International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

Vol. 37 No. 2 March 2023, pp. 188-212

3d Bioprinting In Bone And Cartilage Regeneration Review

Maged Naser[1], Mohamed M. Naser[2], Lamia H. Shehata[3]

[1]Mazahmiya Hospital, Ministry of Health, Kingdom of Saudi Arabia,

[2]Department of Ob/Gyn, King Fahd Hospital, Ministry of Health, Kingdom of Saudi Arabia,

[3]Department of Surgery, Consultant Endoscopic Surgery, Department of Radiology, Care National Hospital, KSA

Abstract – Bone and articular cartilage degeneration and damage are the most common causes of musculoskeletal disability. 3D bioprinting can help regenerate these structures. Autologous/allogeneic bone and cartilage transplantation, vascularized bone transplantation, autologous chondrocyte implantation, mosaicplasty, and joint replacement are all common clinical and surgical procedures. In vitro layer-by-layer printing of biological materials, living cells, and other biologically active substances using 3D bio printing technology is anticipated to replace the aforementioned repair methods. With the ability to prepare various organs and tissue structures, 3D bio printing has largely solved the issue of insufficient organ donors. Researchers use biomedical materials and cells as discrete materials. Bioprinting cell selection and its use in bone and cartilage repair are the primary topics of discussion in this paper.

Keywords – biomaterial, bioprinting, cartilage, bone, regeneration.

I. INTRODUCTION

Bone and articular cartilage degeneration and damage are the most common causes of musculoskeletal impairment [1,2,3] Articular cartilage is a type of hyaline cartilage that is rich in type II collagen and proteoglycan. It is necessary for joint activities because it carries mechanical loads and lubricates joints. Articular cartilage, in contrast to the majority of tissues, lacks blood vessels, nerves, or immune responses. Its ability to self-repair after degeneration or injury is limited within its tissue structure [1]. The majority of large-scale damage to bone and cartilage that results from trauma, disease, or tumor resection exceeds the bone's capacity for self-healing and necessitates surgical repair and reconstruction. Autologous/allogeneic bone and cartilage transplantation, vascularized bone transplantation, autologous chondrocyte implantation, mosaicplasty, and joint replacement are all common clinical and surgical procedures[4].Inadequate tissue in the donor site, additional surgical damage, and disease transmission are issues with the aforementioned bone and cartilage transplantation repair methods. The prosthesis is expensive, and joint replacement is only suitable for advanced cartilage degeneration. In vitro layer-by-layer printing of biological materials, living cells, and other biologically active substances using 3D bio printing technology is anticipated to replace the aforementioned repair methods. Due to its unique advantages, 3D printing technology plays a significant role in the biomedical field [5]. Biomedical materials and cells are used by researchers as distinguished materials. With the ability to prepare various organs and tissue structures, 3D bio printing has largely solved the issue of insufficient organ donors [5,6,7, 8].

The development of 3D printing technology offers a solution for treating patients with complex bone defects, particularly in the use of bones and bone scaffolds. Indeed, a highlight of modern medicine will be the intersection of biomedicine and 3D printing technology. To replace damaged tissue, tissue engineering aims to create natural-looking, three-dimensional, porous composite scaffolds for cell migration, adhesion, and growth [9]. The distribution and movement of cells within a traditional tissue engineering scaffold cannot be precisely controlled, limiting the ability of the cells seeded therein to attach only to the scaffold's surface l10]. In regenerative medicine, 3D bio printing technology has advanced rapidly over the past ten years. Through customized additive manufacturing, this technology can simultaneously combine living cells, extracellular matrix, and

Corresponding Author: Maged Naser

other biomaterials to construct complex biological tissues or 3D artificial implants. 3D bio printing technologies include laser-assisted bioprinting, extrusion bioprinting, and inkjet bioprinting/droplet bioprinting. The ability to print scaffolds with controlled cell distribution, which aids in cartilage tissue regeneration, is the primary advantage of 3D bio printing in bone and cartilage tissue engineering. The selection of printing materials also plays a crucial role, in addition to the limitations of its technology in the application process [11,12, 13,14].

Metal, inorganic non-metallic materials, and polymer materials are currently utilized in 3D printing natural bones and bone scaffolds. Polymer materials are among them, and they are frequently used to make a variety of organizational engineering alloys. Polymer materials, in contrast to ceramics and metal, are extremely adaptable to design because their structure and composition can be altered to meet specific requirements. Polymer materials can have the characteristics of hydrolysed or enzymatic dismissal through molecular design, which is better suited to its metabolism in the body. Side chain decoration can also be used to carry out biologically active factors, drugs, or proteins, enhancing the polymer biomaterial's capacity for tissue regeneration. There are two types of polymers that are frequently used: synthetic polymer and natural polymer. Hyaluronic acid, gum, alginate, shell polycation, and collagen are examples of natural polymers. These polymers are made from natural tissue polymers. Polylactic-co-glycolic acid (PLGA), polyethylene acrylic (PMMA), polyethylene glycol (PEG), and other artificial synthetic polymers are examples of synthetic polymers. Polymer materials are typically produced using biologically squeezed 3D printing methods. It is simple to make hydrogel biological ink from natural or partially synthetic polymer materials. Biocompatibility and hydrophilicity are comparable to those of biological tissue. A stable three-dimensional structure can be created by adjusting the mechanical properties. The majority of biological inks that have been reported are mostly used in vitro in a gas phase environment. It is possible that only a specific liquid-phase solvent can be used for liquid-phase suspended 3D printing, even if it is currently being studied. The biomaterial's actual application environment contains complex ingredients. Different properties and functions will be produced by various printed biomaterial cells and components. The selection of polymer materials, biological printing cells, and their use in the repair of bone and cartilage are the primary subjects of this review. This review explains in detail the characteristics of each component used to develop and implement 3D printing applications for biological bone and cartilage issues.

1. Natural polymer materials

1.1 Collagen

Collagen is the most significant structural protein in human tissue and an essential component of the extracellular matrix, which is the primary component of the cartilage matrix. Due to their weak antigenicity, degradability, excellent biocompatibility, and biomimetic functions, collagen molecules have been widely used in biomedical applications [15,16]. Cells are supported and protected by the scaffold made with collagen as a raw material [17, 18]. However, collagen has a number of drawbacks as well, including a lack of a melting point, a low denaturation temperature, insoluble water, high viscosity, low mechanical stability, rapid degradation, inadequate mechanical strength, and so on. Compounding collagen with other materials is the most common method for addressing these deficiencies.[19] proposed producing 3D printable cell-laden hydrogels by in situ mineralizing blue shark (PG) collagen. The biological performance of the hydrogels showed that the presence of PG collagen helped mouse fibroblast cell line survival both during and after printing. [20] used laser irradiation of the hydrogel to rearrange the collagen fibres to create cavitation gas bubbles and stable microchannels. Organs on a chip and 3D tissue models with intricate structures are made possible by it. [21] came up with a biomimetic micro-fibrous system that could make straight and waveform collagen-based microfibers to help PDL (Population doubling level) cells grow. PDL cell viability was preserved and the tendency to promote healing and regeneration under shear stress was enhanced by waveform microfibers made from 3D-printed collagen. [22] created a 3D bio printed multilayer scaffold filled with bone marrow-derived mesenchymal stem cells (BMSCs) and ketogenic and -TCP (tricalcium phosphate) for each region of osteochondral defect repair. In osteochondral defects of the femoral trochlea, BMSC-laden scaffolds promoted chondrogenesis by suppressing interleukin 1 and promoting collagen II. BMSC-loaded scaffolds significantly improved the injured leg's joint function in terms of the ground support force, paw grip force, and walk gait parameters [23].

1.2 Sodium alginate

Alginate is a characteristic polysaccharide compound extricated from seaweed [24]. It has amazing bond, great biocompatibility, and biodegradability unrivalled by different materials [25,26]. Salt has been generally utilized and created in the

field of biomedicine [27]. Animal tests have shown that high-virtue sodium alginate has great biocompatibility, and no insusceptible dismissal happens when embedded in animals [28,29,30]. Heo et al. [31], incorporated and saved carbohydrazide-changed gelatine (Gel-CDH) into a new multifunctional support bath comprising of gelatine microparticles suspended in an oxidized alginate (OAlg) solution. They offered a clever technique for bioprinting of regular polymer-based hydrogels into 3D complex-moulded biomimetic builds. With different systems, 3D-printed alginate platforms were covered by branch polyethyleneimine to get branch with an enormous number of dynamic N-H gatherings [32,33]. To actuate quick gelation, alginate subordinates were integrated and blended in with silk fibroin. It uncovered improved cell similarity [34]. Besides with silk fibroin, carbon nanotubes were produced into tube shaped frameworks through the coordinated effort to manufacture the crossbreed bio ink with alginate. Checked by mouse models, the legitimate doping of carbon nanotubes could actually expand the mechanical properties of composite scaffolds.

1.3 Chitosan

Chitosan is a sort of organic material with bountiful assets and brilliant execution, non-harmful, biocompatibility, and biodegradability [35,36]. An ideal extracellular lattice material can advance different tissue — cell attachment and expansion [36]. Chitosan has natural action, which can advance the development of vascular endothelium, and the expansion of keratinocytes and osteoblasts, and furthermore has the properties of mitigating, antibacterial, and safe capability guideline. Chitosan has been utilized as a development factor transporter and platform material in the skin, nerve, bone and ligament, and liver tissue designing and can likewise be utilized as wound dressings, drug discharge agents, and defect fillers [38, 39,40]. Be that as it may, scaffolds arranged from pure chitosan additionally have inadequacies, like poor mechanical properties and absence of material surface particularity [35,38]. In this way, when chitosan is utilized in bone tissue designing, it is normally compounded with different materials to accomplish the expected presentation necessities [41,42,43]. [44] designed and created a 3D composite platform with cellulose nanofibrils (TCNFs), chitosan, and casein. This framework can speed up blood clotting and wound recuperating, recommending its expected application in diminishing blood loss during traumatic haemorrhage. Alginate, chitosan, gellan gum, gelatine, and collagen hydrogels were used effectively as core materials-hydrogels which are excessively delicate for 3D plotting of open-permeable designs without an extra mechanical help [45].Although chitosan is plentiful in nature, has brilliant properties, and is harmless to the ecosystem, its mechanical properties are poor, which restricts its use of chitosan. Chitosan has moderately dynamic free extreme gatherings and is generally dynamic [46,47,48,49]. It can likewise be adjusted by chemical reagents to plan comparing composite materials, further growing the chitosan application field [50,51,52].Combining the items in normal and manufactured polymers, itis quite easy to find that polymer materials for organic tissue designing ought to meet the accompanying necessities: 1) Great biocompatibility; 2) Controllable degradability; 3) Mechanical property; 4) Self-development execution and 5) Great cleansing [43].

1.4 Silk fibroin

Silk fibroin is regular macromolecular fibrin with great physical and synthetic properties [34, 53]. Silk fibroin enjoys the accompanying benefits: great biocompatibility, non-poisonousness, biodegradability, no harmful and results of degradation items, slow degradation rate in vivo, and its degradation rate can be changed by changing its primary structure [32,54,55]. Due to its exceptional and brilliant properties, silk fibroin has shown extraordinary application possibilities in biomedicine [32,53,56,57]. However, silk fibroin has lacking mechanical properties. The alteration of silk fibroin by intensifying it with different materials can further develop silk fibroin. Silk fibroin-gelatine (G)- based hydrogel was manufactured as an analytic model to predict the expelled fibre width to augment the printed construction's constancy to the plan. In this review, with gelatine mixed with silk fibroin, hydrogel uncovered capacity to accomplish more controlled and standardized items than old style experimentation approaches in the bio creation of designed constructs [58]. In another review, a kind of three-layered collagen/silk fibroin framework (3D-CF) was created with holes that re-enact the anatomy of ordinary spinal line. With transplantation of brain stem cells (NSCs),3D-CF joined with NSCs can advance the maintenance of harmed spinal cord [59]. In one more fascinating story books with various groupings of silk fibroin and decellularized extracellular matrix (SF-dECM) was ready and mixed with bone marrow mesenchymal stem cells (BMSCs) for 3D bioprinting. With delivering TGF-β3, the SFdECM had the capacity to advance chondrogenic separation ofBMSCs and gave a good ligament fix environment, recommending it is an ideal framework for ligament tissue engineering [60].

1.5 Hyaluronic acid

Hyaluronic acid was first isolated from the ox eye glassy in 1934, and its construction was proposed in 1970 [61]. Hyaluronic acid is plentiful in the extracellular matrix of the human embryo and connective tissues. It likewise exists in a significant amount to assume a part in nourishment, lubrication, and shock absorption on joints [62]. Hyaluronic acid has special physical-chemical properties and great biocompatibility, biological activity, and natural degradability. Its three-layered honeycomb structure pore rate is high, and adequate inward space and surface area conducive to attachment, expansion, and seed cell differentiation [61]. Hyaluronic acid can be joined with CD44. By hindering the expression of interleukin 1β, causing matrix metal prop (MATRIX Metalloproteire-1, MMP-1), MMP-2, MMP-3, MMP-9, andMMP-13 Synthesis diminishes, lessen the activity of alien enzyme in arthritis, and advance the multiplication of cartilage cells while bringing down the apoptosis of cartilage cells and protecting cartilage [63]. Studies have shown that the brackets with hyaluronic acid as the material has apparent bone induction effects during the cartilage repair process, which can essentially advance the maintenance of deformities. It has expansive application possibilities in the field of tissue engineering cartilage repair [64]. Since natural hyaluronic acid is as yet deficient in biocompatibility, biodegradation, mechanical strength, and host integration, it can't meet the prerequisites of superb cartilage repair in organizational engineering. Kim et al. [65], revealed a water-based polyurethane bunch section with hyaluronic acid as a transporter. This bracket is a bracket that is extremely near joint cartilage. Simultaneously, 3D printing innovation can be intended to match the three-layered design of the bracket to match the matching. The state of the ligament deformity gives the best way to repair and reproduce the cartilage tissue. Martyniak et al. [66], proposed the bionic cartoon of the bionic cartilage cells of the emulsion and parts of hyaluronic acid.

Adding super smooth magnetic iron oxide nanoparticles to the further shell shows great cell direction capacities and actuated to initiate it. The two physical stimuli of the static magnetic field and magnetics hear pressure sped up the recovery of cartilage cells. Dynamic useful groups like carboxyl, hydroxyl, and acetylamino in hyaluronic acid molecules can plan new brackets by shaping hydrogen bonds and different polymers by shaping hydrogen bonds [67]. Point anion polysaccharide, so hyaluronic acid can be combined with static power with cation polymers, which is one more standard technique for accomplishing hyaluronic acid composite change. As of late, an electric turning nasoscope has been widely concentrated as a bracket material that advances cell biological activity since it re-enacts collagen nano-fibre networks in an extracellular matrix [65].Wang et al.[67] incorporates 3D-printed islet organoid by joining a pancreatic extracellular framework (pECM) and hyaluronic acid methacrylate (HAMA). After research, the pre-arranged brackets have no cytotoxicity, which can advance the grip, dispersion, and multiplication of seed cells. The above polymers show a huge collaboration in managing cartilage arrangement. An assortment of polymer union bracket scan has greater selectivity in the requirements of their spatial construction, physical and substance properties. Wang et al. [68] fosters a double component situated permeable design of bionic cartilage. Made of sugar and sodium hyaluronate, ready by collagen, chitosan, and sequin protein, the change layer of the microtubule exhibit structure is prepared. Polyinine-sodium nanometre of heparin-sodium nanometre containing change development factor β1, filtering electron microscopy shows that the two-fold layer composite bracket has a double plan like regular cartilage. Simultaneously, expansion and separation, neonatal ligament tissue, and encompassing tissue have accomplished great combination, and the shape is equivalent to natural cartilage. Potyondy et al. [69] incorporates a three-stage hydrogel of collagen, condensate, and hyaluronic acid and afterward involves rabbit' autologous cartilage cells for cartilage deformity repair. Cell activity analysis and in vitro biochemical appraisal show that cartilage cells in hyaluronic acid three-stage water express cell expansion, and the declaration of glucosamine discharge and cartilage contrasts in gel brackets are fundamentally higher than in ordinary gel.

2. Manufactured polymer materials

2.1 Polyetheretherketone

Polyetheretherketone enjoys the benefits of radiation porousness and artefacts in magnetic resonance scanning, which can more readily assess postoperative recuperation [70,71]. It has been utilized in artificial joint jaws, skulls, and spines: lumbar spine, oral imperfection fix, and other fields [72,73,74]. Additionally, contrasted and conventional metal materials (stainless steel, titanium alloy) implanted into human body, polyetheretherketone has great biocompatibility, and its elastic modulus is comparable to human cortical bone [72,73]. It can really diminish the stress shielding impact after implantation into the human body. Polyetheretherketone has turned into the most encouraging artificial bone matrix composite material because of its excellent properties [75]. Clinical polyetheretherketone is the best long-term bone graft material guaranteed by the US Food and Medication Organization. Polyetheretherketone likewise has a few inconveniences, for example, no biological activity, low

surface osteogenic efficiency [76]. The extra biomaterials into Look like calcium hydroxyapatite (cHAp) are successful ways of further developing bone implant interfaces and osseointegration.

The Look/cHAp induced the development of apatite after immersion in the re-enacted body liquid of DMEM for various days to actually look at its organic bioactivity for an implant [77]. In another review, novel amorphous magnesium phosphate [78] particles were mixed into PEEK to foster bioactive and Osseo integrable dental and muscular inserts. AMP-Look composites are great possibility for 3D printing by showing high zero-shear and low endless shear viscosities [75]. Another promising composite is Look HA. Here Look platforms with a progression of hydroxyapatite (HA) contents in slope were made through combined fibre manufacture (FFF) 3D printing methods. Novel frameworks displayed higher Young's modulus and lower compressive strength along Z printing course. The planning relationship among geometric boundaries, HA content, printing bearing, and mechanical properties was laid out, which gave more precise expectations and controllability of the modulus and strength of platforms. The PEEK/HA platforms with the miniature organized surface can advance cell attachment and mineralization in vitro [79]. The composite of polyetheretherketone and inorganic non-metallic materials can work on the physical and chemical properties of artificial bone and artificial bone frameworks and work with the spreading, bond, and development of bone cells [75,77,80].Therefore, the composite of polyetheretherketone and inorganic materials in future improvement will turn into another heading [30, 81,82,83].

2.2 Polylactic acid

Polylactic acid (PLA) is an aliphatic polyester, which can be separated from sustainable plant assets, (for example, corn and potato).Starch in sustainable assets is utilized as natural substance to acquire lactic acid through biological fermentation and following monomer polymerization [84,85].Polylactic acid can be changed over into carbon dioxide and water in both nature and living organisms and is a genuinely harmless to the ecosystem new biodegradable material . The fundamental justification for why polylactic acid can be utilized as a 3printing material is that it has great biocompatibility, sparkle and straightforwardness, mechanical properties, degradability, low softening point, and low thickness [86,87]. While it has imperfections like more noteworthy weakness and unfortunate effect resistance [88].

A progression of multi-zonal and gradient structures was created with bi-phasic and tri-phasic setups. Polylactic acid (PLA) was utilized for the manufacture ozonal/angle frameworks to give mechanical strength. It uncovered primary ordered progression and mechanical strength for bone-cartilage interface engineering [89]. Moreover, an exceptionally permeable framework with physical shape qualities was manufactured with polylactic acid polymer (PLA)and PLA-hydroxyapatite (HA). The HA-integrated platforms showed essentially higher compressive strength, modulus, and osteo-inductivity as proven by more elevated levels of soluble phosphatase movement and calcium deposition [90]. PLA polymer struts on a nanofiber web to create anisosporous channel with a various levelled structure and transparent look. The transparent look conquers the undermining appearance of the masks which can be a possible approach to decreasing the social injury brought about by the flow CoVdisease-19 pandemic [91]. Three gellan gum join poly (d, l-lactide-co-glycolide) copolymers (GGm-PLGA) which varied in the join replacement degree were orchestrated and described. It uncovered that fibroblasts and chondrocytes stayed feasible in the wake of printing and over a culture time of 7 days into platforms [92]. From studies to clinical applications, twenty patients were assessed for the overall materialness and conceivable advantage of PLA in the immobilization of hand surgery patients. It proposed that 3D printed splinting is possible and satisficed in clinical applications [93].

2.3 Polycaprolactone

Polycaprolactone (PCL) is a biodegradable polyester with great biocompatibility and non-harmfulness [94]. As a biodegradable clinical material, it is generally utilized in the clinical field. Processability and great mechanical properties, high crystallinity and low softening point, excellent rheological properties, and viscoelasticity invest it with great dissolve printing capacity [95,96]. Polycaprolactone additionally can store and re-establish twisting, It can adjust to the fast improvement of 3D printing innovation, is reasonable for making tissue engineering platforms, and turns into a typical material for biological 3D printing [97,98].Microstructural frameworks planned with polycaprolactone as unrefined components can offer underlying help and transport channels to incite tissue recovery [74]. They can likewise act as sites for cell adhesion, proliferation, and differentiation, giving a reasonable actual climate to recently framed tissues. Nonetheless, polycaprolactone platforms additionally have weaknesses like unfortunate attachment. Scientists worked on the performance of frameworks by mixing polycaprolactone with different materials. For instance, PCL/HA was manufactured by 3D printing innovation [99]. The surface treatment of the

PCL platform with HA led to an improvement in cell adhesion [100]. A bioprinting methodology to design vascularized tissues was created with PCL. The ability to improve the vascularization and recovery of large bone deformities in vivo was upgraded with co-bio printed containing both HUVECs and hBMSCs [101]. In another review, 3D bioprinting was applied with HUVECs and supporting hBMSCs in the creation for expected remaking [102].

2.4 Polyamide

Polyamide, ordinarily known as nylon, is a typical clinical polymer with high extremity and shows brilliant properties with regards to biocompatibility [103].The polyamide 66/nano-hydroxyapatite composite material consolidates the superb properties of the two materials, has great mechanical properties, and has the biological activity of hydroxyapatite, which has extraordinary expected in the treatment of bone deformities by 3D printing [104]. Poltorak et al. [105] planned and 3D printed a polyamide-based electrochemical cell with polyamide that was utilized as the fluid connection point support during electroanalytical estimations. Switchable, photochromic tungsten oxide nanoparticles, which are colourless even at high concentrations was planned as intertwining agents for polyamide powders in frittage-based 3D printing [106]. Thermoplastic polyurethane (TPU) and Polyamide 11 (PA11) powder was led in the 3D printing cycle of Multi Stream Combination (MJF) [107]. Besides, a polyamide 12-based thermoplastic composite was changed with carbon nanotubes (CNTs), CNTs united onto cleaved carbon filaments (CFs), and graphene nanoplatelets (GNPs) with CNTs to work on its warm conductivity for applications an intensity sinks in electronic parts [108].

2.5 Polylactic acid glycolic acid copolymer

The polylactic acid glycolic acid copolymer is broadly utilized in medication, science, industry, and different fields due to its non-toxic and great biological activity, biocompatibility, and mechanical properties [109,110]. The polylactic acid glycolic acid copolymer can be degraded by breaking the ester bond, and its degradation items are equivalent to those of human metabolism [111]. This strategy has been broadly utilized in the biomedical field by changing the monomer proportion to change the degradation time of PLA-glycolic acid copolymer. The Food and Medication Organization in the US has affirmed the polylactic acid glycolic acid copolymer. It is formally remembered for the US Pharmacopeia as a pharmaceutical excipient [108,112] however its degradation item will produce acid that might cause the potential inflammation [113]. In cancer treatment, imaginative PLGA/Mg permeable frameworks were manufactured for postsurgical the executives of osteosarcoma. PLGA/Mg composite platforms were created with low temperature fast prototyping (LT-RP) 3D-printing technology. It uncovered excellent biodegradability and biocompatibility, showing extraordinary commitment for clinical interpretation [114].

2.6 Conductive polymers

The conductive materials normally imprinted in 3D are made in view of non-metallic 3D printing innovation on the thin film base. The suitable 3Dprinting innovation, scattered fluid or conductive elastic composite material of the conductive filler, could be picked for the adaptable base to get the circuit design and the expected conductive material and device [115]. The 3D printing innovation associated with the assembling of conductive materials basically incorporates melting deposition (FDM), electric field-driven spray deposition (E-JET), polymer infusion forming (Polyjet), direct ink writing (DIW), stereo light carvings (SLA) [115,116,117]. As per the attributes of the material, the proper 3D printing innovation can be chosen to make the conductive material. SLA and Polyjet are reasonable for optical solid restored resin materials. FDM is great for materials that squeezes out the small nozzle in the wake of warming and dissolving [116]. Polyjet, E-Stream, and DIW Necessity materials have the evolving qualities of shear and weaken. Low viscosity ought to be displayed at a high shear rate, similar to fluid, to permit the ink to just barely get through the point by point printing spout. Furthermore, printing ink also needs to have high viscosity, showing a paste at a low shear rate to keep the shape after 3D printing without breakdown [118].

Joined with the E-Fly printing innovation and hybrid hot pressure innovation, Zamboni, F., proposed an inserted silver network producing innovation with no shape, format free, and electroplating [119]. An adaptable transparent electrode with brilliant photograph electric execution, mechanical stability, and environmental adaptability are ready on the customizable transparent base. The transparent electrode with transparent light is amazing [120]. Albeit these standard 3D printing cycles can accomplish higher-accuracy design terminals and microstructure printing, this kind of conductive material in light of the highlight line handling technique isn't just lacking in efficiency. The handling precision is connected with the measurement of the nozzle of the expulsion material, so the higher the printing exactness, the slower the printing speed. Conversely , digital light treatment (DLP) printing shows the upsides of high printing exactness, quick relative speed, and superior surface quality, which gives high

execution conductive material and devices for assembling negative perpopy pine proportion ,complicated geometric shapes, and miniature surface structures[120].The hybrid printed biomass proposed by Professor MauriceN. Collins comprises of algosate and gelatine hydrogel framework containing carbon nanofiber (CNF) to make an electrons and printed 3D brackets [121]. It is vital that the arrangement strategy permits the development of hydrogels with uniform scattering CNF. In view of mechanical, chemical, and cell responses, these hybrid composite material hydrogels were assessed. The doping technique can add electrical fillers to conductive capability through physical or chemical processes [121]. Mixed carboxy-based multiwall carbon nanotubes (C-MWCNTS) to N-acrylceroprid (ACMO) gum can acquire great conductive nano-composite materials for DLP printing and strain sensors, which can be in real time and accurate detection human activity [122].

2.7 Photosensitive resin

Photosensitive resin known as a photocurable solid material mainly comprises of a photo-initiator, oligomer, and responsive diluent [123]. The UV-Curing 3D Printing is the most common way of utilizing the fast cross-connecting of liquid light sensitive resin under ultraviolet light (UV) radiation to solid substances [124]. So as to add optical relieving light-sensitive resin layer by layer, until it frames a total development the course of three – dimensional device [124]. Since the light - touchy sap has one of a kind fluid liquidity and prompt light hardening qualities and how much light sensitive resin can precisely control the amount and space of the light sensitivity resin [125]. The optical solidification 3D printing can make a model with any complex geometric shape that is difficult to get ready with traditional processing techniques. The optical solidification 3D printing innovation is the longest history; however, the advancement speed is the quickest. It is additionally the most generally utilized kind of 3D printing innovation. It predominantly incorporates SLA, DLP, LCD, ClIP and other strategies [125]. Its essence is a colloidal substance made out of macromolecules [126]. The molecules are dissipated and cross-connected together like a fence. When the photosensitive resin is irradiated by ultraviolet light, the photo-initiator absorbs energy, forms excited molecules, and disintegrates active groups [127]. Besides, it is appeared as the change of colloidal resin into a solid item. The light source in the 3D printer persistently crosslinks the photosensitive resin by scanning layer by layer, there by accumulating a three-dimensional solid item [124].

As a brilliant 3D printing consumable, the photosensitive resin enjoys the benefits of high shape in precision and short curing time and is reasonable for processing precision devices [128]. Albeit the use of photosensitive resin in the field of 3D printing has been boundless, the performance of photosensitive resin has certain abandons because of the actual material. Scientists have defeated these imperfections through strategies like surface change and doping [48,129]. Mahmoudi et al. [130] detailed a photo-initiator process for the 3D printing of pure commercial epoxy polymer. A clever radical free/cationic hybrid photosensitive resin was created by a cationic curing system with the course of UV-curing. It was planned and demonstrated as a minimal expense one-step printing process. With chemical modification, NR was changed to photosensitive NR (PNR), which was mixed with a commercial resin (CR) at different rubber items (0-3 wt%) by a simple mixing approach. The synthesized photosensitive natural rubber could be utilized as a toughness modifier utilized in ultraviolet-curable resin for the light-based 3D printing innovation [131].

3. Bioprinting cell determination

3.1 Mesenchymal stem cells

Human bone marrow mesenchymal stem cells can be isolated from adult mesenchymal tissue, which has been demonstrated of good expansion potential. It won't lose its multi-directional differentiation capacity within several generations and is generally applied as one of the ideal cell sources for cartilage tissue engineering [132].Recently, an ever increasing number of studies have been led on the chondrogenic capability of MSCs in bone marrow, fat, synovium, periosteum, umbilical cord, and muscle [132, 133].In view of mesenchymal stem cells have been produced for the recovery of cartilage defects. Synovial MSCs (SMSCs) have strong articular explicitness and chondrogenic differentiation ability. A chitosan hydrogel/3D-printed poly (ε-caprolactone) hybrid containing SMSCs and enrolling tetrahedral outline work nucleic acid was created for the cartilage regenerative system [134,135]. MSCs have been applied in the therapy of osteoarthritis as seed cells to rescue the defect and chronic inflammation in the joint. Bone marrow-determined mesenchymal stem cells (BMSC)- loaded 3D-bioprinted multilayer platform with methacrylate hyaluronic acid (MeHA)/polycaprolactone consolidating ketogenic and β-TCP for osteochondral deformity fix inside every area. In addition, MSCs have been taken as bio-ink cells for bone recovery. Bone tissue engineering frameworks with MSCs can be unequivocally created with SLA, SLM, and STL advances [136].

3.2 Chondrocytes

As of now, chondrocytes are fundamentally utilized in the field of cartilage bioprinting [137]. In 1994, Brittberg originally presented autologous chondrocyte transplantation [138]. During the arthroscopy of the patient, healthy chondrocytes would be taken out from the patient's injured knee, while the chondrocytes were infused into the patient's deformity with14-21 days of culture [139]. Autologous chondrocyte transplantation essentially diminished swelling and pain in patients. Biodegradable waterborne polyurethane (WBPU) was changed utilizing a water-based green chemistry interaction to shape the capacity for 3D printing. The flexibility of this material supplies extraordinary consistence with tissue in the scratching of wounds [140]. Silk fibroin as a natural polymer manufactured with glycidyl-methacrylate (Silk-GMA) was exhibited for digital lighting processing 3D printing. New cartilage-like tissue and epithelium were found encompassing transplanted Silk-GMA hydrogel [141]. Cell-laden alginate hydrogel containing chondrocytes was infused into 3D PCL cross breed platforms to help the mechanical properties of their producing auricle ligament [142]. The above models delineate that the implantation of chondrocytes can advance the maintenance of ligament defect tissue.

3.3 Embryonic stem cells/incited pluripotent stem cells

Embryonic stem cells (ESCs) can be incited to separate into mesenchymal stem cells and chondrocytes and are frequently utilized in cartilage tissue engineering [143]. Gene expression and immunostaining analysis affirmed that this co-culture system could structure the cell colonies and emit extracellular matrix (ECM) containing glycosaminoglycan (GAG) [144]. The dynamic expression of chondrocyte-specific genes was seen during the cell monolayer extension in this co-culture framework, completely affirming the chondrogenic differentiation of human early stage stem cells (hESCs) [145]. Fiber impedimetric reactions related with the bio inks that contained separated mESCs were created with 3D bioprinting. Multifunctional fiber impedimetric sensors empowered the characterization of stem cells with separation marker expression [146]. Human pluripotent stem cells (hPSC)-based way to deal with produce organoids that cooperate with vascular cells in a spatially resolved way. Specially designed 3D printed chip was applied for spatial communication among organoid and vasculature with a matched co-culture framework .Studies have shown that during the co-culture of hESCs and chondrocytes (Chds), morphogenetic factors emitted by chondrocytes can incite hESCs to separate into the chondrocyte lineage [147].

4. Application in bone and cartilage repair

4.1 Supporting construction

To develop customized regenerative articular cartilage tissue, exact control of the shape and interior construction of the platform is critical [148]. 3D printing innovation can print an assortment of bio-inks containing different biological materials, cells, and bioactive variables to build 3D platforms with complex anatomical designs. Rastogi et al., revealed alginate hydrogel stacked with chondrocytes and osteoblasts utilized 3D printing innovation to develop a non-uniform hydrogel framework [149]. 3D frameworks with different pore sizes and flexible modulus were gotten by changing the dispersing and point of the printed lines. To mimic the osteochondral structure, the development of various tissues was seen in various areas of a similar framework after 6 weeks of subcutaneous transplantation [149]. Moreover, the co-printing of various bio inks likewise gives a decent stage to developing the interstitial design of articular cartilage [24]. Articular cartilage shows contrasts in composition and mechanical properties from top to base. The development of such heterogeneous 3D designs is challenging to accomplish by traditional tissue engineering techniques [134]. The Nakamura, A. group involved gradient bioprinting to control cell density distribution in a same framework and exactly controlled the cell density by changing the mixing proportion of cell-free bio ink and cell-loaded bio ink at the printing needle [59]. The chondrocytes from various interstitial spaces were extricated, and these 3 cells were printed layer by layer to frame interstitial structures. The trial results showed that chondrocytes from various sources could create specific interstitial ECM. Notwithstanding cell determination and control, studies have shown that providing cells with proper biological signals or ECM parts can stimulate cells to create a zonal phenotype [150]. For instance, adding chondroitin sulfate and metalloproteinase-sensitive peptides to Fix hydrogel scan prompt MSCs to secrete external ECM parts, while doping chondroitin sulfate or HA alone can incite cells to deliver moderate and profound ECM components [151,152]. Consequently, in future research, printing different biomaterials and cells from various sources combinations to stimulate the articular cartilage physiological function and mechanical properties will turn into a research heading for tissue engineering to repair articular cartilage.

4.2 Mechanical support

To reproduce the mechanical properties of articular cartilage, many studies have utilized profoundly versatile hydrogels to develop 3Dplatforms by 3D printing to mimic the mechanical properties of joints [131]. Shan et al. [153], utilized a natural polymer, alginate, supported with an extracellular matrix got from decellularized tissue (rECM) for 3D bioprinting. Depending on the curing time, the elastic modulus of the platform can be adjusted from 73.2 kPa to 40 MPa, and the framework has great flexible recuperation, which can resemble the MR of the natural articular cartilage mechanical properties. Co-printing thermoplastic materials with hydrogel materials with weak mechanical properties is likewise a typical way to improve the mechanical properties of cartilage repair scaffolds [154]. The thermoplastic material is utilized as the scaffold's skeleton to endure the primary mechanical stress. The research shows that the mechanical properties of the hybrid printed platform are like those of pure thermoplastic frameworks. Monfared et al. [155], introduced a double cross-linkable hydrogel ink made of PEG star polymer and TEMPO oxidized nanocellulose strands (CNFs). In no time, hydrogels with Young's modulus somewhere in the range of ~10 and 30 kPa were acquired by simply modifying the CNF and Ca2+ content. The exploratory outcomes showed that elements, for example, the heading and dividing of the bio ink printed lines would influence the mechanical properties of the last platform [156]. Consequently, notwithstanding the mechanical properties of the actual material, proper printing settings and structural layout additionally influence the mechanical properties of the platform [155,157].

4.3 Enlistment of cell function

Bioactive designs are developed in view of 3D printing innovation. Different parts with biological regulation capabilities, for example, growth factors, proteins, peptides, medications, and ECM parts are usually doped into bio inks [158]. The ideal bone fix polychole ought to have a large hole with countless pores with specific pores more noteworthy than 100 μm. The large opening permits cells to relocate inside the bracket, advances the integration of frames and host tissues, and guides new bone and blood vessels to fill in the shelf; the microphone can adsorb the protein on the outer layer of the material and influence cell expansion, separation, and different ways of behaving through connection with cell protein [159,160]. Expanded pore rate will build the penetrability and degradability of calcium phosphate-based organic ceramic permeable stents, which will help cells' connection, expansion, and separation. In any case, it will diminish the mechanical strength of the brackets. Consequently, the degree and mechanical strength of calcium phosphate-based organic ceramic permeable brackets are still very testing [161]. The entire design of calcium phosphate-based biological permeable stents decides their mechanical strength and regular qualities. In this manner, exactly controlling the permeable bracket' shole structure is essential for getting ready brilliant bone fix permeable brackets. TGF (transforming growth factors)- factors are frequently doped into hydrogel bio inks to incite chondrogenic separation of MSCs. Macromolecules comprising the natural cartilage matrix, like HA, are a sort of cartilage prompting ideal biomaterial [162]. Adding these natural macromolecules can work on the rheological properties what's more, printing properties of bio inks [163]. It is quite important that while utilizing bioactive elements to incite cells to play biological capabilities, consideration ought to be paid to the printing conditions for these Impact factors [164,165]. As bio-ink and thermoplastic materials are coprinted, the high-temperature printing states of thermoplastic materials might influence the biological activity of factors. Post-printing change and different strategies are required to stay away from the peculiarity of component inactivation [166].In option to adding different biological signs, decellularized extracellular matrix (dECM) bio inks have step by step pulled in the consideration of scientists lately [167].dECM is like natural ECM in composition and topology and can improve cell-matrix collaboration and give a reasonable microenvironment to cell growth and differentiation [135,168,169].Obtaining dECM from different tissues to plan bio-ink and the nusing 3D printing innovation to fabricate a profoundly open and permeable 3Ddesign to advance the exchange of supplements inside and outside the framework has turned into another system for cartilage tissue repair[170]. Through 3D printing, they were printed as a single-material framework or a high-mechanical-strength platform dmixed with PCL. The exploratory outcomes show that dECM got from cartilage and fat can give a reasonable growth environment to MSCs, really initiating MSCs to differentiate into cartilage [171].

5.Three-layered Bioprinting Strategies

5.1 Extrusion based Printing

Extrusion based bioprinting is a pressure based bioprinting strategy that has filled being used over the course of the past 10 years. Utilizing a robotic system connected to a liquid administering array, cells can be saved in a 3D shaped structures in view of computer aided plan modeling. This cycle is finished by utilizing the shear-thinning way of behaving of the bio ink and is for the

most part plotted in cylindrical lines. This framework is controlled by pneumatic, solenoid, or mechanical control. Every framework has its own advantages and disadvantages relying upon the spatial build to be printed or bio ink to be used.[172,173] Because of the adaptable and bigger diameter nozzle, and the capacity to extrude bio ink in a close to solid state ,bio inks, like hydrogels, microcarriers ,tissue spheroids, and tissue stands can be generally utilized. This procedure has exhibited accomplishment with printing various tissues including cartilage, lipid bilayers ,lungs, and liver tissue deposition among others.[174,175,176] While contrasting extrusion based bioprinting with different strategies, this printing technique enjoys the benefit of more noteworthy statement and printing speed as well as anatomically correct permeable construct generation .Monetarily, this printing strategy is financially accessible and has high flexibility taking into consideration the utilization of different bio inks. At long last, the innovation stays safe by a novice client. Disadvantages incorporate restricted resolution which diminishes the accuracy of designing and organization of the cells, hydrogel use is complicated by the gelation and hardening prerequisites, and cells can be impacted by the dehydration and the lack of nutrients. [172,173]

5.2 Droplet/Inkjet-based Printing

Droplet-based bioprinting is an umbrella term that includes inkjet, acoustic-drop ejection, and microvalve bioprinting.[172] Improvement of this printing should be possible by change on a conventional printer by the option of a regulator to the print head for production of a two-dimensional bioprinter.[177] The bio ink is then added to the printer by means of a storing cartridge .Inkjet printing is further subclassified into persistent, drop-on-request ,and electrohydrodynamic printing methods.[172] This technique utilizes gravity, atmospheric pressure, and liquid mechanics to create drops that are delivered to a substrate. Constant inkjet printing powers the bio ink under pressure through a nozzle which then, at that point, breaks into drops as the potential energy is lessened. Drop-on-request printing attempts to convey single drops on request by utilizing a tension pulses to push a drop through a nozzle that is held into place by surface tension. These strain pulses are variable considering the framework and can be piezoelectric, electrostatic, or thermal in nature. Electrohydrodynamic stream bioprinting utilizes an electric field to maneuver the bio ink droplets onto the substrate, which again makes the drop by disturbing the surface strain at the nozzle tip. At the point when the generation of the electric field overcomes the surface strain, the drop is launched out. Acoustic bioprinting launch drops from a pool by generating of an acoustic field. This cycle assists with limiting exposure to excess pressure, voltage, heat, or shear. when the focal point of convergence from a round wave surpasses surface strain, the bead is ejected. At last, microwave bioprinting utilizes an electromechanical valve to control drop release. This process occurs by the generation of a magnetic field with the utilization of a solenoid coil that discharges bio ink drops from the gated microvalve.

5.3 Laser-based

Printing Laser-based bioprinting is a type of bioprinting in which droplet release is initiated by laser-based modalities. There are two layers involved in this process. The selected bio ink is in the bottom layer, which is made up of an energy-absorbing donor layer. When a laser pulse is emitted onto the top donor surface layer, the bioindroplet is released. When the top layer is vaporized, this process creates a bubble at the interface, propelling the droplet onto the substrate. There are several advantages to laser-based bioprinting over other bioprinting techniques. The ability to avoid mechanical stress by avoiding direct contact with the printer is the first. Even though resolution and precision are crucial in bioprinting, the laser-base modality has several drawbacks. These drawbacks include the fact that droplets can be printed to the template with greater precision and resolution. The cost of laser-based systems is the most formidable. Because of its size and complexity, the equipment's use in typical research settings is limited. In addition, there have been fewer applications for research. Also, unknown, the cellular effects on the bio inks' viable components.

6. Added substance Assembling Ideas

6.1 Biomimicry

Hydrogels cultivated with viable cells take into consideration patterning of cells. This cell course of action can recapitulate native anatomy. However, this by itself is insufficient for fruitful bioprinting. The ensuing extracellular matrix (ECM) arrangement, the absorption and debasement of the hydrogel matrix, and the connections and expansion of encapsulated cells are similarly basic to the suitability and useful outcome of the printed tissues. Impediments of tissue strand/spheroid development utilizing hydrogels incorporate confined cell interactions, proliferation, and colonization of immobilized cells inside the hydrogel framework, also as the powerlessness of cells to spread, stretch, and relocate to effectively create the new tissue, especially at high hydrogel concentrations. Bio inks created with cell totals, without hydrogels, display better biomimetic qualities working with

both homo-and hetero-cellular collaborations as a result of the great cell densities and the absence of exogenous matrix immobilization seen when encapsulated in hydrogels. These tissue constructs closely look like the native tissue and protect cell phenotype and functionality for expanded periods.

6.2 Biologic Self-assembly

Organ and complex tissue development evolution is generally founded on cell self-assembly mechanisms. The tissue builds environment of the cells necessities to look like its native counterpart for cells to keep up with their phenotype, lay out suitable cell collaborations, and express tissue explicit proteins alongside ECM. Three-layered cell total aggregates allow for a more friendly and more local anatomic environment for tissue self-assembly to occur contrasted with monolayer cell cultures. Tissue morphogenesis is dependent on the development of multicellular aggregates. These aggregates are limited by cadherin particles which facilitate strong intercellular adhesion. This cadherin interceded aggregates empower signal transduction, an increase in integrin expression as well as binding to arginyl-glycyl-aspartic corrosive motifs in the deposited ECM parts.

6.3 Building Blocks

To bio print scalable tissue, "minitissues" which address the smallest composite tissue units can and ought to be utilized as building blocks. Such building blocks can be in spheroid or tube-shaped structure. Both the structures have been utilized in bioprinting. Tissue spheroids address a platform free bio ink-type, where the cells are coordinated circularly into 200-to 400-mm-diameter cell conglomerations. Several various creation methods have been utilized for manufacture of tissue spheroids incorporating refined cells in microwells with roundedness on a cell adhesion dormant shape made of hydrogels, for example, agarose, methacrylate hyaluronic acid, and alginate. In this methodology, millions of cells are cultivated into an array of microwells and cultured for 24 to 48hours to work with cell accumulation. Cells will sediment to the lower part of the microwells and get comfortable close contact with one another, driving the cells to suddenly stick to each other to limit free energy and develop into a neo-tissue.[178] Due to intracellular cytoskeletal reorganization from cadherin interceded cell restricting, tissue spheroids will lessening size due to spiral compression. [179] Different methodologies which have additionally exhibited outcome in tissue spheroid creation incorporate the hanging drop strategy, microfluidic helped innovation, and acoustic wave-helped cell assembly. Tissue strands are barrel shaped neotissue building blocks that are utilized for bioprinting increase tissues like ink in an ink-jet printer.[179,180] To manufacture the tissue strands for bioprinting, cells at exceptionally high thickness are infused and stuffed into empty alginate tubules.[180]Semipermeable alginate tubules stimulated as these consider exchange of nutrition and oxygen. The cells that are set into the tubules will frame into round and hollow neo-tissue strands as the cells self-adhere and pull away from the tubule walls. Similarly, as with tissue spheroids, tissue strands won't tie to the alginate luminal surface. After cells have aggregated into the neotissue strand, the tube is dissolved utilizing a decross-linker arrangement. The formed tissue strand is then loaded into a specially designed bioprinter head and mechanically extrusion printed.

6.4 Cartilage Rebuilding and Reconstruction

Injury to the articular cartilage of joints is common. Current clinical restorative choices for articular cartilage injury incorporate marrow stimulating techniques, osteochondral grafting (auto and allogeneic), and cell-based techniques. These choices all have eminent deficiencies to incorporate expense, durability, potential disease transmission, and most prominently the failure to re-make local articular cartilage design frequently bringing about a transient arrangement that needs durability.[181.182,183] construction and piece of sound articular cartilage is vital to its function.[182,183,184] This intricate design shifts along the osteochondral axis, and a considerable lot of the restrictions of current methods can be credited to the absence of the local spatiotemporal control of biologic signs for directing cell differentiation, hyaline cartilage formation, explicit zonal biomechanical properties, and coordination with the underlying bone. [181,182,183,184] The heterogeneous and anisotropic cartilage is made of anatomic zones that have zone-explicit mechanical and biologic properties mirroring each zone's composition and architecture, which to date current clinical treatment innovations and tissue engineering strategies have been not able to recapulate. Current cell-based procedures bring about a scattered repair tissue that has poor durability.[183] Presently, osteoarticular allografts the clinical technique MOs frequently utilized for recreation of large osteochondral defects and injury.[185]Though this can yield great outcomes, there stays a restricted supply of these live osteoarticular allografts, with wait times frequently of a year or longer for unite coordinating, during which time critical impediment to the adjacent joint surfaces and global environment of the knee occurs, also extra pain and enduring, with lost work time/wages. Besides, likewise with all allograft tissues, disease transmission stays an issue and particularly so with osteoarticular allografts this includes live bone and

cartilage transfers. Given the restricted clinical progress of current framework and cell-based techniques, there stays a neglected requirement for chondral and osteochondral develops that recapitulate life systems, histology, and biology, which advance fast coordination, and give a durable clinical answer for articular cartilage injury. The added substance producing methodology of 3D bioprinting gives a potential solution.

6.5 Bionics

The foundation of biologic printing rotates around the utilization of bionics. Bonaire the combination of inert printing medium seeded with living cells. Together these parts structure the raw material which are stored onto the collection substrate. The formative permitted control of living cells to make biologic develops. The ideal bio ink is printable; has high mechanical integrity, high stability, insoluble in cell culture medium, nontoxic, and nonimmunogenic and can advance cell adhesion. For the bio ink to be successful, it should keep up with its plan strength and integrity for implementation in vivo. Several studies have assessed different bio inks for their viability in cartilage restoration. Alginate and agarose may better help hyaline-cartilage while gelatinmethacryloyl-and poly(ethylene glycol) methacrylate-based bio inks may support more fibro-cartilaginous tissues.[186] These bionics have likewise been demonstrated to be biocompatible for cartilage growth.[187] Two significant types have been created, which include platform and platform free techniques. Their implications for cartilage rebuilding are talked about later.

7. Platform and platform free

7.1 In Vitro Work

Bioprinting can be performed regardless of a platform. Frameworks utilized for manufacture of articular cartilage alludes to biomaterials, either engineered or natural occurring, that are utilized to help the cartilage construct or perhaps used to help with inducing repair from native host cells. Platform based bioprinting involved the loading of cells into hydrogels or other transporter that can be saved onto earlier construct designs. These hydrogels can work with the generation of tissues by means of cell expansion and development Hydrogels arrive in a wide assortment of substrates and types, all with different benefits and disadvantages. Platforms are attractive in tissue engineering as they allow for immediate structural integrity and can be utilized to control the spatiotemporal construction, advancement, and interactions of the cells and the creating ECM. Several criteria can be utilized in choosing the proper framework. Contemplations incorporate bio capability, porosity, pore size, mechanical strength, biodegradability, and capacity to advance cartilage tissue formation.[185] The framework likewise offers "Time Zero" mechanical loadbearing properties, a characteristic that bio printed tissues frequently at initially lack. Frameworks can be created with angles in structure and/or architecture to copy the mechanical properties of native cartilage and permit the dissemination of suitable mechanical and biologic signals to cells all through the different zonal design. Total porosity and interconnectivity of the pores likewise assume a huge part in effectivity of a platform. This characteristic helps with cell adhesion and seeding as well as keeping up with proximity to blood supply for efficient oxygen and nutrient delivery.[188]

Various studies have taken a gander at in vitro bioprinting utilizing framework. Abbadessa et al [189] tried hydrogels containing polyethylene glycol and to some degree (10%) methacrylatedpoly(N-(2-hydroxypropyl) methacrylamidemono/dilactate) (M10P10) and methacrylate hyaluronic acid which expanded storage modulus, slowed degradation, and further developed printability versusM10P10 alone. These authors exhibited chondrocyte growth at 42 days of culture. This information base keeps on growing a different laboratories examine the various parts of the platforms to enhance cartilage cell development. Framework free strategies use nonissues deposit them in specifications on a substrate. These tissues are then fused and mature over the long term into larger functional tissues by idea of mini tissue units as building blocks. Framework free strategies permit a high-density deposition of cells on beginning print without the requirement for biomaterials, which was achieved earlier by the utilization of tissue spheroids that are imprinted in proximity and fuse over the long term. Spheroids really do have several issues, notwithstanding. They require a delivery medium for extrusion which complicates the printing process. Since fusion happens by proximity, premature fusion can cause nozzle clogging. At last, gaps between printed spheroids have been displayed from tissues with gaps which can leak.

Yu et al.,[180] fostered a clever method which allowed the printing of bio strands, which prompts various benefits which included help of fast combination and development through self-assembly, bioprinting in solid structure, extrusion of the fluid delivery medium and don't need a support molding construction during bioprinting for cell aggregate and fusion. In their review, the strands were kept and refined in vitro. Like in vitro, cells exhibited great survivability. Following fourteen days, histological staining was finished exhibiting substantial proteoglycan statement with positive staining for Safranin-O, like native cartilage

control. Aggrecan and type II collagen were likewise present on immunohistological staining further describing the cartilage material. Self-assembly was tried and exhibited as soon as 12 hours post printing. On day 7, a practically complete tissue patch was available, permitting biomechanical testing of the item. The Young's modulus of the printed cartilage was tried in pressure and viewed as 1,094 6 26.33 kPa like native cartilage. The authors proposed that the Young's modulus would be more comparable assuming strands were cultured for longer. The remarkable ability of bioprinting permits the improvement of precise pattern of cartilage cells with the complex design of the cartilage layers to deliver mimicry of the native construction of cartilage. The framework free procedure has permitted printing of close to solid state tissue which doesn't need a liquid medium for cell facilitation, viability, or fusion. Current framework based bioprinting mechanisms require a form to have the cells which might restrict the size of the printable develops. Framework free procedures may give an approach to printing of larger implantable cartilage patches with similar biomechanical and histological properties to that of native cartilage.

7.2 In Vivo Work

In vivo transplantation of chondrocytes has begun to be studied by several researchers as we continue to search for the ideal parameters and conditions for the bioprinting process. With the transplantation of cartilage constructs, in vivo survivability has been evaluated using rat, mouse, and rabbit models. [190,191] Two distinct types of in vivo studies have been attempted thus far. The 3D bio prosthetic's survival has been the focus of most research. After that, these constructs were left on for a variety of times, and the cells were examined histologically when they were taken off. Shim etal.[190] implanted 3D printed cartilage cells into rabbit knee joints, which demonstrated the development of vascular membranes, chondrocyte proliferation, and lacunae without cell integrity loss. Neocartilage formation, osteochondral integration, lacuna formation, and a smooth cartilage cap in the defect area were observed in the test group upon examination. With the use of a hydrogel scaffold, bio printed cartilage cells have been shown to survive and integrate in vivo. Future cartilage tissue engineering methods and potential treatment alternatives may benefit from this discovery.

7.3 Bone Replacement and Reconstruction

Outstanding weaknesses remain with bone grafting choices for bone restoration and reconstruction. Autograft bone keeps on being utilized much of the time however has the significant drawback of donor site morbidity. Allograft bone has been utilized widely, yet disease transmission, lack of osteogenicity, cost, and an all-around restricted supply notwithstanding quickly developing interest are remarkable worries. The field of bone tissue engineering tries to accommodate these difficulties and the developing neglected need for viable bone grafting alternative by combining (1) a biocompatible framework that restates the natural bone ECM niche, (2) consideration of osteogenic cells to secrete the necessaries, (3)morphogenic signals that spatiotemporally bio direct the cells to the phenotypically helpful type, and (4) adequate vascularization to meet the developing tissue supplement supply and metabolic necessities. Three-layered bioprinting allows for added substance manufacturing of this dynamic tissue that incorporates a highly complex microarchitecture integral to its function. However various tissue engineering systems perhaps utilized to handle the difficulties of bone tissue engineering, 3Dbioprinting offers a superior command over the structural and mechanical properties of the platform over other recently portrayed methods counting gas foaming, salt leaching, and freeze drying. Besides, 3Dbioprinting considers better cell-cell interconnection, further developed oxygen diffusion, and nutrient transportation and gives cells the essential connection, expansion, and tissue formation factors.[192] Bone grafts have been made utilizing natural hydrogels, for example, fibrin oralginate. Nonetheless, the frameworks made in vitro have poor compressive modulus making them deficient for bone tissue engineering.[193] Alternatively,3D bioprinting utilizing manufactured polymeric polyethylene glycol dimethacrylatehydrogel gives compressive modulus that can exceed500 kPa.[194,195] This cycle approximates human tissue compressive moduli.[196] Moreover, the utilization of polyethylene glycol hydrogel will provide better cell viability and advance ECM production.[194,197,198]

Expansion of human mesenchymal stem cells(hMSCs) can recover bone tissues when animated by a ceramic scaffold.[199] Bioactive glass and hydroxyapatite(HA) have both been displayed to advance bone tissue formation.[193,200]Collectively, HA in polyethylene glycol hydrogel can keep up with MScs reasonability and advances hMSC osteogenic differentiation and biosynthetic function.[201] Qi et al., showed that utilizing hB MSCs in conjunction with calcium sulfate hydrate/mesoporous bioactive glass platforms animated the adhesion, proliferation, alkaline phosphatase activity and osteogenesis-related gene expression of hB MSCs. The authors likewise exhibited that calcium sulfate hydrate/mesoporous bioactive glass platforms could markedly upgrade new bone development in vivo bony imperfections contrasted with controls.[202]As in cartilage, bioprinting without framework gives the benefit of keeping away from cytotoxic or generally biological deleterious breakdown byproducts of

the framework. This approach leads top reservation of cell aggregates and capability through a help of cell connections and a stronger statement of ECM. Evinger et al [203] demonstrated the utilization of Novo Gen bioprinting stage with adipose derived mesenchymal immature microorganisms as well as endothelial cells to deliver osteopontin and alkaline phosphatase positive cells after 5 days post bioprinting. Osteogenesis was likewise confirmed by measuring bone modeling biochemical markers including interleukin (IL)- 1a, IL-6, IL-8, C motif chemokine ligand 2, and chemokine(C-X-C theme) ligand 1.

[203] Keriquel et al. [204] have recently displayed that laser-assisted bioprinting is an attractive tool for the in-situ printing of a bone substitute. These authors effectively utilized the laser-assisted bioprinting technique to bio print mesenchymal stromal cells, related with collagen and nano-HA in a calvarial deformity displaying mice.[204] Utilizing droplet based bioprinting , Herberg et al[205] added growth factors, including bone morphogenetic protein (BMP)- 2,transforming growth factor-b1, and stromal cell-derived factor-1 beta(SDF-1b) on 5-mmdiameter acellular Derma Network plates, which the authors then implanted into osseous defects in mice. The co-delivery ofBMP-2 and SDF-1 was superior toBMP-2 and SDF-b-only gatherings in bone formation.[205] The expansion of a bio ink carrier to the combination considers solidification by polymerization to guarantee the maintenance of the construct. MSCs co-printed with HA can make frameworks with Young's modulus upsides of 1 to 2 MPa.These builds additionally were displayed to create significant bone tissues. Another significant component of the development process was the fuse of type I collagen with thermo-responsive agarose hydrogels bio inks. This combination with high-collagen proportions enhances the mechanical stiffness required for differentiation and gives exact shapes to the constructs.[206]

Das et al. [207], showed osteogenic differentiation of mesenchymal stem cells embodied in silk fibroin-gelatin which was cross-connected either by the enzyme tyrosinase during bioprinting or by sonication post bioprinting.[206] The authors likewise exhibited that by changing the way of culture media, they had the option to differentiate cells with a develop that differs in mechanical properties and function.[208]. Raja and Yun [209], additionally utilized this procedure by keeping in a coaxial way calcium-lacking HA and alginate loaded down with pre-osteoblastMC3T3-E1 cells, prompting the designing of bone tissue composites with the compressive modulus of 7.01 6 0.82 MPa. Added substance assembling of bone utilizing 3D bioprinting offers the upside of making composite tissues including the ability to incorporate essential vascularity to the bone tissue creation. Kolesky et al., have shown this with the ability to make a 1-cm thick tissue with implanted vasculature for tissue perfusion. [208]

8. Clinical Application and Future Heading

A critical headway in clinical bioprinting of muscular tissues, whether bone or cartilage, will be joining with computer-aided design, where medical pictures gained by CT, MRI, positron emission tomography, and ultrasonography can be straightforwardly taken care of into a processor, which can quickly create the design through image reconstruction algorithms. This step includes image segmentation and mesh generation followed by mesh optimization re-making exceptionally intricate irregular mathematical models. The mesh is then changed over into a path plan for 3D bioprinting which can be straightforwardly taken care of into a bioprinter. These designs would show restraint specific regarding the geometry of implant as well as the degree of tissue inadequacy and the anatomy of the composite tissue as well as the vascular network. Several advances in tissue segmentation algorithms from various imaging modalities have recently arose that may ultimately be utilized for bioprinting of composite vascularized tissues.

II. Conclusion

Striking shortcomings exist in the right now accessible surgical choices for reconstruction of bone and articular cartilage defects. Three-layered bioprinting as an added substance producing tissue designing procedure incorporates viable cells and ECM for layer-by-layer manufacture of highly complex tissues like bone and ligament. On account of the adaptability of 3D bioprinting, this innovation has the capacity to fabricate tissues in clinically pertinent volumes and addresses the imperfections of changing sizes and geometries. Sticking to the standards of biomimicry, biologic self-assembly, and the utilization of mini- tissues as building blocks, striking achievement has proactively been accomplished with cartilage and bone tissue bioprinting utilizing extrusion based bioprinting utilizing alginate carriers and platform free bio inks. Fabrication of composite tissues has been accomplished which incorporates vascularity, an important essential to tissue viability. As this innovation develops, and we can coordinate excellent radiographic imaging, computer-assisted design, computer assisted fabricating, with realtime3D bioprinting and eventually in situ surgical printing, this added substance producing method can be utilized to reproduce both bone and

articular cartilage and has the potential to succeed where our presently available clinical advancements and tissue producing systems come up short.

Conflict Of Interest

All authors declare no conflicts of interest.

Authors Contribution

Authors have equally participated and shared every item of the work.

References

[1] Zhang, Juan, et al. "A 3D printable, highly stretchable, self-healing hydrogel-based sensor based on polyvinyl alcohol/sodium tetraborate/sodium alginate for human motion monitoring." *International Journal of Biological Macromolecules* 219 (2022): 1216-1226.

[2] Zhu, Tengjiao, et al. "High efficacy of tetra-PEG hydrogel sealants for suture less dural closure." *Bioactive Materials* 8 (2022): 12-19.

[3] Siegel, Mark G., et al. "Articular cartilage restoration requires cells, scaffolds, growth factors, and mechanical stimulation." *Arthroscopy: The Journal of Arthroscopic & Related Surgery*37.5 (2021): 1359-1360.

[4] Bei, Ho Pan, et al. "Bone-a-Petite: Engineering Exosomes towards Bone, Osteochondral, and Cartilage Repair." *Small*17.50 (2021): 2101741.

[5] Critchley, Susan, et al. "3D printing of fibre-reinforced cartilaginous templates for the regeneration of osteochondral defects." *Acta Biomaterialia* 113 (2020): 130-143.

[6] Ruiz-Cantu, Laura, et al. "Multi-material 3D bioprinting of porous constructs for cartilage regeneration." *Materials Science and Engineering: C* 109 (2020): 110578.

[7] Liu, Xiaoyun, et al. "3D bio printed neural tissue constructs for spinal cord injury repair." *Biomaterials* 272 (2021): 120771.

[8] Potyondy, Tyler, et al. "Recent advances in 3D bioprinting of musculoskeletal tissues." *Bio fabrication* 13.2 (2021): 022001.

[9] Su, Xin, Ting Wang, and Shu Guo. "Applications of 3D printed bone tissue engineering scaffolds in the stem cell field." *Regenerative therapy* 16 (2021): 63-72.

[10] Yanyu, Yang, Wang Xing, and Wu Decheng. "Chitosan-based high-mechanical double-network hydrogels: Construction, modulation and applications." *Acta Chimica Sinica* 79.1 (2021): 1.

[11] De Angelis, Elena, et al. "Cultured Horse Articular Chondrocytes in 3D-Printed Chitosan Scaffold with Hyaluronic Acid and Platelet Lysate." *Frontiers in Veterinary Science* 8 (2021): 671776.

[12] Jang, Chul Ho, YoungWon Koo, and GeunHyung Kim. "ASC/chondrocyte-laden alginate hydrogel/PCL hybrid scaffold fabricated using 3D printing for auricle regeneration." *Carbohydrate polymers* 248 (2020): 116776.

[13] Cao, Yanyan, et al. "Mesenchymal stem cells loaded on 3D-printed gradient poly (ε-caprolactone)/methacrylated alginate composite scaffolds for cartilage tissue engineering." *Regenerative Biomaterials* 8.3 (2021): rbab019.

[14] Golebiowska, Aleksandra A., and Syam P. Nukavarapu. "Bio-inspired zonal-structured matrices for bone-cartilage interface engineering." *Biofabrication* 14.2 (2022): 025016.

[15] Wang, Shao-Jie, et al. "Biomimetic nanosilica–collagen scaffolds for in situ bone regeneration: toward a cell-free, one-step surgery." *Advanced Materials* 31.49 (2019): 1904341.

[16] Burdis, Ross, Farhad Chariyev-Prinz, and Daniel J. Kelly. "Bioprinting of biomimetic self-organised cartilage with a supporting joint fixation device." *Biofabrication* 14.1 (2021): 015008.

[17] Su, Chunyu, et al. "Natural Materials for 3D Printing and Their Applications." *Gels* 8.11 (2022): 748.

[18] Lee, Jia Min, et al. "Bioprinting of collagen: considerations, potentials, and applications." *Macromolecular Bioscience* 21.1 (2021): 2000280.

[19] Diogo, Gabriela S., et al. "Cell-laden biomimetically mineralized shark-skin-collagen-based 3D printed hydrogels for the engineering of hard tissues." *ACS Biomaterials Science & Engineering* 6.6 (2020): 3664-3672.

[20] Enrico, Alessandro, et al. "3D Microvascularized Tissue Models by Laser-Based Cavitation Molding of Collagen." *Advanced Materials* 34.11 (2022): 2109823.

[21] Lin, Hsu-Hsiang, et al. "3D-printed collagen-based waveform microfibrous scaffold for periodontal ligament reconstruction." *International Journal of Molecular Sciences* 22.14 (2021): 7725.

[22] Liu, Xiaoyun, et al. "3D bioprinted neural tissue constructs for spinal cord injury repair." *Biomaterials* 272 (2021): 120771.

[23] Heinrich, Marcel Alexander, et al. "3D bioprinting: from benches to translational applications." *Small* 15.23 (2019): 1805510.

[24] Piras, Carmen C., and David K. Smith. "Multicomponent polysaccharide alginate-based bioinks." *Journal of Materials Chemistry B* 8.36 (2020): 8171-8188.

[25] Olmos-Juste, R., et al. "3D printed alginate-cellulose nanofibers-based patches for local curcumin administration." *Carbohydrate Polymers* 264 (2021): 118026.

[26] Rastin, Hadi, et al. "3D bioprinting of a cell-laden antibacterial polysaccharide hydrogel composite." *Carbohydrate Polymers*264 (2021): 117989.

[27] Zhang, Jianhua, et al. "3D Bioprinting of human tissues: Biofabrication, bioinks, and bioreactors." *International Journal of Molecular Sciences* 22.8 (2021): 3971.

[28] Chen, You, et al. "Hybridizing gellan/alginate and thixotropic magnesium phosphate-based hydrogel scaffolds for enhanced osteochondral repair." *Materials Today Bio* 14 (2022): 100261.

[29] Erkoc, Pelin, et al. "3D Printing of Cytocompatible Gelatin-Cellulose-Alginate Blend Hydrogels." *Macromolecular Bioscience* 20.10 (2020): 2000106.

[30] Gao, Xinshuai, et al. "Preparation of Amorphous Poly (aryl ether nitrile ketone) and Its Composites with Nano Hydroxyapatite for 3D Artificial Bone Printing." *ACS Applied Biomaterials* 3.11 (2020): 7930-7940.

[31] Heo, Dong Nyoung, et al. "3D bioprinting of carbohydrazide-modified gelatin into microparticle-suspended oxidized alginate for the fabrication of complex-shaped tissue constructs." *ACS applied materials & interfaces* 12.18 (2020): 20295-20306.

[32] Ni, Tianyu, et al. "3D bioprinting of bone marrow mesenchymal stem cell-laden silk fibroin double network scaffolds for cartilage tissue repair." *Bioconjugate Chemistry*31.8 (2020): 1938-1947.

[33] Khoshnood, Negin, Ali Zamanian, and Maryam Abbasi. "The potential impact of polyethylenimine on biological behavior of 3D-printed alginate scaffolds." *International Journal of Biological Macromolecules* 178 (2021): 19-28.

[34] Kim, Eunu, et al. "Silk fibroin enhances cytocompatibilty and dimensional stability of alginate hydrogels for light-based three-dimensional bioprinting." *Biomacromolecules* 22.5 (2021): 1921-1931.

[35] Demirtaş, Tuğrul Tolga, Gülseren Irmak, and Menemşe Gümüşderelioğlu. "A bioprintable form of chitosan hydrogel for bone tissue engineering." *Biofabrication* 9.3 (2017): 035003.

[36] Yang, Yanyu, et al. "Robust, anti-freezing and conductive bonding of chitosan-based double-network hydrogels for stable-performance flexible electronic." *Carbohydrate Polymers* 276 (2022): 118753.

[37] Xu, Jiaqi, et al. "Chitosan-based high-strength supramolecular hydrogels for 3D bioprinting." *International Journal of Biological Macromolecules* (2022).

[38] Liu, Ye, et al. "Fabrication of gelatin-based printable inks with improved stiffness as well as antibacterial and UV-shielding properties." *International Journal of Biological Macromolecules* 186 (2021): 396-404.

[39] Liu, Yanzhi, et al. "3D-bioprinted BMSC-laden biomimetic multiphasic scaffolds for efficient repair of osteochondral defects in an osteoarthritic rat model." *Biomaterials* 279 (2021): 121216.

[40] Neufurth, Meik, et al. "3D bioprinting of tissue units with mesenchymal stem cells, retaining their proliferative and differentiating potential, in polyphosphate-containing bio-ink." *Biofabrication* 14.1 (2021): 015016.

[41] Jin, Jing, et al. "Two series of microporous lanthanide–organic frameworks with different secondary building units and exposed Lewis base active sites: sensing, dye adsorption, and magnetic properties." *Inorganic Chemistry* 58.1 (2018): 339-348.

[42] Yang, Yanyu, et al. "Anti-freezing, resilient and tough hydrogels for sensitive and large-range strain and pressure sensors." *Chemical Engineering Journal* 403 (2021): 126431.

[43] Yang, Zhen, et al. "3D-bioprinted difunctional scaffold for in situ cartilage regeneration based on aptamer-directed cell recruitment and growth factor-enhanced cell chondrogenesis." *ACS applied materials & interfaces* 13.20 (2021): 23369-23383.

[44] Biranje, Santosh Shivaji, et al. "Development of cellulose nanofibril/casein-based 3D composite hemostasis scaffold for potential wound-healing application." *ACS applied materials & interfaces* 14.3 (2022): 3792-3808.

[45] Akkineni, Ashwini Rahul, et al. "A versatile method for combining different biopolymers in a core/shell fashion by 3D plotting to achieve mechanically robust constructs." *Biofabrication* 8.4 (2016): 045001.

[46] Lee, Ju-Yeon, et al. "Customized biomimetic scaffolds created by indirect three-dimensional printing for tissue engineering." *Biofabrication* 5.4 (2013): 045003.

[47] Hafezi, Forough, et al. "Bioprinting and preliminary testing of highly reproducible novel bioink for potential skin regeneration." *Pharmaceutics* 12.6 (2020): 550.

[48] Hua, Wenqiang, et al. "Exceptional mechanical properties and heat resistance of photocurable bismaleimide ink for 3D printing." *Materials* 14.7 (2021): 1708.

[49] Castillo-Henríquez, Luis, et al. "Exploration of bioengineered scaffolds composed of thermo-responsive polymers for drug delivery in wound healing." *International Journal of Molecular Sciences* 22.3 (2021): 1408.

[50] Shen, Yi, et al. "DLP printing photocurable chitosan to build bio-constructs for tissue engineering." *Carbohydrate polymers*235 (2020): 115970.

[51] Poongodi, Raju, et al. "Bio-scaffolds as cell or exosome carriers for nerve injury repair." *International Journal of Molecular Sciences* 22.24 (2021): 13347.

[52] Nakielski, Paweł, et al. "Laser-Assisted Fabrication of Injectable Nanofibrous Cell Carriers." *Small* 18.2 (2022): 2104971.

[53] Kim, Hyun Seung, and Kuen Yong Lee. "Stretchable and self-healable hyaluronate-based hydrogels for three-dimensional bioprinting." *Carbohydrate Polymers* 295 (2022): 119846.

[54] Deng, Changxu, et al. "3D bio-printed biphasic scaffolds with dual modification of silk fibroin for the integrated repair of osteochondral defects." *Biomaterials Science* 9.14 (2021): 4891-4903.

[55] Guo, Maoze, et al. "One-step 3D printed intelligent silk fibroin artificial skin with built-in electronics and microfluidics." *Analyst* 146.19 (2021): 5934-5941.

[56] Sakai, S., et al. "Silk fibroin nanofibers: A promising ink additive for extrusion three-dimensional bioprinting." *Materials Today Bio* 8 (2020): 100078.

[57] Rajput, Monika, et al. "Light-based 3D bioprinting of bone tissue scaffolds with tunable mechanical properties and architecture from photocurable silk fibroin." *International Journal of Biological Macromolecules* 202 (2022): 644-656.

[58] Trucco, Diego, et al. "Modeling and fabrication of silk fibroin–gelatin-based constructs using extrusion-based three-dimensional bioprinting." *ACS Biomaterials Science & Engineering* 7.7 (2021): 3306-3320.

[59] Jiang, Guangyao, et al. "A 3D-printed PRP-GelMA hydrogel promotes osteochondral regeneration through M2 macrophage polarization in a rabbit model." *Acta biomaterialia*128 (2021): 150-162.

[60] Zhang, Jianhua, et al. "3D Bioprinting of human tissues: Biofabrication, bioinks, and bioreactors." *International Journal of Molecular Sciences* 22.8 (2021): 3971.

[61] Desai, Nina, et al. "New hyaluronan-based biomatrix for 3-D follicle culture yields functionally competent oocytes." *Reproductive Biology and Endocrinology* 20.1 (2022): 1-14.

[62] Flégeau, Killian, Anna Puiggali-Jou, and Marcy Zenobi-Wong. "Cartilage tissue engineering by extrusion bioprinting utilizing porous hyaluronic acid microgel bioinks." *Biofabrication* 14.3 (2022): 034105.

[63] Huang, Haokun, et al. "In vitro application of drug-loaded hydrogel combined with 3D-printed porous scaffolds." *Biomedical Materials* 17.6 (2022): 065019.

[64] Janarthanan, Gopinathan, et al. "Manufacturing of self-standing multi-layered 3D-bioprinted alginate-hyaluronate constructs by controlling the cross-linking mechanisms for tissue engineering applications." *Biofabrication* 14.3 (2022): 035013.

[65] Kim, Hyun Seung, and Kuen Yong Lee. "Stretchable and self-healable hyaluronate-based hydrogels for three-dimensional bioprinting." *Carbohydrate Polymers* 295 (2022): 119846.

[66] Martyniak, Kari, et al. "Biomaterial composition and stiffness as decisive properties of 3D bioprinted constructs for type II collagen stimulation." *Acta Biomaterialia* 152 (2022): 221-234.

[67] Wang, Dongzhi, et al. "Hyaluronic acid methacrylate/pancreatic extracellular matrix as a potential 3D printing bioink for constructing islet organoids." *Acta biomaterialia* (2022).

[68] Wang, Hufei, et al. "Multifunctional microcapsules: a theranostic agent for US/MR/PAT multi-modality imaging and synergistic chemo-photothermal osteosarcoma therapy." *Bioactive materials* 7 (2022): 453-465.

[69] Potyondy, Tyler, et al. "Recent advances in 3D bioprinting of musculoskeletal tissues." *Biofabrication* 13.2 (2021): 022001.

[70] Fairag, Rayan, et al. "A composite lactide-mineral 3D-printed scaffold for bone repair and regeneration." *Frontiers in Cell and Developmental Biology* 9 (2021): 654518.

[71] Han, Xingting, et al. "Tailoring the biologic responses of 3D printed PEEK medical implants by plasma functionalization." *Dental Materials* 38.7 (2022): 1083-1098.

[72] He, Dali, et al. "3D-printed PEEK extravascular stent in the treatment of nutcracker syndrome: imaging evaluation and short-term clinical outcome." *Frontiers in bioengineering and biotechnology* 8 (2020): 732.

[73] Li, Feng, et al. "Cryogenic 3D Printing of ß-TCP/PLGA Composite Scaffolds Incorporated with BpV (Pic) for Treating Early Avascular Necrosis of Femoral Head." *Frontiers in Bioengineering and Biotechnology* 9 (2022): 1354.

[74] Li, Wenfeng, et al. "Pore Size of 3D-Printed Polycaprolactone/Polyethylene Glycol/Hydroxyapatite Scaffolds Affects Bone Regeneration by Modulating Macrophage Polarization and the Foreign Body Response." *ACS Applied Materials & Interfaces* 14.18 (2022): 20693-20707.

[75] Sikder, Prabaha, et al. "Bioactive amorphous magnesium phosphate-polyetheretherketone composite filaments for 3D printing." *Dental Materials* 36.7 (2020): 865-883.

[76] Prechtel, Alexander, et al. "Comparison of various 3D printed and milled PAEK materials: Effect of printing direction and artificial aging on Martens parameters." *Dental Materials* 36.2 (2020): 197-209.

[77] Oladapo, Bankole I., et al. "Lattice design and 3D-printing of PEEK with Ca10 (OH)(PO4) 3 and in-vitro bio-composite for bone implant." *International Journal of Biological Macromolecules* 165 (2020): 50-62.

[78] Puertas-Bartolomé, María, et al. "Development of bioactive catechol functionalized nanoparticles applicable for 3D bioprinting." *Materials Science and Engineering: C* 131 (2021): 112515.

[79] Zheng, Jibao, et al. "Additively-manufactured PEEK/HA porous scaffolds with excellent osteogenesis for bone tissue repairing." *Composites Part B: Engineering* 232 (2022): 109508.

[80] Yang, Weiwei, et al. "Fabrication of smart components by 3D printing and laser-scribing technologies." *ACS applied materials & interfaces* 12.3 (2019): 3928-3935.

[81] Sharma, Neha, et al. "Quantitative assessment of point-of-care 3D-printed patient-specific polyetheretherketone (PEEK) cranial implants." *International Journal of Molecular Sciences*22.16 (2021): 8521.

[82] Zhu, Ce, et al. "3D-Printed multifunctional polyetheretherketone bone scaffold for multimodal treatment of osteosarcoma and osteomyelitis." *ACS Applied Materials & Interfaces* 13.40 (2021): 47327-47340.

[83] Wang, Mian, et al. "Molecularly cleavable bioinks facilitate high-performance digital light processing-based bioprinting of functional volumetric soft tissues." *Nature communications*13.1 (2022): 3317.

[84] Aihemaiti, Patiguli, et al. "Optimization of 3D printing parameters of biodegradable polylactic acid/hydroxyapatite composite bone plates." *International Journal of Bioprinting*8.1 (2022).

[85] Buj-Corral, Irene, et al. "Characterization of 3D Printed Metal-PLA Composite Scaffolds for Biomedical Applications." *Polymers* 14.13 (2022): 2754.

[86] Chang, Po-Chun, et al. "Preclinical evaluation of a 3D-printed hydroxyapatite/poly (lactic-co-glycolic acid) scaffold for ridge augmentation." *Journal of the Formosan Medical Association*120.4 (2021): 1100-1107.

[87] Wang, Yihan, et al. "Approaches to Biofunctionalize Polyetheretherketone for Antibacterial: A Review." *Frontiers in Bioengineering and Biotechnology* 10 (2022).

[88] Custodio, Cyron L., et al. "Powder loading effects on the physicochemical and mechanical properties of 3D printed poly lactic acid/hydroxyapatite biocomposites." *International Journal of Bioprinting* 7.1 (2021).

[89] Golebiowska, Aleksandra A., and Syam P. Nukavarapu. "Bio-inspired zonal-structured matrices for bone-cartilage interface engineering." *Biofabrication* 14.2 (2022): 025016.

[90] Grottkau, Brian E., et al. "Rapid fabrication of anatomically-shaped bone scaffolds using indirect 3D printing and perfusion techniques." *International Journal of Molecular Sciences* 21.1 (2020): 315.

[91] He, Haijun, et al. "3D printed and electrospun, transparent, hierarchical polylactic acid mask nanoporous filter." *International Journal of Bioprinting* 6.4 (2020).

[92] Rodríguez-Merchán, Emérito Carlos. "Bone healing materials in the treatment of recalcitrant nonunions and bone defects." *International Journal of Molecular Sciences* 23.6 (2022): 3352.

[93] Waldburger, Leonie, et al. "3D-Printed Hand Splints versus Thermoplastic Splints: A Randomized Controlled Pilot Feasibility Trial." *International Journal of Bioprinting* 8.1 (2022).

[94] Chiesa-Estomba, Carlos M., et al. "Three-dimensional bioprinting scaffolding for nasal cartilage defects: a systematic review." *Tissue Engineering and Regenerative Medicine* 18 (2021): 343-353.

[95] Cui, Yuecheng, et al. "Crystallization enhanced thermal-sensitive hydrogels of PCL-PEG-PCL triblock copolymer for 3D printing." *Biomedical Materials* 16.3 (2021): 035006.

[96] Hamid, Omar A., et al. "3D bioprinting of a stem cell-laden, multi-material tubular composite: An approach for spinal cord repair." *Materials Science and Engineering: C* 120 (2021): 111707.

[97] Koch, Fritz, et al. "Mechanical properties of polycaprolactone (PCL) scaffolds for hybrid 3D-bioprinting with alginate-gelatin hydrogel." *journal of the mechanical behavior of biomedical materials* 130 (2022): 105219.

[98] Xu, Bingbing, et al. "Protein-spatiotemporal partition releasing gradient porous scaffolds and anti-inflammatory and antioxidant regulation remodel tissue engineered anisotropic meniscus." *Bioactive Materials* 20 (2023): 194-207.

[99] Bandyopadhyay, Amit, Indranath Mitra, and Susmita Bose. "3D printing for bone regeneration." *Current osteoporosis reports* 18 (2020): 505-514.

[100] Mousavi Nejad, Zohre, et al. "3D bioprinting of polycaprolactone-based scaffolds for pulp-dentin regeneration: investigation

[101] of physicochemical and biological behavior." *Polymers* 13.24 (2021): 4442.

[102] Waldburger, Leonie, et al. "3D-Printed Hand Splints versus Thermoplastic Splints: A Randomized Controlled Pilot Feasibility Trial." *International Journal of Bioprinting* 8.1 (2022).

[103] Nulty, Jessica, et al. "3D bioprinting of prevascularised implants for the repair of critically-sized bone defects." *Acta biomaterialia* 126 (2021): 154-169.

[104] Dann, Tyler, et al. "Anatase titanium dioxide imparts photoluminescent properties to PA2200 commercial 3D printing material to generate complex optical imaging phantoms." *Materials* 14.7 (2021): 1813.

[105] Helal, Mohamed A., et al. "In-vitro comparative evaluation for the surface properties and impact strength of CAD/CAM milled, 3D printed, and polyamide denture base resins." *Journal of International Society of Preventive & Community Dentistry* 12.1 (2022): 126.

[106] Poltorak, Lukasz, et al. "Electrochemical study of ephedrine at the polarized liquid-liquid interface supported with a 3D printed cell." *Journal of Hazardous Materials* 402 (2021): 123411.

[107] Powell, Alexander W., et al. "On-demand activation of photochromic nanoheaters for high color purity 3D printing." *Nano Letters* 20.5 (2020): 3485-3491.

[108] Tey, Wei Shian, Chao Cai, and Kun Zhou. "A comprehensive investigation on 3D printing of polyamide 11 and thermoplastic polyurethane via multi jet fusion." *Polymers* 13.13 (2021): 2139.

[109] Zhang, Yunfan, et al. "Facile fabrication of a biocompatible composite gel with sustained release of aspirin for bone regeneration." *Bioactive materials* 11 (2022): 130-139.

[110] Barati, Danial, et al. "Injectable and Crosslinkable PLGA-Based Microribbons as 3D Macroporous Stem Cell Niche." *Small* 16.22 (2020): 1905820.

[111] Carlier, Emeric, et al. "Development of mAb-loaded 3D-printed (FDM) implantable devices based on PLGA." *International journal of pharmaceutics* 597 (2021): 120337.

[112] Jiang, Ji-Peng, et al. "Three-dimensional bioprinting collagen/silk fibroin scaffold combined with neural stem cells promotes nerve regeneration after spinal cord injury." *Neural regeneration research* 15.5 (2020): 959.

[113] Koons, Gerry L., et al. "Effect of 3D printing temperature on bioactivity of bone morphogenetic protein-2 released from polymeric constructs." *Annals of Biomedical Engineering* (2021): 1-12.

[114] Li, Pinxue, et al. "Chitosan hydrogel/3D-printed poly (ε-caprolactone) hybrid scaffold containing synovial mesenchymal stem cells for cartilage regeneration based on tetrahedral framework nucleic acid recruitment." *Biomaterials*278 (2021): 121131.

[115] Long, Jing, et al. "Multifunctional magnesium incorporated scaffolds by 3D-Printing for comprehensive postsurgical management of osteosarcoma." *Biomaterials* 275 (2021): 120950.

[116] Abbasi-Ravasjani, Sonia, et al. "Sulfated carboxymethyl cellulose and carboxymethyl κ-carrageenan immobilization on 3D-printed poly-ε-caprolactone scaffolds differentially promote pre-osteoblast proliferation and osteogenic activity." *Frontiers in Bioengineering and Biotechnology* 10 (2022): 1662.

[117] Andjela, Lalatovic, et al. "A review on Vat Photopolymerization 3D-printing processes for dental application." *Dental Materials* (2022).

[118] Deng, Changxu, et al. "3D bio-printed biphasic scaffolds with dual modification of silk fibroin for the integrated repair of osteochondral defects." *Biomaterials Science* 9.14 (2021): 4891-4903.

[119] Gong, Haihuan, et al. "3D bio-printing of photocrosslinked anatomically tooth-shaped scaffolds for alveolar ridge preservation after tooth extraction." *Journal of Materials Chemistry B* 10.41 (2022): 8502-8513.

[120] Zamboni, Fernanda, et al. "Curcumin encapsulated polylactic acid nanoparticles embedded in alginate/gelatin bioinks for in situ immunoregulation: Characterization and biological assessment." *International Journal of Biological Macromolecules* 221 (2022): 1218-1227.

[121] Murab, Sumit, et al. "Alginate based hydrogel inks for 3D bioprinting of engineered orthopedic tissues." *Carbohydrate Polymers* (2022): 119964.

[122] Serafin, Aleksandra, et al. "Printable alginate/gelatin hydrogel reinforced with carbon nanofibers as electrically conductive scaffolds for tissue engineering." *Materials Science and Engineering: C* 122 (2021): 111927.

[123] Zhang, Zhenxue, et al. "3D printing processability of a thermally conductive compound based on carbon nanofiller-modified thermoplastic polyamide 12." *Polymers* 14.3 (2022): 470.

[124] Abdallah, Mira, et al. "Coumarins as powerful photosensitizers for the cationic polymerization of epoxy-silicones under near-UV and visible light and applications for 3D printing technology." *Molecules* 25.9 (2020): 2063.

[125] Dadras-Toussi, Omid, et al. "Multiphoton Lithography of Organic Semiconductor Devices for 3D Printing of Flexible Electronic Circuits, Biosensors, and Bioelectronics." *Advanced Materials* 34.30 (2022): 2200512.

[126] Foster, Jeffrey C., et al. "Continuous Additive Manufacturing using Olefin Metathesis." *Advanced Science* 9.14 (2022): 2200770.

[127] Liu, Yi, et al. "An injectable, self-healing phenol-functionalized chitosan hydrogel with fast gelling property and visible light-crosslinking capability for 3D printing." *Acta Biomaterialia* 122 (2021): 211-219.

[128] Bud, Eugen S., et al. "Accuracy of three-dimensional (3D) printed dental digital models generated with three types of resin polymers by extra-oral optical scanning." *Journal of Clinical Medicine* 10.9 (2021): 1908.

[129] Fang, Zheng, et al. "Effect of reconstruction algorithm on the identification of 3D printing polymers based on hyperspectral CT technology combined with artificial neural network." *Materials* 13.8 (2020): 1963.

[130] Fleck, Elyse, et al. "Advancing 3D-Printed Microfluidics: Characterization of a Gas-Permeable, High-Resolution PDMS Resin for Stereolithography." *Micromachines* 12.10 (2021): 1266.

[131] Mahmoudi, Mohammadreza, et al. "Additive-free and support-free 3D printing of thermosetting polymers with isotropic mechanical properties." *ACS Applied Materials & Interfaces*13.4 (2021): 5529-5538.

[132] Shan, Junyang, et al. "Design and synthesis of free-radical/cationic photosensitive resin applied for 3D printer with liquid crystal display (LCD) irradiation." *Polymers* 12.6 (2020): 1346.

[133] Tessanan, Wasan, Philippe Daniel, and Pranee Phinyocheep. "Development of photosensitive natural rubber as a mechanical modifier for ultraviolet-curable resin applied in digital light processing-based three-dimensional printing technology." *ACS omega* 6.23 (2021): 14838-14847.

[134] Fitzpatrick, Vincent, et al. "Functionalized 3D-printed silk-hydroxyapatite scaffolds for enhanced bone regeneration with innervation and vascularization." *Biomaterials* 276 (2021): 120995.

[135] Fazal, Faraz, et al. "A modified 3D printer as a hybrid bioprinting-electrospinning system for use in vascular tissue engineering applications." *Medical Engineering & Physics* 94 (2021): 52-60.

[136] He, Xiao-Yu, et al. "Advances in the application of mesenchymal stem cells, exosomes, biomimetic materials, and 3D printing in osteoporosis printing in osteoporosis treatment." *Cellular & Molecular Biology Letters* 26.1 (2021): 1-23.

[137] Su, Xin, Ting Wang, and Shu Guo. "Applications of 3D printed bone tissue engineering scaffolds in the stem cell field." *Regenerative therapy* 16 (2021): 63-72.

[138] De Angelis, Elena, et al. "Cultured Horse Articular Chondrocytes in 3D-Printed Chitosan Scaffold with Hyaluronic Acid and Platelet Lysate." *Frontiers in Veterinary Science* 8 (2021): 671776.

[139] Li, Qiushi, et al. "Laser-induced corrugated graphene films for integrated multimodal sensors." *ACS Applied Materials & Interfaces* 13.31 (2021): 37433-37444.

[140] Diloksumpan, Paweena, et al. "Combining multi-scale 3D printing technologies to engineer reinforced hydrogel-ceramic interfaces." *Biofabrication* 12.2 (2020): 025014.

[141] Dudman, Joseph PR, et al. "Reliable inkjet printing of chondrocytes and MSCs using reservoir agitation." *Biofabrication* 12.4 (2020): 045024

[142] Feng, Zhaoxuan, et al. "A novel waterborne polyurethane with biodegradability and high flexibility for 3D printing." *Biofabrication* 12.3 (2020): 035015.

[143] Jang, Chul Ho, YoungWon Koo, and GeunHyung Kim. "ASC/chondrocyte-laden alginate hydrogel/PCL hybrid scaffold fabricated using 3D printing for auricle regeneration." *Carbohydrate polymers* 248 (2020): 116776.

[144] Hong, Heesun, et al. "Digital light processing 3D printed silk fibroin hydrogel for cartilage tissue engineering." *Biomaterials*232 (2020): 119679.

[145] Abdelrahman, Sherin, et al. "A Parkinson's disease model composed of 3D bioprinted dopaminergic neurons within a biomimetic peptide scaffold." *Biofabrication* 14.4 (2022): 044103

[146] Mabrouk, Mohamed H. Elsafi, et al. "The spatial self-organization within pluripotent stem cell colonies is continued in detaching aggregates." *Biomaterials* 282 (2022): 121389.

[147] Edgar, L., et al. "Regenerative medicine, organ bioengineering and transplantation." *Journal of British Surgery* 107.7 (2020): 793-800.

[148] Haring, Alexander P., et al. "3D bioprinting using hollow multifunctional fiber impedimetric sensors." *Biofabrication* 12.3 (2020): 035026.

[149] Bliley, Jacqueline, et al. "FRESH 3D bioprinting a contractile heart tube using human stem cell-derived cardiomyocytes." *Biofabrication* 14.2 (2022): 024106.

[150] Han, Yu, et al. "High-precision, gelatin-based, hybrid, bilayer scaffolds using melt electro-writing to repair cartilage injury." *Bioactive Materials* 6.7 (2021): 2173-2186.

[151] Rastogi, Prasansha, and Balasubramanian Kandasubramanian. "Review of alginate-based hydrogel bioprinting for application in tissue engineering." *Biofabrication*11.4 (2019): 042001.

[152] Fan, Daoyang, et al. "Progressive 3D printing technology and its application in medical materials." *Frontiers in pharmacology*11 (2020): 122.

[153] Nakamura, Anna, et al. "Bio-3D printing iPSC-derived human chondrocytes for articular cartilage regeneration." *Biofabrication* 13.4 (2021): 044103.

[154] Beh, Cyrus W., et al. "A fluid-supported 3D hydrogel bioprinting method." *Biomaterials* 276 (2021): 121034.

[155] Shan, Junyang, et al. "Design and synthesis of free-radical/cationic photosensitive resin applied for 3D printer with liquid crystal display (LCD) irradiation." *Polymers* 12.6 (2020): 1346.

[156] De Santis, Martina M., et al. "Extracellular-matrix-reinforced bioinks for 3D bioprinting human tissue." *Advanced materials*33.3 (2021): 2005476.

[157] Monfared, Marzieh, et al. "3D bioprinting of dual-crosslinked nanocellulose hydrogels for tissue engineering applications." *Journal of Materials Chemistry B* 9.31 (2021): 6163-6175.

[158] Park, Jeong Hun, et al. "3D bioprinting of a trachea-mimetic cellular construct of a clinically relevant size." *Biomaterials*279 (2021): 121246.

[159] Shin, Yu Jung, et al. "3D bioprinting of mechanically tuned bioinks derived from cardiac decellularized extracellular matrix." *Acta biomaterialia* 119 (2021): 75-88.

[160] Soman, Soja Saghar, and Sanjairaj Vijayavenkataraman. "Perspectives on 3D bioprinting of peripheral nerve conduits." *International journal of molecular sciences* 21.16 (2020): 5792.

[161] Barreiro Carpio, Mabel, et al. "3D Bioprinting strategies, challenges, and opportunities to model the lung tissue microenvironment and its function." *Frontiers in Bioengineering and Biotechnology* (2021): 1097.

[162] Potyondy, Tyler, et al. "Recent advances in 3D bioprinting of musculoskeletal tissues." *Biofabrication* 13.2 (2021): 022001.

[163] Ghorbani, Farnaz, et al. "Tuning the biomimetic behavior of hybrid scaffolds for bone tissue engineering through surface modifications and drug immobilization." *Materials Science and Engineering: c* 130 (2021): 112434.

[164] Murphy, Caroline A., et al. "Regional dependency of bovine meniscus biomechanics on the internal structure and glycosaminoglycan content." *Journal of the Mechanical Behavior of Biomedical Materials* 94 (2019): 186-192.

[165] Davidson, Sean M., et al. "Progress in cardiac research: from rebooting cardiac regeneration to a complete cell atlas of the heart." *Cardiovascular research* 117.10 (2021): 2161-2174.

[166] Gurlin, Rachel E., Jaime A. Giraldo, and Esther Latres. "3D bioprinting and translation of beta cell replacement therapies for type 1 diabetes." *Tissue Engineering Part B: Reviews* 27.3 (2021): 238-252.

[167] Liu, Gele, et al. "Advances in pluripotent stem cells: history, mechanisms, technologies, and applications." *Stem cell reviews and reports* 16 (2020): 3-32.

[168] Jin, Zhizhong, et al. "Engineering the fate and function of human T-Cells via 3D bioprinting." *Biofabrication* 13.3 (2021): 035016.

[169] Mandrycky, Christian, et al. "3D bioprinting for engineering complex tissues." *Biotechnology advances* 34.4 (2016): 422-434.

[170] Neufurth, Meik, et al. "3D bioprinting of tissue units with mesenchymal stem cells, retaining their proliferative and differentiating potential, in polyphosphate-containing bio-ink." *Biofabrication* 14.1 (2021): 015016.

[171] Suarez-Martinez, Ariana D., et al. "Bioprinting on live tissue for investigating cancer cell dynamics." *Tissue Engineering Part A*27.7-8 (2021): 438-453.

[172] Tang, Min, et al. "Three-dimensional bioprinted glioblastoma microenvironments model cellular dependencies and immune interactions." *Cell research* 30.10 (2020): 833-853.

[173] Leberfinger, Ashley N., et al. "Concise review: bioprinting of stem cells for transplantable tissue fabrication." *Stem cells translational medicine* 6.10 (2017): 1940-1948.

[174] Ozbolat, Ibrahim T., and Monika Hospodiuk. "Current advances and future perspectives in extrusion-based bioprinting." *Biomaterials* 76 (2016): 321-343.

[175] Horváth, Lenke, et al. "Engineering an in vitro air-blood barrier by 3D bioprinting." *Scientific reports* 5.1 (2015): 1-8.

[176] Billiet, Thomas, et al. "The 3D printing of gelatin methacrylamide cell-laden tissue-engineered constructs with high cell viability." *Biomaterials* 35.1 (2014): 49-62.

[177] Durmus, Naside Gozde, Savas Tasoglu, and Utkan Demirci. "Functional droplet networks." *Nature materials* 12.6 (2013): 478-479.

[178] Mattimore, Justin P., et al. "A general-purpose driver board for the HP26 ink-jet cartridge with applications to bioprinting." *Proceedings of the IEEE SoutheastCon 2010 (SoutheastCon)*. IEEE, 2010.

[179] Athanasiou, Kyriacos A., et al. "Self-organization and the self-assembling process in tissue engineering." *Annual review of biomedical engineering* 15 (2013): 115-136.

[180] Akkouch, A., Y. Yu, and I. T. Ozbolat. "Microfabrication of scaffold-free tissue strands for three-dimensional tissue engineering. Biofabrication 7, 31002." (2015).

[181] Yu, Yin, et al. "Three-dimensional bioprinting using self-assembling scalable scaffold-free “tissue strands” as a new bioink." *Scientific reports* 6.1 (2016): 1-11.

[182] Makris, Eleftherios A., et al. "Repair and tissue engineering techniques for articular cartilage." *Nature Reviews Rheumatology* 11.1 (2015): 21-34.

[183] Farr, Jack, et al. "Clinical cartilage restoration: evolution and overview." *Clinical Orthopaedics and Related Research®* 469 (2011): 2696-2705.

[184] Nehrer, Stefan, Myron Spector, and Tom Minas. "Histologic analysis of tissue after failed cartilage repair procedures." *Clinical Orthopaedics and Related Research (1976-2007)* 365 (1999): 149-162.

[185] Cole, Brian J., Cecilia Pascual-Garrido, and Robert C. Grumet. "Surgical management of articular cartilage defects in the knee." *JBJS* 91.7 (2009): 1778-1790.

[186] Izadifar, Zohreh, Xiongbiao Chen, and William Kulyk. "Strategic design and fabrication of engineered scaffolds for articular cartilage repair." *Journal of functional biomaterials* 3.4 (2012):

[187] Daly, Andrew C., et al. "A comparison of different bioinks for 3D bioprinting of fibrocartilage and hyaline cartilage." *Biofabrication* 8.4 (2016): 045002.

[188] Markstedt, Kajsa, et al. "3D bioprinting human chondrocytes with nanocellulose–alginate bioink for cartilage tissue engineering applications." *Biomacromolecules* 16.5 (2015): 1489-1496.

[189] El-Sherbiny, Ibrahim M., and Magdi H. Yacoub. "Hydrogel scaffolds for tissue engineering: Progress and challenges." *Global Cardiology Science and Practice* 2013.3 (2013): 38.

[190] Abbadessa, A., et al. "A thermo-responsive and photo-polymerizable chondroitin sulfate-based hydrogel for 3D printing applications." *Carbohydrate polymers* 149 (2016): 163-174.

[191] Shim, Jin-Hyung, et al. "Three-dimensional bioprinting of multilayered constructs containing human mesenchymal stromal cells for osteochondral tissue regeneration in the rabbit knee joint." *Biofabrication* 8.1 (2016): 014102.

[192] Xu, Tao, et al. "Hybrid printing of mechanically and biologically improved constructs for cartilage tissue engineering applications." *Biofabrication* 5.1 (2012): 015001.

[193] 192- Bose, Susmita, Sahar Vahabzadeh, and Amit Bandyopadhyay. "Bone tissue engineering using 3D printing." *Materials today*16.12 (2013): 496-504.

[194] Khanarian, Nora T., et al. "A hydrogel-mineral composite scaffold for osteochondral interface tissue engineering." *Tissue Engineering Part A* 18.5-6 (2012): 533-545.

[195] Cui, Xiaofeng, et al. "Direct human cartilage repair using three-dimensional bioprinting technology." *Tissue Engineering Part A* 18.11-12 (2012): 1304-1312.

[196] Cui, Xiaofeng, et al. "Thermal inkjet printing in tissue engineering and regenerative medicine." *Recent patents on drug delivery & formulation* 6.2 (2012): 149-155.

[197] Hoenig, Elisa, et al. "High amplitude direct compressive strain enhances mechanical properties of scaffold-free tissue-engineered cartilage." *Tissue Engineering Part A* 17.9-10 (2011): 1401-1411.

[198] Bryant, Stephanie J., and Kristi S. Anseth. "Hydrogel properties influence ECM production by chondrocytes photoencapsulated in poly (ethylene glycol) hydrogels." *Journal of Biomedical Materials Research: An Official Journal of The Society for Biomaterials and The Japanese Society for Biomaterials* 59.1 (2002): 63-72.

[199] Elisseeff, J., et al. "Photoencapsulation of chondrocytes in poly (ethylene oxide) -based semi-interpenetrating networks." *Journal of Biomedical Materials Research: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials* 51.2 (2000): 164-171.

[200] Leboy, Phoebe S., et al. "Dexamethasone induction of osteoblast mRNAs in rat marrow stromal cell cultures." *Journal of cellular physiology* 146.3 (1991): 370-378.

[201] 200- Jiang, Jie, et al. "Bioactive stratified polymer ceramic-hydrogel scaffold for integrative osteochondral repair." *Annals of biomedical engineering* 38 (2010): 2183-2196.

[202] Gao, Guifang, and Xiaofeng Cui. "Three-dimensional bioprinting in tissue engineering and regenerative medicine." *Biotechnology letters* 38 (2016): 203-211.

[203] Qi, Xin, et al. "Three-dimensional printing of calcium sulfate and mesoporous bioactive glass scaffolds for improving bone regeneration in vitro and in vivo." *Scientific reports* 7.1 (2017): 1-12.

[204] Evinger, Albert J., et al. "Osteogenic differentiation of mesenchymal stem/stromal cells within 3D bioprinted neotissues." (2013): 193-2.

[205] Keriquel, Virginie, et al. "In vivo bioprinting for computer-and robotic-assisted medical intervention: preliminary study in mice." *Biofabrication* 2.1 (2010): 014101.

[206] Herberg, Samuel, et al. "Inkjet-based biopatterning of SDF-1β augments BMP-2-induced repair of critical size calvarial bone defects in mice." *Bone* 67 (2014): 95-103.

[207] Duarte Campos, Daniela Filipa, et al. "Bioprinting organotypic hydrogels with improved mesenchymal stem cell remodeling and mineralization properties for bone tissue engineering." *Advanced healthcare materials* 5.11 (2016): 1336-1345.

[208] Das, Sanskrita, et al. "Bioprintable, cell-laden silk fibroin–gelatin hydrogel supporting multilineage differentiation of stem cells for fabrication of three-dimensional tissue constructs." *Acta biomaterialia* 11 (2015): 233-246.

[209] Kolesky, David B., et al. "Three-dimensional bioprinting of thick vascularized tissues." *Proceedings of the national academy of sciences* 113.12 (2016): 3179-3184.

[210] Raja, Naren, and Hui-suk Yun. "A simultaneous 3D printing process for the fabrication of bioceramic and cell-laden hydrogel core/shell scaffolds with potential application in bone tissue regeneration." *Journal of Materials Chemistry B* 4.27 (2016): 4707-4716