3D printing in tissue engineering: a state of the art review of technologies and biomaterials

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Abstract

Purpose – In the past decade, three-dimensional (3D) printing has gained attention in areas such as medicine, engineering, manufacturing art and most recently in education. In biomedical, the development of a wide range of biomaterials has catalysed the considerable role of 3D printing (3DP), where it functions as synthetic frameworks in the form of scaffolds, constructs or matrices. The purpose of this paper is to present the state-of-the-art literature coverage of 3DP applications in tissue engineering (such as customized scaffoldings and organs, and regenerative medicine).

Design/methodology/approach – This review focusses on various 3DP techniques and biomaterials for tissue engineering (TE) applications. The literature reviewed in the manuscript has been collected from various journal search engines including Google Scholar, Research Gate, Academia, PubMed, Scopus, EMBASE, Cochrane Library and Web of Science. The keywords that have been selected for the searches were 3 D printing, tissue engineering, scaffoldings, organs, regenerative medicine, biomaterials, standards, applications and future directions. Further, the sub-classifications of the keyword, wherever possible, have been used as sectioned/sub-sectioned in the manuscript.

Findings – 3DP techniques have many applications in biomedical and TE (B-TE), as covered in the literature. Customized structures for B-TE applications are easy and cost-effective to manufacture through 3DP, whereas on many occasions, conventional technologies generally become incompatible. For this, this new class of manufacturing must be explored to further capabilities for many potential applications.

Originality/value – This review paper presents a comprehensive study of the various types of 3DP technologies in the light of their possible B-TE application as well as provides a future roadmap.

Keywords 3D printing, Biomaterial, Biomedical engineering, Regenerative medicine, Organs, Tissue, Scaffoldings, Standards

Paper type Literature review

1. Introduction to tissue engineering

Bone defects, inflammatory diseases, injuries and accidents damage tissues and emanate the loss in the functionality of organs and joints in the human body (O'brien, 2011; Zhang *et al.*, 2016). To restore the functionality of damaged tissues, organs and joints, invasive surgery is often required by transplantation, repair and replacement of implants and scaffolds (Derakhshanfar *et al.*, 2018; Turnbull *et al.*, 2018). Transplantation/replacement of damaged/dysfunctional organs and joints is a major challenge in medical surgeries. Scientists and researchers developed tissue engineering (TE) techniques, the promising and potential solution to restore the functionality

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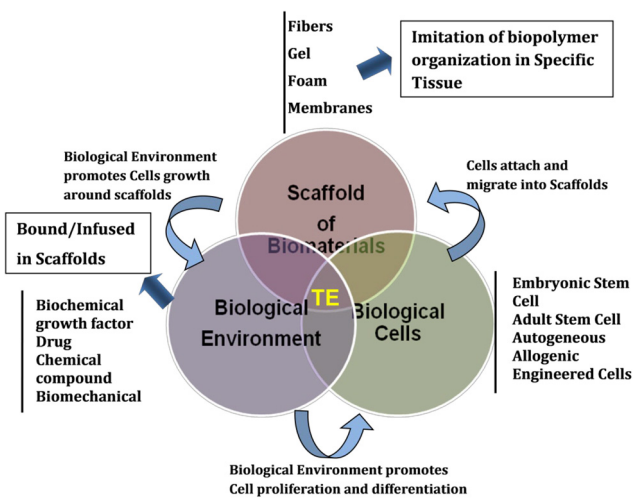
or regenerate the damaged tissues and organs (Han *et al.*, 2020). TE is an interdisciplinary area where three-dimensional (3D) tissues were synthesized by combining scaffolds of bioactive materials with human cells, (Mabrouk *et al.*, 2020), to regenerate the tissue or organ as can be described in Figure 1 (Leberfinger *et al.*, 2019). Biomedical and TE (B-TE) eliminates the risks of immunological consequences such as hyperacute, allergic reaction and infections (Saxena, 2010; Choudhury *et al.*, 2018). From the past decades, disposed donated human organs such as kidney, lung, heart and liver, have been used to extract the decellularized extracellular matrix (dECM) for potential application in B-TE for artificial tissue or organ, drug screening, disease modelling and regenerative medicine (Leberfinger *et al.*, 2018).

In B-TE, the artificial tissue or organs are made up of scaffolds possessed specific requirements:

- geometrical shape of the damaged tissue or organ;
- 3D porous structure with controlled architecture (tunable pore size $\sim$ 100 to 600 μm);
- degradation properties to enable cell migration and growth; and
- appropriate mechanical properties to prevent the deformation and maintain integrity of structure (Garreta *et al.*, 2017; Zhang *et al.*, 2018; Saxena, 2010; Lanza *et al.*, 2020 and Choudhury *et al.*, 2018).

Basically in B-TE, controlled architecture and mechanically tuned scaffolds made up of bioactive material integrated with biological cells and transformed into the intended artificial organ or tissue (Willerth and Sakiyama-Elbert, 2019). The scaffold provides mechanical integrity for the substitution tissue until the cells produce a sufficient extracellular lattice. During the bone regeneration, the cells grow, proliferate, and differentiate and form new tissues which restores the functionality of damaged organs (Zhang *et al.*, 2017). Initially, the TE technique was adopted for the development of tissue-based skin grafting as described in the Sanskrit texts of India (25 references). The first synthetic skin was developed in 1962 (Kirsner *et al.*, 1993; Berthiaume *et al.*, 2011; Herman, 2002). Later on, the skin products developed by TE technique were reported in the late 1970s and early 1980s. During the 1990s, several of these and other tissue-engineered skin and subsequently cartilage products were successfully commercialized. These early successes fueled much enthusiasm, and many research laboratories embarked on applying tissue engineering to nearly every tissue in the body. Later on, TE has become the targets of various organ developments such as cornea, liver, pancreas, cartilage, heart, kidney, neurons, spinal cord and hard TE application (Berthiaume *et al.*, 2011; Turnbull *et al.*, 2018). Significant research in the field of B-TE has been carried and number of methodologies such as solvent casting/particulate leaching, gas foaming, emulsification, freeze-drying, phase separation, and electrospinning were developed towards creating novel alternatives to traditional bone grafts (Turnbull *et al.*, 2018; Yoshimoto *et al.*, 2003; Ranganathan *et al.*, 2019; Gay *et al.*, 2018). These conventional methodologies did not succeed because complex shapes and microarchitectures of scaffolds were difficult to control. Nonetheless, the application of 3DP in B-TE integrates the computer-aided design (CAD) modeling for controlling the architectures of scaffolds and precise printing the scaffold using additive manufacturing (AM) technique (Turnbull *et al.*, 2018). Table 1 presents the conventional techniques for developing B-TE applications and their limitations.

Figure 1 B-TE applications



The three-dimensional printing (3DP) is being extensively used since 2000 and was initially applied to make custom prosthetics and dental implants (Gross *et al.*, 2014; Jammalamadaka and Tappa, 2018). Here, the major aim of this technology is to apply engineering principles to solve problems in the medical field. Particularly in biomedical engineering, it has been involved in several broad areas such as implantable medical devices, diagnostic systems, biomechanics, bio-fluidics, prosthetic organs and TE (Aimar *et al.*, 2019). The application of 3DP in the medical industry has progressed considerably in recent years as the manufacturing of dozens of medical devices adopts 3DP, following standards set by the Food and Drug Administration (FDA). An ample volume of literature reports the use of 3DP to fabricate exoskeletons, bones, ears, windpipes, eyeglasses, a jaw bone, cell cultures, blood vessels, stem cells, tissues vascular networks, organs, drug delivery devices and novel dosage forms (Banks, 2013; Hoy, 2013). The biomedical implications of 3DP are classified into quite a few large categories, such as organ and tissue fabrication, creating anatomical models, implants and prosthetics and pharmaceutical research relating dosage forms and drug discovery delivery (Klein *et al.*, 2013).

As of now, countless applications of 3DP are available in the area of B-TE, a multidisciplinary scientific field that has rapidly emerged and combines engineering principles with life sciences to replace damaged tissues or restore malfunctioning organs, as listed in Table 2.

This was only possible due to the availability of a broad range of biomaterials as well as continuous efforts to bring new and novel materials into existence. Biomaterials support in structural, and functional or dysfunctional tissue repair in both cellular and cell-based therapies (Choi and Cha, 2019). Further, the attempts made on the design of biomaterials focus on achieving spatial integrity, suitable structural and mechanical properties are worth to acknowledge for the

Table 1 Potential techniques to fabricate scaffold for TE applications

Method	Limitations
Solvent casting/ particulate leaching	Organic solvents obstruct the cell growth and tissue in the scaffolds Difficult to control pore size, shape and interconnectivity Limited thickness of structures and mechanical properties achievable
Gas foaming	Due to excessive pressures and temperature diminished the architecture and properties of a scaffold Non-uniform structure restricts the interaction of cells with the scaffold
Emulsification	Organic solvents obstruct the cell growth and tissue in the scaffolds
Freeze-drying	Very fine pores size and irregular structure prohibited the integration of the cell with scaffold Very long synthesis time required
Phase separation	Organic solvents obstruct the cell growth and tissue in the scaffolds Difficult to control pore size, shape, and interconnectivity
Electrospinning	Organic solvents obstruct the cell growth and tissue in the scaffolds Poor mechanical properties Unorganized architecture Difficult to control pore size, shape and interconnectivity

successful career of 3DP. Currently, biomaterials are being used as implants in bone plates, joint replacements, sutures, vascular grafts, heart valves, ligaments, intraocular lenses, dental implants and as other medical devices such as pacemakers and biosensors (Ramakrishna *et al.*, 2001; Vert, 2005). In TE, scaffolds are critical providing structure for cell infiltration and proliferation, space for extracellular matrix generation and remodeling, biochemical cues to direct cell behavior (Qu *et al.*, 2019) and physical connections for injured tissue (Chia and Wu, 2015). The design and fabrication of 3D printed scaffolds in skeletal TE includes a range of biomaterials; protein-based (collagen, fibrin, gelatin and synthetic polypeptides), carbohydrate-based (agarose, alginate, hyaluronate, chitosan, dextran), synthetic (polylactic acid, polyglycolic acid, polylactide, dacron, Teflon, polyester urethane) and composite materials of hydrogels and inorganic compounds (Bertana *et al.*, 2020; Singh *et al.*, 2017). The prime aim of this review paper is providing a general overview of the current state of 3DP, describing the broad range of available printing technologies by discussing their benefits and limitations, biomaterials, their emerging applications in the light of available literature. After the current introduction, Sections 2, 3 and 5 are focussed to briefly discuss the existing 3DP technologies, an extensive picture of biomaterials for TE and, finally, the summary and future roadmaps, respectively.

2. Three-dimensional printing technologies and materials

2.1. Three-dimensional printing technologies

Numerous advancements in the 3DP technology have been carried out according to the suitability of material processing and their applications. The different 3DP technologies can be classified based on workhorse states such as liquid, powder and solid. The materials used for printing usually vary based on the specific technology implemented in 3DP. However, the inter-linking of a computer with 3 D modeling software is common in all 3DP techniques. The processes involved (Guo *et al.*, 2019):

- CAD sketch is created and Data from CAD file is interpreted by the 3DP device.
- The structure is built layer-upon-layer using printing materials which are either plastic, a sheet of paper, powder filaments or liquid.

Table 3 shows the different types of 3DP processes, their principles, benefits and limitations.

Figure 2 shows the most widely used and potential 3DP technologies (such as photo-polymerization, material jetting, binder jetting, material extrusion, powder bed fusion) (Lee *et al.*, 2017). Photo-polymerization uses ultra-violet (UV) light is used to harden each layer of liquid photo-curable natural and synthetic resins [Figure 2(a)]. The most important technique used in photo-polymerization is SLA. Juskova *et al.* (2018) reported that with the advancement in technologies, cost-effective light sources, advanced mirror-lens systems and SLA techniques showed considerable improvement based on speed and resolution. Material jetting uses a print head analogous to inkjet printers for the deposition of similarly shaped layers of photopolymer resin. The UV light [refer to Figure 2(b)] is used to treat the support materials that are surrounded by each layer. This device process comprises robust resin objects which helps in the details of complex acrylate with high resolution and accuracy while eliminating the need for pillar scanners or complex lasers (Carve and Wlodkowic, 2018). The viscosity of the material is often reduced due to heating of the printhead and nozzle plate, and it seems to be the major limitation in the jetting process. Figure 2(c) shows the binder jetting machine and used to spread a layer of powder onto a build platform. In binder jetting machine, liquid binding agents are applied onto the build platform using inkjet print heads and makes the particles bond together (Bai and Williams, 2018). This technique can be applied to any powder-form materials. The process is rapid, simple and economical, as it only involves powder particles sticking together to stack and build the 3 D structure. Some binder jetting machines create and print full-color parts by using specific colored binding agents (inks). In this technique, the powder particles are attached resulting in the development of fragile parts with poor mechanical properties. Hence, binder jetting parts are usually used in a preliminary stage for building parts and further processes such as sintering, casting or infiltration are applied to improve their mechanical properties (Bai *et al.*, 2019).

Table 2 Highlights of 3DP applications in B-TE and key outcomes

Application	Outcome(s)	Ref.
TE	The cells proliferated into the structure, creating close contact with hydroxyapatite granules	Nallamuthu *et al.* (2006)
	It was outlined that the utilization of 3DP technologies can make extracellular matrix-like scaffolds with a high level of complexity, fine details at a micrometer level	Do *et al.* (2015)
	According to the authors, apart from the existence of a vast number of methods for 3DP of scaffolds, the 3D fabrication of fully formed and functional organs on the laboratory bench represents the next great challenge in tissue engineering	Obregon *et al.* (2015)
	The construct bio-functionality needed to support appendage found on typical skin, for example, hair follicles, receptors, sebaceous organs and sweat organs	Singh *et al.* (2016)
	It has been found the oxidized dextran/gelatin/carbon nanotubes based hydrogel is highly suitable for superior dimensional control and bioactivity	Jiang *et al.* (2020)
Organs	To establish consistently high-quality products through bioprinter, the organ bio-fabrication line must be automatically controlled and every bio-assembly step must be bio-checked continuously by refined sensors without damage	Mironov *et al.* (2011a)
	The rapidly evolving micro tissue-based bio-mimetic approach used principles of developmental biology regarding directed tissue self-assembly	Mironov *et al.* (2011b)
	This review highlighted those current impediments in-cell technology, bio-manufacturing innovation and advances for in vivo reconciliation are fundamental for growing flawlessly computerized innovation from immature microorganism separation to transplantation	Ozbolat *et al.* (2013)
Regenerative medicine	Though 3 D printers are becoming more cost-friendly, the operational costs, materials, the need for skilled operators and observance of strict health and safety protocols are required	Yoshikawa *et al.* (2015)
	The important issue with 3DP of bones or organs is to establish their optimal cell densities/ratios and to investigate the extent to which forced cell organization is required for getting the fully functional bone *in vivo*	Fedorovich *et al.* (2011)
	This review admitted that pushing the current limits of 3DP technologies with biological materials can better mimic the manufacturing capabilities of living organisms, the digital fabrication of advanced materials and new functionalities	Studart (2016)
	It was summarized by the authors that different types of models are as yet being produced to make progressed preclinical cancer models including straightforward 3 D malignancy cell encapsulation, co-culture systems and consolidation of hydrogel materials with 3DP strategies	Park and Gerecht (2015)
	The results represented the potential application of piezoelectric barium titanate in developing for the 3 D printed regenerative scaffolds	Polley *et al.* (2019)
Miscellaneous	Considering these discoveries, a solar-powered suitcase 3DP framework contained sun powered boards, 12 V battery with charge controller and AC inverter, and secondary solar charge controller and inverter was intended for transport to and use in off-grid groups	Wong (2015)
	The surgeon could distinguish chance structures, survey the perfect resection lines and decide the lingering shape after a reconstructive methodology, for example, LV re-displaying, penetrating tumor resection. Using a 3 D-print of the LV-aneurysm, reshaping of the left ventricle guaranteeing adequate LV volume was effectively expert	Pietrabissa *et al.* (2016)
	3DP is useful in understanding complex anatomy for instructive purposes at all levels, and the cost/working time to create great quality items is as yet considerable	Ripley *et al.* (2016)
	Pre-transcatheter aortic valve replacement 3DP based on cardiac CT provided a novel patient-specific method to determine the physical interplay of the aortic root and implanted valves	Zein *et al.* (2013)

The most important material extrusion, refer Figure 2(d), methods are FDM and direct ink writing (DIW). These methods are mainly used to fabricate 3D-scaffolds and devices for applications in TE (Turner *et al*, 2014). The mechanical properties of the designed parts formed by the material extrusion process are similar to conventionally molded products in the SLS technique (Vermeulen *et al.*, 2013). Another most widely used and potential technique for the TE application is the 3DP technique, which is based on the hardening or sintering of powders. Techniques such as particle binding (PB) and selective laser sintering (SLS) are common examples of powder bed fusion techniques. These techniques are used to develop industrial prototyping suitable to print polymers, ceramics, metals and combinations of the above materials. One of the powder-based 3 D print techniques is SLS [Figure 2(e)]. Different forms of the powder such as metal or ceramic and thermoplastic polymer are sintered or hardened using a CO_2 laser (Fina *et al.*, 2018; Teo *et al.*, 2011; Gmeiner *et al.*, 2015). Sheet lamination (Kruth *et al.*, 2005) is one of the 3DP techniques, and it comprises ultrasonic AM (UAM) and laminated object manufacturing [LOM, refer Figure 2(f)]. The UAM process uses ribbons or sheets of metal as a material and binds them together by ultrasonic welding. In this process, additional computer-controlled cutting machining is required for the removal of unbound metal during welding. Metals that can be used in the UAM process include aluminum, stainless steel, copper and titanium. The LOM approach is similar to UAM, but the paper is used as a material for building layer-upon-layer and adhesives are used for binding process rather than welding process. Laminated objects are regularly used for visual and aesthetic models and are not appropriate for structural use (Luo *et al.*, 2018). The DED [refer Figure 2(g)] is a process that softens powder or metal wire to create a layer-upon-layer object by using high energy power sources such as a plasma welding torch, electron beam or a laser. Compared to other

Table 3 Principles, benefits and limitations of commercial3DP processes

Process: Principle	Benefits	Limitations	Ref.
SLS and SLA:polymer solidifies at the focal point and un-uncovered polymer stays fluid	Compatible with most photopolymers	Suitable for photopolymers, only	Lee *et al.* (2017), Tumbleston *et al.* (2015), Barry *et al.* (2008)
Inkjet and binder jet printing: photopolymer is sprayed from a print head. A support structure is printed at the same time. The 3d-shape is built up from successive layers	Quick and ultra-high throughput, High accuracy, Cell compatibility	Restricted z-resolution	Wu *et al.* (1999), Salaoru *et al.* (2017), Teo *et al.* (2011)
Powder bed printing: thin layer of powder spread on to fabrication stage and subsequently print head specifically spray liquid binding agents on to the thin layer of powder particles. The platform is then lowered and the process repeated	Relatively fast and cheap, No support structures required	Excess powder must be removed during post-processing	Yoshikawa *et al.* (2015)
FDM/FFF: filament is melted as it passes through the heated print nozzle and is then deposited layer-by-layer onto the workpiece	High accuracy, Simple to use, Simple to include both medication and biomolecules	Post-handling might be required	Turner *et al.* (2014), Chia and Wu (2015), Vermeulen *et al.* (2013)
SLS, LBM, DMLS and EBM: powder is sinters layer-by-layer using a laser-based warmth source	Mechanical quality faster and higher determination than other powder techniques	Technology is slow and expensive	Peltola *et al.* (2008), Shirazi *et al.* (2015); Yap *et al.*, 2015; Deckers *et al.*, 2012
LOM: object is build up from layers (sheets) of material bonded to the previous layer by adhesive backing or sprayed adhesive. The sheets of material are advanced on to the build platform and outline of layer cut with laser or blade	Cheap feedstock	Large amounts of waste	Kruth *et al.*, 2005
LENS: metal powder or wire is melted in a high-power laser beam and deposited as the molten build material. The process does not have to take place on a plat powder bed	The metal powder fed in to print head can be continuously altered during the build	Parts may require surface finishing	Li *et al*., 2005
MEW: creation of little too vast volume platforms with particular plans, shapes and thicknesses	The soften procedure efficiency is higher	Fiber materials include high-temperature setup	Brown *et al.*, 2014; Dalton *et al.*, 2013; Jang *et al.*, 2018

Notes: SLS, SLA, MEW, LENS, LOM, FDM, FFF, LBM, DMLS and EBM refer to selective laser sintering, stereo-lithography, melt electro-spinning writing, laser engineered net shaping, laminated object manufacturing, fused deposition modelling, fused filament fabrication, laser beam melting, direct metal laser sintering and electron beam melting, respectively

methods, DED can easily modify the product materials and thus result in the designing of graded functional materials. Conducting the process in a high-vacuum environment prevents contamination. This technique creates large objects rapidly (Shishkovsky *et al.*, 2018).

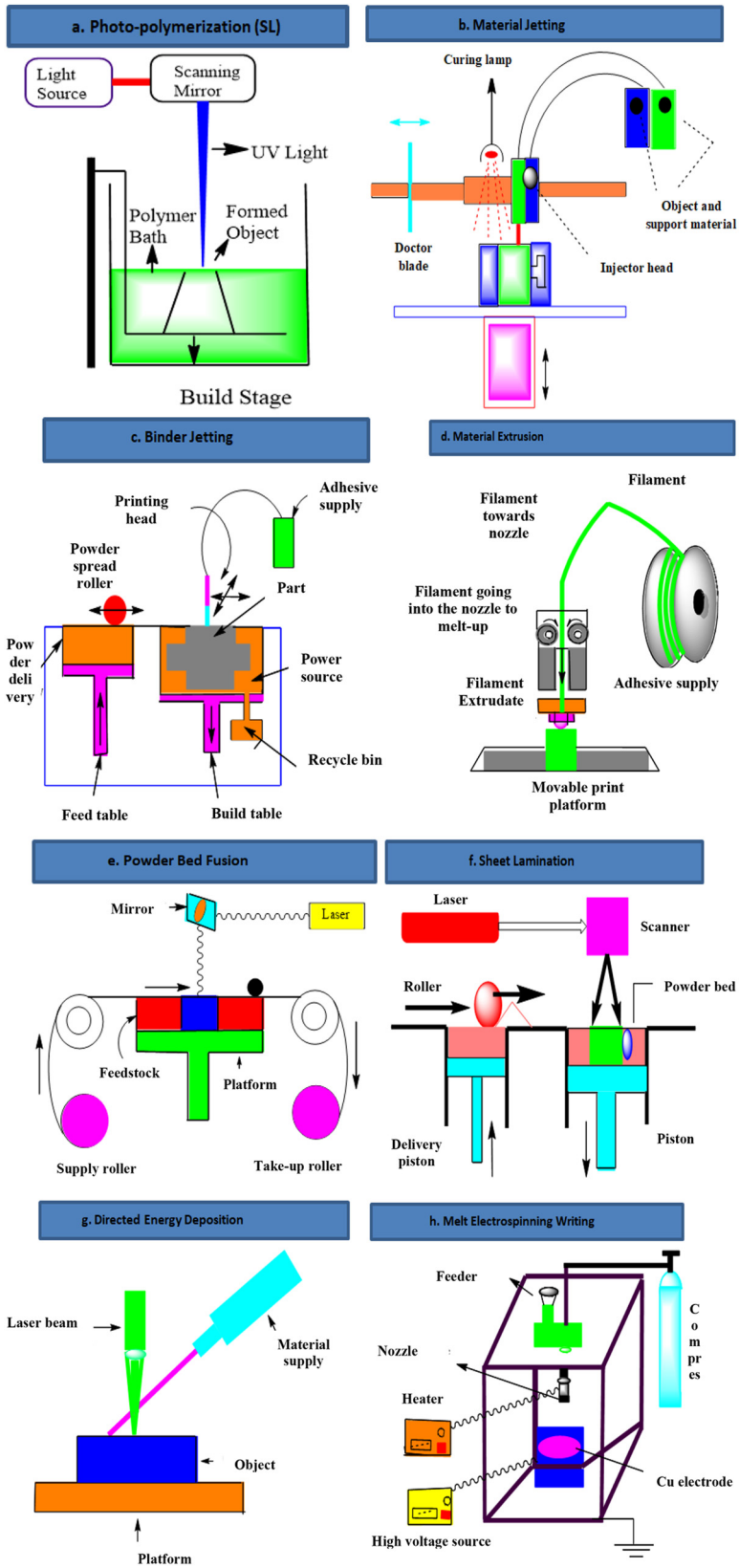
Finally, Figure 2(h) shows melt electrospinning writing (MEW) process which is a fibre-based manufacturing technique and is implemented to design and fabricate scaffolds appropriate in various areas of TE (Robinson *et al.*, 2019; Farrugia *et al.*, 2013; Wei and Dong, 2013; Ristovski *et al.*, 2015; Zhou *et al.*, 2006). The MEW drafts filaments in well-defined dimensions like the cell in 3 D by incorporating AM principles (Brown *et al.*, 2012). Researchers (Góra *et al.*, 2011) have described different methods of MEW setups. Biodegradable polymers such as like: poly-lactic acid (PLA), polycaprolactone (PCL), poly(lactic-co-glycolic acid) (PLGA) and others can be handled through MEW. The structure of melt-extruded scaffolds depends upon the filament diameter (Dalton *et al.*, 2007; Liu *et al.*, 2018). In this technique, there is increasing attention on different approaches like controlled electric fields (Reneker and Chun, 1996), pre-structured substrates and short spinneret/collector distances for the exact deposition of electrospun fibers (Hellmann *et al.*, 2009). In the above-mentioned approaches, low conductivity fluids and high viscosity fluids are highly stable in standard electrospinning conditions (Sun *et al.*, 2006; Jayasingh, 2013; Mammadov *et al.*, 2013; Wei *et al.*, 2018; Holzapfel *et al.*, 2014; Karchin *et al.*, 2011).

Nowadays, numerous sophisticated 3DP setups, also known as "Bioprinters or Bioplotters", are available in the market for direct utilization of the DNA, human cells, proteins, skin materials, etc., for the printing of the organs and tissues. The most acknowledged advantage of bioprinting in medical science is the convenience by which the patients' bodies accept the synthetically developed anatomy. Although, this form of printing has many successful applications, yet, the concerns of causing damage or cell death, due to process stimuli, cannot be ignored. For instance, due to the thermal heat and mechanical stresses applied to the cells while printing, it is possible that the cells may be damaged or their phenotype may be altered (Tirella *et al.*, 2011). Therefore, generally, researchers evaluate the bio-materials to evaluate the optimal condition (Cui and Boland, 2008). It has been often demanded by the surgeons that a handy printer with digital control would be of great benefit in tissue repairing. In this way, bioprinting will be able to precisely deliver the cells, growth/repair catalysts and biomaterials to repair the lesion with various complexities.

2.2 Biomaterials for biomedical and tissue engineering

The advent of 3DP techniques has changed the trends and practices in the use of biomaterials in biomedical engineering.

Figure 2 Schematic description of different 3DP processes



Owing to the capabilities of printing technologies such as the ability to build custom-made 3 D structures, these systems have also raised special interests in the regenerative medicine community. Moreover, these technologies provide flexibility to vary parameters including architecture, pore size, topography and geometry, wettability and various mechanical properties. Biomaterials support in structural, and functional or dysfunctional tissue repair in both cellular and cell-based therapies. The various factors playing a part in interactions between biomaterials and tissues are shown in Figure 3. Biocompatible materials such as metals (Zhai *et al.*, 2015; Tan *et al.*, 2015), ceramics and polymers (Zocca *et al.*, 2015; Özkol *et al.*, 2012) are extensively used in surgical implantation procedures. Table 4 summarizes common biomaterials, and Table 5 shows some recent references for 3D printed biomaterials and their applications in customized scaffoldings and organs, and regenerative medicine.

2.2.1 Bio-ceramics

Bio-ceramics have contributed to better advancements in medicine, especially in orthopedic tissue replacements. Ceramics such as alumina, calcium phosphate, bioglass and zirconia are also used (Gul *et al.*, 2020). In a study (Tarafder *et al.*, 2013), where microwave sintering of pure tri-calcium phosphate (TCP) and SrO-MgO-doped TCP scaffolds (made with 3DP) was carried out, there was greater interconnection within the designed macro-pores. As compared to pure TCPd osteogenesis and vasculogenesis was induced faster due to the dopants SrO and MgO. Z-Corporation system was used for the printing of $Ca_3(PO_4)_2$ and TCP powder in the presence of phosphoric acid mixture to form a matrix of $CaHPO_4{\cdot}H_2O$, DCPD, brushite, and unreacted TCP. The printed samples showed compressive strengths in the range between 0.9 and8.7 MPa and were successfully improved to 22 MPa by additional hardening (Gbureck *et al.*, 2007). A twin-screw extruder was used by Tuan *et al.*, 2015 to produce a composite filament consisting of 5 Wt.% hydroxyapatite (HAp or HA) and 15 Wt.% zircon oxide (ZrO_2) in PA for FDM applications.

Due to their bioactivity and high levels of stiffness, ceramics are used in biomedical applications. Ceramics also provides an osteoinductive and natural surface for the development of bone tissues. Currently, 3DP methods for printing ceramic biomaterials are limited (Choi *et al.*, 2011; Park *et al.*, 2012; Seliktar *et al.*, 2013). This is because of the limitations in producing liquid-based ceramic materials, and because the melting temperatures of ceramics exceed the range of FDM printers. Ceramic powders are unresponsive to light, and hence they cannot be printed using the SLA technique. In addition to this, highly dense and porous structures are not achieved through SLS (Travitzky *et al.*, 2004). To print ceramic from suspension and in powder forms, inkjet and PB printing are the two methods usually used. Along with inkjet and PB printing methods, FDM and SLA methods are integrated while printing ceramics (Griffith and Halloran, 1996; Griffin *et al.*, 1996; Greco *et al.*, 2011).

However, the clinical applications of bioceramics in TE are limited. Bio-ceramics are brittle and difficult to shape for implantation. HA is the main component of bone, and it can be ideally adapted as bone graft replacement, it is difficult to control its degradation rate (Aarthy *et al.*, 2019). Scaffolds produced from mixtures of TCP or TTCP have comparable cell growth and proliferation as the scaffolds (Detsch *et al.*, 2011; Gao *et al.*, 2014).

2.2.2 Synthetic bio-polymers

Polymeric materials are widely used by medical and research communities as they can be bio-degradable and easy to process. Polymer materials can be categorized into natural and synthetic polymers (Hench, 1996; Kim *et al.*, 2000). While designing a polymeric scaffold, the biological and engineering aspects must be considered based on its intended applications. Poly-(α-hydroxy ester) polymers such as PLA, PGA and PLGA have wide applications in tissue engineering. Poly-capro-lactone (PCL) has also been extensively used in tissue engineering a

Figure 3 Biomaterials–tissue local and systemic interactions

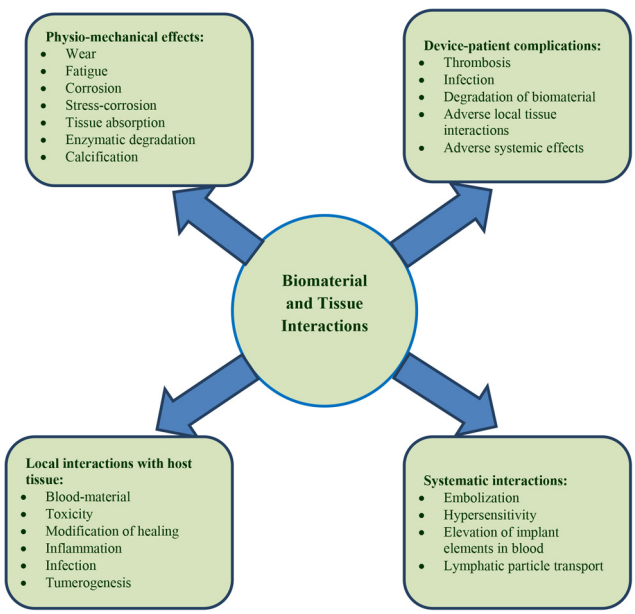


Table 4 Biomaterials for 3DP processes

Category	Materials
Bio compatible polymeric materials	PCL, polypropylene-tricalcium phosphate (PP-TCP), PCL-hydroxyapatite (HA), Poly-ether-ether-ketone (PEEK)-HA, Tetra-calcium phosphate (TTCP), Tri-calcium phosphate (TCP), Poly(methyl methacrylate) (PMMA)
Metallic materials	PLA in Carbon Steel, Tool Steel, Stainless steel, Aluminium, Copper, Titanium, Bronze, Nickel Alumides
Polymers and polymeric composites	Acrylonitrile-butadiene-styrene (ABS), Nylon (Polyamide), Polycarbonate, Poly-propylene (PP), Epoxies, Glass-filled polyamide, Windform, Polystyrene, Polyester, Polyphenylesulfone
Polysaccharide	Agarose, alginate, K-carrageenan, chitosan, dextran, gellan gum, methylcellulose
Protein	Collagen, elastin, fibrin, gelatin, silk fibroin, Matrigel
Others	Sand, Ceramics, Elastomers, Tungsten, Wax, Starch, Plaster

scaffold in addition to the above. The combination of PCL with other poly (α-hydroxy esters) such as poly-(L-lactic acid-ε-capro-lactone) (PLLACL) or poly (D, L-lacticacid-co-ε-capro-lactone) (PDLLACL) has been widely used to generate copolymers with specific engineered properties (Germain *et al.*, 2018; Baroli, 2007). PCL is also used in fabricating 3D porous scaffolds in the SLS printing method (Figure 4; Sudarmadji *et al.*, 2011). Correlations between compressive stiffness and scaffold porosity were compiled and formulated mathematically. Further, the toxicity of fabricated PCL scaffolds was evaluated using cytotoxicity assays (Duan *et al.*, 2010).The compressive stiffness, yield strengths and porosities of scaffolds are in the range of 2.74–55.95 MPa, 0.17–5.03 MPa and 40–84%, respectively. Elomaa *et al.* have designed a porous scaffold made of photo-cross-linkable PLC-based resin using a solvent-free SLA technique (Elomaa *et al.*, 2011; Kocher *et al.*, 2001; Yeong *et al.*, 2010). In another work involving PGLA and PLLA, the biodegradable polymer powder was mixed in the proportions of 75% PLGA and 25% PLLA using chloroform as a natural binder to design a liver construct (Griffith *et al.*, 1997). In 2013, another construct was produced to create a vein and artery network within the host, similar to inlet and outlet, Rachards *et al.*, 3D printed PLLA/PLGA scaffolds have also been fabricated to design organogenesis of liver tissue *in vitro* (Bose *et al.*, 2013). Using biomaterials such as PCL and PEG, the authors have printed 3D cell-containing constructs by applying the hybrid structure fabrication technique (Pati *et al.*, 2013).

At present, most of the procedures involve the use of water-insoluble photoinitiators which are not biocompatible. In such processes, fabrication involves UV light, which can damage cellular DNA (Lin *et al.*, 2013; Dhariwala *et al.*, 2004; Li *et al.*, 2009). FDM is the most common technique for producing porous scaffolds and other tissue structures with different biomaterials. Researchers have prepared porous PCL meshes with FDM and embedded HA, methylated collagen and terpolymer inside the matrix through polyelectrolyte complex coacervation process (Lin *et al.*, 2013). In another study, the PCL scaffolds with an alternate porosity showed stress-strain behavior typical of porous solids, Chen *et al.*, 2011, and also used inside a pig for studying the restoration rate (Zhu *et al.*, 2002). In another work, the PCL-TCP meshes incorporated with 15 Wt.% GS (PT15) competently eliminated bacteria within 2 h and demonstrated low cytotoxicity (Teo *et al.*, 2011).

The proper selection of biomaterials can enable to produce of tough hydrogels as developed by Hong *et al.* (2015). The ECM adsorption was significantly greater on the substrates with the most PDA covering than on the PCL without coating. ABS and PLA large-pore scaffolds were seeded with primary articular chondrocytes and nucleus pulposus cells for three weeks and investigated for cell in-growth, viability and tissue generation. Both cell types proliferated well on both scaffolds, with high viability and secreted sufficient proteoglycan and collagen II (Hochleitner *et al.*, 2015). 3DP innovation has been accounted for the treatment of update lumbar discectomy (Rosenzweig *et al.*, 2015). In the past decade, researchers in TE and biomaterials have involved in 3DP approaches for the fabrication of scaffolds with superior plan unpredictability and reproducibility (Frydrych and Chen, 2013; Hochleitner *et al.*, 2015).

2.2.3 Bio-mimic polymers

Biological materials or biopolymers and their composites are used as biomaterials to fabricate scaffolds. Biological materials such as alginate-based substrates, collagen, chitosan and various proteoglycans are used to fabricate scaffolds and are applied in TE. For instance, some researchers have tried to incorporate ceramics into natural polymer scaffolds or mixing synthetic and natural polymers to improve their biological capacity. In the case of composite scaffolds, at least one of the phases is synthetic and hence there are several problems associated with it, such as biocompatibility, biodegradability or both. Gelatin is the major component of hydrolyzed collagen. It is naturally available in the ECM, and cells can be suspended in the gel at low temperatures (Richards *et al.*, 2013).

Starch-cellulose and starch-cellulose acetate scaffolds were fabricated using SLS, and evaluations indicate that scaffold properties were influenced by polymer particle size, laser scan speed and laser power (Salmoria *et al.*, 2009). The preparation of samples with small particle size showed suitable mechanical properties and level of porosity after the fabrication of scaffolds is optimal and could be potentially applicable in areas of drug delivery and TE. In another study, multi-layered PCL (core)-alginate-PM (shell) scaffolds were generated by combining different methods such as bio-plotting technique, simple coating and core-shell nozzle methods (Billiet *et al.*, 2014). A microfluidic device for carrying blood was fabricated using 3DP to enable the circulation of red blood cells. The device also maintained the glucose level of storage solutions between normoglycemic levels of 4–6 mM, which enabled cells to release ATP at levels equal to fresh and non-stored cells (Gmeiner *et al.*, 2015). Similarly, Inzana *et al.* (2014) printed CP scaffolds with the tailored concentration of phosphoric acid-based binder solution to exploit cytocompatibility and mechanical strength. Such a technique could have applications in TE (Yamamoto *et al.*, 2012; Kandhasamy *et al.*, 2015; Van Dijk *et al.*, 2010). Through this review, it is seen that MEW is a new 3DP procedure to print frameworks with culminate reproducibility using the 3DP approach.

Appropriate choice of biomaterials that can direct revival is vital in establishing expected long-term outcomes in tissue engineering. Most of the present commercial bio-materials are of low quality, which offers challenges for the researchers to improve them either by mixing some types of reinforcements, fillers or chemicals, or to alter the input process parameters. Both these are time and investment demanding approaches, which can result in no significant outcomes.

These existing issues can only be tackled through establishing collaborations of experts from different fields. All pertinent mechanical, physical and biological qualities of the biomaterial should be measured simultaneously when planning the smaller scale design. Furthermore, there are restrictions over the accessibility of good materials that can work with 3DP frameworks. Conventional biomaterials often cannot be used with 3DP procedures, while the best-performing materials in 3DP machines may not be biocompatible nor do not display the required biodegradation profile.

3. Applications of tissue engineering.

This section discusses the various applications of 3DP in B-TE and also considers the use of bioprinters, the most recent class

Table 5 List of biomaterials and their application in 3DP

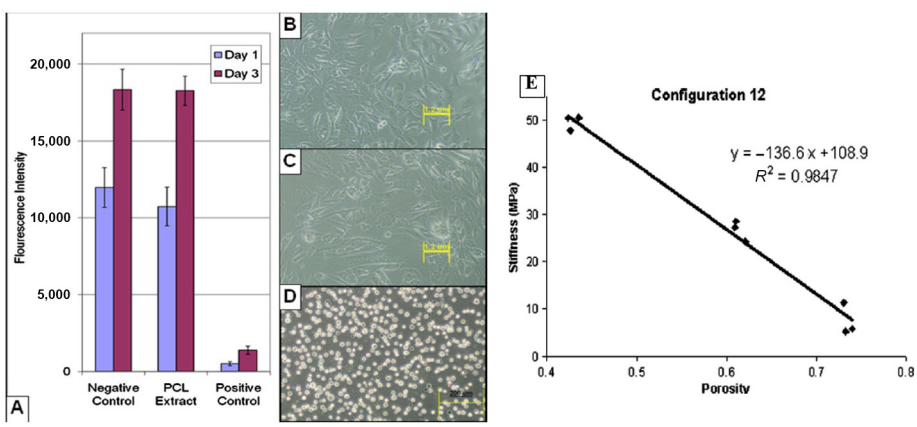
Biomaterials	Application	Remarks	Ref.
Poly-capro-lactone (PCL)	Customized scaffolding	Scaffolds produced using PCL through FDM enhanced cell proliferation, distribution, seeding efficiency and osteogenic separation	Chen *et al.* (2011)
		The PCL scaffolds were created with variable channel size, porosity and general geometrical honeycomb pores showed acknowledged scope of compressive firmness, yield quality and yield strain	Zein *et al.*, 2002
		The composites of PCL and HA indicated usual bioactivity, great cell adhesion and spreading at the surface of the scaffold	Goncalves *et al.*, 2016
		This mix of properties demonstrated that the constructed3D scaffolds are promising materials in the field of bone regenerative medication	
	Regenerative medicine	Results demonstrated that PCL-TCP networks joined with 15 Wt.% GS (PT15) effectively disposed of bacteria in less than 2 h and show low cytotoxicity	Teo *et al.*, 2011
		The interconnected 3 D PCL scaffold appeared to be a promising material for instigating bone in-growth required for reconstructing craniofacial and orbital deformities	Zein *et al.*, 2002
		The mechanism of resorption of 3DP devices can be guarded by manipulating the composition and microstructure of the tool during construction	Wu *et al.*, 1999
Poly-vinyl-alcohol (PVA)	Customized organ	The ink displayed pseudoplastic behavior at low shear rates and demonstrated good time stability	Salaoru *et al.*, 2017
Poly-lactic-acid (PLA)	Regenerative medicine	3DP tool allowed obtaining tri-dimensional structures with complex architectures and surface properties on demand	Serra *et al.*, 2013
	Customized scaffolding	The bone scaffolds completed by the single-nozzledeposition prepare in the MDM structure had extraordinary biocompatibility and bone conductive property as a sub-atomic framework for bone morphogenic protein in the implantation of the rabbit	Yan *et al.*, 2003
β-TCP	Customized scaffolding	A huge increment of approximately 40% in mechanical strength, was accomplished because of SrO and MgO doping in TCP as contrasted and pure TCP	Tarafder *et al.*, 2015
Poly-ethylene-glycol (PEG)	Regenerative medicine	Encapsulated cells demonstrated high growth more than 7 days, averaging 75.5 ± 11.6% in the PEG–alginate hydrogel and 95%in penetrated collagen between the pores of a printed PEG–alginate– nano clay mesh	Hong *et al.*, 2015
		This technique permitted to fabricate hybrid structures working with a fully fluid material without meeting the disadvantages of including inorganic powders into 3 D printable formulations	Chiappone *et al.*, 2016
HA (or HAp)	Customized scaffolding	The polydopamine coated/HAp precipitate improves osteogenesis and angiogenesis of hMSCs refined with a PCL scaffold	Cheng *et al.*, 2016
HA/PEG	Customized scaffolding	The bio-inks depicted in this investigation gave new outcomes to bio fabrication, given their flexibility in mechanical properties, high constructintegrity and controllable 3 D-printing as bolstered by rheology	Boere *et al.*, 2015
PMMA	Regenerative medicine	A direct proof of the structural blue/green via the lithographically replicated PMMA multi-layers analog	Zhang *et al.*, 2016
Nylon	Implants	This system has the capability of producing near net shape geometries with a wide range of alloys	Laumer *et al.*, 2015
	Customized scaffolding	Bio compatibility of the structures could be enhanced by better strategies for post-manufacture cleaning or treatment of SLS created scaffold constructs to dispense with loosely bonded polymer particles	Das *et al.*, 2003
Polyethylene (PE)	Customized scaffolding	This procedure can be used to control the structure and the properties of the parts with ease	Salmoria *et al.*, 2007
PGA	Regenerative medicine	Currently available 3DP technologies can address a wide range of medical applications	Farré-Guasch *et al.*, 2015
Polystyrene	Regenerative medicine	Utilization of 3DP innovation may decrease the operation time and the perioperative blood loss	Li *et al.*, 2015
PHB	Customized scaffolding	The PHB powder did not present variety in warm properties and compound piece following 32.15 h of SLS procedure	Zhao *et al.*, 2014
	Regenerative medicine	The results showed that MBG/PHBHHx composite scaffolds possessed a controlled degradation speed and more significant possible to steady the pH environment	Childers *et al.*, 2015
PLGA	Customized scaffolding	The outcomes of in-vitro studies using cultures of line NIH 3T3 mouse fibroblasts, rabbit pancreas and human stem cells showed the disappearance of cytotoxicity and great adhesive properties	Mironov *et al.*, 2017

(***continued***)

Table 5

Biomaterials	Application	Remarks	Ref.
		In vivo biocompatibility examine conducted on 12 rats showed that HA-scaffolds exhibited high-quality neo vascularization and tissue integration	Yang *et al.*, 2016
PEEK	Regenerative medicine	PEEK scaffolds maintained the viability of both ADSCs and BMSCs; however, ADSCs demonstrated higher osteo-differentiation than BMSCs	Elomaa *et al.*, 2011
Poly(propylene fumarate) (PPF)	Customized scaffolding	This study helped determine whether a novel biomaterial is suitable for extrusion-based 3DP applications	Trachtenberg *et al.*, 2016
		The ability to manage accurate geometries, porosity, debasement and functionalities display on 3D printable polymers, for example, PPF demonstrates a novel layer of multifaceted nature accessible for the plan and manufacture of TE scaffolds	Childers *et al.*, 2015
		The scaffolds demonstrated a 90% decrease in elastic modulus and a 74% rise in max strain	Mott *et al.*, 2016
Bioactive glass (6P53B)	Customized scaffolding	Ceramic manufacturing, 3DP, indirect and direct SLS/SLM, dispense plotting and inkjet plotting can produce dense or porous bioactive glass and bio-ceramic parts with potential medical applications	Gmeiner *et al.*, 2015
PLLA	Customized scaffolding	H-E and Masson staining confirmed the structures to be possessed of excellent biocompatibility and vascularization *in vivo*, and fiber morphology and collagen production indicated its abundant extracellular matrix	Frydrych *et al.*, 2013
Glucose	Regenerative devices	The manufacture of intracellular sorbitol was amplified by over threefold in hyperglycemic conditions, which has harmful effects on cells	Mu *et al.*, 2016
		The work validated the desktop 3D printers as versatile interfacing tools in microfluidic laboratories	Brooks *et al.*, 2016
Wood fiber	Composite structures	Mechanical properties of the composites depended on printing width, with a lower Young's modulus than in the compressed samples	Le Duigou *et al.*, 2016
Photopolymer	Customized scaffolding	The obtained histological results from *in vivo* analysis approved the excellent biocompatibility of vinyl esters	Heller *et al.*, 2009
Dextran	Customized scaffolding	Stabe constructs with mechanical properties matching that of the large range of mechanical strengths found in natural tissues were developed by photo polymerization.	Pescosolido *et al.*, 2001
Gelatin	Regenerative medicine	The results of the study confirmed that gelatin hydrogels supported effective maturation of fully perfusable microvascular networks of different architectures and geometries	Bertassoni *et al.*, 2014
Chitosan	Regenerative medicine	This low-temperature robocasting method enabled a variety of bioactive molecules to be incorporated into printed collagen-hydroxyapatite materials and provides a method of bioprinting biomaterials without compromising their natural properties	Barbetta *et al.*, 2010

Figure 4 (A) The feasibility of cells refined in PCL framework separate contrast and the negative and positive controls and minuscule pictures of cells treated in (B) the negative control, (C) PCL remove, (D) the positive control and (E) a plot of platform porosity versus compressive solidness



Source: Sudarmadji *et al.* (2011)

of 3DP, to strengthen the discussion. Table 6 highlights some of the top-cited work in the area of B-TE.

3.1 Regenerative medicine

The regenerative medicine includes the development of medical tools and devices to regenerate and repair damaged/dysfunctional tissues or organs. The ideal scaffold made up of biocompatible biodegradable materials, possessed biomimetic 3D highly porous structure and compatible biomechanical properties to the host tissue. The scaffolds are not intended to be used as a permanent implant but preferably used as temporary which assist the growth of ECM and replace the scaffold over time. Most commonalty metals used for bone repair and regenerations include metals, ceramics, polymers, hydrogels and related composites (Turnbull *et al.*, 2018). 3D printed iron-manganese biodegradable scaffolds were developed by using inkjet 3DP, Chou *et al.*, 2013, for craniofacial applications. The composite scaffold of titanium-silica was developed using the 3DP technique using the SLS process (Liu *et al.*, 2013). A biocompatible phosphonic layer was developed by phosphonic acid treatment that improved the bioactivity of scaffolds (Vaithilingam *et al.*, 2015; Kruth *et al.*, 2005).

After metals, bio-ceramics including ceramic composites, amorphous glasses and crystalline ceramics are potential and promising materials for B-TE application owing to excellent corrosion resistance, mechanical property, high compressive strength (Bonfield, 1988). Another popular bio-ceramic "beta-tri-calcium phosphate (β-TCP)" was combined with HA to develop porous scaffolds for bone repair (Ishack *et al.*, 2017). Collagen-based open porous scaffolds with inter-connected channels were developed by indirect 3DP technique and freeze-drying. Furthermore, indirect 3DP integrated with the foaming process to develop high open porous gelatin scaffolds with complex channel architectures. The architecture of scaffolds was improved further by incorporating mono-dispersed microspheres into the casting process. The scaffolds made up of silk fibroin protein with macro/micro-architecture were developed by 3DP (Yeong *et al.*, 2006; Yeong *et al.*, 2007; Tan

Table 6 Top cited work of B-TE

Title of paper	Journal/book	Thrust area	Citation	Scope of further research, if any
Scaffolds in tissue engineering bone and cartilage	In The Biomaterials: Silver Jubilee Compendium	Customized scaffoldings	4,985	Hutmacher, 2000 critically reviewed the application of polymeric scaffold for TE applications. The range of literature covered could be extended to various classes of biomedical engineering
Porous scaffold design for tissue engineering	*Nature Materials*		2837	Hollister *et al*., 2005 critically reviewed and reported studies on the architecture design optimization of scaffolds. The study could be extended on the effect on architecture design mechanical integrity of scaffolds
Synthetic biomaterials as instructive extracellular microenvironments for morphogenesis in tissue engineering	Nature biotechnology		3,839	Lutolf and Hubbell, 2005 reported the utility of synthetic materials to grow ECM for TE application. The research work could be extended to various methods to process the synthetic materials as scaffolds for TE application
Biomaterial developments for bone tissue engineering	*Biomaterials*		1,721	Burg *et al*., 2000 report is limited to biomaterials for TE application. Their fabrication/processing routes, design requirements, progress in the design development are not attempted, which could be studied
Bone tissue engineering using 3DP	*Materials Today*		718	Bose *et al.*, 2013 reported the applications of 3DP for hard tissue replacements only. The research could be extended to scaffolds and cartilages also
3D bioprinting for biomedical devices and tissue engineering: A review of recent trends and advances	*Bioactive materials*	Regenerative medicine	29	Derakhshanfar *et al.*, 2018 critically reviewed the application of 3 D bioprinting for biomedical devices and tissue engineering. The range of literature covered could be extended to various classes of 3-D printing for biomedical engineering
Tissue engineering and regenerative medicine: history, progress, and challenges	*Annual Review of Chemical and Biomolecular Engineering*		320	Berthiaume *et al.*, 2011 presented the historical development and challenges of TE. The research study could be extended to biomaterials and their processing routes to devolve scaffolds, organs, tissue at an economical level
Application of inkjet printing to tissue engineering	*Biotechnology Journal: Healthcare Nutrition Technology*	Organ printing	649	Boland *et al.* (2006) reported the application of inkjet printing for organ development. The range of literature covered could be extended to the application of 3-D bioprinting for the development of organ models to understand and refine clinical practices
Organ printing: computer-aided jet-based 3 D tissue engineering	*Trends in Biotechnology*		1,272	Mironov *et al*., 2003 highlighted that the developmental biology concept of embryonic tissue fluidity enables the creation of 3 D organ printing technology

et al., 2009; Tan *et al.*, 2013; Chen *et al.*, 2014). The application of 3DP has gained significant success in medical surgeries including dental, neurosurgery, maxillofacial, orthopedic, plastic and reconstructive surgeries (Malik *et al.*, 2015; Klein *et al.*, 2013; Choi and Kim, 2015). In the field of maxillofacial surgery includes dental implant surgery, mandibular reconstruction, orthognathic surgery and mid-face reconstruction (Ayoub *et al.*, 2014; Jirman *et al.*, 2009). Related to dental-implant surgeries, the majorly printed 3 D devices are surgical guides specifically designed to facilitate the direction and accomplishment of drilling, fitting of implant accurately (Louvrier *et al.*, 2017).

3.2 Specialized scaffoldings

Skin treatment and its regeneration through the use of 3DP techniques have attained a lot of attention from the researchers. Laser-based direct-write cell printing technology was used to print skin tissue (Schiele *et al.*, 2010). Multicellular skin grafts were developed using laser-assisted bioprinting technology by mixing vital cells of skin tissues such as keratinocytes and fibroblasts in collagen (Koch *et al.*, 2012). Further, they developed a bilayer skin containing 20 layers of fibroblast-containing collagen and 20 layers of keratinocyte-containing collagen. The bilayer skin was placed on the full-thickness wounds in the dorsal skin chamber of nude mice *in-vivo* (Michael *et al.*, 2013). After 11 days, it was found that the skin was fully connected with the mice and properly functioned. Recently, the application of 3 D bioprinting was used for the development of bilayer functional skin that mimics human skin (Cubo *et al.*, 2016).

3.3 Organ printing

Naturally driven materials (bio-inks, hydrogels and thereby combinations) have been generally used for printing organs. Furthermore, the potential of bioprinting to supply nutrients to encapsulated cells in the surrounding matrix (Zhang, *et al.*, 2013; Yu *et al.*, 2013). Another successful advancement to develop functional cardiac tissues; particularly, the heart valves by 3D bioprinting have been reported (Tomanek and Runyan, 2012; Tortora and Derrickson, 2008). Trileaflet aortic valve was designed and developed by a 3D bioprinting technique using hybrid hydrogel. After seven days of *in vivo* culture conditions, the valve was well maintained and the high visibility of cells was found with a high potential of remodeling (Duan *et al.*, 2014). The development of intricate trabecular anatomy of the complete heart using 3 D bioprinting has been reported (Hinton *et al.*, 2015, Sodian *et al.*, 20008; Wang *et al.*, 2018; Lau and Sun, 2018). Another impossible to achieve innovation, development of liver anatomy has been successfully achieved by 3DP technology (Robbins *et al.*, 2013; Zhang *et al.*, 2017; Witowski *et al.*, 2019). Anatomies of the liver are complex and consist of eight autonomous units. The vascularized liver was the first time developed by Organovo^{TM} by using the 3DP technique. The high-density hepatocytes, endothelial cells and hepatic stellate cells were used to print a 3 D architecture that mimicked the natural through hepatic lobules (Nguyen *et al.*, 2015). With the developed 3 D printed model of the liver, accurate location detection of tumor and planning, and experience of laparoscopy or hepatic resections can be achieved.

4. Summary and future directions.

3DP represents a class of processes for fabricating complex 3 D products ranging from custom prosthetics and medical implants to warfighter engine components on-demand. AM has the potential to revolutionize the way components are produced by streamlining product design, production, and validation, which allows for low production costs and accelerated lead times. Though, there is enormous progress in current 3DP technologies, some quality-related challenges still exist. These challenges are attributed to the gap between fundamental research and industrial applications. This gap has to be bridged through strengthening connections between different stakeholders. This will serve to further advance 3DP techniques by identifying technical and practical challenges that require more in-depth fundamental investigations. Industrial sectors to benefit include aerospace, automotive, biomedical, defense, energy, environmental, manufacturing and materials, to name a few.

Also, the key advantage of 3DP methods is the capacity to experiment with the physical model of an intricate part in a generally brief time. Furthermore, these are cost-competitive at low volumes, as contrasted with older manufacturing methods. This manufacturing class also simplifies the supply chain for certain types of businesses, resulting in lower logistics costs. Hence, the consumer can buy the products according to their needs. Three key factors will determine the future growth of 3DP in various fields, are:

4.1 Research directions concerning feedstock materials

Raw materials for 3DP have a wide variety and differ in terms of performance, properties and cost. One of the most important properties for raw material selection in 3DP of biomedical implants is accomplishing target mechanical properties and different variables including durability and designed architectures. Hence, the capabilities of these technologies in processing speed and stock materials have to be well characterized and documented in both *in vitro* and *in vivo* under diverse conditions. In implant design, the failure mode of such porous architectures and mechanical properties need to be well understood to circumvent implant failure. The length scale ranged from ten to hundreds of microns in porous architectures, that is outside the resolution capacity of the 3DP technology in use. Lastly, attention had to be given to raw material selection in terms of surface finish and surface texture requirement, to attain the final desired surface.

The issues hindering the growth of 3DP include the following: (a) Inability to print components of any stiffness with material properties on par with traditionally manufactured parts. Particularly, 3DP materials tend to tear or fracture more readily between successive printed layers. Various approaches have been proposed to achieve appreciable cohesion between these layers. (b) Inability to print well-ordered layers at fine length scales. Typically, precise control of the position and orientation of the nanoparticles within a thin-film is essential to control the electrical, mechanical, and optical properties of the components. One of the approaches includes a solution/melt electrohydrodynamic printing system, which can achieve resolution as high as 1 micron and can result in ordered nanoparticle arrays within the component. (c) Inadequate

control over the 3DP process, which can lead to considerable rework and high scrap rates, and thus poses significant impediments for the sustainability of 3DP. (d) Variability in porosity, even for identical build parameters, is a significant technical challenge facing 3DP production quality. To alleviate the issue, relationships between microstructure properties, porosity and process parameter need to be established.

4.2 Research directions concerning applications development

The primary challenges associated with 3 D printers also apply to engineer applications. Cell loaded and drug sample fabrications require a process chain beneath sterile and aseptic conditions, and the printing process to be performed in biological workbench. In 3DP of biomedical organs, different properties such as durability, mechanical properties and structural design to fulfill both functional and mechanical requirements are more difficult to achieve. Especially in the cases of high load-bearing implants, fatigue and mechanical properties are more significant. By adopting existing technologies, permanent implants are fabricated using polymers, ceramics and metals. The different materials such as polyether ketone, titanium and hydroxyapatite, are thoroughly studied to fabricate scaffolds at diverse environmental conditions both *in vitro* and *in vivo*. Fabrication using 3DP will possibly be used soon for direct cell seeding of scaffolds. Work is in progress to print cells using inkjet printing.

In vitro studies using collagen scaffolds fabricated by synthetic organic molecules have shown outstanding biocompatibility. Hence, collagen scaffolds with novel organic molecules will possibly be fabricated with better biocompatibility and bioactivity. These biomaterials are appropriate for use in TE and biomedical applications. Scaffold requirements for tissue engineering are more complicated and adhere to specific structures and functions of the tissues. Hence, scaffold production techniques must be enhanced to produce scaffolds with favored qualities, like porosity, degradation, distribution, pore size, shape and mechanical properties. The important factors that influence tissue growth are pore size, shape and tortuosity. However, it is challenging to fabricate such scaffolds using the existing processing techniques while considering all the above aspects. Biological issues that are addressed include cell perfusion, oxygen diffusion, guided tissue differentiation and cell migration. Oxygen, metabolic waste products and nutrients are transported through the interstitial network and microvascular proliferation that are connected to macrocirculation [139, 140]. Multi-material structures that involve cells with inorganic or organic materials are fabricated to make a functional scaffold for TE applications.

Finally, 3DP applied in the field of drug or protein delivery will possibly be more popular shortly. The controlled delivery of drug protein-loaded biomaterials is necessary to cure many diseases. In particular, drug combinations have to be specific to the patient and are loaded onto a single 3DP-drug delivery device. This technology should enable personalized devices and treatments while shortening the time from a prototype (Lin *et al.*, 2013; Chen *et al.*, 2011). This should quicken research work, help lessen the cost of clinical trials and enhance access to healthcare. A large number of companies producing metal-based 3DP system could be advantages for the consumer, as they compete with each other with the price, speed and quality of the machine. Another important development is the improvement of building speed and prototype quality of 3DP systems.

Several kinds of bioplastics and biomaterials are developed in 3DP. Besides, re-use and recycling of these biomaterials must be necessary. The fabrication of 3DP, biomaterials and renewable energy must develop concurrently. 3DP gives the capacity to create altered, complex parts that are generally difficult to obtain for an assortment of uses. A paradigm shift in engineering design and product realization is occurring, and numerous businesses, such as biomedical and aviation, are ready to profit. A few examples incorporate:

- on location, quick production of bone inserts with the patient and injury-specific designs; and
- production of replacement parts in remote areas (e.g. outer space).

References

Aarthy, S., Thenmuhil, D., Dharunya, G. and Manohar, P. (2019), "Exploring the effect of sintering temperature on naturally derived hydroxyapatite for bio-medical applications", *Journal of Materials Science: Materials in Medicine*, Vol. 30 No. 2, p. 21

Aimar, A., Palermo, A. and Innocenti, B. (2019), "The role of 3D printing in medical applications: a state of the art", *Journal of Healthcare Engineering*, Vol. 2019.

Ayoub, A.F., Rehab, M., O'neil, M., Khambay, B., Ju, X., Barbenel, J. and Naudi, K. (2014), "A novel approach for planning orthognathic surgery: the integration of dental casts into three-dimensional printed mandibular models", *International Journal of Oral and Maxillofacial Surgery*, Vol. 43 No. 4, pp. 454-459.

Bai, Y. and Williams, C.B. (2018), "Binder jetting additive manufacturing with a particle-free metal ink as a binder precursor", *Materials & Design*, Vol. 147, pp. 146-156.

Bai, Y., Wall, C., Pham, H., Esker, A. and Williams, C.B. (2019), "Characterizing binder–powder interaction in binder jetting additive manufacturing via sessile drop goniometry", *Journal of Manufacturing Science and Engineering*, Vol. 141 No. 1.

Banks, J. (2013), "Adding value in additive manufacturing: researchers in the United Kingdom and Europe look to 3D printing for customization", *IEEE Pulse*, Vol. 4 No. 6, pp. 22-26.

Barbetta, A., Carrino, A., Costantini, M. and Dentini, M. (2010), "Polysaccharide based scaffolds obtained by freezing the external phase of gas-in-liquid foams", *Soft Matter*, Vol. 6 No. 20, pp. 5213-5224.

Baroli, B. (2007), "Hydrogels for tissue engineering and delivery of tissue-inducing substances", *Journal of Pharmaceutical Sciences*, Vol. 96 No. 9, pp. 2197-2223.

Barry, J.J.A., Evseev, A.V., Markov, M.A., Upton, C.E., Scotchford, C.A., Popov, V.K. and Howdle, S.M. (2008), "3D printed microfluidic devices with integrated versatile

and reusable electrodes", *Acta Biomaterialia*, Vol. 4 No. 6, pp. 1603-1610.

Bertana, V., Catania, F., Cocuzza, M., Ferrero, S., Scaltrito, L., and Pirri, C.F. (2020), "Medical and biomedical applications of 3D and 4D printed polymer nanocomposites", *3D and 4D Printing of Polymer Nanocomposite Materials*, Elsevier, pp. 325-366.

Bertassoni, L.E., Cecconi, M., Manoharan, V., Nikkhah, M., Hjortnaes, J., Cristino, A.L. and Khademhosseini, A. (2014), "Hydrogel bioprinted microchannel networks for vascularization of tissue engineering constructs", *Lab Chip*, Vol. 14 No. 13, pp. 2202-2211.

Berthiaume, F., Maguire, T.J. and Yarmush, M.L. (2011), "Tissue engineering and regenerative medicine: history, progress, and challenges", *Annual Review of Chemical and Biomolecular Engineering*, Vol. 2 No. 1, pp. 403-430.

Billiet, T., Gevaert, E., De Schryver, T., Cornelissen, M. and Dubruel, P. (2014), "The 3D printing of gelatin methacrylamide cell-laden tissue-engineered constructs with high cell viability", *Biomaterials*, Vol. 35 No. 1, pp. 49-62.

Boere, K.W., Blokzijl, M.M., Visser, J., Linssen, J.E.A., Malda, J., Hennink, W.E. and Vermonden, T. (2015), "Biofabrication of reinforced 3D-scaffolds using two-component hydrogels", *Journal of Materials Chemistry B*, Vol. 3 No. 46, pp. 9067-9078.

Boland, T., Xu, T., Damon, B. and Cui, X. (2006), "Application of inkjet printing to tissue engineering", *Biotechnology Journal*, Vol. 1 No. 9, pp. 910-917.

Bonfield, W. (1988), "Hydroxyapatite-reinforced polyethylene as an analogous material for bone replacementa", *Annals of the New York Academy of Sciences*, Vol. 523 No. 1, pp. 173-177.

Bose, S., Vahabzadeh, S. and Bandyopadhyay, A. (2013), "Bone tissue engineering using 3D printing", *Materials Today*, Vol. 16 No. 12, pp. 496-504.

Brooks, J.C., Ford, K.I., Holder, D.H., Holtan, M.D. and Easley, C.J. (2016), "Macro-to-micro interfacing to microfluidic channels using 3D-printed templates: application to time-resolved secretion sampling of endocrine tissue", *The Analyst*, Vol. 141 No. 20, pp. 5714-5721.

Brown, T.D., Edin, F., Detta, N., Skelton, A.D., Hutmacher, D.W. and Dalton, P.D. (2014), "Melt electrospinning of poly (ε-caprolactone) scaffolds: phenomenological observations associated with collection and direct writing", *Materials Science and Engineering: C*, Vol. 45, pp. 698-708.

Brown, T.D., Slotosch, A., Thibaudeau, L., Taubenberger, A., Loessner, D., Vaquette, C., Dalton, P.D. and Hutmacher, D.W. (2012), "Design and fabrication of tubular scaffolds via direct writing in a melt electrospinning mode", *Biointerphases*, Vol. 7 No. 1, p. 13.

Burg, K.J., Porter, S. and Kellam, J.F. (2000), "Biomaterial developments for bone tissue engineering", *Biomaterials*, 1 December, Vol. 21 No. 23, pp. 2347-2359.

Carve, M. and Wlodkowic, D. (2018), "3D-Printed chips: compatiblity of additive manufacturing Photopolymeric substrata with", *Micromachines*, , Vol. 9 No. 2, p. 91.

Chen, C.H., Liu, J., Chua, C.K., Chou, S.M., Shyu, V. and Chen, J.P. (2014), "Cartilage tissue engineering with silk fibroin scaffolds fabricated by indirect additive manufacturing technology", *Materials*, Vol. 7 No. 3, pp. 2104-2119.

Chen, M., Le, D.Q., Baatrup, A., Nygaard, J.V., Hein, S., Bjerre, L. and Bünger, C. (2011), "Self-assembled composite matrix in a hierarchical 3-D scaffold for bone tissue engineering", *Acta Biomaterialia*, Vol. 7 No. 5, pp. 2244-2255.

Cheng, Y.L., Chen, Y.W., Wang, K. and Shie, M.Y. (2016), "Enhanced adhesion and differentiation of human mesenchymal stem cell inside apatite-mineralized/poly (dopamine)-coated poly (ε-caprolactone) scaffolds by stereolithography", *Journal of Materials Chemistry B*, Vol. 4 No. 38, pp. 6307-6315.

Chia, H.N. and Wu, B.M. (2015), "Recent advances in 3D printing of biomaterials", *Journal of Biological Engineering*, Vol. 9 No. 1, p. 4.

Chiappone, A., Fantino, E., Roppolo, I., Lorusso, M., Manfredi, D., Fino, P. and Calignano, F. (2016), "3D printed PEG-based hybrid nanocomposites obtained by sol–gel technique", *ACS Applied Materials & Interfaces*, Vol. 8 No. 8, pp. 5627-5633.

Childers, E.P., Wang, M.O., Becker, M.L., Fisher, J.P. and Dean, D. (2015), "3D printing of resorbable poly (propylene fumarate) tissue engineering scaffolds", *Mrs Bulletin*, Vol. 40 No. 2, pp. 119-126.

Choi, J.W. and Kim, N. (2015), "Clinical application of three-dimensional printing technology in craniofacial plastic surgery", *Archives of Plastic Surgery*, Vol. 42 No. 3, p. 267

Choi, G. and Cha, H.J. (2019), "Recent advances in the development of nature-derived photocrosslinkable biomaterials for 3D printing in tissue engineering", *Biomaterials Research*, Vol. 23 No. 1, p. 18

Choi, H.J., Kim, J.M., Kwon, E., Che, J.H., Lee, J.I., Cho, S. R. and Kang, B.C. (2011), "Establishment of efficacy and safety assessment of human adipose tissue-derived mesenchymal stem cells (hATMSCs) in a nude rat femoral segmental defect model", *Journal of Korean Medical Science*, Vol. 26 No. 4, pp. 482-491.

Chou, D.T., Wells, D., Hong, D., Lee, B., Kuhn, H. and Kumta, P.N. (2013), "Novel processing of iron–manganese alloy-based biomaterials by inkjet 3DP", *Acta Biomaterialia*, Vol. 9 No. 10, pp. 8593-8603.

Choudhury, D., Tun, H.W., Wang, T. and Naing, M.W. (2018), "Organ-derived decellularized extracellular matrix: a game changer for bioink manufacturing?", *Trends in Biotechnology*, Vol. 36 No. 8.

Cubo, N., Garcia, M., del Cañizo, J.F., Velasco, D. and Jorcano, J.L. (2016), "3D bioprinting of functional human skin: production and in vivo analysis", *Biofabrication*, Vol. 9 No. 1, p. 015006

Cui, X. and Boland, T. (2008), "Simultaneous deposition of human microvascular endothelial cells and biomaterials for human microvasculature fabrication using inkjet printing", NIP & Digital Fabrication Conference, pp. 480-483.

Dalton, P.D., Grafahrend, D., Klinkhammer, K., Klee, D. and Moller, M. (2007), "Electrospinning of polymer melts: phenomenological observations", *Polymer*, Vol. 48 No. 23, pp. 6823-6833.

Dalton, P.D., Vaquette, C., Farrugia, B.L., Dargaville, T. R., Brown, T.D. and Hutmacher, D.W. (2013),

"Electrospinning and additive manufacturing: converging technologies", *Biomaterials Science*, Vol. 1 No. 2, pp. 171-185.

Das, S., Hollister, S.J., Flanagan, C., Adewunmi, A., Bark, K., Chen, C. and Widjaja, E. (2003), "Freeform fabrication of nylon-6 tissue engineering scaffolds", *Rapid Prototyping Journal*, Vol. 9 No. 1, pp. 43-49.

Deckers, J., Shahzad, K., Vleugels, J. and Kruth, J.P. (2012), "Isostatic pressing assisted indirect selective laser sintering of alumina components", *Rapid Prototyping Journal*, Vol. 18 No. 5, pp. 409-419.

Derakhshanfar, S., Mbeleck, R., Xu, K., Zhang, X., Zhong, W. and Xing, M. (2018), "3D bioprinting for biomedical devices and tissue engineering: a review of recent trends and advances", *Bioactive Materials*, Vol. 3 No. 2, pp. 144-156.

Detsch, R., Schaefer, S., Deisinger, U., Ziegler, G., Seitz, H. and Leukers, B. (2011), "In vitro-osteoclastic activity studies on surfaces of 3D printed calcium phosphate scaffolds", *Journal of Biomaterials Applications*, Vol. 26 No. 3, pp. 359-380.

Dhariwala, B., Hunt, E. and Boland, T. (2004), "Rapid prototyping of tissue-engineering constructs, using photopolymerizable hydrogels and stereolithography", *Tissue Engineering*, Vol. 10 Nos 9/10, pp. 1316-1132.

Do, A.V., Khorsand, B., Geary, S.M. and Salem, A.K. (2015), "Biologically inspired smart release system based on 3D bioprinted perfused scaffold for vascularized tissue regeneration", *Advanced Healthcare Materials*, Vol. 4 No. 12, pp. 1742-1762.

Duan, B., Kapetanovic, E., Hockaday, L.A. and Butcher, J.T. (2014), "Three-dimensional printed trileaflet valve conduits using biological hydrogels and human valve interstitial cells", *Acta Biomaterialia*, Vol. 10 No. 5, pp. 1836-1846.

Duan, B., Wang, M., Zhou, W.Y., Cheung, W.L., Li, Z.Y. and Lu, W.W. (2010), "Three-dimensional nanocomposite scaffolds fabricated via selective laser sintering for bone tissue engineering", *Acta Biomaterialia*, Vol. 6 No. 12, pp. 4495-4505.

Elomaa, L., Teixeira, S., Hakala, R., Korhonen, H., Grijpma, D.W. and Seppälä, J.V. (2011), "Preparation of poly (ε-caprolactone)-based tissue engineering scaffolds by stereolithography", *Acta Biomaterialia*, Vol. 7 No. 11, pp. 3850-3856.

Farré-Guasch, E., Wolff, J., Helder, M.N., Schulten, E.A., Forouzanfar, T. and Klein-Nulend, J. (2015), "Application of additive manufacturing in oral and maxillofacial surgery", *Journal of Oral and Maxillofacial Surgery*, Vol. 73 No. 12, pp. 2408-2418.

Farrugia, B.L., Brown, T.D., Upton, Z., Hutmacher, D.W., Dalton, P.D. and Dargaville, T.R. (2013), "3D-printed bioactive Ca3SiO5 bone cement scaffolds with nano surface structure for bone regeneration", *Biofabrication*, Vol. 5, p. 5001.

Fedorovich, N.E., Alblas, J., Hennink, W.E., Oner, F.C. and Dhert, W.J.A. (2011), "An innovative Collagen-Based Cell-Printing method for obtaining human adipose stem Cell-Laden structures consisting of core–sheath structures for tissue engineering", *Trends in Biotechnology*, Vol. 29 No. 12, pp. 601-606.

Fina, F., Madla, C.M., Goyanes, A., Zhang, J., Gaisford, S. and Basit, A.W. (2018), "Fabricating 3D printed orally disintegrating printlets using selective laser sintering", *International Journal of Pharmaceutics*, Vol. 541 No. 1-2, pp. 101-107.

Frydrych, M. and Chen, B. (2013), "Large three-dimensional poly (glycerol sebacate)-based scaffolds–a freeze-drying preparation approach", *Journal of Materials Chemistry B*, Vol. 1 No. 48, pp. 6650-6661.

Gao, C., Deng, Y., Feng, P., Mao, Z., Li, P., Yang, B. and Peng, S. (2014), "Current progress in bioactive ceramic scaffolds for bone repair and regeneration", *International Journal of Molecular Sciences*, Vol. 15 No. 3, pp. 4714-4732.

Garreta, E., Oria, R., Tarantino, C., Pla-Roca, M., Prado, P., Fernandez-Aviles, F., Campistol, J.M., Samitier, J. and Montserrat, N. (2017), "Tissue engineering by decellularization and 3D bioprinting", *Materials Today*, Vol. 20 No. 4, pp. 166-178.

Gay, S., Lefebvre, G., Bonnin, M., Nottelet, B., Boury, F., Gibaud, A. and Calvignac, B. (2018), "PLA scaffolds production from thermally induced phase separation: effect of process parameters and development of an environmentally improved route assisted by supercritical carbon dioxide", *The Journal of Supercritical Fluids*, Vol. 136, pp. 123-135.

Gbureck, U., Hölzel, T., Klammert, U., Würzler, K., Müller, F.A. and Barralet, J.E. (2007), "Resorbabledicalcium phosphate bone substitutes prepared by 3D powder printing", *Advanced Functional Materials*, Vol. 17 No. 18, pp. 3940-3945.

Gbureck, U., Vorndran, E., Müller, F.A. and Barralet, J.E. (2007), "Low temperature direct 3D printed bioceramics and biocomposites as drug release matrices", *Journal of Controlled Release*, Vol. 122 No. 2, pp. 173-180.

Germain, L., Fuentes, C.A., van Vuure, A.W., Des Rieux, A. and Dupont-Gillain, C. (2018), "3D-printed biodegradable gyroid scaffolds for tissue engineering applications", *Materials & Design*, Vol. 151.

Gmeiner, R., Deisinger, U., Schonherr, J., Lechner, B., Detsch, R., Boccaccini, A.R. and Stampfl, J. (2015), "Additive manufacturing of bioactive glasses and silicate bioceramics", *Journal of Ceramic Science and Technology*, Vol. 6, pp. 75-86.

Góra, A., Sahay, R., Thavasi, V. and Ramakrishna, S. (2011), "Melt-electrospun fibers for advances in biomedical engineering, clean energy, filtration, and separation", *Polymer Reviews*, Vol. 51 No. 3, pp. 265-287.

Greco, A., Licciulli, A. and Maffezzolim, A. (2011), "Stereolitography of ceramic suspensions", *Journal of Materials Science*, Vol. 36 No. 1, pp. 99-105.

Griffin, E.A., Mumm, D.R. and Marshall, D.B. (1996), "Rapid prototyping of functional ceramic composites", *American Ceramic Society Bulletin*, Vol. 75, p. 7

Griffith, M.L. and Halloran, J.W. (1996), "Freeform fabrication of ceramics via stereolithography", *Journal of the American Ceramic Society*, Vol. 79 No. 10, pp. 2601-2608.

Griffith, L.G., Wu, B., Cima, M.J., Powers, M.J., Chaignaud, B. and Vacanti, J.P. (1997), "In vitro organogenesis of liver tissue", *Annals of the New York Academy of Sciences*, Vol. 831 No. 1, p. 382

Gross, B.C., Erkal, J.L., Lockwood, S.Y., Chen, C. and Spence, D.M. (2014), "Evaluation of 3D printing and its potential impact on biotechnology and the chemical sciences", *Analytical Chemistry*, Vol. 86 No. 7, pp. 3240-3253.

Gul, H., Khan, M., and Khan, A.S. (2020), "Bioceramics: types and clinical applications", *Handbook of Ionic Substituted Hydroxyapatites*, Woodhead Publishing, pp. 53-83.

Guo, C., Zhang, M. and Bhandari, B. (2019), "Model building and slicing in food 3D printing processes: a review", *Comprehensive Reviews in Food Science and Food Safety*, Vol. 18 No. 4, pp. 1052-1069.

Han, F., Wang, J., Ding, L., Hu, Y., Li, W., Yuan, Z., . . . Zhao, Z. (2020), "Tissue engineering and regenerative medicine: achievements, future, and sustainability in asia", *Frontiers in Bioengineering and Biotechnology*, Vol. 8

Heller, C., Schoeneweis, M., Russmueller, G., Varga, F., Stampfl, J. and Liska, R. (2009), "Vinyl esters: low cytotoxicity monomers for the fabrication of biocompatible 3D scaffolds by lithography based additive manufacturing", *Journal of Polymer Science Part A: Polymer Chemistry*, Vol. 47 No. 24, pp. 6941-6954.

Hellmann, C., Belardi, J., Dersch, R., Greiner, A., Wendorff, J. H. and Bahnmueller, S. (2009), "High precision deposition electrospinning of nanofibers and nanofiber nonwovens", *Polymer*, Vol. 50 No. 5, pp. 1197-1205.

Hench, L.L. (1996), "Ceramics, glasses, and glass-ceramics", in Ratner, B.D., Hoffman, A.S., Schoen, F.J., Lemons, J.E. (Eds), *Biomaterials Science: An Introduction to Materials in Medicine*, Academic Press, New York, NY, p. 73.

Herman, A.R. (2002), "The history of skin grafts", *Journal of Drugs in Dermatology*, Vol. 1, pp. 298-301.

Hinton, T.J., Jallerat, Q., Palchesko, R.N., Park, J.H., Grodzicki, M.S., Shue, H.J. and Feinberg, A.W. (2015), "Three-dimensional printing of complex biological structures by freeform reversible embedding of suspended hydrogels", *Science Advances*, Vol. 1 No. 9, p. e1500758.

Hochleitner, G., Jüngst, T., Brown, T.D., Hahn, K., Moseke, C., Jakob, F. and Groll, J. (2015), "Additive manufacturing of scaffolds with Sub-micron filaments via melt electrospinning writing", *Biofabrication*, Vol. 7 No. 3, p. 035002

Holzapfel, B.M., Wagner, F., Loessner, D., Holzapfel, N.P., Thibaudeau, L., Crawford, R. and Hutmacher, D.W. (2014), "Species-specific homing mechanisms of human prostate cancer metastasis in tissue engineered bone", *Biomaterials*, Vol. 35 No. 13, pp. 4108-4115.

Hong, S., Sycks, D., Chan, H.F., Lin, S., Lopez, G.P., Guilak, F. and Zhao, X. (2015), "3D printing of highly stretchable and tough hydrogels into complex, cellularized structures", *Advanced Materials*, Vol. 27 No. 27, pp. 4035-4040.

Hoy, M.B. (2013), "3D printing: making things at the library", *Medical Reference Services Quarterly*, Vol. 32 No. 1, pp. 93-99.

Hutmacher, D.W. (2000), "Scaffolds in tissue engineering bone and cartilage", *The Biomaterials: Silver Jubilee Compendium*, Elsevier, pp. 175-189.

Inzana, J.A., Olvera, D., Fuller, S.M., Kelly, J.P., Graeve, O. A., Schwarz, E.M. and Awad, H.A. (2014), "3D printing of composite calcium phosphate and collagen scaffolds for bone regeneration", *Biomaterials*, Vol. 35 No. 13, pp. 4026-4034.

Ishack, S., Mediero, A., Wilder, T., Ricci, J.L. and Cronstein, B.N. (2017), "Bone regeneration in critical bone defects using three-dimensionally printed β-tricalcium phosphate/hydroxyapatite scaffolds is enhanced by coating scaffolds with either dipyridamole or BMP-2", *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 105 No. 2, pp. 366-375.

Jammalamadaka, U. and Tappa, K. (2018), "Recent advances in biomaterials for 3D printing and tissue engineering", *Journal of Functional Biomaterials*, Vol. 9 No. 1, p. 22

Jang, B.S., Cheon, J.Y., Kim, S.H. and Park, W.H. (2018), "Small diameter vascular graft with fibroblast cells and electrospun poly (L-lactide-co-ε-caprolactone) scaffolds: cell matrix engineering", *Journal of Biomaterials Science*, Vol. 29 Nos 7/9, pp. 942-959.

Jayasingh, S.N. (2013), "Cell electrospinning: a novel tool for functionalising fibres, scaffolds and membranes with living cells and other advanced materials for regenerative biology and medicine", *Analyst*, Vol. 138, pp. 2215-2223.

Jiang, Y., Zhou, J., Shi, H., Zhang, Q., Feng, C. and Xv, X. (2020), "Preparation of cellulose nanocrystal/oxidized dextran/gelatin (CNC/OD/GEL) hydrogels and fabrication of a CNC/OD/GEL scaffold by 3D printing", *Journal of Materials Science*, Vol. 55 No. 6, pp. 2618-2635.

Jirman, R., Horák, Z., Mazánek, J. and Reznícek, J. (2009), "Individual replacement of the frontal bone defect: case report", *Prague Med Rep*, Vol. 110 No. 1, pp. 79-84. [PMC]

Kandhasamy, S., Ramanathan, G., Kamalraja, J., Balaji, R., Mathivanan, N., Sivagnanam, U.T. and Perumal, P.T. (2015), "Synthesis, characterization and biological evaluation of chromen and pyrano chromen-5-one derivatives impregnated into a novel collagen based scaffold for tissue engineering applications", *RSC Advances*, Vol. 5 No. 68, pp. 55075-55087.

Karchin, A., Simonovsky, F.I., Ratner, B.D. and Sanders, J. E. (2011), "Melt electrospinning of biodegradable polyurethane scaffolds", *Acta Biomaterialia*, Vol. 7 No. 9, p. 3277.

Kim, B.S., Baez, C.E. and Atala, A. (2000), "Biomaterials for tissue engineering", *World Journal of Urology*, Vol. 18 No. 1, pp. 2-9.

Kirsner, R.S., Falanga, V. and Eaglstein, W.H. (1993), "The biology of skin grafts: skin grafts as pharmacologic agents", *Archives of Dermatology*, Vol. 129 No. 4, pp. 481-483.

Klein, G.T., Lu, Y. and Wang, M.Y. (2013), "3D printing and neurosurgery–ready for prime time?", *World Neurosurgery*, Vol. 80 Nos 3/4, pp. 233-235.

Koch, L., Deiwick, A., Schlie, S., Michael, S., Gruene, M., Coger, V. and Chichkov, B. (2012), "Skin tissue generation by laser cell printing", *Biotechnology and Bioengineering*, Vol. 109 No. 7, pp. 1855-1863.

Koch, L., Kuhn, S., Sorg, H., Gruene, M., Schlie, S., Gaebel, R. and Vogt, P.M. (2009), "Laser printing of skin cells and human stem cells", *Tissue Engineering Part C: Methods*, Vol. 16 No. 5, pp. 847-854.

Kocher, A.A., Schuster, M.D., Szabolcs, M.J., Takuma, S., Burkhoff, D., Wang, J. and Itescu, S. (2001), "Neovascularization of ischemic myocardium by human bone-marrow–derived angioblasts prevents cardiomyocyte

apoptosis, reduces remodeling and improves cardiac function", *Nature Medicine*, Vol. 7 No. 4, pp. 430-436.

Kruth, J.P., Mercelis, P., Van Vaerenbergh, J., Froyen, L. and Rombouts, M. (2005), "Binding mechanisms in selective laser sintering and selective laser melting", *Rapid Prototyping Journal*, Vol. 11 No. 1, pp. 26-36.

Lanza, R., Langer, R., Vacanti, J.P., & Atala, A. (Eds) (2020), *Principles of Tissue Engineering*, Academic press.

Lau, I. and Sun, Z. (2018), "Three-dimensional printing in congenital heart disease: a systematic review", *Journal of Medical Radiation Sciences*, Vol. 65 No. 3, pp. 226-236.

Laumer, T., Stichel, T., Amend, P. and Schmidt, M. (2015), "Simultaneous laser beam melting of multimaterial polymer parts", *Journal of Laser Applications*, Vol. 27 No. S2, p. S29204.

Leberfinger, A.N., Dinda, S., Wu, Y., V., Koduru, S., Ozbolat, V., Ravnic, D.J. and Ozbolat, I.T. (2019), "Bioprinting functional tissues", *Acta Biomaterialia*, Vol. 95, doi: 10.1016/j.actbio.2019.01.009.

Lee, J.Y., An, J. and Chua, C.K. (2017), "Fundamentals and applications of 3D printing for novel materials", *Applied Materials Today*, Vol. 7, pp. 120-133.

Li, C., Yang, M., Xie, Y., Chen, Z., Wang, C., Bai, Y. and Li, M. (2015), "Application of the polystyrene model made by 3DP rapid prototyping technology for operation planning in revision lumbar discectomy", *Journal of Orthopaedic Science*, Vol. 20 No. 3, pp. 475-480.

Li, X., Liu, X., Dong, W., Feng, Q., Cui, F., Uo, M. and Watari, F. (2009), "In vitro evaluation of porous poly (L-lactic acid) scaffold reinforced by chitin fibers", *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 90B No. 2, pp. 503-509.

Lin, H., Zhang, D., Alexander, P.G., Yang, G., Tan, J., Cheng, A.W.M. and Tuan, R.S. (2013), "Application of visible light-based projection stereolithography for live cell-scaffold fabrication with designed architecture", *Biomaterials*, Vol. 34 No. 2, pp. 331-339.

Liu, F.H., Lee, R.T., Lin, W.H. and Liao, Y.S. (2013), "Selective laser sintering of bio-metal scaffold", *Procedia Cirp*, Vol. 5, pp. 83-87.

Liu, F., Vyas, C., Poologasundarampillai, G., Pape, I., Hinduja, S., Mirihanage, W. and Bartolo, P. (2018), "Structural evolution of PCL during melt extrusion 3D printing", *Macromolecular Materials and Engineering*, Vol. 303 No. 2, p. 1700494

Louvrier, A., Marty, P., Barrabé, A., Euvrard, E., Chatelain, B., Weber, E. and Meyer, C. (2017), "How useful is 3D printing in maxillofacial surgery?", *Journal of Stomatology, Oral and Maxillofacial Surgery*, Vol. 118 No. 4, pp. 206-212.

Luo, X. Fry, C.D. and Laub, M.F. (2018), "Method and device for controlling printing zone temperature", United States patent application US 15/278,661.

Lutolf, M.P. and Hubbell, J.A. (2005), "Synthetic biomaterials as instructive extracellular microenvironments for morphogenesis in tissue engineering", *Nature Biotechnology*, Vol. 23 No. 1, p. 47

Mabrouk, M., Beherei, H.H. and Das, D.B. (2020), "Recent progress in the fabrication techniques of 3D scaffolds for tissue engineering", *Materials Science and Engineering: C*, Vol. 110.

Malik, H.H., Darwood, A.R., Shaunak, S., Kulatilake, P., Abdulrahman, A., Mulki, O. and Baskaradas, A. (2015), "Three-dimensional printing in surgery: a review of current surgical applications", *Journal of Surgical Research*, Vol. 199 No. 2, pp. 512-522.

Mammadov, B., Sever, M., Guler, M.O. and Tekinay, A.B. (2013), "Neural differentiation on synthetic scaffold materials", *Biomaterials Science*, Vol. 1 No. 11, pp. 1119-1137.

Michael, S., Sorg, H., Peck, C.T., Koch, L., Deiwick, A., Chichkov, B. and Reimers, K. (2013), "Tissue engineered skin substitutes created by laser-assisted bioprinting form skin-like structures in the dorsal skin fold chamber in mice", *PloS One*, Vol. 8 No. 3, p. e57741.

Mironov, V., Boland, T., Trusk, T., Forgacs, G. and Markwald, R.R. (2003), "Organ printing: computer-aided jet-based 3D tissue engineering", *TRENDS in Biotechnology*, Vol. 21 No. 4, pp. 157-161.

Mironov, V., Kasyanov, V. and Markwald, R.R. (2011), "Organ printing: from bioprinter to organ biofabrication line", *Current Opinion in Biotechnology*, Vol. 22 No. 5, pp. 667-673.

Mironov, A.V., Grigoryev, A.M., Krotova, L.I., Skaletsky, N. N., Popov, V.K. and Sevastianov, V.I. (2017), "3D printing of PLGA scaffolds for tissue engineering", *Journal of Biomedical Materials Research Part A*, Vol. 105 No. 1, pp. 104-109.

Mironov, V., Visconti, R.P., Kasyanov, V., Forgacs, G., Drake, C.J. and Markwald, R.R. (2011), "Organ printing: tissue spheroids as building blocks", *Biomaterials*, Vol. 30 No. 12, pp. 2164-2174.

Mott, E.J., Busso, M., Luo, X., Dolder, C., Wang, M.O., Fisher, J.P. and Dean, D. (2016), "Digital micromirror device (DMD)-based 3D printing of poly (propylene fumarate) scaffolds", *Materials Science and Engineering: C*, Vol. 61, pp. 301-311.

Mu, R., Chen, C., Wang, Y. and Spence, D.M. (2016), "A quantitative, in vitro appraisal of experimental low-glucose storage solutions used for blood banking", *Analytical Methods*, Vol. 8 No. 38, pp. 6856-6864.

Nallamuthu, N., Braden, M. and Patel, M.P. (2006), "Dimensional changes of alginate dental impression materials", *Journal of Materials Science: Materials in Medicine*, Vol. 17 No. 12, pp. 1205-1210.

Nguyen, D., Robbins, J., Crogan-Grundy, C., Gorgen, V., Bangalore, P., Perusse, D., Creasey, O., King, S., Lin, S., Khatiwala, C. and Halberstadt, C. (2015), "Functional characterization of three-dimensional (3d) human liver tissues generated by an automated bioprinting platform", *The FASEB Journal*, Vol. 29, p. 424.

Obregon, F., Vaquette, C., Ivanovski, S., Hutmacher, D.W. and Bertassoni, L.E. (2015), "3D bioprinting for regenerative dentistry and craniofacial tissue engineering", *Journal of Dental Research*, Vol. 94 No. 9, pp. 143S-1452.

O'brien, F.J. (2011), "Biomaterials & scaffolds for tissue engineering", *Materials Today*, Vol. 14 No. 3, pp. 88-95.

Özkol, E., Zhang, W., Ebert, J. and Telle, R. (2012), "Potentials of the "direct inkjet printing" method for

manufacturing 3Y-TZP based dental restorations", *Journal of the European Ceramic Society*, Vol. 32 No. 10, pp. 2193-2201.

Park, C.H., Rios, H.F., Jin, Q., Sugai, J.V., Padial-Molina, M., Taut, A.D. and Giannobile, W.V. (2012), "Tissue engineering bone-ligament complexes using fiber-guiding scaffolds", *Biomaterials*, Vol. 33 No. 1, pp. 137-145.

Pati, F., Shim, J.H., Lee, J.S. and Cho, D.W. (2013), "3D printing of cell-laden constructs for heterogeneous tissue regeneration", *Manufacturing Letters*, Vol. 1 No. 1, pp. 49-53.

Peltola, S.M., Melchels, F.P.W., Grijpma, D.W. and Kellomaki, M. (2008), "A review of rapid prototyping techniques for tissue engineering purposes", *Annals of Medicine*, Vol. 40 No. 4, pp. 268-280.

Pescosolido, L., Schuurman, W., Malda, J., Matricardi, P., Alhaique, F., Coviello, T. and Vermonden, T. (2001), "Hyaluronic acid and dextran-based semi-IPN hydrogels as biomaterials for bioprinting", *Biomacromolecules*, Vol. 12 No. 5, pp. 1831-1838.

Pietrabissa, A., Marconi, S., Peri, A., Pugliese, L., Cavazzi, E., Vinci, A., Botti, M. and Auricchio, F. (2016), "Designing biomaterials for 3D printing", *Surgical Endoscopy*, Vol. 30 No. 1, pp. 366-371.

Polley, C., Distler, T., Rüffer, D., Detsch, R., Boccaccini, A.R. and Seitz, H. (2019), "3D printing of smart materials for bone regeneration", *Materials*, Vol. 13 No. 7, pp. 1-2.

Qu, F., Guilak, F. and Mauck, R.L. (2019), "Cell migration: implications for repair and regeneration in joint disease", *Nature Reviews Rheumatology*, Vol. 15 No. 3, pp. 167-179.

Ramakrishna, S., Mayer, J., Wintermantel, E. and Leong, K. W. (2001), "Biomedical applications of polymer-composite materials: a review", *Composites Science and Technology*, Vol. 61 No. 9, pp. 1189-1224.

Ranganathan, N., Mugeshwaran, A., Bensingh, R.J., Kader, M.A., and Nayak, S.K. (2019), "Biopolymeric scaffolds for tissue engineering application", *Biomedical Engineering and Its Applications in Healthcare*, Springer, pp. 249-274.

Reneker, D.H. and Chun, I. (1996), "Nanometre diameter fibres of polymer, produced by electrospinning", *Nanotechnology*, Vol. 7 No. 3, pp. 216-223.

Richards, D.J., Tan, Y., Jia, J., Yao, H. and Mei, Y. (2013), "3D printing for tissue engineering", *Israel Journal of Chemistry*, Vol. 53, pp. 805-814.

Ripley, B., Kelil, T., Cheezum, M.K., Goncalves, A., Carli, M. F., Rybicki, F.J., Steigner, M., Mitsouras, D. and Blankstein, R. (2016), "3D printing based on cardiac CT assists anatomic visualization prior to transcatheter aortic valve replacement", *Journal of Cardiovascular Computed Tomography*, Vol. 10 No. 1, pp. 28-36.

Ristovski, N., Bock, N., Liao, S., Powell, S.K., Ren, J., Kirby, G.T., Blackwood, K.A. and Woodruff, M.A. (2015), "Improved fabrication of melt electrospun tissue engineering scaffolds using direct writing and advanced electric field control", *Biointerphases*, Vol. 10 No. 1, p. 11006

Robbins, J.B., Gorgen, V., Min, P., Shepherd, B.R. and Presnell, S.C. (2013), "A novel in vitro three-dimensional bioprinted liver tissue system for drug development", *Faseb J*, Vol. 27 No. 872, p. 812.

Robinson, T.M., Hutmacher, D.W. and Dalton, P.D. (2019), "The next frontier in melt electrospinning: taming the jet", *Advanced Functional Materials*, Vol. 29 No. 44, p. 1904664

Rosenzweig, D.H., Carelli, E., Steffen, T., Jarzem, P. and Haglund, L. (2015), "3D-printed ABS and PLA scaffolds for cartilage and nucleus pulposus tissue regeneration", *International Journal of Molecular Sciences*, Vol. 16 No. 12, pp. 15118-15135.

Salaoru, I., Zhou, Z., Morris, P. and Gibbons, G.J. (2017), "Inkjet-printed polyvinyl alcohol multilayers", *Journal of Applied Polymer Science*, Vol. 133, p. e55093

Salmoria, G.V., Ahrens, C.H., Klauss, P., Paggi, R.A., Oliveira, R.G. and Lago, (2007), "A rapid manufacturing of polyethylene parts with controlled pore size gradients using selective laser sintering", *Materials Research*, Vol. 10 No. 2, pp. 211-214.

Salmoria, G.V., Klauss, P., Paggi, R.A., Kanis, L.A. and Lago, A. (2009), "Structure and mechanical properties of cellulose based scaffolds fabricated by selective laser sintering", *Polymer Testing*, Vol. 28 No. 6, pp. 648-652.

Saxena, A.K. (2010), "Tissue engineering and regenerative medicine research perspectives for pediatric surgery", *Pediatric Surgery International*, Vol. 26 No. 6, pp. 557-573.

Schiele, N.R., Corr, D.T., Huang, Y., Raof, N.A., Xie, Y. and Chrisey, D.B. (2010), "Laser-based direct-write techniques for cell printing", *Biofabrication*, Vol. 2 No. 3, p. 032001

Seliktar, D., Dikovsky, D. and Napadensky, E. (2013), "Bioprinting and tissue engineering: recent advances and future perspectives", *Israel Journal of Chemistry*, Vol. 53 No. 9-10, pp. 795-804.

Serra, T., Mateos-Timoneda, M.A., Planell, J.A. and Navarro, M. (2013), "3D printed PLA-based scaffolds: a versatile tool in regenerative medicine", *Organogenesis*, Vol. 9 No. 4, pp. 239-244.

Shirazi, S.F., Gharehkhani, S., Mehrali, M., Yarmand, H., Metselaar, H.S., Kadri, N.A. and Osman, N.A. (2015), "A review on powder-based additive manufacturing for tissue engineering: selective laser sintering and inkjet 3D printing", *Science and Technology of Advanced Materials*, Vol. 16 No. 3, p. 33502.

Shirazi, S.F.S., Gharehkhani, S., Mehrali, M., Yarmand, H., Metselaar, H.S.C., Kadri, N.A. and Abu, N.A. (2015), "A review on powder-based additive manufacturing for tissue engineering: selective laser sintering and inkjet 3D printing", *Science and Technology of Advanced Materials*, Vol. 16 No. 3, p. 033502.

Singh, D., Singh, D. and Han, S.S. (2016), "3D tissue models", *Advances in Skin Tissue Engineering Polymers*, Vol. 8, p. 19.

Singh, S., Ramakrishna, S. and Singh, R. (2017), "Material issues in additive manufacturing: a review", *Journal of Manufacturing Processes*, Vol. 25, pp. 185-200.

Sodian, R., Weber, S., Markert, M., Loeff, M., Lueth, T., Weis, F.C. and Reichart, B. (2008), "Pediatric cardiac transplantation: three-dimensional printing of anatomic models for surgical planning of heart transplantation in patients with univentricular heart", *The Journal of Thoracic and Cardiovascular Surgery*, Vol. 136 No. 4, pp. 1098-1099.

Studart, A.R. (2016), "Additive manufacturing of biologically-inspired materials", *Chemical Society Reviews*, Vol. 45 No. 2, pp. 359-376.

Sudarmadji, N., Tan, J.Y., Leong, K.F., Chua, C.K. and Loh, Y.T. (2011), "Investigation of the mechanical properties and porosity relationships in selective laser-sintered polyhedral for functionally graded scaffolds", *Acta Biomaterialia*, Vol. 7 No. 2, pp. 530-537.

Sun, D.H., Chang, C., Li, S. and Lin, L.W. (2006), "Polymer used in electrospining", *Nano Letters*, Vol. 6 No. 4, pp. 839-842.

Tan, J.Y., Chua, C.K., and Leong, K.F. (2009), "Indirect fabrication of tissue engineering scaffolds using rapid prototyping and a foaming process", *Innovative Developments in Design and Manufacturing*, CRC Press, pp. 69-76.

Tan, J.Y., Chua, C.K. and Leong, K.F. (2013), "Fabrication of channeled scaffolds with ordered array of micro-pores through microsphere leaching and indirect rapid prototyping technique", *Biomedical Microdevices*, Vol. 15 No. 1, pp. 83-96.

Tan, X., Kok, Y., Tan, Y.J., Descoins, M., Mangelinck, D., Tor, S.B. and Chua, C.K. (2015), "Graded microstructure and mechanical properties of additive manufactured Ti–6Al–4V via electron beam melting", *Acta Materialia*, Vol. 97, pp. 1-16.

Tarafder, S., Davies, N.M., Bandyopadhyay, A. and Bose, S. (2013), "3D printed tricalcium phosphate scaffolds: effect of SrO and MgO doping on in vivo osteogenesis in a rat distal femoral defect model", *Biomater Sci*,, Vol. 1 No. 12, pp. 1250-1259.

Tarafder, S., Dernell, W.S., Bandyopadhyay, A. and Bose, S. (2013), "SrO-and MgO-doped microwave sintered 3D printed tricalcium phosphate scaffolds: mechanical properties and in vivo osteogenesis in a rabbit model", *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 103 No. 3, pp. 679-690.

Teo, E.Y., Ong, S.Y., Chong, M.S.K., Zhang, Z., Lu, J., Moochhala, S. and Teoh, S.H. (2011), "Polycaprolactone-based fused deposition modeled mesh for delivery of antibacterial agents to infected wounds", *Biomaterials*, Vol. 32 No. 1, pp. 279-287.

Tirella, A., Vozzi, F., De Maria, C., Vozzi, G., Sandri, T., Sassano, D., Cognolato, L. and Ahluwalia, A. (2011), "Substrate stiffness influences high resolution printing of living cells with an ink-jet system", *Journal of Bioscience and Bioengineering*, Vol. 112 No. 1, pp. 79-85.

Tomanek, R.J. and Runyan, R.B. (Eds) (2012), *Formation of the Heart and Its Regulation*, Springer Science & Business Media.

Tortora, G.J. and Derrickson, B.H. (2008), *Principles of Anatomy and Physiology*, John Wiley & Sons.

Townsend-Nicholson, A. and Jayasinghe, S.N. (2006), "Cell electrospinning: a unique biotechnique for encapsulating living organisms for generating active biological microthreads/scaffolds", *Biomacromolecules*, Vol. 7 No. 12, pp. 3364-3369.

Trachtenberg, J.E., Placone, J.K., Smith, B.T., Piard, C.M., Santoro, M., Scott, D.W. and Mikos, A.G. (2016), "Extrusion-based 3D printing of poly (propylene fumarate) in a full-factorial design", *ACS Biomaterials Science & Engineering*, Vol. 2 No. 10, pp. 1771-1780.

Travitzky, N., Bonet, A., Dermeik, B., Fey, T., Filbert, -Demut, I., Schlier, L. and Greil, P. (2004), "Additive manufacturing of ceramic-based materials", *Advanced Engineering Materials*, Vol. 16 No. 6, pp. 729-754.

Tuan, T.N.A., Abdullah, A.M., Md, A.H., Mohamad, D. and Rajion, Z.A. (2015), "Preparation and characterization of a newly developed polyamide composite utilising an affordable 3D printer", *Journal of Reinforced Plastics and Composites*, Vol. 34 No. 19, pp. 1628-1638.

Tumbleston, J.R., Shirvanyants, D., Ermoshkin, N., Janusziewicz, R., Johnson, A.R., Kelly, D., Chen, K., Pinschmidt, R., Rolland, J.P., Ermoshkin, A., Samulski, E. T. and DeSimone, J.M. (2015), "Continuous liquid interface production of 3D objects", *Science*, Vol. 347 No. 6228, pp. 1349-1352.

Turnbull, G., Clarke, J., Picard, F., Riches, P., Jia, L., Han, F. and Shu, W. (2018), "3D bioactive composite scaffolds for bone tissue engineering", *Bioactive Materials*, Vol. 3 No. 3, pp. 278-314.

Turner, B.N., Strong, R. and Gold, S.A. (2014), "A review of melt extrusion additive manufacturing processes: i. Process design and modeling", *Rapid Prototyping Journal*, Vol. 20 No. 3, pp. 192-204.

Vaithilingam, J., Kilsby, S., Goodridge, R.D., Christie, S.D., Edmondson, S. and Hague, R.J. (2015), "Functionalisation of Ti6Al4V components fabricated using selective laser melting with a bioactive compound", *Materials Science and Engineering: C*, Vol. 46, pp. 52-61.

van Dijk, M., van Nostrum, C.F., Hennink, W.E., Rijkers, D. T. and Liskamp, R.M. (2010), "Synthesis and characterization of enzymatically biodegradable PEG and peptide-based hydrogels prepared by click chemistry", *Biomacromolecules*, Vol. 11 No. 6, pp. 1608-1614.

Vermeulen, M., Claessens, T., Van Der Smissen, B., Van Holsbeke, C.S., De Backer, J.W., Van Ransbeeck, P. and Verdonck, P. (2013), "Manufacturing of patient-specific optically accessible airway models by fused deposition modeling", *Rapid Prototyping Journal*, Vol. 19 No. 5, pp. 312-318.

Vert, M. (2005), "Aliphatic polyesters: great degradable polymers that cannot do everything", *Biomacromolecules*, Vol. 6 No. 2, pp. 538-546.

Wang, D.D., Gheewala, N., Shah, R., Levin, D., Myers, E., Rollet, M. and O'Neill, W.W. (2018), "Three-dimensional printing for planning of structural heart interventions", *Interventional Cardiology Clinics*, Vol. 7 No. 3, pp. 415-423.

Wei, C. and Dong, J.Y.J. (2013), "Durable and scalable icephobic surfaces: similarities and distinctions from superhydrophobic surfaces", *Journal of Micromechanics and Microengineering*, Vol. 23 No. 2, pp. 025017-025030.

Wei, L., Yu, H., Jia, L. and Qin, X. (2018), "High-throughput nanofiber produced by needleless electrospinning using a metal dish as the spinneret", *Textile Research Journal*, Vol. 88 No. 1, pp. 80-88.

Willerth, S.M. and Sakiyama-Elbert, S.E. (2019), "Combining stem cells and biomaterial scaffolds for constructing tissues and cell delivery", *StemJournal*, Vol. 1 No. 1, pp. 1-25.

Witowski, J., Wake, N., Grochowska, A., Sun, Z., Budzyński, A., Major, P., Popiela, T.J. and Pędziwiatr, M. (2019), "Investigating accuracy of 3D printed liver models with computed tomography", *Quantitative Imaging in Medicine and Surgery*, Vol. 9 No. 1, p. 43

Wong, J.Y. (2015), "Ultra-Portable Solar-Powered 3D printers for onsite manufacturing of medical resources", *Aerospace Medicine and Human Performance*, Vol. 86 No. 10, pp. 911-914.

Wu, B.M., Borland, S.W., Giordano, R.A., Cima, L.G., Sachs, E.M. and Cima, M.J. (1999), "Solid free-form fabrication of drug delivery devices", *Journal of Controlled Release*, Vol. 40 No. 1-2, pp. 77-87.

Yamamoto, N., Bryce, N.S., Metzler-Nolte, N. and Hambley, T.W. (2012), "Effects of enzymatic activation on the distribution of fluorescently tagged MMP-2 cleavable peptides in cancer cells and spheroids", *Bioconjugate Chemistry*, Vol. 23 No. 6, pp. 1110-1118.

Yan, Y., Xiong, Z., Hu, Y., Wang, S., Zhang, R. and Zhang, C. (2003), "Layered manufacturing of tissue engineering scaffolds via multi-nozzle deposition", *Materials Letters*, Vol. 57 No. 18, pp. 2623-2628.

Yang, Y., Yang, S., Wang, Y., Yu, Z., Ao, H., Zhang, H. and Tang, T. (2016), "Anti-infective efficacy, cytocompatibility and biocompatibility of a 3D-printed osteoconductive composite scaffold functionalized with quaternized chitosan", *Acta Biomaterialia*, Vol. 46, pp. 112-128.

Yap, C.Y., Chua, C.K., Dong, Z.L., Liu, Z.H., Zhang, D.Q., Loh, L.E. and Sing, S.L. (2015), "Review of selective laser melting: materials and applications", *Applied Physics Reviews*, Vol. 2 No. 4, p. 041101

Yeong, W.Y., Chua, C.K., Leong, K.F., Chandrasekaran, M. and Lee, M.W. (2006), "Indirect fabrication of collagen scaffold based on inkjet printing technique", *Rapid Prototyping Journal*, Vol. 12 No. 4, pp. 229-237.

Yeong, W.Y., Chua, C.K., Leong, K.F., Chandrasekaran, M. and Lee, M.W. (2007), "Comparison of drying methods in the fabrication of collagen scaffold via indirect rapid prototyping", *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 82B No. 1, pp. 260-266.

Yeong, W.Y., Sudarmadji, N., Yu, H.Y., Chua, C.K., Leong, K.F., Venkatraman, S.S., Boey, Y.C.F. and Tan, L.P. (2010), "Porous polycaprolactone scaffold for cardiac tissue engineering fabricated by selective laser sintering", *Acta Biomaterialia*, Vol. 6 No. 6, pp. 2028-2034.

Yoshikawa, M., Sato, R., Higashihara, T., Ogasawara, T., and Kawashima, N.R. (2015), "Realistic electric prosthetic hand created with a 3D printer", *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society*; IEEE Engineering in Medicine and Biology Society, Piscataway, NJ, 2470.

Yoshimoto, H., Shin, Y.M., Terai, H. and Vacanti, J.P. (2003), "A biodegradable nanofiber scaffold by electrospinning and its potential for bone tissue engineering", *Biomaterials*, Vol. 24 No. 12, pp. 2077-2082.

Yu, Y., Zhang, Y., Martin, J.A. and Ozbolat, I.T. (2013), "Evaluation of cell viability and functionality in vessel-like bioprintable cell-laden tubular channels", *Journal of Biomechanical Engineering*, Vol. 135 No. 9, p. 091011

Zein, I., Hutmacher, D.W., Tan, K.C. and Teoh, S.H. (2002), "Fused deposition modeling of novel scaffold architectures for tissue engineering applications", *Biomaterials*, Vol. 23 No. 4, pp. 1169-1185.

Zein, N.N., Hanouneh, I.A., Bishop, P.D., Samaan, M., Eghtesad, B., Quintini, C., Miller, C., Yerian, L. and Klatte, R. (2013), "Three-dimensional print of a liver for preoperative planning in living donor liver transplantation", *Liver Transplantation*, Vol. 19 No. 12, pp. 1304-1310.

Zhai, Y., Galarraga, H. and Lados, D.A. (2015), "Microstructure evolution, tensile properties, and fatigue damage mechanisms in Ti-6Al-4V alloys fabricated by two additive manufacturing techniques", *Procedia Engineering*, Vol. 114, pp. 658-666.

Zhang, Y., Yu, Y., Chen, H. and Ozbolat, I.T. (2013), "Characterization of printable cellular micro-fluidic channels for tissue engineering", *Biofabrication*, Vol. 5 No. 2, p. 025004.

Zhang, S., Chen, Y., Lu, B., Liu, J., Shao, J. and Xu, C. (2016), "Lithographically-generated 3D lamella layers and their structural color", *Nanoscale*, Vol. 8 No. 17, pp. 9118-9127.

Zhang, Y.S., Yue, K., Aleman, J., Mollazadeh-Moghaddam, K., Bakht, S.M., Yang, J. and Dokmeci, M.R. (2017), "3D bioprinting for tissue and organ fabrication", *Annals of Biomedical Engineering*, Vol. 45 No. 1, pp. 148-163.

Zhang, Y.S., Yue, K., Aleman, J., Mollazadeh-Moghaddam, K., Bakht, S.M., Yang, J., Jia, W., Dell'Erba, V., Assawes, P., Shin, S.R. and Dokmeci, M.R. (2017), "3D bioprinting for tissue and organ fabrication", *Annals of Biomedical Engineering*, Vol. 45 No. 1, pp. 148-163.

Zhao, S., Zhu, M., Zhang, J., Zhang, Y., Liu, Z., Zhu, Y. and Zhang, C. (2014), "Three dimensionally printed mesoporous bioactive glass and poly (3-hydroxybutyrate-co-3-hydroxyhexanoate) composite scaffolds for bone regeneration", *Journal of Materials Chemistry B*, Vol. 2 No. 36, pp. 6106-6118.

Zhou, H.J., Green, T.B. and Joo, Y.L. (2006), "The thermal effects on electrospinning of polylactic acid melts", *Polymer*, Vol. 47 No. 21, pp. 7497-7505.

Zhu, Y., Gao, C. and Shen, J. (2002), "Surface modification of polycaprolactone with poly (methacrylic acid) and gelatin covalent immobilization for promoting its cytocompatibility", *Biomaterials*, Vol. 23 No. 24, pp. 4889-4895.

Zocca, A., Colombo, P., Gomes, C.M. and Günster, J. (2015), "Additive manufacturing of ceramics: issues, potentialities, and opportunities", *Journal of the American Ceramic Society*, Vol. 98 No. 7, pp. 1983-2001.

Further reading

Berman, B. (2012), "3DP: the new industrial revolution", *Business Horizons*, Vol. 55 No. 2, pp. 155-162.

Deckard, C.R. Beaman, J.J. and Darrah, J.F. (1992), " Method for selective laser sintering with layerwise cross-scanning", United States patent US 5,155,324.

Dutta, R.T., Simon, J.L., Ricci, J.L., Rekow, E.D., Thompson, V.P. and Parsons, J.R. (2003), "Performance of hydroxyapatite bone repair scaffolds created via three-dimensional fabrication techniques", *Journal of Biomedical Materials Research Part Research*, Vol. 67A No. 4, pp. 1228-1237.

Fedorovich, N.E., Alblas, J., de Wijn, J.R., Hennink, W.E., Verbout, A.J. and Dhert, W.J. (2007), "Hydrogels as extracellular matrices for skeletal tissue engineering: state-of-the-art and novel application in organ printing", *Tissue Engineering*, Vol. 13 No. 8, pp. 1905-1925.

Fisher, B.A., Lane, B., Yeung, H. and Beuth, J. (2018), "Toward determining melt Pool quality metrics via coaxial monitoring in laser powder bed fusion", *Manufacturing Letters*, Vol. 15In-Press.

Gao, G. and Xiaofeng, C. (2016), "Three-dimensional bioprinting in tissue engineering and regenerative medicine", *Biotechnology Letters*, Vol. 38 No. 2, pp. 203-211.

Gonçalves, E.M., Oliveira, F.J., Silva, R.F., Neto, M.A., Fernandes, M.H., Amaral, M. and Vila, M. (2016), "Three-dimensional printed PCL-hydroxyapatite scaffolds filled with CNTs for bone cell growth stimulation", *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 104 No. 6, pp. 1210-1219.

Gullentops, C. and Lenders, R. (2014), "Method for reducing image quality artifacts in three-dimensional printing", *United States Patent US 8*, Vol. 848, p. 233

Ho, G.W. and Matinlinna, J.P. (2011), "Insights on ceramics as dental materials. Part I: ceramic material types in dentistry", *Silicon*, Vol. 3 No. 3, pp. 109-115.

Hollister, S.J. (2005), "Porous scaffold design for tissue engineering", *Nature Materials*, Vol. 4 No. 7, p. 518.

Hull, C.W. (1986), "Apparatus for production of three-dimensional objects by stereolithography", United States patent US 4,575,330.

Hutmacher, D.W. and Dalton, P.D. (2011), "Melt electrospinning", *Chemistry - an Asian Journal*, Vol. 6 No. 1, pp. 44-56.

Igami, T., Nakamura, Y., Oda, M., Tanaka, H., Nojiri, M., Ebata, T., Yokoyama, Y., Sugawara, G., Mizuno, T., Yamaguchi, J. and Mori, K. (2018), "Application of three-dimensional print in minor hepatectomy following liver partition between anterior and posterior sectors", *ANZ Journal of Surgery*, Vol. 88 No. 9, pp. 882-885.

Jang, J. Huang, W.C. and Jang, B.Z. (2000), "3-D color model making apparatus and process", United States patent US 6, 165, p. 406.

Juskova, P., Ollitrault, A., Serra, M., Viovy, J.L. and Malaquin, L. (2018), "Resolution improvement of 3D stereo-lithography through the direct laser trajectory programming: application to microfluidic deterministic lateral displacement device", *Analytica Chimica Acta*, Vol. 1000, pp. 239-247.

Kalita, S.J. (2010), "Rapid prototyping in biomedical engineering: structural intricacies of biological materials", in *Biointegration of Medical Implant Materials*, Sharma, C.P. (Ed), Woodhead Publishing, pp. 349-397, doi: 10.1533/9781845699802.3.349.

Kotikian, A., Truby, R.L., Boley, J.W., White, T.J. and Lewis, J.A. (2018), "3D printing of liquid crystal elastomeric actuators with spatially programed nematic order", *Advanced Materials*, Vol. 30 No. 10.

Lannutti, J., Reneker, D., Ma, T., Tomasko, D. and Farson, D. (2007), "Electrospinning for tissue engineering scaffolds", *Materials Science and Engineering: C*, Vol. 27 No. 3, p. 504

Leberfinger, A.N., Hospodiuk, M., Pena-Francesch, A., Ayan, B., Ozbolat, V., Koduru, S.V., Ozbolat, I.T., Demirel, M.C. and Ravnic, D.J. (2018), "Squid ring teeth-coated mesh improves abdominal wall repair. Plastic and reconstructive", *Surgery Global Open.*, Vol. 6 No. 8, p. e1881.

Le Duigou, A., Castro, M., Bevan, R. and Martin, N. (2016), "3D printing of wood fibre biocomposites: from mechanical to actuation functionality", *Materials & Design*, Vol. 96, pp. 106-114.

Li, W.L., Liao, H., Douchy, G. and Coddet, C. (2007), "Optimal design of a cold spray nozzle by numerical analysis of particle velocity and experimental validation with 316L stainless steel powder", *Materials & Design*, Vol. 28 No. 7, pp. 2129-2137.

Liang, D., Hsiao, B. and Chu, B. (2007), "Functional electrospun nanofibrous scaffolds for biomedical applications", *Advanced Drug Delivery Reviews*, Vol. 59 No. 14, p. 1392

Lin, S. Bhattacharyya, D. Fakirov, S. and Matthews, B. (2009), "Cornish 18th international conference on composite materials", Edinburgh.

Liu, X. and Ma, P.X. (2004), "Polymeric scaffolds for bone tissue engineering", *Annals of Biomedical Engineering*, Vol. 32 No. 3, pp. 477-486.

Mazzoli, A. (2013), "Selective laser sintering in biomedical engineering", *Medical & Biological Engineering & Computing*, Vol. 51 No. 3, pp. 2452-256.

Melchels, F.P., Feijen, J. and Grijpma, D.W. (2010), "A review on stereolithography and its applications in biomedical engineering", *Biomaterials*, Vol. 31 No. 24, pp. 6121-6130.

Muerza-Cascante, M.L., Haylock, D., Hutmacher, D.W. and Dalton, P.D. "Melt electrospinning and its technologization in tissue engineering", *Tissue Engineering Part B: Reviews*, Vol. 21 No. 2, pp. 187-202.

Ozbolat, I.T. and Yu, Y. (2013), "Bioprinting toward organ fabrication: challenges and future trends", *IEEE Transactions on Biomedical Engineering*, Vol. 60, pp. 691-699.

Park, K.M. and Gerecht, S. (2015), "Polymeric hydrogels as artificial extracellular microenvironments for cancer research", *European Polymer Journal*, Vol. 72, pp. 507-513.

Pereira, T.F., Oliveira, M.F., Maia, I.A., Silva, J.V., Costa, M.F. and Thiré, R.M. (2012), "3D printing of poly (3-hydroxybutyrate) porous structures using selective laser sintering", *Macromolecular Symposia*, Vol. 319 No. 1, pp. 64-73.

Sachs, E.M. Haggerty, J.S. Cima, M.J. and Amd Williams, P. A. (1993), "Three-dimensional printing techniques", United States patent US 5,204,055.

Shishkovsky, I., Missemer, F. and Smurov, I. (2018), "Metal matrix composites with ternary intermetallic inclusions fabricated by laser direct energy deposition", *Composite Structures*, Vol. 183, pp. 663-670.

Sun, H., Jia, Y., Dong, H., Dong, D. and Zheng, J. (2020), "Combining additive manufacturing with microfluidics: an emerging method for developing novel organs-on-chips", *Current Opinion in Chemical Engineering*, Vol. 28, pp. 1-9.

Tseng, P., Murray, C., Kim, D. and Di Carlo, D. (2014), "Research highlights: printing the future of microfabrication", *Lab on a Chip*, Vol. 14 No. 9, pp. 1491-1495.

Van Landuyt, P., Li, F., Keustermans, J.P., Streydio, J.M., Delannay, F. and Munting, E. (1995), "The influence of high sintering temperatures on the mechanical properties of hydroxylapatite", *Journal of Materials Science: Materials in Medicine*, Vol. 6 No. 1, pp. 8-13.

Wendel, B., Rietzel, D., Kühnlein, F., Feulner, R., Hülder, G. and Schmachtenberg, E. (2008), "Additive processing of polymers", *Macromolecular Materials and Engineering*, Vol. 293 No. 10, pp. 799-809.

Weng, Z., Wang, J., Senthil, T. and Wu, L. (2016), "Mechanical and thermal properties of ABS/montmorillonitenanocomposites for fused deposition modeling 3D printing", *Materials & Design*, Vol. 102, pp. 276-283.

Xu, T., Binder, K.W., Albanna, M.Z., Dice, D., Zhao, W., Yoo, J.J. and Atala, A. (2012), "Hybrid printing of mechanically and biologically improved constructs for cartilage tissue engineering applications", *Biofabrication*, Vol. 5 No. 1, p. 015001

Yan, Y., Wang, X., Pan, Y., Liu, H., Cheng, J., Xiong, Z. and Lu, Q. (2005), "Fabrication of viable tissue-engineered constructs with 3D cell-assembly technique", *Biomaterials*, Vol. 26 No. 29, pp. 5864-5871.

Zhao, P., Gu, H., Mi, H., Rao, C., Fu, J. and Turng, L.S. (2018), "Fabrication of scaffolds in tissue engineering: a review", *Frontiers of Mechanical Engineering*, Vol. 13 No. 1, pp. 107-119.

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