native Joint: A Numerical Study. Journal of Cranio-Maxillofacial Surgery 2015, 43 (8), 1384–1391. https://doi.org/10.1016/j.jcms.2015.06.042.

[77] Huang, H.-L.; Su, K.-C.; Fuh, L.-J.; Chen, M. Y. C.; Wu, J.; Tsai, M.-T.; Hsu, J.-T. Biomechanical Analysis of a Temporomandibular Joint Condylar Prosthesis during Various Clenching Tasks. Journal of Cranio-Maxillofacial Surgery 2015, 43 (7), 1194–1201. https://doi.org/10.1016/j.jcms.2015.04.016.

[78] Ackland, D. C.; Robinson, D.; Redhead, M.; Lee, P. V. S.; Moskaljuk, A.; Dimitroulis, G. A Personalized 3D-Printed Prosthetic Joint Replacement for the Human

Temporomandibular Joint: From Implant Design to Implantation. Journal of the Mechanical Behavior of Biomedical Materials 2017, 69, 404–411. https://doi.org/10.1016/j.jmbbm.2017.01.048.

[79] Wu, Y.; Liu, J.; Kang, L.; Tian, J.; Zhang, X.; Hu, J.; Huang, Y.; Liu, F.; Wang, H.; Wu, Z. An Overview of 3D Printed Metal Implants in Orthopedic Applications: Present and Future Perspectives. Heliyon 2023, 9 (7), e17718–e17718. https://doi.org/10.1016/j.heliyon.2023.e17718.

[80] Jiang, J.; Jiao, Z.; Cheng, B.; Han, J.; Xu, X.; Guo, C. Design, Fabrication and Evaluation of a Novel 3D-Printed Temporomandibular Joint Prosthesis Enhanced with Elastic Layers. International Journal of Bioprinting 2024, 0 (0), 4899. https://doi.org/10.36922/ijb.4899.

[81] Kazuo Tanne; Tanaka, E.; Sakuda, M. Stress Distribution in the Temporomandibular Joint Produced by Orthopedic Chincup Forces Applied in Varying Directions: A Three-Dimensional Analytic Approach with the Finite Element Method. American Journal of Orthodontics and Dentofacial Orthopedics 1996, 110 (5), 502–507. https://doi.org/10.1016/s0889-5406(96)70056-2.

[82] Tanaka, E.; Sasaki, A.; K Tahmina; Yamaguchi, K.; K Tanne. Mechanical Properties of Human Articular Disk and Its Influence on TMJ Loading Studied with Finite Element Method. Journal of Oral Rehabilitation 2001, 28 (3), 273–279. https://doi.org/10.1111/j.1365-2842.2001.tb01677.x.

[83] Capsi-Morales, P.; Piazza, C.; Sjoberg, L.; Catalano, M. G.; Grioli, G.; Bicchi, A.; Hermansson, L. M. Functional Assessment of Current Upper Limb Prostheses: An Integrated Clinical and Technological Perspective. PLOS ONE 2023, 18 (8), e0289978. https://doi.org/10.1371/journal.pone.0289978.

[84] Yildiz, K. A.; Shin, A. Y.; Kaufman, K. R. Interfaces with the Peripheral Nervous System for the Control of a Neuroprosthetic Limb: A Review. Journal of NeuroEngineering and Rehabilitation 2020, 17 (1). https://doi.org/10.1186/s12984-020-00667-5.

[85] Kumar, D. K.; Jelfs, B.; Sui, X.; Arjunan, S. P. Prosthetic Hand Control: A Multidisciplinary Review to Identify Strengths, Shortcomings, and the Future. Biomedical Signal Processing and Control 2019, 53, 101588. https://doi.org/10.1016/j.bspc.2019.101588.

[86] Miller, L. A.; Stubblefield, K. A.; Lipschutz, R. D.; Lock, B. A.; Kuiken, T. A. Improved Myoelectric Prosthesis Control Using Targeted Reinnervation Surgery: A Case Series. IEEE Transactions on Neural Systems and Rehabilitation Engineering 2008, 16 (1), 46–50. https://doi.org/10.1109/tnsre.2007.911817.

[87] Chilmakuri, L.; Mishra, A. K.; Shokeen, D. .; Gupta, P. .; Wadhwa, H. H.; Dhingra, K. .; Verma, S. A Wearable EMG Sensor for Continuous Wrist Neuromuscular Activity for Monitoring. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 148-159. https://doi.org/10.60087/jklst.v3.n4.p148.

[88] Dongre, A. .; Nale, T. . .; Ramavajhala, A.; Mahanta, D. .; Sharma, . O. .; Wadhwa, H. H. .; Dhingra, K. .; Verma, S. . The Evolution of Transdermal Drug Delivery: From Patches to Smart Microneedle-Biosensor Systems. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 160-168. https://doi.org/10.60087/jklst.vol3.n4.p160.

[89] Frost, C. M.; Ursu, D. C.; Flattery, S. M.; Nedic, A.; Hassett, C. A.; Moon, J. D.; Buchanan, P. J.; Brent Gillespie, R.; Kung, T. A.; Kemp, S. W. P.; Cederna, P. S.; Urbanchek, M. G. Regenerative Peripheral Nerve Interfaces for Real-Time, Proportional Control of a Neuroprosthetic Hand. Journal of NeuroEngineering and Rehabilitation 2018, 15 (1). https://doi.org/10.1186/s12984-018-0452-1.

[90] Vu, P. P.; Vaskov, A. K.; Irwin, Z. T.; Henning, P. T.; Lueders, D. R.; Laidlaw, A. T.; Davis, A. J.; Nu, C. S.; Gates, D. H.; Gillespie, R. B.; Kemp, S. W. P.; Kung, T. A.; Chestek, C. A.; Cederna, P. S. A Regenerative Peripheral Nerve Interface Allows Real-Time Control of an Artificial Hand in Upper Limb Amputees. Science Translational Medicine 2020, 12 (533). https://doi.org/10.1126/scitranslmed.aay2857.

[91] Periketi, P.; Kaur, K. .; Naseer Vaid, F. .; Sree M, Y. .; Madhu, M. .; Verma, S. .; Dhingra, K. . Blood Brain Barrier-on-a-Chip Permeation to Model Neurological Diseases Using Microfluidic Biosensors. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 78-93. https://doi.org/10.60087/jklst.v3.n4.p78.

[92] Green, R. A.; Lim, K. S.; Henderson, W. C.; Hassarati, R. T.; Martens, P. J.; Lovell, N. H.; Poole-Warren, L. A. Living Electrodes: Tissue Engineering the Neural Interface. 2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2013. https://doi.org/10.1109/embc.2013.6611158.

[93] Wei, Y.; Li, B.; Domingos, M.; Qian, Z.; Zhu, Y.; Yan, L.; Ren, L.; Wei, G. Fully 3D Printed Flexible, Conformal and Multi-Directional Tactile Sensor with Integrated Biomimetic and Auxetic Structure. Communications Engineering 2023, 2 (1). https://doi.org/10.1038/s44172-023-00131-x.

[94] Mutlu, R.; Singh, D.; Charbel Tawk; Emre Sarıyıldız. A 3D-Printed Soft Haptic Device with Built-in Force Sensing Delivering Bio-Mimicked Feedback. Biomimetics 2023, 8 (1), 127–127. https://doi.org/10.3390/biomimetics8010127.

[95] Moeinnia, H.; Su, H.; Kim, W. S. Novel Grasping Mechanisms of 3D-Printed Prosthetic Hands. Advanced Intelligent Systems 2022, 4 (11), 2200189. https://doi.org/10.1002/aisy.202200189.

[96] Nagarajan, Y. R.; Farukh Farukh; Buis, A.; Karthikeyan Kandan. Single Polymer Composites: An Innovative

Solution for Lower Limb Prosthetic Sockets. Prosthesis 2024, 6 (3), 457–477. https://doi.org/10.3390/prosthesis6030033.

[97] Noshin Tasnim Tuli; Khatun, S.; Adib Bin Rashid. Unlocking the Future of Precision Manufacturing: A Comprehensive Exploration of 3D Printing with Fiber-Reinforced Composites in Aerospace, Automotive, Medical, and Consumer Industries. Heliyon 2024, e27328–e27328. https://doi.org/10.1016/j.heliyon.2024.e27328.

[98] Kazim, I.; Gande, T.; Reyher, E. .; Gyatsho Bhutia, K. .; Dhingra, K.; Verma, S. Advancements in Sequencing technologies:: From Genomic Revolution to Single-Cell Insights in Precision Medicine. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 108-124. https://doi.org/10.60087/jklst.v3.n4.p108.

[99] Griffet, J. Amputation and Prosthesis Fitting in Paediatric Patients. Orthopaedics & Traumatology: Surgery & Research 2016, 102 (1), S161–S175. https://doi.org/10.1016/j.otsr.2015.03.020.

[100] Ngo, T. D.; Kashani, A.; Imbalzano, G.; Nguyen, K. T. Q.; Hui, D. Additive Manufacturing (3D Printing): A Review of Materials, Methods, Applications and Challenges. Composites Part B: Engineering 2018, 143 (1359-8368), 172–196. https://doi.org/10.1016/j.compositesb.2018.02.012.

[101] Owen, M. K.; DesJardins, J. D. Transtibial Prosthetic Socket Strength. Journal of Prosthetics and Orthotics 2020, 32 (2), 93–100. https://doi.org/10.1097/jpo.0000000000000306.

[102] Allum, J.; Gleadall, A.; Silberschmidt, V. V. Fracture of 3D-Printed Polymers: Crucial Role of Filament-Scale Geometric Features. Engineering Fracture Mechanics 2020, 224, 106818. https://doi.org/10.1016/j.engfracmech.2019.106818.

[103] Ramlee, M. H.; Ammarullah, M. I.; Mohd Sukri, N. S.; Faidzul Hassan, N. S.; Baharuddin, M. H.; Abdul Kadir, M. R. Investigation on Three-Dimensional Printed Prosthetics Leg Sockets Coated with Different Reinforcement Materials: Analysis on Mechanical Strength and Microstructural. Scientific Reports 2024, 14 (1), 6842. https://doi.org/10.1038/s41598-024-57454-8.

[104] Dey, A.; Roan Eagle, I. N.; Yodo, N. A Review on Filament Materials for Fused Filament Fabrication. Journal of Manufacturing and Materials Processing 2021, 5 (3), 69. https://doi.org/10.3390/jmmp5030069.

[105] Rodzeń, K.; Harkin-Jones, E.; Wegrzyn, M.; Sharma, P. K.; Zhigunov, A. Improvement of the Layer-Layer Adhesion in FFF 3D Printed PEEK/Carbon Fibre Composites. Composites Part A: Applied Science and Manufacturing 2021, 149, 106532. https://doi.org/10.1016/j.compositesa.2021.106532.

[106] Tripathi, S.; Dash, M.; Chakraborty, R.; Lukman, H. J.; Kumar, P.; Hassan, S.; Mehboob, H.; Singh, H.; Nanda, H. S. Engineering Considerations in the Design of Tissue Specific Bioink for 3D Bioprinting Applications. Biomaterials Science 2024. https://doi.org/10.1039/d4bm01192a.

[107] Augustine, R.; Alhussain, H.; Zahid, A. A.; Raza Ur Rehman, S.; Ahmed, R.; Hasan, A. Crosslinking Strategies to Develop Hydrogels for Biomedical Applications. Gels Horizons: From Science to Smart Materials 2021, 21–57. https://doi.org/10.1007/978-981-15-7138-1_2.

[108] Mancha Sánchez, E.; Gómez-Blanco, J. C.; López Nieto, E.; Casado, J. G.; Macías-García, A.; Díaz Díez, M. A.; Carrasco-Amador, J. P.; Torrejón Martín, D.; Sánchez-Margallo, F. M.; Pagador, J. B. Hydrogels for Bioprinting: A Systematic Review of Hydrogels Synthesis, Bioprinting Parameters, and Bioprinted Structures Behavior. Frontiers in Bioengineering and Biotechnology 2020, 8, 776. https://doi.org/10.3389/fbioe.2020.00776.

[109] Theus, A. S.; Ning, L.; Hwang, B.; Gil, C.; Chen, S.; Wombwell, A.; Mehta, R.; Serpooshan, V. Bioprintability: Physiomechanical and Biological Requirements of Materials for 3D Bioprinting Processes. Polymers 2020, 12 (10), 2262. https://doi.org/10.3390/polym12102262.

[110] Hwang, J.-H.; Byun, M. R.; Kim, A. R.; Kim, K. M.; Cho, H. J.; Lee, Y. H.; Kim, J.; Jeong, M. G.; Hwang, E. S.; Hong, J.-H. Extracellular Matrix Stiffness Regulates Osteogenic Differentiation through MAPK Activation. PLOS ONE 2015, 10 (8), e0135519. https://doi.org/10.1371/journal.pone.0135519.

[111] Walma, D. A. C.; Yamada, K. M. The Extracellular Matrix in Development. Development 2020, 147 (10), dev175596. https://doi.org/10.1242/dev.175596.

[112] Diller, R. B.; Tabor, A. J. The Role of the Extracellular Matrix (ECM) in Wound Healing: A Review. Biomimetics 2022, 7 (3), 87. https://doi.org/10.3390/biomimetics7030087.

[113] Barceló, X.; Eichholz, K. F.; Garcia, O.; Kelly, D. J. Tuning the Degradation Rate of Alginate-Based Bioinks for Bioprinting Functional Cartilage Tissue. Biomedicines 2022, 10 (7), 1621. https://doi.org/10.3390/biomedicines10071621.

[114] Hou, Y.; Cui, X.; Qin, Z.; Su, C.; Zhang, G.; Tang, J.; Li, J.; Zhang, J. Three-Dimensional Bioprinting of Artificial Blood Vessel: Process, Bioinks, and Challenges. International Journal of bioprinting 2023, 9 (4). https://doi.org/10.18063/ijb.740.

[115] Bosmans, C.; Núria Ginés Rodriguez; Karperien, M.; Malda, J.; Liliana Moreira Teixeira; Levato, R.; Jeroen Leijten. Towards Single-Cell Bioprinting: Micropatterning Tools for Organ-On-Chip Development. Trends in Biotechnology 2024. https://doi.org/10.1016/j.tibtech.2023.11.014.

[116] Zhang, P.; Abate, A. R. High-Definition Single-Cell Printing: Cell-By-Cell Fabrication of Biological Structures.

Advanced Materials 2020, 32 (52), 2005346. https://doi.org/10.1002/adma.202005346.

[117] Xu, H.-Q.; Liu, J.-C.; Zhang, Z.-Y.; Xu, C.-X. A Review on Cell Damage, Viability, and Functionality during 3D Bioprinting. Military Medical Research 2022, 9 (1). https://doi.org/10.1186/s40779-022-00429-5.

[118] Li, Y.; Ma, Z.; Ren, Y.; Lu, D.; Li, T.; Li, W.; Wang, J.; Ma, H.; Zhao, J. Tissue Engineering Strategies for Peripheral Nerve Regeneration. Frontiers in Neurology 2021, 12. https://doi.org/10.3389/fneur.2021.768267.

[119] Zhang, H.; Wu, C. 3D Printing of Biomaterials for Vascularized and Innervated Tissue Regeneration. International Journal of Bioprinting 2023, 9 (3). https://doi.org/10.18063/ijb.706.

[120] Ng, W. L.; Qi, J. T. Z.; Yeong, W. Y.; Naing, M. W. Proof-of-Concept: 3D Bioprinting of Pigmented Human Skin Constructs. Biofabrication 2018, 10 (2), 025005. https://doi.org/10.1088/1758-5090/aa9e1e.

[121] Kaufmann, B. K.; Rudolph, M.; Pechtl, M.; Geronimo Wildenburg; Hayden, O.; Hauke Clausen-Schaumann; Sudhop, S. MSLAb – an Open-Source Masked Stereolithography (MSLA) Bioprinter. HardwareX 2024, 19, e00543–e00543. https://doi.org/10.1016/j.ohx.2024.e00543.

[122] Rahimeh Rasouli; Sweeney, C.; Frampton, J. P. Heterogeneous and Composite Bioinks for 3D-Bioprinting of Complex Tissue. Deleted Journal 2024. https://doi.org/10.1007/s44174-024-00171-7.

[123] Zheng, K.; Chai, M.; Luo, B.; Cheng, K.; Wang, Z.; Li, N.; Shi, X. Recent Progress of 3D Printed Vascularized Tissues and Organs. Smart Materials in Medicine 2024, 5 (2). https://doi.org/10.1016/j.smaim.2024.01.001.

[124] Gilbert, F.; O'Connell, C. D.; Mladenovska, T.; Dodds, S. Print Me an Organ? Ethical and Regulatory Issues Emerging from 3D Bioprinting in Medicine. Science and Engineering Ethics 2017, 24 (1), 73–91. https://doi.org/10.1007/s11948-017-9874-6.

[125] Nale, T. .; Dhingra, K.; Verma, S. CRISPR-Cas9 As a Gene Editing Tool Using Cardiac Glycoside Reductase Operon for Digoxin Metabolism. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 224-232. https://doi.org/10.60087/jklst.v3.n4.p224.

[126] Mehta, A.; da Silva Dias, L.; Espinal, M.; Jillellamudi, R.; Mathew, R. .; Chauhan, A.; Dhingra, K.; Verma, S. E-Health Implementation Challenges: A Comprehensive Review of Digital Healthcare in the United States. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 233–246. https://doi.org/10.60087/jklst.v2.n3.p233.

[127] Precision Medicine With Data-driven Approaches: A Framework For Clinical Translation - Simranjit Kaur, Rowan Kim, Nisha Javagal, Joseph Calderon, Senia Rodriguez, Nithin Murugan, Kelsang Gyatsho Bhutia, Karan Dhingra, Saloni Verma - AIJMR Volume 2, Issue 5, September-October 2024. https://www.aijmr.com/research-paper.php?id=1077

[128] Kirillova, A.; Bushev, S.; Abubakirov, A.; Sukikh, G. Bioethical and Legal Issues in 3D Bioprinting. International Journal of Bioprinting 2020, 6 (3). https://doi.org/10.18063/ijb.v6i3.272.

[129] Chandna, R. .; Bansal, A.; Kumar, A.; Hardia, S.; Daramola, O.; Sahu, A.; Verma, K.; Dhingra, K.; Verma, S. Skin Disease Classification Using Two Path Deep Transfer Learning Models. J. Knowl. Learn. Sci. Technol. 2024, 3 (4), 169-187. https://doi.org/10.60087/jklst.v3.n4.p169.

[130] Zuniga, J. M.; Peck, J. L.; Srivastava, R.; Pierce, J. E.; Dudley, D. R.; Than, N. A.; Stergiou, N. Functional Changes through the Usage of 3D-Printed Transitional Prostheses in Children. Disability and Rehabilitation: Assistive Technology 2017, 14 (1), 68–74. https://doi.org/10.1080/17483107.2017.1398279.

[131] De Vivo Nicoloso, L. G.; Pelz, J.; Barrack, H.; Kuester, F. Towards 3D Printing of a Monocoque Transtibial Prosthesis Using a Bio-Inspired Design Workflow. Rapid Prototyping Journal 2021, 27 (11), 67–80. https://doi.org/10.1108/rpj-06-2021-0136.

[132] Górski, F.; Wichniarek, R.; Kuczko, W.; Żukowska, M. Study on Properties of Automatically Designed 3D-Printed Customized Prosthetic Sockets. Materials 2021, 14 (18), 5240. https://doi.org/10.3390/ma14185240.

[133] Cabibihan, J.-J.; Alkhatib, F.; Mudassir, M.; Lambert, L. A.; Al-Kwifi, O. S.; Diab, K.; Mahdi, E. Suitability of the Openly Accessible 3D Printed Prosthetic Hands for War-Wounded Children. Frontiers in Robotics and AI 2021, 7. https://doi.org/10.3389/frobt.2020.594196.

[134] AOPA Statement on 3-D Printing in Prosthetics and Frequent Errant Estimates of the Average Cost of Upper and Lower Limb Custom-Fabricated Prosthetic Devices | AOPA – AMERICAN ORTHOTIC & PROSTHETIC ASSOCIATION. Aopanet.org. https://www.aopanet.org/2015/02/aopa-statement-on-3-d-printing-in-prosthetics-and-frequent-errant-estimates-of-the-average-cost-of-upper-and-lower-limb-custom-fabricated-prosthetic-devices/ (accessed 2024-12-14).

[135] e-Nable. Enabling The Future. Enabling The Future. https://enablingthefuture.org/.

[136] Hoque, M. E.; Riham, S. A. H.; Shuvo, Md. A. A. A Cost-Effective Prosthetic Leg: Design and Development. Hybrid Advances 2023, 2, 100017. https://doi.org/10.1016/j.hybadv.2022.100017.

[137] van der Stelt, M.; Grobusch, Martin. P.; Koroma, Abdul. R.; Papenburg, M.; Kebbie, I.; Slump, Cornelis. H.; Maal, T. J. J.; Brouwers, L. Pioneering Low-Cost 3D-Printed Transtibial Prosthetics to Serve a Rural Population in

Sierra Leone – an Observational Cohort Study. EClinicalMedicine 2021, 35, 100874. https://doi.org/10.1016/j.eclinm.2021.100874.

[138] How Long Does It Take to Get a Prosthetic Leg? | PrimeCare Orthotics & Prosthetics. primecareprosthetics.com. https://primecareprosthetics.com/blog/how-long-does-it-take-to-get-a-prosthetic-leg.

[139] Andrés-Esperanza, J.; Iserte-Vilar, J. L.; Llop-Harillo, I.; Pérez-González, A. Affordable 3D-Printed Tendon Prosthetic Hands: Expectations and Benchmarking Questioned. Engineering Science and Technology, an International Journal 2021. https://doi.org/10.1016/j.jestch.2021.08.010.

[140] Omar, S.; Kasem, A.; Ahmad, A.; Seri Rahayu Ya'akub; Safwan Ahman; Yunus, E. Implementation of Low-Cost 3D-Printed Prosthetic Hand and Tasks-Based Control Analysis. Advances in intelligent systems and computing 2018, 213–223. https://doi.org/10.1007/978-3-030-03302-6_19.

[141] How Long Does It Take to Get Fitted for an Upper Limb Prosthesis? www.armdynamics.com. https://www.armdynamics.com/upper-limb-library/how-long-does-it-take-to-get-fitted-for-an-upper-limb-prosthesis.

[142] Alghothani, Y.; El Zamly, A. Abstract. Plastic and Reconstructive Surgery - Global Open 2016, 4, 131–132. https://doi.org/10.1097/01.gox.0000503056.86814.c5.

[143] Ruthwik Guntupalli, Saloni Verma and Karan Dhingra 2024. Impact of Healthcare Digitization: Systems Approach for Integrating Biosensor Devices and Electronic Health with Artificial Intelligence. American Scientific Research Journal for Engineering, Technology, and Sciences. 98, 1 (Aug. 2024), 246–257, https://asrjetsjournal.org/index.php/American_Scientific_Journal/article/view/10786/2789

[144] N. Ashammakhi, S. Ahadian, C. Xu, H. Montazerian, H. Ko, R. Nasiri, N. Barros, A. Khademhosseini, Bioinks and bioprinting technologies to make heterogeneous and biomimetic tissue constructs, Materials Today Bio, Volume 1, 2019, https://doi.org/10.1016/j.mtbio.2019.100008.