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## Development of Bioimplants with 2D, 3D, and 4D Additive Manufacturing Materials



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### ABSTRACT

Over the past 30 years, additive manufacturing (AM) has developed rapidly and has demonstrated great potential in biomedical applications. AM is a materials-oriented manufacturing technology, since the solidification mechanism, architecture resolution, post-treatment process, and functional application are based on the materials to be printed. However, 3D printable materials are still quite limited for the fabrication of bioimplants. In this work, 2D/3D AM materials for bioimplants are reviewed. Furthermore, inspired by Tai Chi, a simple yet novel soft/rigid hybrid 4D AM concept is advanced to develop complex and dynamic biological structures in the human body based on 4D printing hybrid ceramic precursor/ceramic materials that were previously developed by our group. With the development of multi-material printing technology, the development of bioimplants and soft/rigid hybrid biological structures with 2D/3D/4D AM materials can be anticipated.

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### 1. Introduction

Bioimplants are implants for medical or clinical therapy applications, such as porous bone implants, prosthetics, wearable biosensors, and drug delivery systems. They are usually implanted into the human body for a period of more than 30 days [1]. They are designed to fix, support, reproduce, or improve the functions of human tissues by integrating the human body, properties of materials, and intactness of bioimplants. Recently, the demand for bioimplants has grown tremendously due to an aging population [2] and a shortage of donor organs in medical treatment [3]. With the study and expansion of the biomaterials field [4], various bioimplants, such as brain/neural implants [5], bone/cartilage implants [6], dental implants [7], and other structural implants, have been developed. Proper selection of biomaterials, manufacturing method [8], surface treatment [9], and biological evaluations [5–8] is the major challenge with bioimplants.

According to differences in the amounts of cellular components in implants [3], bioimplants are categorized into biological implants, biologized implants, and biofunctional implants [10]. Biological implants are prepared from natural biological materials including cell proteins or others by bioprinting. They usually contain two key components: a bioprinter containing living cells and biodegradable scaffolds/matrices (hydrogels). Until now, biological implants could not be used within the human body, although bioprinting has been accepted as a robust potential technology. Biologized implants are fabricated using cellular components and biomaterials that are permanent and non-biodegradable. Bioinert materials, including stainless steel (SS; 316L), tantalum, gold, cobalt–chromium (Co–Cr) alloys, titanium (Ti), and nitinol, are widely applied as biologized implants [11]. Biofunctional implants are implants that have undergone a surface treatment by which bioactive surfaces are prepared after implantation. The surface treatments facilitate cell attachment and proliferation, which are key preconditions for tissue engineering.

Additive manufacturing (AM) technologies, which are methods that add materials onto the substrate rather than subtracting materials as in traditional manufacturing [3], provide more possibilities for the production of bioimplants with complex geometry

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or custom requirements with high efficiency. Recently, two inspiring papers on the 3D bioprinting of tissues or organs were published. Lee et al. [12] presented a method of printing human heart components at various scales, based on suspended hydrogels. Grigoryan et al. [13] established intravascular and multivascular architectures of an alveolar model with photopolymerizable hydrogels; this model was also used in a rodent model of chronic liver injury. At present, fused deposition modeling (FDM), selective laser melting (SLM), stereolithography (SLA), and other AM technologies [14] are being applied successfully to manufacture bioimplants, including cortical bone [15], skull [16], cartilage [17], and surgical tools [18]. However, some drawbacks exist, including additional processing, high cost, and limitations of printable materials [3]. Therefore, new printing methods and materials must be developed to overcome these limitations.

In this paper, two-dimensional (2D) and three-dimensional (3D) AM materials for bioimplants are reviewed. Furthermore, with novel ceramic inks as four-dimensional (4D) AM materials, both rigid and soft bioimplants have been developed, and the combination of soft and rigid segments within one model has been successfully achieved. These novel ceramic inks show great potential in the manufacturing of bioimplants consisting of different segments with various mechanical modules, such as knee joints and vertebral implants.

## 2. 2D AM materials for bioimplants

2D AM is regarded as a matter of applying materials to the surface of an object, typically by coating or other surface-treatment techniques. As shown in Fig. 1 [19–22], 2D AM materials are widely applied in biomedical fields. Corrosion behavior, excellent mechanical properties, and biocompatibility are vital preconditions for the performance of bioimplants in the internal fluid environment of the human body [23]. Surface chemistry and physical topography of the surface play a vital role [9]. Thus, various coating and surface-treatment methods [8], including plasma spraying, sputter coating, and ion-beam-assisted deposition, among others, have been applied to optimize the mechanical properties, biofunctionality, and biocompatibility of biomaterials such as bioceramics, bioglasses, biopolymers, and metal alloys [5,8,9,23], and to enhance the performance of bioimplants or other medical devices. Biodegradable magnesium (Mg) [24] and Ti alloys [25,26] are typical bioimplant materials due to their long-term structural and mechanical durability [24–27]. Coatings on the abovementioned metal-alloy biomaterials have been the subject of much study recently, and include a pulse-potential coating of calcium phosphate on the surface of a Mg alloy (AZ91) [28] and an ultrathin film coating of hydroxyapatite (HAp) on a magnesium–calcium (Mg–Ca) alloy [29]. Both coatings have better performance than their uncoated counterparts in a simulated internal body-fluid environment. In addition, films of Ti alloys have been fabricated onto commercial purity (CP)-Ti substrates via the magnetron sputtering method to enhance the corrosion-resistance properties [30].

Research shows that Mg in bioimplants can promote osteogenic differentiation and improve bone-fracture healing in rats [19]. Development of a supra-nanometer-sized dual-phase Mg alloy using the magnetron sputtering method was reported; this alloy exhibited near-ideal strength at ambient temperature [20]. This supra-nanometer-sized Mg alloy offers great manufacturing potential as a coating on biodegradable implants to improve wear resistance and osteogenic differentiation ability.

Natural and synthetic polymers are widely used as scaffolds or bioimplants in regeneration medicine and the field of tissue engineering [31,32]. Polymer coatings can also promote the biocompatibility and biofunctionality of bioimplants. Tremendous advances

have been achieved in the polymer coating of implants. For example, polymer-coated stents can slowly release anti-stenosis pharmaceuticals [33]. Furthermore, biodegradable elastomeric polyurethanes were reported as drug-eluting coatings for degradable vascular stents based on Mg [21].

In addition to their performance on bioimplants, coatings have great potential in the fields of tissue engineering and cell therapy [34,35] as smart microrobots [36,37]. A porous microrobot fabricated by photoresist SU-8 and coated with nickel (Ni) and Ti can achieve motion control under an external magnetic field [22]. With this microrobot, targeted cells delivery *in vivo* can be achieved successfully under an external magnetic gradient field. A magnetically driven micro-swimmer with a Ni coating was also reported [33], and can potentially be used in medical diagnosis and treatment.

## 3. 3D AM materials for bioimplants

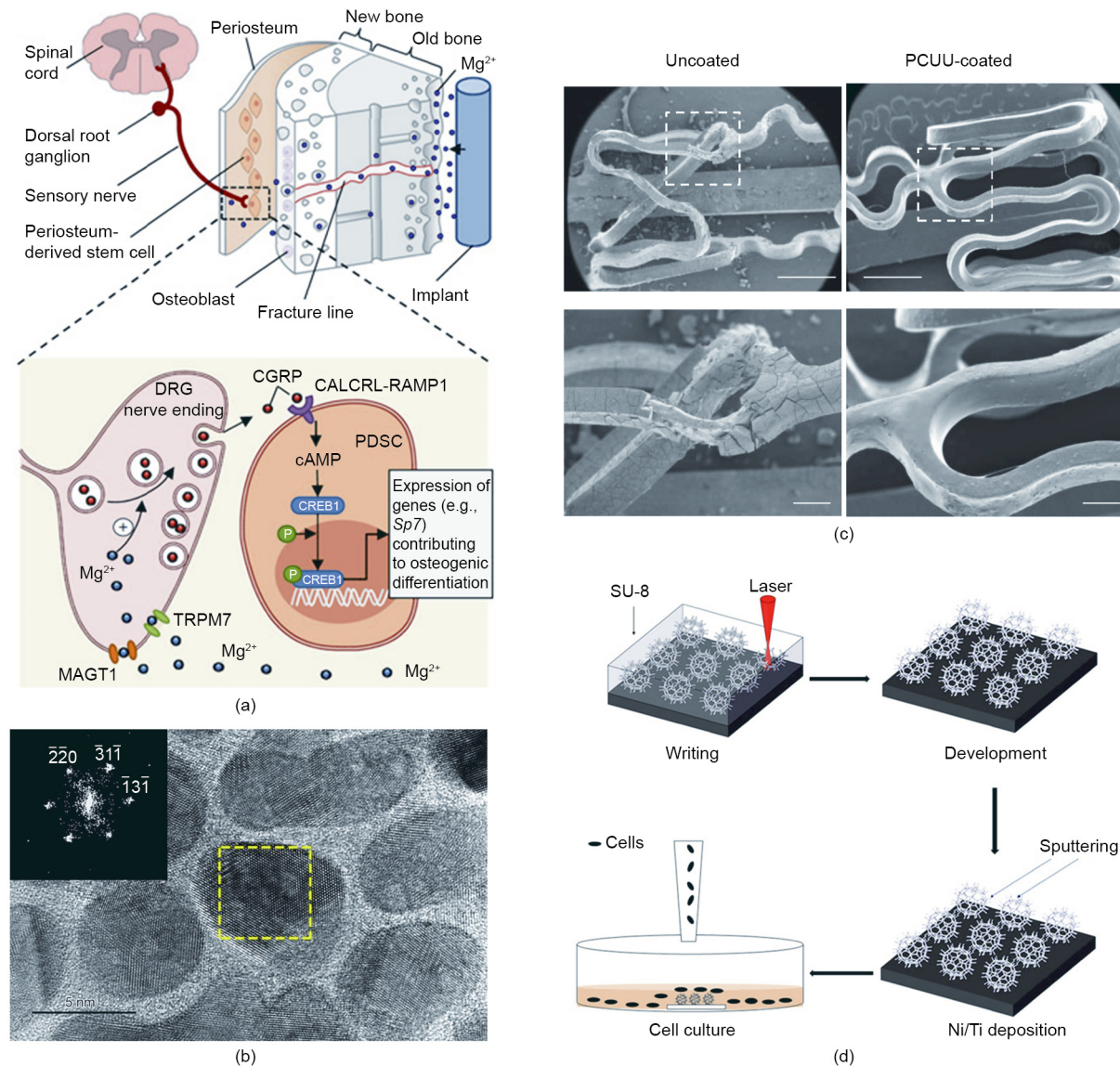
Although many biomaterials have been reported, not all are available for the 3D printing of bioimplants. Materials for the preparation of bioimplants should first have good biocompatibility and low toxicity. Cells should be able to adhere to the surface easily and proliferate well. As they will remain in the human body over the long term, materials should not release toxic elements, and should possess an appropriate degradation rate and wear resistance. To meet the requirements of different locations within the human body (e.g., bone [38], cartilage [39], blood vessel [40,41], joint [42,43], and other focal zones), the application environment should also be considered. Regarding the implants, a mismatch of stiffness between tissue and implants can influence the load sharing in the process of implant use. The materials for load-bearing implants (e.g., bone implants [38,44]) should have high mechanical strength. Therefore, metals and ceramics are good candidates for load-bearing implants. Polymer materials must also be considered due to their appropriate tensile strength and an elastic modulus that is similar to that of host tissues.

To fabricate implants by 3D printing methods, the chemical and physical properties of materials must also be considered. Several materials that have been used in bioimplants or have potential for bioimplant use in the near future are introduced in the following discussion.

### 3.1. Polymers

Polymers that are commonly used to prepare scaffolds by 3D printing include polyetheretherketone (PEEK), polycaprolactone (PCL), poly(vinyl alcohol) (PVA), and poly(L-lactic acid) (PLLA) [3].

PEEK, which has been approved by the US Food and Drug Administration (FDA), is a thermoplastic biomaterial with mechanical properties that have been highlighted for use in artificial bone implants, especially at human load-bearing sites. The Young's modulus and tensile strength of PEEK are 3.3 GPa and 110 MPa, respectively, which are in close proximity to the corresponding values of 3.75 GPa and 100 MPa for collagen [45]. Owing to its mechanical proximity with natural collagen, PEEK is a suitable candidate for replacement of collagen in artificial bone implants. Processability is a significant challenge for PEEK due to its high glass-transition temperature and melting temperature, at 143 and 343 °C [46], respectively. In cranio-maxillofacial (CMF) surgery, patient-specific implants have been fabricated by FDM [47], with collection bed and print temperatures of 100 and 400 °C, respectively. Haleem and Javaid [46] also reviewed the promising application of 3D-printed PEEK in dental implants. Zhang et al. [48] developed a new method of designing costal cartilage prostheses with wavy elastic structure by means of FDM.



**Fig. 1.** 2D AM materials in biomedical applications. (a) Schematic showing diffusion of implant-derived  $Mg^{2+}$  contributing to osteogenic differentiation; (b) structure of supra-nanometer-sized dual-phase glass-crystal; (c) scanning electron microscopy images of corrosion regions on stents with various coatings under a simulated body environment; (d) fabrication process of microrobots including Ni/Ti deposition. DRG: dorsal root ganglion; CGRP: calcitonin gene-related peptide; TRPM7: transient receptor potential-melastatin-like 7; MAGT1: magnesium transporter subtype 1; CALCRL: calcitonin receptor-like receptor; RAMP1: receptor activity modifying protein 1; PDSC: periosteum-derived stem cell; cAMP: cathelicidin antimicrobial peptide; CREB: cAMP-regulated enhancer B. (a)–(d) Reproduced from Refs. [19–22] with permission of the authors.

PCL is the most commonly used thermoplastic polymer for the 3D printing of bone scaffolds due to its prior FDA approval, good biocompatibility, and slow biodegradation. Its low melting temperature (60 °C) eases its fabrication by means of benchtop FDM. Zamani et al. [49] prepared a PCL scaffold with gradient mechanical properties by FDM for use as potential mandibular bone implants. The PCL material lacks osteo-inductivity, so functionalized mineral additives had to be incorporated in the matrix, including tricalcium phosphates (TCPs), HAp crystals, decellularized bone matrix (DCB) [50], and trace elements (such as strontium (Sr), Mg, zinc (Zn), silver (Ag), and silicon (Si)) in the human body [51]. PCL scaffolds can also be used in the clinical application of augmentation rhinoplasty [52].

Poly(lactic acid) (PLA) is a semi-crystalline polymer with melting and glass-transition temperatures of 174 and 57 °C,

respectively. PLA has two different stereoisomers, PLLA and poly-D-lactide (PLDA). PLLA degrades much slower than PLDA in the human body, so PLLA is usually made into orthopedic implants. PLA has been approved by the FDA for use as a human biomedical material, and shows promising application for fixation devices such as screws, pins, sutures, and arrows in orthopedics and dentistry due to its good biocompatibility and low toxicity. However, it presents a problem similar to that encountered with PCL: namely, its lack of mechanical strength and functionality limit its further applications [47,53].

In addition to the aforementioned polymers, poly(methyl methacrylate) (PMMA), PVA, and poly(lactic-co-glycolic acid) (PLGA) are widely used in 3D-printed implants. The usage of PMMA in cranioplasty can be dated back to the 1940s. Petersmann et al. [54] prepared cranial implants using PMMA by means of FDM. PVA shows excellent potential for cartilage repair.

### 3.2. Ceramics

Ceramics are preferred for the preparation of bone implants, because natural bone is composed of ceramic (HAp, ~80% wet weight of bone) and collagen. Ideal bioceramics should be not only biocompatible, but also osteoconductive and osteoinductive, without releasing toxic elements during application. Initially, bioinert bioceramics were represented by zirconia ( $ZrO_2$ ) [55] and alumina ( $Al_2O_3$ ) [56] for the production of femoral heads of total hip arthroplasty prostheses. Later, bioactive ceramic materials were developed, which can form strong chemical-force bone bonding to host bone tissue without causing inflammation. Ca–P-based ceramics are a well-known group including HAp [57], TCP [58], and bioglass as bone-replacement materials. These bioactive ceramics have a significantly lower mechanical strength compared with  $ZrO_2$  and  $Al_2O_3$ , but show better biological response, production of proteins, and cell adhesion (osteoconduction). Chen et al. [59] reviewed the 3D printing technologies of ceramics in 2019, including slurry-, powder-, and bulk solid-based methods

### 3.3. Metals

The 3D printing of metals or their alloys materials is usually realized by SLM or electron beam melting (EBM) [60]. Several common metals and alloys (Ti-based, SS, and Co-based) and biodegradable metals (Mg-based, Zn-based, and iron-based) for bioimplants are introduced in the following subsections.

#### 3.3.1. Titanium-based alloys

Ti alloys have been used as biomaterials due to their good biocompatibility, low modulus, and resistance to corrosion. Ti–6Al–4V is used to fabricate clavicular implants, mandibular implants, in foot osteotomy, as flanged acetabular cups, and in other focal zones such as dental and hip implants [61]. However, Alzheimer's, osteomalacia, and other neurological issues occur due to the release of Al and V [62–64]. Currently, Ti–6Al–7Nb [65] and Ti–5Al–2.5Fe [66] without V are fabricated and applied in femoral prosthesis stems. Surface modifications and the addition of refractory metal elements in Ti alloys are usually necessary for better wear resistance.

#### 3.3.2. Stainless steel

Austenitic 316L SS alloys (containing 2%–3% molybdenum (Mo)) are the most commonly used implant materials to fabricate internal fixation devices (stents, bone plates, and artificial joints) [67,68]. Because 316L SS cannot promote new tissue growth, Hao et al. [69] presented a combination material comprising 316L SS and HAp bioceramic for manufacturing load-bearing and bioactive composite implants by SLM. 317L SS alloys (containing 3%–4% Mo) are better than 316L in terms of pitting and general corrosion resistance [70]. To reduce bacterial infections of bone implants, Chai et al. [70] studied the biocompatibility and antibacterial activity of 317L SS–Cu *in vitro* and *in vivo*. Localized corrosion effect, causing 24% [71] of implant failures, is a major issue impairing the performance of SS alloys as implant materials [72]. Surface modification [73], coating, and surface texture modification (at the nanoscale) [74,75] can be adopted to improve the corrosion resistance of SS.

#### 3.3.3. Cobalt-based alloys

Co–Cr alloys, consisting of Co, Cr, Ni, and Mo, are commonly used biomaterials for orthopedic implants. Compared with SS, Co-based alloys have better biocompatibility, abrasion resistance, corrosion resistance, and mechanical strength [72]. Co–Cr alloys have two basic types: Co–Cr–Mo alloys and Co–Ni–Cr–Mo alloys. Co–Cr–Mo alloys have been used in dental implants and artificial

joints, with element contents of 27%–30% Co, 2.5% Ni, and 5%–7% Mo [76]. Co–Ni–Cr–Mo alloys have been used for heavy load-bearing joints (hip and knee joints) [77], composed of 19%–21% Cr, 33%–37% Ni, and 9%–11% Mo [76]. Xiang et al. [78] manufactured a Co–Cr–Mo alloy with an anisotropy microstructure and mechanical properties by means of EBM. Biocorrosion is one of the major problems for Co-based alloys due to the release of positively charged metal ions in the process of binding to proteins or cells in the human body [79].

#### 3.3.4. Magnesium-based alloys

Pure Mg has a similar density to natural bone, at slightly less than  $1.74 \text{ g}\cdot\text{cm}^{-3}$  in comparison with  $1.8\text{--}2.1 \text{ g}\cdot\text{cm}^{-3}$  [80]. However, its application for implants in the human body is restricted by its rapid corrosion, which causes quick degradation. If researchers can control the corrosion rate of Mg, it could be an appropriate candidate for bone implants, as its elastic modulus (45 GPa) is similar to that of cortical bone. This would allow the stress-shielding effect to be avoided effectively. Mg alloys (Mg–Zn- [81], Mg–Ca- [82], Mg–Si- [83], and Mg–Sr-based alloys) [84] provide good solutions to control the corrosion of pure Mg, and have shown great potential in the tissue engineering, orthopedic, and cardiovascular fields. In bioimplants, Al and rare-earth elements cannot be alloyed with Mg, because these two components result in neurotoxicity and hepatotoxicity, respectively, although the mechanical strength is increased. In addition, hydrogen formation is usually a common challenge in research on Mg alloys [5,85]. As an alternative material, Mg glasses can be applied as implants without the formation of hydrogen [86].

#### 3.3.5. Zinc-based alloys

Zn-based alloys hold tremendous potential as tissue implant materials due to their good biodegradability and biocompatibility [87]. In 2013, Bowen et al. [88] reported Zn as a superior applicant material for the fabrication of stents. Pure Zn has an ultimate tensile strength of 20 MPa by casting and 120 MPa by wrought operation [89,90]. However, it is not strong enough for application in stents (i.e., 300 MPa is required for a vascular stent). Thus, Zn needs to be combined with other metals to form alloys for biomedical applications. Zn–Mg, Zn–Ca/Sr, Zn–Al, Zn–Li, Zn–Ag, Zn–Cu, and Zn–Mn alloy systems have been reviewed in some papers [87,91]. Zn–Cu alloys show potential application in craniomaxillofacial osteosynthesis implants [92]. Interfacial Zn–P provides a key controlling biocompatibility for Zn implants, and can be used as a promising coating material with stable chemical properties for other biomedical applications [93].

#### 3.3.6. Iron-based alloys

Iron and its alloys, which do not promote hydrogen evolution and which have better mechanical properties than Mg-based alloys, are another type of biodegradable metal that can be used as cardiovascular stent or bone implants [94] due to their low hemolysis ratio and excellent anticoagulant property [95,96]. The elastic modulus of pure Fe (211.4 GPa) is higher than that of pure Mg (41 GPa) or 316L SS (190 GPa) [97]. Mn, carbon (C), Si, and palladium (Pd) elements are commonly alloyed with Fe in order to enhance the degradation rate of pure Fe material ( $0.16 \text{ mm}\cdot\text{a}^{-1}$  [97] in an osteogenic environment) and reduce its magnetic susceptibility in clinical application. When an open cell structure is designed for Fe-based alloys, they can show mechanical properties close to those of natural bone [98]. Li et al. [99] fabricated Fe scaffolds by direct metal printing with an ordered porous structure, and studied their biodegradation behaviors and mechanical properties. Hong et al. [100] fabricated Fe–Mn and Fe–Mn–Ca-based constructs by 3D printing, and found that Ca addition could enhance the degradation rate of Fe. Usually, modification needs

to be done to improve the surface bioactivity by stimulating bone formation. Yang et al. [101] presented a HAp coating method based on a hydrothermal procedure to improve 3D-printed Fe scaffolds, and demonstrated potential application in bone engineering.

### 3.3.7. Bulk metallic glasses

Bulk metallic glasses (BMGs) are a kind of metallic material with a strength, elasticity, and Young's modulus of ~2 GPa, ~2%, and 50–100 GPa, respectively [102]. They have high wear- and corrosion-resistance ability due to their unique disordering atomic structure. Therefore, BMGs can be used as novel implant materials with better biocompatibility than their crystalline bulk.  $Zr_{44}Ti_{11}Cu_{10}Ni_{10}Be_{25}$  BMG exhibits better cell growth and attachment support ability [103].  $Pt_{57.5}Cu_{14.7}Ni_{5.3}P_{22.5}$  BMG with micro-/nano-patterns surface shows enhanced angiogenic performance [104].

## 3.4. 3D AM technologies for bioimplants

Several representative 3D AM technologies that are commonly used for bioimplant manufacturing are summarized in Table 1 [14–17,105–113], along with their advantages, limitations, and current applications.

### 3.4.1. Fused deposition modeling

FDM is an AM process in which a thin filament of polymer is formed after melting and extrusion [114]. Thermoplastic polymers are usually used, such as polycarbonate (PC), acrylonitrile butadiene styrene (ABS), PCL, polyamide (PA), and PLA. Zeng et al. [115] built an artificial human ear using FDM technology, in which polyurethane was adopted to prepare the auricular framework, due to its good flexibility and biocompatibility. This experiment indicated an efficient way to achieve macrotia reconstruction and mitigate other cartilage defects in orthopedic surgery. Gronet et al. [116] fabricated acrylic cranial implants for two patients that facilitated the restoration of large or complicated cranial defects. Tan et al. [16] produced patient-specific acrylic cranioplasty implants. The advantages of these implants included no required chemical post-treatment and cost efficiency, while their main

limitation was the inferiority of the mechanical properties of the products [117].

### 3.4.2. Direct ink writing

Direct ink writing (DIW) is an AM process in which the suspension or melts of the material are extruded from the machine as filaments [105]. There are abundant sources of materials for DIW, including hydrogels, ceramic/metal powder suspensions in polymer solution, and thermoplastic polymer melts. Recently, a melt-electrospinning-based DIW method [118] was developed that allowed high resolution to be obtained due to the melt's stretching under a high-voltage electric field. Similar to FDM, the printing resolution is subject to, for example, the pressure, moving velocity of the stage, and diameter of printing nozzles. For ceramic and metal parts, post-treatment is required to remove the polymer composition in the printing inks by sintering or other methods. The DIW method has been applied in developing bioimplants, including in cartilage [17], bone tissue [106], and vascularization [107].

### 3.4.3. Stereolithography

SLA, one of the earliest AM methods, was developed in 1986 [119]. It uses ultraviolet (UV) light to initiate polymerization on a thin layer of photosensitive resin or monomer solution. An acrylic or epoxy group is usually contained in the monomers, which can be activated to polymerize and form long-chain polymers. Bone [15] and dental implants [108] have been developed using the SLA method. To prepare ceramic-based implants, ceramic powders can be dispersed in the photosensitive resin, and the polymers are removed by subsequent sintering. Winder and Bibb [120] summarized the potential applications of SLA in maxillofacial prosthodontics, including auricular and nasal prosthesis, obturators, and surgical tents. Post-treatments sometimes include, for example, polishing, painting, and sanding. The advantage of SLA is the production of implants with a high resolution of 10  $\mu\text{m}$  [119], while its disadvantages are a high cost and limited material resources.

### 3.4.4. Selective laser melting

During SLM processes, the laser fuses the powder, which lies loosely in the bed, at a specific location for each layer to form

**Table 1**  
Several representative 3D AM technologies for bioimplant manufacturing.

3D AM technology	Materials	Basic principle	Advantages	Disadvantages	Application in bioimplants
FDM [14]	Thermoplastic filaments, including ABS, PLA, PC, and PA	Selectively depositing melted material in a pre-determined path layer-by-layer	Cost-effective; wide range of materials	Lowest-dimensional resolution	Skull [16], vertebrae
DIW [105]	Hydrogel, HAp, polymer nanocomposites, sol-gel, ceramic inks	Liquid-phase "ink" is dispensed out under controlled pressure and deposited layer-by-layer	Bulk with high density; porous scaffold	Limited selection of ink with rheological properties; post-processing needed to remove polymer composition for ceramic and metal printing	Cartilage [17], bone tissue [106], vascularization [107]
SLA [14]	Photo-reactive resin	Using light processing to crosslink monomers and form parts layer-by-layer	High speed; high resolution; smooth surface	High cost; brittle; post-processing needed to remove supporting part	Bone implants [15], dental implants [108]
SLM [14]	Mg, Ti, Al alloys, Ti alloys, SS	Using a laser to scan and selectively fuse the metal powder particles, bonding them to build model layer-by-layer	Complex geometries; lightweight structure; good mechanical performance	High cost; small manufacturing size	Locking plate [18], acetabular cups [109], spinal surgery template [110], dental alloys [111]
EBM [112]	Co–Cr–Mo alloy, Ti–6Al–4V, Ni–Ti alloy	Components are built within a powder bed by selectively melting the powder with a high power electron beam	Extremely high velocities under vacuum condition; high working temperature; low residual stress	Restricted to conductive materials (metals and alloys)	Orthopedic implants [78], dental implants [113]

designed structures. Pure metal powders and laser beams (generally neodymium-doped yttrium aluminum garnet, 1.064  $\mu\text{m}$ ) with a higher absorptivity to metals or fiber lasers (1.09  $\mu\text{m}$ ) with a shorter wavelength are commonly used in the SLM process. Researchers produced the first patient-specific Ti-6Al-4V jaw implant using SLM technology [121]. The advantages of SLM include a wide range of materials to use and the recyclability of unused particles. Its disadvantages are that the printing accuracy depends on particle size and the printing environment is inert gas, preventing the oxidation of particles. Applications of SLM in bioimplants include the development of locking plates [18], acetabular cups [109], spinal surgery templates [110], and dental alloys [111].

#### 3.4.5. Electron beam melting

EBM, which was developed by Arcam AB Corporation (Sweden) in 1997, is a powder-bed-based AM technology [112]. It is similar to the SLM process. However, an electron beam is the heat source in EBM instead of a laser beam. Moreover, EBM is only applied for the preparation of metals and alloys, while SLM is used for polymers, metals, and ceramics. EBM can operate at extremely high velocities (up to  $10^5 \text{ m}\cdot\text{s}^{-1}$ ) under vacuum conditions [112]. Co-Cr-Mo alloys [78], Ti-6Al-4V [113,122,123], and Ni-Ti alloys [124] have been reported to be fabricated by EBM as orthopedic and dental implants. A noteworthy advantage of EBM is that the level of residual stresses in the parts made by EBM is much lower than that in those made by SLM.

#### 3.4.6. 3D bioprinting

Unlike other 3D printing technologies, 3D bioprinting uses bioinks as printing materials. Bioinks consist of biological materials, biochemicals, and living cells. The central challenge in 3D bioprinting is recapitulating biological function based on the production of structures [125]. Based on the work principles, 3D bioprinting methods can be classified as inkjet-based [126], microextrusion-based [127], and laser-assisted bioprinting [128]. An ideal bioink is important for bioprinting; it should meet requirements such as an adequate mechanical strength, adjustable gelation process, biocompatibility, and so on. Researchers can refer to some reviews [129–132] on bioinks for 3D bioprinting. Kang et al. [133] invented an integrated tissue-organ printer system, which was used for the potential reconstruction of mandible bone, calvarial bone, ear cartilage, and skeletal muscle. Lee et al. [12] presented a new 3D bioprinting method with freeform reversible embedding of suspended hydrogels as a supporting printing medium, and printed a human heart at various scales. Grigoryan et al. [13] established intravascular and multivascular structures with photopolymerizable hydrogels by means of SLA. 3D bioprinting technology has shown a flourishing foreground, although it has not been used for real application in clinics.

## 4. 4D AM materials for bioimplants

In 4D printing, a 3D-printed material autonomously and programmably changes its configuration or function in response to environmental stimuli, such as stress, light, liquids, temperature changes, magnetic fields, gas pressure, embedded circuitry, or a combination of these stimuli. The first demonstration of 4D printing was a multi-material strand folded into the letter “MIT” in 2014 [134]. Thus far, many materials, including polymers [135–143], metals [143–145], and ceramics [146], have been developed for 4D AM. The shape-morphing capabilities of 4D AM materials [147] can be applied in dynamic and versatile human environments, such as for drug delivery [148] and stent insertion [149]. However, the response speed and mechanical robustness of

shape-morphing materials are usually critical limitations in developing practical applications.

Gladman et al. [135] reported a biomimetic 4D printing system made of hydrogel composite materials, in which the orientation of embedded non-swelling cellulose fibers was precisely patterned for anisotropic swelling behavior. Complex-shaped overall architectures with mixed Gaussian curvature were designed and achieved with this system. Another kind of widely used 4D AM polymer is shape memory polymers (SMPs) and their composites, which have many advantages, including large deformation, multi-stimuli response, biocompatibility, light weight, and low cost [150]. Ge et al. [136] developed printed active composite materials with multi-material printing technology. The printed SMP fibers in an elastomer matrix could drive the shape-morphing behavior of the composite materials, resulting in the thermo-mechanical programming of origami patterns [137]. Ding et al. [138] designed a direct 4D printing method that integrated the programming steps into the 3D printing process, resulting in permanent programmed shapes. Lin et al. [139] introduced magnetic powders into an SMP matrix to achieve remote control of 4D-printed biomedical devices. Huang et al. [140] proposed a kind of novel 4D AM polymer made from hydrogel and SMPs; the ultra-fast digital printing that was used for this polymer overcame the limitations in AM speed by avoiding layer-by-layer printing in the vertical dimension and line-by-line printing in the planar dimension. Furthermore, some works on the 3D printing of shape memory alloys (SMAs) suggest potential for developing 4D AM metallic materials [143], including Ni-Mn-Ga SMAs using the binder jetting printing method [144] and NiTi alloys using SLM methods [145]. In these works, 3D-printed SMAs exhibit shape memory behavior resulting from martensitic transformation with temperature changes.

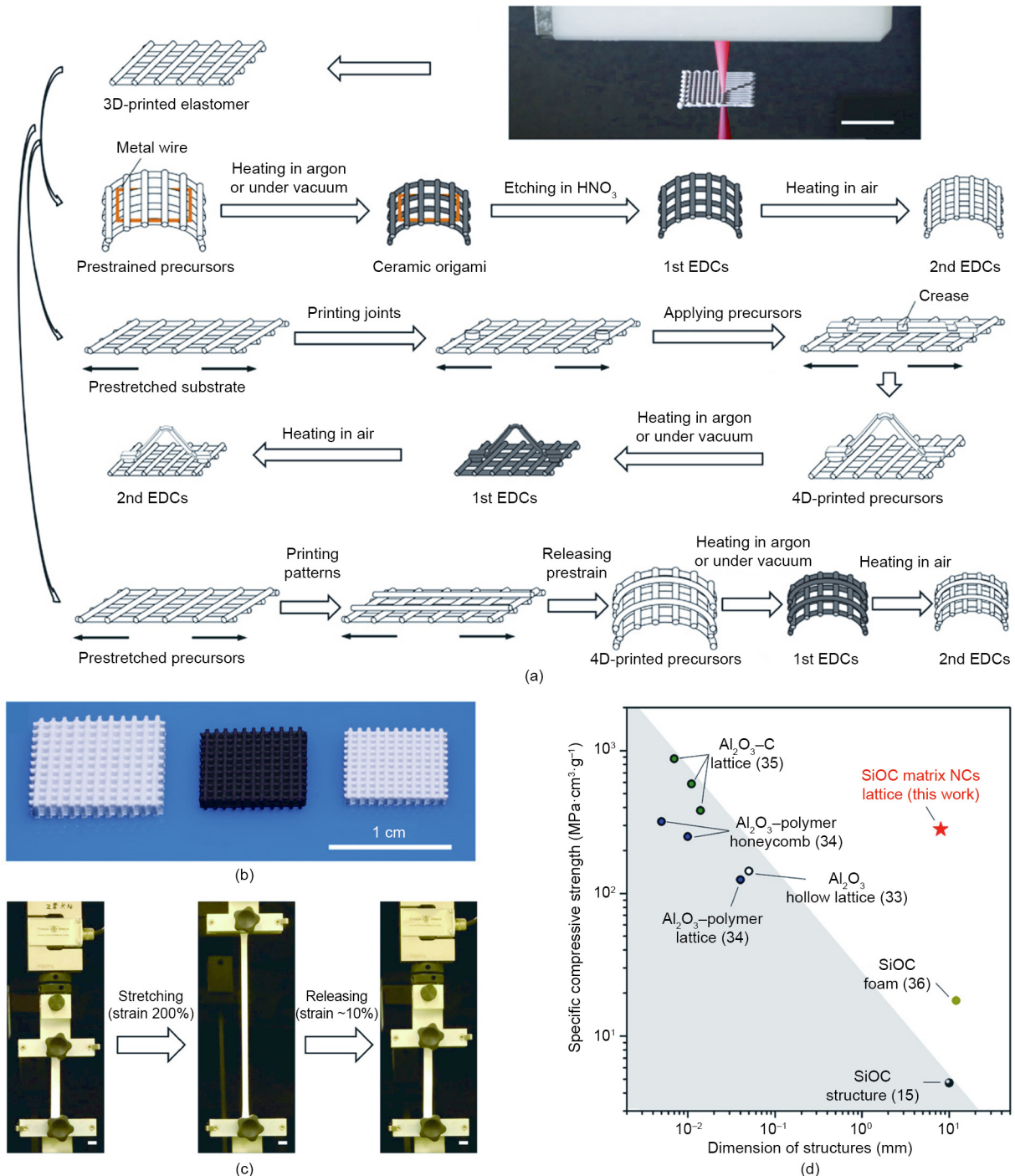
4D AM techniques are developed with the shape-morphing capability of the relevant 4D AM materials. Various materials and technologies provide tremendous possibilities for designing and fabricating 4D smart structural materials such as soft robots, controlled grippers, programmable shape change patterns, and more. Heat is the most common and readily accessible stimulus for 4D printing, and a large number of heat-responsive 4D materials have been reported, including hydrogels [135], SMAs [151], and SMPs [138]. However, the relatively slow response speed of heat-driven 4D printing technologies is a major limitation in their broad application.

Light-driven 4D technology has attracted a great deal of attention due to advantages such as a fast response, wireless control, accurate focusing, and sustainable properties [152–154]. Graphene and carbon nanotube-based composites [155–157], liquid crystal elastomer-based composites [158–160], SMPs [161], and hydrogels [162] are commonly used in light-triggered 4D systems. A light-sensitive printed micro-swimmer [163] was reported. Humidity has also been used to drive the deformation of 4D printed actuators. Mao et al. [142] demonstrated a hydrophilic/hydrophobic bilayer under a humidity stimulus, which showed potential application in soft actuators. Magnetic fields are another important strategy for 4D material development, as their delicate control and excellent biocompatibility for living organisms meet the preconditions for their biomedical and therapy use. 4D magnetic butterfly structures [164,165] and a 4D flower-like magnetic actuator [166] were printed by DIW. Various biomimetic 4D structures controlled by a magnetic field were also reported, including spirulina cells [167], caterpillars [168,169], starfish [170], and jelly fish [171]. Besides these technologies, stress- [146], electricity- [172], and gas-driven [173] 4D printing technologies have also been studied. These 4D-driven technologies have progressed a great deal recently; however, most existing smart 4D structures are only responsive to one stimulus, which limits their interaction capacity

with the surroundings and their adaptability under multiple environmental stimuli [174]. The development of multi-responsive materials and technologies has promoted a new generation of 4D-printed structures, including light-thermal dual-responsive hydrogels, electrothermal and electrochemical actuation materials [175], magnetic-photo/thermal dual stimuli actuators [176–180], temperature-pH sensitive fluorescence bilayer actuators [181], and humidity-temperature-light triple-responsive hydrogels [174]. A biomimetic shape-color double-responsive 4D composite based on SMPs and thermochromic pigments was printed by

means of FDM [182]. Meanwhile, some problems for 4D AM techniques still remain to be overcome; for example, the wavelength limitation and biological toxicity of light, reactive nature concerns, and frequency control of a magnetic field.

The first ceramic 4D printing system was previously developed by our group. In this system, elastic ceramic precursors were printed, deformed, and then transformed into rigid ceramic structures, as shown in Fig. 2 [146]. The shape-morphing process can be achieved by releasing the elastic energy stored in the pre-stretched ceramic precursors, which can be stretched to over 200% strain.



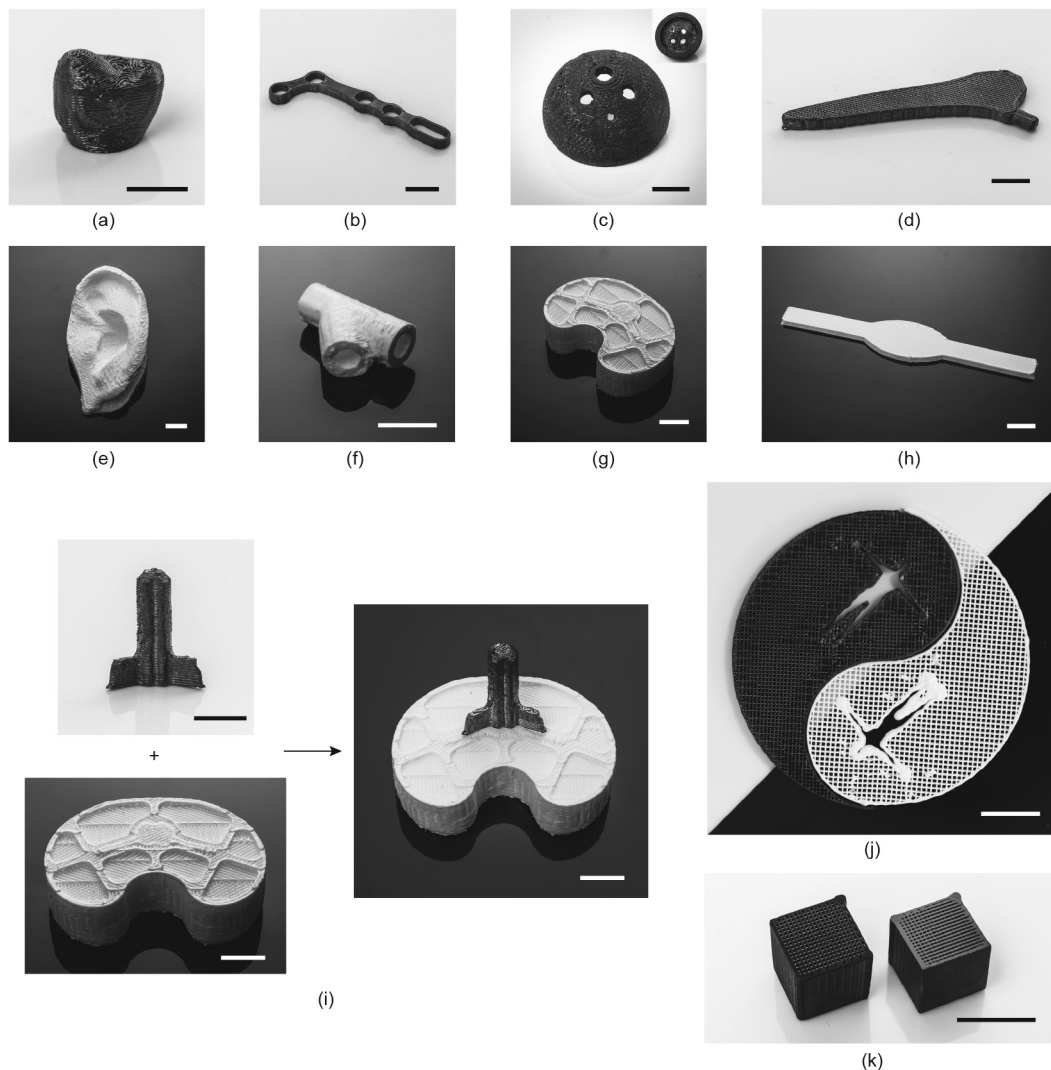
**Fig. 2.** A ceramic 4D printing system. (a) DIW-morphing-heat treatment method. (b) Printed micro-lattice of ceramic precursors and two types of corresponding EDCs (left to right). (c) Printed ceramic precursors can be stretched to 200% strain. (d) Strength-scalability synergy is achieved. Scale bars, 1 cm. NCs: nanocomposites. Reproduced from Ref. [146] with permission of the authors.

Moreover, strength-scalability synergy is achieved in 4D printed elastomer-derived ceramics (EDCs). Hierarchical EDCs with printed architectures from 200  $\mu\text{m}$  to tens of centimeters, as well as a compressive strength of 547 MPa at  $1.6 \text{ g}\cdot\text{cm}^{-3}$ , can be prepared by this method [146].

Compared with other 4D AM polymeric and metallic materials, the abovementioned ceramic 4D AM system has advantages for high-temperature structural applications, since polymer-derived ceramics exhibit remarkable thermal, chemical, and mechanical stability [183]. The DIW and heat treatment process of the ceramic precursors is more cost-effective than other high-melting-point material 4D AM systems, because it does not require expensive laser energy for the 3D printing process, or sintering of high-melting-point material powders for post-processing. Moreover, the ceramic 4D AM system can be extended to develop various material and shape-morphing systems, due to its open-end feed-stock system for ink materials. The disadvantages of the current ceramic 4D AM system include its deformation control accuracy, because the shape-morphing system relies on a homemade biaxial stretch device. With the involvement of a new deformation mechanism and high-accuracy machining technologies, improvement is expected in the shape-morphing programming accuracy.

The above-described ceramic 4D printing work could drive innovation in the AM of bioimplants. With the printability of both ceramics and ceramic precursors, the AM of rigid bioimplants with ceramics, including crowns, locking plates, acetabular cups, and bone plates (as shown in Figs. 3(a)–(d)), as well as soft ones with ceramic precursors, including ears, tracheas, meniscuses, and ligaments (as shown in Figs. 3(e)–(h)), can be anticipated. Moreover, bioimplants with simultaneously soft and rigid parts can be printed, since the “ceramic inks” used for printing ceramic precursors and ceramics can fuse these parts together, resulting in a homologous sandwich structure (as shown in Fig. 3(i)). The inks for these results were prepared by mixing liquid PDMS (SE1700 clear, Dow Corning Co., USA) with 10 wt%  $\text{ZrO}_2$  nanoparticles (Tong Li Tech Co. Ltd., China). The 3D printing of the ceramic precursors was conducted with a DIW-based 3D printer. After ink deposition, the formed structures were post-cured at  $150^\circ\text{C}$  for 30 min. Ceramics were generated by heating the ceramic precursors to  $1300^\circ\text{C}$  for 1 h under argon (Ar) flow.

Furthermore, these printed ceramics can achieve a compressive strength of 34–547 MPa and a tensile strain of 200% [146]. According to a related report, the ultimate tensile strains for tendons/ligaments and articular cartilage are 10%–15% and 60%–120%



**Fig. 3.** Development of representative bioimplants with 4D printing hybrid ceramic precursor/ceramic materials. Printed rigid ceramic-made (a) crown, (b) locking plate, (c) acetabular cup, and (d) bone plate. Printed soft ceramic precursor-made (e) external ear, (f) trachea, (g) meniscus, and (h) ligaments. (i) Printable “ceramic inks” as adhesives to fuse printed rigid and soft bioimplants together. (j) Printed Yin/Yang symbol for Tai Chi with white/black hybrid ceramic precursor/ceramic materials demonstrating soft/rigid hybrid biological structures in the human body. (k) Comparison of printed ceramic lattice structure without (left) or with (right) polishing. Scale bars, 1 cm.



[184], respectively, while the compressive strengths of cortical bone tissue and dental tissue are 88–164 and 295 MPa, respectively [185]. All these parameters are within the mechanical properties range of this material, which indicates its potential use in bioimplants of various tissues, especially parts with both soft and rigid segments.

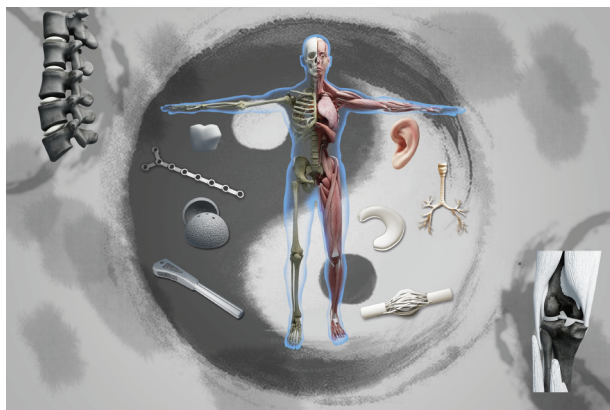
Similar to the philosophical relationship between the two fundamental elements Yin and Yang in Tai Chi, soft and rigid biological structures in the human body fuse and function together, resulting in a comprehensive balance in the form of soft/rigid hybrid biological components such as knee joints and vertebrae (Fig. 4). A Yin/Yang symbol for Tai Chi with white/black hybrid ceramic precursor/ceramic materials demonstrating soft/rigid hybrid biological structures in the human body was printed (Fig. 3(j)). Soft/rigid hybrid structural materials based on AM techniques will be desirable for a diversity of fields, including bio-inspired tough or otherwise superior materials [186–189], as well as actuators [190–192].

Post-treatment of printed structures can be applied to obtain good mechanical properties or biocompatibility. For example, post-treatment with surface mechanical attrition treatment [193] of 3D-printed components in Ti alloys can introduce a nanostructured layer to the metal surface [194] and drastically enhance fatigue resistance [195]. Furthermore, printed ceramic structures with good polishing can be prepared with an average surface roughness (Ra) on the polished samples of 0.06  $\mu\text{m}$  (Fig. 3(k)).

## 5. Conclusions

The present soft/rigid hybrid 4D AM concept that is achieved by the 4D printing of hybrid ceramic precursor/ceramic materials can be extended to other binary and multiple-component systems. Assisted by other technologies, such as multi-material printing and local ceramization, more kinds of soft/rigid hybrid structures with functional gradient interfaces can be additively manufactured. More innovations in the development of bioimplants for complex and dynamic biological environments in the human body could be generated together with a combination of 2D/3D/4D AM materials.

In future research, multi-material printing would include material combinations among not only printing host materials but also printing support materials and printing medium materials. With the development of multi-modulus ink material systems, AM of bio-inspired tough hybrid systems could be applied in structural materials to overcome the strength-toughness tradeoff. Multidimensional AM will drive the printing dimension to increase from



**Fig. 4.** Soft and rigid biological structures in the human body fuse and function together, resulting in a comprehensive balance like the Yin and Yang symbols in Tai Chi.

2D/3D/4D to even higher dimensions and the printing strategy to change from dot-by-dot/line-by-line/sheet-by-sheet/volume-by-volume AM to AM with even higher dimensional elements, resulting in a high level of structural freedom and printing efficiency. Furthermore, the involvement of other manufacturing strategies such as subtractive manufacturing, together with the pre-programming, real-time treatment, or post-processing of printed materials for various functional applications, will offer promising research and industrial opportunities for future study on AM materials and technologies.

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## Compliance with ethics guidelines

Guo Liu, Yunhu He, Pengchao Liu, Zhou Chen, Xuliang Chen, Lei Wan, Ying Li, and Jian Lu declare that they have no conflict of interest or financial conflicts to disclose.

## References

- [1] Kolan KCR, Leu MC, Hilmas GE, Brown RF, Velez M. Fabrication of 13–93 bioactive glass scaffolds for bone tissue engineering using indirect selective laser sintering. *Biofabrication* 2011;3(2):025004.
- [2] Kang CW, Fang FZ. State of the art of bioimplants manufacturing: part I. *Adv Manuf* 2018;6(1):20–40.
- [3] Ho CMB, Ng SH, Yoon YJ. A review on 3D printed bioimplants. *Int J Precis Eng Manuf* 2015;16(5):1035–46.
- [4] Gilbert F. A threat to autonomy? The intrusion of predictive brain implants. *AJOB Neurosci* 2015;6(4):4–11.
- [5] Prakasam M, Locs J, Salma-Ancane K, Loca D, Largeteau A, Berzina-Cimdina L. Biodegradable materials and metallic implants—a review. *J Funct Biomater* 2017;8(4):44.
- [6] Wang X, Xu S, Zhou S, Xu W, Leary M, Choong P, et al. Topological design and additive manufacturing of porous metals for bone scaffolds and orthopaedic implants: a review. *Biomaterials* 2016;83:127–41.
- [7] Lee DJ, Lee JM, Kim EJ, Takata T, Abiko Y, Okano T, et al. Bio-implant as a novel restoration for tooth loss. *Sci Rep* 2017;7:7414.
- [8] Kang C, Fang F. State of the art of bioimplants manufacturing: part II. *Adv Manuf* 2018;6(2):137–54.
- [9] Kurella A, Dahotre NB. Review paper: surface modification for bioimplants: the role of laser surface engineering. *J Biomater Appl* 2005;20(1):5–50.
- [10] German Society for Biomedical Engineering, National Academy of Science and Engineering. *Bioimplants: biological, biologised and bio functionalised implants*. Frankfurt: Association for Electrical, Electronic and Information Technologies (VDE); 2011.
- [11] Saini M, Singh Y, Arora P, Arora V, Jain K. Implant biomaterials: a comprehensive review. *World J Clin Cases* 2015;3(1):52–7.
- [12] Lee A, Hudson AR, Shiwarski DJ, Tashman JW, Hinton TJ, Yerneni S, et al. 3D bioprinting of collagen to rebuild components of the human heart. *Science* 2019;365(6452):482–7.
- [13] Grigoryan B, Paulsen SJ, Corbett DC, Sazer DW, Fortin CL, Zaita AJ, et al. Multivascular networks and functional intravascular topologies within biocompatible hydrogels. *Science* 2019;364(6439):458–64.
- [14] Ngo TD, Kashani A, Imbalzano G, Nguyen KTO, Hui D. Additive manufacturing (3D printing): a review of materials, methods, applications and challenges. *Compos Part B Eng* 2018;143:172–96.
- [15] Song WW, Heo JH, Lee JH, Park YM, Kim YD. Osseointegration of magnesium-incorporated sand-blasted acid-etched implant in the dog mandible: resonance frequency measurements and histomorphometric analysis. *Tissue Eng Regen Med* 2016;13(2):191–9.
- [16] Tan ETW, Ling JM, Dinesh SK. The feasibility of producing patient-specific acrylic cranioplasty implants with a low-cost 3D printer. *J Neurosurg* 2016;124(5):1531–7.
- [17] Chen L, Deng C, Li J, Yao Q, Chang J, Wang LM, et al. 3D printing of a lithium–calcium–silicate crystal bioscaffold with dual bioactivities for osteochondral interface reconstruction. *Biomaterials* 2019;196:138–50.

- [18] Smith KE, Dupont KM, Safranski DL, Blair JW, Buratti DR, Zeetser V, et al. Use of 3D printed bone plate in novel technique to surgically correct hallux valgus deformities. *Tech Orthop* 2016;31(3):181–9.
- [19] Zhang Y, Xu J, Ruan Y, Yu MK, O'Laughlin M, Wise H, et al. Implant-derived magnesium induces local neuronal production of CGRP to improve bone-fracture healing in rats. *Nat Med* 2016;22(10):1160–9.
- [20] Wu G, Chan KC, Zhu L, Sun L, Lu J. Dual-phase nanostructuring as a route to high-strength magnesium alloys. *Nature* 2017;545(7652):80–3.
- [21] Gu X, Mao Z, Ye S, Koo Y, Yun Y, Tiasha TR, et al. Biodegradable, elastomeric coatings with controlled anti-proliferative agent release for magnesium-based cardiovascular stents. *Colloids Surf B Biointerfaces* 2016;144:170–9.
- [22] Li J, Li X, Luo T, Wang R, Liu C, Chen S, et al. Development of a magnetic microrobot for carrying and delivering targeted cells. *Sci Robot* 2018;3(19):eaat8829.
- [23] Mudali UK, Sridhar TM, Raj B. Corrosion of bio implants. *Sadhana* 2003;28(3):601–37.
- [24] Ding W. Opportunities and challenges for the biodegradable magnesium alloys as next-generation biomaterials. *Regen Biomater* 2016;3(2):79–86.
- [25] Kulkarni M, Mazare A, Gongadze E, Perutkova S, Kralj-Igljic V, Milosevic I, et al. Titanium nanostructures for biomedical applications. *Nanotechnology* 2015;26(6):062002.
- [26] Kwasniak P, Garbacz H, Kurzydowski KJ. Solid solution strengthening of hexagonal titanium alloys: restoring forces and stacking faults calculated from first principles. *Acta Mater* 2016;102:304–14.
- [27] Mao L, Shen L, Chen JH, Zhang X, Kwak M, Wu Y, et al. A promising biodegradable magnesium alloy suitable for clinical vascular stent application. *Sci Rep* 2017;7:46343.
- [28] Kannan MB. Enhancing the performance of calcium phosphate coating on a magnesium alloy for bioimplant applications. *Mater Lett* 2012;76:109–12.
- [29] Surmeneva MA, Muhametkaliyev TM, Khakbaz H, Sumenev RA, Kannan MB. Ultrathin film coating of hydroxyapatite (HA) on a magnesium–calcium alloy using RF magnetron sputtering for bioimplant applications. *Mater Lett* 2015;152:280–2.
- [30] Subramanian B, Muraleedharan CV, Ananthakumar R, Jayachandran M. A comparative study of titanium nitride (TiN), titanium oxy nitride (TiON) and titanium aluminum nitride (TiAlN), as surface coatings for bio implants. *Surf Coat Tech* 2011;205(21–22):5014–20.
- [31] Cheung HY, Lau KT, Lu T, Hui D. A critical review on polymer based bio-engineered materials for scaffold development. *Compos Part B Eng* 2007;38(3):291–300.
- [32] Wong JY, Bronzino JD, Peterson DR, editors. *Biomaterials: principles and practices*. Boca Raton: CRC Press; 2012.
- [33] Liao P, Xing L, Zhang S, Sun D. Magnetically driven undulatory microswimmers integrating multiple rigid segments. *Small* 2019;15(36):1901197.
- [34] Doucet C, Ernou I, Zhang Y, Llense JR, Begot L, Lataillade JJ. Platelet lysates promote mesenchymal stem cell expansion: a safety substitute for animal serum in cell-based therapy applications. *J Cell Physiol* 2005;205(2):228–36.
- [35] Dimmeler S, Burchfield J, Zeiher AM. Cell-based therapy of myocardial infarction. *Arterioscler Thromb Vasc Biol* 2008;28(2):208–16.
- [36] Kim S, Qiu F, Kim S, Ghanbari A, Moon C, Zhang L, et al. Fabrication and characterization of magnetic microrobots for three-dimensional cell culture and targeted transportation. *Adv Mater* 2013;25(41):5863–8.
- [37] Nelson BJ, Kaliakatsos IK, Abbott JJ. Microrobots for minimally invasive medicine. *Annu Rev Biomed Eng* 2010;12:55–85.
- [38] Martinez-Marquez D, Mirnajafizadeh A, Carty CP, Stewart RA. Application of quality by design for 3D printed bone prostheses and scaffolds. *PLoS ONE* 2018;13(4):e0195291.
- [39] Correa D, Lietman SA. Articular cartilage repair: current needs, methods and research directions. *Semin Cel Dev Biol* 2017;62:67–77.
- [40] Awad NK, Niu H, Ali U, Morsi YS, Lin T. Electrospun fibrous scaffolds for small-diameter blood vessels: a review. *Membranes* 2018;8(1):15.
- [41] Wu J, Hu C, Tang Z, Yu Q, Liu X, Chen H. Tissue-engineered vascular grafts: balance of the four major requirements. *Colloid Interface Sci Commun* 2018;23:34–44.
- [42] Steines D, Lang P, Fitz W, inventors; ConforMIS Inc., Steines D, Lang P, Fitz W, assignees. Interpositional joint implant. World Intellectual Property Organization patent WO2007/064349. 2007 Sep 27.
- [43] Bojarski RA, Fitz W, inventors; ConforMIS, Inc., assignee. Devices, techniques and methods for assessing joint spacing, balancing soft tissues and obtaining desired kinematics for joint implant components. United States patent US 13/915609. 2013 Dec 12.
- [44] Soro N, Attar H, Brodie E, Veidt M, Molotnikov A, Dargusch MS. Evaluation of the mechanical compatibility of additively manufactured porous T-25Ta alloy for load-bearing implant applications. *J Mech Behav Biomed Mater* 2019;97:149–58.
- [45] Svensson RB, Hassenkam T, Grant CA, Magnusson SP. Tensile properties of human collagen fibrils and fascicles are insensitive to environmental salts. *Biophys J* 2010;99(12):4020–7.
- [46] Haleem A, Javid M. Polyether ether ketone (PEEK) and its manufacturing of customised 3D printed dentistry parts using additive manufacturing. *Clin Epidemiol Glob Health* 2019;7(4):654–60.
- [47] Meboldt M, Klahn C, editors. *Industrializing additive manufacturing—proceedings of additive manufacturing in products and applications—AMPA2017*. Cham: Springer; 2017.
- [48] Zhang C, Wang L, Kang J, Fuentes OM, Li D. Bionic design and verification of 3D printed PEEK costal cartilage prosthesis. *J Mech Behav Biomed Mater* 2020;103:103561.
- [49] Zamani Y, Amoabediny G, Mohammadi J, Seddiqi H, Helder MN, Zandieh-Doulabi B, et al. 3D-printed poly( $\epsilon$ -caprolactone) scaffold with gradient mechanical properties according to force distribution in the mandible for mandibular bone tissue engineering. *J Mech Behav Biomed Mater* 2020;104:103638.
- [50] Nyberg E, Rindone A, Dorafshar A, Grayson WL. Comparison of 3D-printed poly- $\epsilon$ -caprolactone scaffolds functionalized with tricalcium phosphate, hydroxyapatite, bio-oss, or decellularized bone matrix. *Tissue Eng Part A* 2017;23(11–12):503–14.
- [51] Liu D, Nie W, Li D, Wang W, Zheng L, Zhang J, et al. 3D printed PCL/SrHA scaffold for enhanced bone regeneration. *Chem Eng J* 2019;362:269–79.
- [52] Park YJ, Cha JH, Bang SI, Kim SY. Clinical application of three-dimensionally printed biomaterial polycaprolactone (PCL) in augmentation rhinoplasty. *Aesthetic Plast Surg* 2019;43(2):437–46.
- [53] Chen X, Gao C, Jiang J, Wu Y, Zhu P, Chen G. 3D printed porous PLA/nHA composite scaffolds with enhanced osteogenesis and osteoconductivity *in vivo* for bone regeneration. *Biomed Mater* 2019;14(6):065003.
- [54] Petersmann S, Spoerk M, Huber P, Lang M, Pinter G, Arbeiter F. Impact optimization of 3D-printed poly(methyl methacrylate) for cranial implants. *Macromol Mater Eng* 2019;304(11):1900263.
- [55] Zhu Y, Liu K, Deng J, Ye J, Ai FR, Ouyang H, et al. 3D printed zirconia ceramic hip joint with precise structure and broad-spectrum antibacterial properties. *Int J Nanomed* 2019;14:5977–87.
- [56] Liu X, Zou B, Xing H, Huang C. The preparation of ZrO<sub>2</sub>-Al<sub>2</sub>O<sub>3</sub> composite ceramic by SLA-3D printing and sintering processing. *Ceram Int* 2020;46(1):937–44.
- [57] Chen S, Shi Y, Luo Y, Ma J. Layer-by-layer coated porous 3D printed hydroxyapatite composite scaffolds for controlled drug delivery. *Colloids Surf B Biointerfaces* 2019;179:121–7.
- [58] Daher S, Leary J, Ewers R, Coelho PG, Bonfante EA. Histological analysis of an implant retrieved from a  $\beta$ -tricalcium phosphate graft after 4 years: a case study. *J Long Term Eff Med Implants* 2019;29(2):135–40.
- [59] Chen Z, Li Z, Li J, Liu C, Lao C, Fu Y, et al. 3D printing of ceramics: a review. *J Eur Ceram Soc* 2019;39(4):661–87.
- [60] Martinez-Marquez D, Jokymaityte M, Mirnajafizadeh A, Carty CP, Lloyd D, Stewart RA. Development of 18 quality control gates for additive manufacturing of error free patient-specific implants. *Materials* 2019;12(19):3110.
- [61] Popov VV Jr, Muller-Kamskii G, Kovalevsky A, Dzhenzhera G, Strokin E, Kolomiets A, et al. Design and 3D-printing of titanium bone implants: brief review of approach and clinical cases. *Biomed Eng Lett* 2018;8(4):337–44.
- [62] Gupta VB, Anita S, Hegde ML, Zecca L, Garruto RM, Ravid R, et al. Aluminium in Alzheimer's disease: are we still at a crossroad? *Cell Mol Life Sci* 2005;62(2):143–58.
- [63] Tomljenovic L. Aluminium and Alzheimer's disease: after a century of controversy, is there a plausible link? *J Alzheimers Dis* 2011;23(4):567–98.
- [64] Avila-Costa MR, Fortoul TI, Colin-Barenque L, Ordoñez-Librado JL, Gutiérrez-Valdez AL. Vanadium and the nervous system. In: Fortoul TI, Avila-Costa MR, editors. *Vanadium: its impact on health*. New York: Nova Science Publishers; 2007. p. 29–42.
- [65] Shen X, Shukla P, Swanson P, An Z, Prabhakaran S, Waugh D, et al. Altering the wetting properties of orthopaedic titanium alloy (Ti-6Al-7Nb) using laser shock peening. *J Alloys Compd* 2019;801:327–42.
- [66] Yamanoglu R, Efendi E, Kolayli F, Uzuner H, Daoud I. Production and mechanical properties of Ti-5Al-2.5Fe-xCu alloys for biomedical applications. *Biomed Mater* 2018;13(2):025013.
- [67] Hao L, Lawrence J, Phua YF, Chian KS, Lim GC, Zheng HY. Enhanced human osteoblast cell adhesion and proliferation on 316 LS stainless steel by means of CO<sub>2</sub> laser surface treatment. *Biomed Mater Res B* 2005;73(1):148–56.
- [68] Parsapour A, Khorasani SN, Fathi MH. Effect of surface treatment and metallic coating on corrosion behavior and biocompatibility of surgical 316L stainless steel implant. *J Mater Sci Technol* 2012;28(2):125–31.
- [69] Hao L, Dadbakhsh S, Seaman O, Flestead M. Selective laser melting of a stainless steel and hydroxyapatite composite for load-bearing implant development. *J Mater Process Technol* 2009;209(17):5793–801.
- [70] Chai H, Guo L, Wang X, Fu Y, Guan J, Tan L, et al. Antibacterial effect of 317L stainless steel contained copper in prevention of implant-related infection *in vitro* and *in vivo*. *J Mater Sci Mater Med* 2011;22(11):2525–35.
- [71] Lodhi MJK, Deen KM, Greenlee-Wacker MC, Haider W. Additively manufactured 316L stainless steel with improved corrosion resistance and biological response for biomedical applications. *Addit Manuf* 2019;27:8–19.
- [72] Manivasagam G, Dhinasekaran D, Rajamanickam A. Biomedical implants: corrosion and its prevention—a review. *Recent Pat Corros Sci* 2010;2:40–54.
- [73] McCafferty E. Effect of ion implantation on the corrosion behavior of iron, stainless steels, and aluminum—a review. *Corrosion* 2001;57(12):1011–29.
- [74] Mohan CC, Prabhath A, Cherian AM, Vadukumpully S, Nair SV, Chennazhi K, et al. Nanotextured stainless steel for improved corrosion resistance and biological response in coronary stenting. *Nanoscale* 2015;7(2):832–41.
- [75] Misra RDK, Nune C, Pesacreta TC, Somani MC, Karjalainen LP. Understanding the impact of grain structure in austenitic stainless steel from a nanograined regime to a coarse-grained regime on osteoblast functions using a novel metal deformation-annealing sequence. *Acta Biomater* 2013;9(4):6245–58.

- [76] Manam N, Harun WSW, Shri DNA, Ghani SAC, Kurniawan T, Ismail MH, et al. Study of corrosion in biocompatible metals for implants: a review. *J Alloys Compd* 2017;701:698–715.
- [77] Alvarado R, Maldonado R, Marxuach J, Otero R. Biomechanics of hip and knee prostheses [dissertation]. Mayaguez: University of Puerto Rico Mayaguez; 2003.
- [78] Xiang DD, Wang P, Tan X, Chandra S, Wang C, Nai MLS, et al. Anisotropic microstructure and mechanical properties of additively manufactured Co–Cr–Mo alloy using selective electron beam melting for orthopedic implants. *Mater Sci Eng A* 2019;765:138270.
- [79] Sargeant A, Goswami T. Hip implants—paper VI—ion concentrations. *Mater Des* 2007;28(1):155–71.
- [80] Li L, Zhang M, Li Y, Zhao J, Qin L, Lai Y. Corrosion and biocompatibility improvement of magnesium-based alloys as bone implant materials: a review. *Regen Biomater* 2017;4(2):129–37.
- [81] Wang H, Zhu S, Wang L, Feng Y, Ma X, Guan S. Formation mechanism of Ca-deficient hydroxyapatite coating on Mg–Zn–Ca alloy for orthopaedic implant. *Appl Surf Sci* 2014;307:92–100.
- [82] Rad HRB, Idris MH, Kadir MRA, Farahany S. Microstructure analysis and corrosion behavior of biodegradable Mg–Ca implant alloys. *Mater Des* 2012;33:88–97.
- [83] Gil-Santos A, Marco I, Moelans N, Hort N, van der Biest O. Microstructure and degradation performance of biodegradable Mg–Si–Sr implant alloys. *Mater Sci Eng C* 2017;71:25–34.
- [84] Brar HS, Wong J, Manuel MV. Investigation of the mechanical and degradation properties of Mg–Sr and Mg–Zn–Sr alloys for use as potential biodegradable implant materials. *J Mech Behav Biomed Mater* 2012;7:87–95.
- [85] Yazdimamaghani M, Razavi M, Vashae D, Moharamzadeh K, Boccaccini AR, Tayebi L. Porous magnesium-based scaffolds for tissue engineering. *Mater Sci Eng C* 2017;71:1253–66.
- [86] Yang Y, Scenini F, Curioni M. A study on magnesium corrosion by real-time imaging and electrochemical methods: relationship between local processes and hydrogen evolution. *Electrochim Acta* 2016;198:174–84.
- [87] Mostaed E, Sikora-Jasinska M, Drelich JW, Vedani M. Zinc-based alloys for degradable vascular scent applications. *Acta Biomater* 2018;71:1–23.
- [88] Bowen PK, Drelich J, Goldman J. Zinc exhibits ideal physiological corrosion behavior for bioabsorbable stents. *Adv Mater* 2013;25(18):2577–82.
- [89] Vojtěch D, Kubasek J, Serak J, Novak P. Mechanical and corrosion properties of newly developed biodegradable Zn-based alloys for bone fixation. *Acta Biomater* 2011;7(9):3515–22.
- [90] Mostaed E, Sikora-Jasinska M, Mostaed A, Loffredo S, Demir AG, Preuitali B, et al. Novel Zn-based alloys for biodegradable stent applications: design, development and *in vitro* degradation. *J Mech Behav Biomed Mater* 2016;60:581–602.
- [91] Levy GK, Goldman J, Aghion E. The prospects of zinc as a structural material for biodegradable implants—a review paper. *Metals* 2017;7(10):402.
- [92] Li P, Zhang W, Dai J, Xepapadeas AB, Schweizer E, Alexander D, et al. Investigation of zinc-copper alloys as potential materials for craniomaxillofacial osteosynthesis implants. *Mater Sci Eng C* 2019;103:109826.
- [93] Su Y, Yang H, Gao J, Qin Y, Zheng Y, Zhu D. Interfacial zinc phosphate is the key to controlling biocompatibility of metallic zinc implants. *Adv Sci* 2019;6(14):1900112.
- [94] Gorejová R, Haverová L, Oriňáková R, Oriňák A, Oriňák M. Recent advancements in Fe-based biodegradable materials for bone repair. *J Mater Sci* 2019;54(3):1913–47.
- [95] Cheng J, Liu B, Wu Y, Zheng Y. Comparative *in vitro* study on pure metals (Fe, Mn, Mg, Zn and W) as biodegradable metals. *J Mater Sci Technol* 2013;29(7):619–27.
- [96] Nie F, Zheng Y, Wei S, Hu C, Yang G. *In vitro* corrosion, cytotoxicity and hemocompatibility of bulk nanocrystalline pure iron. *Biomed Mater* 2010;5(6):065015.
- [97] Purnama A, Herrmawan H, Couet J, Mantovani D. Assessing the biocompatibility of degradable metallic materials: state-of-the-art and focus on the potential of genetic regulation. *Acta Biomater* 2010;6(5):1800–7.
- [98] Quadbeck P, Kümmel K, Hauser R, Standke G, Adler J, Stephani G, et al. Structural and material design of open-cell powder metallurgical foams. *Adv Eng Mater* 2011;13(11):1024–30.
- [99] Li Y, Jahr H, Lieaeart K, Pavanram P, Yilmaz A, Li F, et al. Additively manufactured biodegradable porous iron. *Acta Biomater* 2018;77:380–93.
- [100] Hong D, Chou DT, Velikokhatnyi OI, Roy A, Lee B, Swink I, et al. Binder-jetting 3D printing and alloy development of new biodegradable Fe–Mn–Ca/Mg alloys. *Acta Biomater* 2016;45:375–86.
- [101] Yang C, Huang Z, Wang X, Wu C, Chang J. 3D printed Fe scaffolds with HA nanocoating for bone regeneration. *ACS Biomater Sci Eng* 2018;4(2):608–16.
- [102] Wang WH, Dong C, Shek C. Bulk metallic glasses. *Mater Sci Eng R Rep* 2004;44(2–3):45–89.
- [103] Schroers J, Hodges TM, Chan S, Kyriakides TR. Bulk metallic glasses for biomedical applications. *JOM* 2009;61(9):21–9.
- [104] Wang J, Loye AM, Ketkaew J, Schroers J, Kyriakides TR. Hierarchical micro- and nano-patterning of metallic glass to engineer cellular responses. *ACS Appl Bio Mater* 2018;1(1):51–8.
- [105] Studart AR. Additive manufacturing of biologically-inspired materials. *Chem Soc Rev* 2016;45(2):359–76.
- [106] Ma H, Feng C, Chang J, Wu C. 3D-printed bioceramic scaffolds: from bone tissue engineering to tumor therapy. *Acta Biomater* 2018;79:37–59.
- [107] Zhang W, Feng C, Yang G, Li G, Ding X, Wang S, et al. 3D-printed scaffolds with synergistic effect of hollow-pipe structure and bioactive ions for vascularized bone regeneration. *Biomaterials* 2017;135:85–95.
- [108] Faveri M, Figueiredo LC, Feres M. Considerations about designing and reporting randomized clinical trials—response to the letter to the editor from Preus et al. *J Evid Based Dent Pract* 2015;15(2):87–8.
- [109] Khorasani AM, Gibson I, Goldberg M, Littlefair G. A comprehensive study on surface quality in 5-axis milling of SLM Ti–6Al–4V spherical components. *Int J Adv Manuf Technol* 2017;94(9–12):3765–84.
- [110] Wang D, Wang Y, Wang J, Song C, Yang Y, Zhang Z, et al. Design and fabrication of a precision template for spine surgery using selective laser melting (SLM). *Materials* 2016;9(7):608.
- [111] Koutsoukis T, Zinelis S, Eliades G, Al-Wazzan K, Al Rifai M, Al Jabbari YS. Selective laser melting technique of Co–Cr dental alloys: a review of structure and properties and comparative analysis with other available techniques. *J Prosthodont* 2015;24(4):303–12.
- [112] Körner C. Additive manufacturing of metallic components by selective electron beam melting—a review. *Int Mater Rev* 2016;61(5):361–77.
- [113] Ramakrishnaiah R, Al Kheraif AA, Mohammad A, Divakar DD, Kotha SB, Celur SL, et al. Preliminary fabrication and characterization of electron beam melted Ti–6Al–4V customized dental implant. *Saudi J Biol Sci* 2017;24(4):787–96.
- [114] Wong KV, Hernandez A. A review of additive manufacturing. *ISRN Mech Eng* 2012;2012:208760.
- [115] Zeng W, Lin F, Shi T, Zhang R, Nian Y, Ruan J, et al. Fused deposition modelling of an auricle framework for microtia reconstruction based on CT images. *Rapid Prototyping J* 2008;14(5):280–4.
- [116] Gronet PM, Waskewicz GA, Richardson C. Preformed acrylic cranial implants using fused deposition modeling: a clinical report. *J Prosthet Dent* 2003;90(5):429–33.
- [117] Singh S, Ramakrishna S, Singh R. Material issues in additive manufacturing: a review. *J Manuf Process* 2017;25:185–200.
- [118] Brown TD, Dalton PD, Hutmacher DW. Direct writing by way of melt electrosintering. *Adv Mater* 2011;23(47):5651–7.
- [119] Melchels FP, Feijen J, Grijpma DW. A review on stereolithography and its applications in biomedical engineering. *Biomaterials* 2010;31(24):6121–30.
- [120] Winder J, Bibb R. Medical rapid prototyping technologies: state of the art and current limitations for application in oral and maxillofacial surgery. *J Oral Maxillofac Surg* 2005;63(7):1006–15.
- [121] Nickels L. World's first patient-specific jaw implant. *Met Powder Rep* 2012;67(2):12–4.
- [122] Tang H, Zhao P, Xiang C, Liu N, Jia L. Ti–6Al–4V orthopedic implants made by selective electron beam melting. In: Froes FH, Qian M, editors. *Titanium in medical and dental applications*. Cambridge: Woodhead Publishing Ltd.; 2018. p. 239–49.
- [123] Zhang X, Leary M, Tang HP, Song T, Qian M. Selective electron beam manufactured Ti–6Al–4V lattice structures for orthopedic implant applications: current status and outstanding challenges. *Curr Opin Solid State Mater Sci* 2018;22(3):75–99.
- [124] Hayat MD, Chen G, Khan S, Liu N, Tang H, Cao P. Physical and tensile properties of NiTi alloy by selective electron beam melting. *Key Eng Mater* 2018;770:148–54.
- [125] Murphy SV, Atala A. 3D bioprinting of tissues and organs. *Nat Biotechnol* 2014;32(8):773–85.
- [126] Jiang J, Bao B, Li M, Sun J, Zhang C, Li Y, et al. Fabrication of transparent multilayer circuits by inkjet printing. *Adv Mater* 2016;28(7):1420–6.
- [127] Liu P, Shen H, Zhi Y, Si J, Shi J, Guo L, et al. 3D bioprinting and *in vitro* study of bilayered membranous construct with human cells-laden alginate/gelatin composite hydrogels. *Colloids Surf B Biointerfaces* 2019;181:1026–34.
- [128] Sorkio A, Koch L, Koivusalo L, Deiwick A, Miettinen S, Chichkov B, et al. Human stem cell based corneal tissue mimicking structures using laser-assisted 3D bioprinting and functional bioinks. *Biomaterials* 2018;171:57–71.
- [129] Gungor-Ozkerim PS, Inci I, Zhagn YS, Khademhosseini A, Dokmeci MR. Bioinks for 3D bioprinting: an overview. *Biomater Sci* 2018;6(5):915–46.
- [130] Chimene D, Lennox KK, Kaunas RR, Gaharwar AK. Advanced bioinks for 3D printing: a materials science perspective. *Ann Biomed Eng* 2016;44(6):2090–102.
- [131] Faramarzi N, Yazdi IK, Nabavinia M, Gemma A, Fanelli A, Caizzone A, et al. Patient-specific bioinks for 3D bioprinting of tissue engineering scaffolds. *Adv Healthc Mater* 2018;7(11):1701347.
- [132] Parak A, Pradeep P, du Toit LC, Kumar P, Choonara YE, Pillay V, et al. Functionalizing bioinks for 3D bioprinting applications. *Drug Discov Today* 2019;24(1):198–205.
- [133] Kang HW, Lee SJ, Ko IK, Kengla C, Yoo JJ, Atala A. A 3D bioprinting system to produce human-scale tissue constructs with structural integrity. *Nat Biotechnol* 2016;34(3):312–9.
- [134] Tibbitts S. 4D printing: multi-material shape change. *Architectural Design* 2014;84(1):116–21.
- [135] Gladman AS, Matsumoto EA, Nuzzo RG, Mahadevan L, Lewis JA. Biomimetic 4D printing. *Nat Mater* 2016;15(4):413–8.
- [136] Ge Q, Qi HJ, Dunn ML. Active materials by four-dimension printing. *Appl Phys Lett* 2015;103(13):131901.
- [137] Ge Q, Dunn CK, Qi HJ, Dunn ML. Active origami by 4D printing. *Smart Mater Struct* 2014;23(9):094007.

- [138] Ding Z, Yuan C, Peng X, Wang T, Qi HJ, Dunn ML. Direct 4D printing via active composite materials. *Sci Adv* 2017;3(4):e1602890.
- [139] Lin C, Lv J, Li Y, Zhang F, Li J, Liu Y, et al. 4D-printed biodegradable and remotely controllable shape memory occlusion devices. *Adv Funct Mater* 2019;29(51):1906569.
- [140] Huang L, Jiang R, Wu J, Song J, Bai H, Li B, et al. Ultrafast digital printing toward 4D shape changing materials. *Adv Mater* 2017;29(7):1605390.
- [141] Wan X, Wei H, Zhang F, Liu Y, Leng J. 3D printing of shape memory poly (*D, L*-lactide-co-trimethylene carbonate) by direct ink writing for shape-changing structures. *J Appl Polym Sci* 2019;136(44):48177.
- [142] Mao Z, Zhu K, Pan L, Liu G, Tang T, He Y, et al. Direct-ink written shape-morphing film with rapid and programmable multimotion. *Adv Mater Tech* 2020;5(2):1900974.
- [143] Lee AY, An J, Chua CK. Two-way 4D printing: a review on the reversibility of 3D-printed shape memory materials. *Engineering* 2017;3(5):663–74.
- [144] Caputo MP, Berkowitz AE, Armstrong A, Mullner P, Solomon CV. 4D printing of net shape parts made from Ni–Mn–Ga magnetic shape-memory alloys. *Addit Manuf* 2018;21:579–88.
- [145] Dadbakhsh S, Speirs M, Kruth JP, Schrooten J, Luyten J, Van Humbeeck J. Effect of SLM parameters on transformation temperatures of shape memory nickel titanium parts. *Adv Eng Mater* 2014;16(9):1140–6.
- [146] Liu G, Zhao Y, Wu G, Lu J. Origami and 4D printing of elastomer-derived ceramic structures. *Sci Adv* 2018;4(8):eaat0641.
- [147] Truby RL, Lewis JA. Printing soft matter in three dimensions. *Nature* 2016;540(7633):371–8.
- [148] Randall CL, Gultepe E, Gracias DH. Self-folding devices and materials for biomedical applications. *Trends Biotechnol* 2012;30(3):138–46.
- [149] Rapp B. Nitinol for stents. *Mater Today* 2004;7(5):13.
- [150] Leng J, Lu H, Liu Y, Huang W, Du S. Shape-memory polymers—a class of novel smart materials. *MRS Bull* 2009;34(11):848–55.
- [151] Jani JM, Leary M, Subic A, Gibson MA. A review of shape memory alloy research, applications and opportunities. *Mater Des* 2014;56:1078–113.
- [152] Zhao Y, Xuan C, Qian X, Alsaïd Y, Hua M, Jin L, et al. Soft phototactic swimmer based on self-sustained hydrogel oscillator. *Sci Robot* 2019;4(33):eaax7112.
- [153] Kwan KW, Li SJ, Hau NY, Li W, Feng SP, Ngan AHW. Light-stimulated actuators based on nickel hydroxide-oxyhydroxide. *Sci Robot* 2018;3(18):eaat4051.
- [154] Wani OM, Zeng H, Priimagi A. A light-driven artificial flytrap. *Nat Commun* 2017;8:15546.
- [155] Chen L, Weng M, Zhou P, Huang F, Liu C, Fan S, et al. Graphene-based actuator with integrated-sensing function. *Adv Funct Mater* 2019;29(5):1806057.
- [156] Liang J, Xu Y, Huang Y, Zhang L, Wang Y, Ma Y, et al. Infrared-triggered actuators from graphene-based nanocomposites. *J Phys Chem C* 2009;113(22):9921–7.
- [157] Wang E, Desai MS, Lee SW. Light-controlled graphene-elastin composite hydrogel actuators. *Nano Lett* 2013;13(6):2826–30.
- [158] Jiang H, Li C, Huang X. Actuators based on liquid crystalline elastomer materials. *Nanoscale* 2013;5(12):5225–40.
- [159] Dong L, Zhao Y. Photothermally driven liquid crystal polymer actuators. *Mater Chem Front* 2018;2(11):1932–43.
- [160] Gelebart AH, Mulder DJ, Vantomme G, Schenning APHJ, Broer DJ. A rewritable, reprogrammable, dual light-responsive polymer actuator. *Angew Chem Int Ed Engl* 2017;56(43):13436–9.
- [161] Iqbal D, Samiullah MH. Photo-responsive shape-memory and shape-changing liquid-crystal polymer networks. *Materials* 2013;6(1):116–42.
- [162] Li L, Scheiger JM, Levkin PA. Design and applications of photoresponsive hydrogels. *Adv Mater* 2019;31(26):e1807333.
- [163] Nishiguchi A, Zhang H, Schweizerhof S, Schulte MF, Mourran A, Moller M. 4D printing of a light-driven soft actuator with programmed printing density. *ACS Appl Mater Interfaces* 2020;12(10):12176–85.
- [164] Zhu P, Yang W, Wang R, Gao S, Li B, Li Q. 4D printing of complex structures with a fast response time to magnetic stimulus. *ACS Appl Mater Interfaces* 2018;10(42):36435–42.
- [165] Zhang Y, Wang L, Gao W, Gu T, Li Z, Li X, et al. Bioinspired from butterfly wings: programmable actuation of isolated rods architectures for magnetic-assisted microswitches. *Smart Mater Struct* 2019;28(7):075014.
- [166] Gao W, Wang L, Wang X, Liu H. Magnetic driving flowerlike soft platform: biomimetic fabrication and external regulation. *ACS Appl Mater Interfaces* 2016;8(22):14182–9.
- [167] Gong D, Cai J, Celi N, Feng L, Jiang Y, Zhang D. Bio-inspired magnetic helical microswimmers made of nickel-plated *Spirulina* with enhanced propulsion velocity. *J Magn Magn Mater* 2018;468:148–54.
- [168] Joyee EB, Pan Y. A fully three-dimensional printed inchworm-inspired soft robot with magnetic actuation. *Soft Robot* 2019;6(3):333–45.
- [169] Lu H, Zhang M, Yang Y, Huang Q, Fukuda T, Wang Z, et al. A bioinspired multilegged soft millirobot that functions in both dry and wet conditions. *Nat Commun* 2018;9:3944.
- [170] Tognato R, Armiento AR, Bonfrate V, Levato R, Malda J, Alini M, et al. A stimuli-responsive nanocomposite for 3D anisotropic cell-guidance and magnetic soft robotics. *Adv Funct Mater* 2019;29(9):1804647.
- [171] Ren Z, Hu W, Dong X, Sitti M. Multi-functional soft-bodied jellyfish-like swimming. *Nat Commun* 2019;10:2703.
- [172] Xia X, Afshar A, Yang H, Portela CM, Kochmann DM, Di Leo CV, et al. Electrochemically reconfigurable architected materials. *Nature* 2019;573(7773):205–13.
- [173] Schaffner M, Faber JA, Pianegonda L, Ruhs PA, Coulter F, Studart AR. 3D printing of robotic soft actuators with programmable bioinspired architectures. *Nat Commun* 2018;9:878.
- [174] Dong Y, Wang J, Guo X, Yang S, Ozen MO, Chen P, et al. Multi-stimuli-responsive programmable biomimetic actuator. *Nat Commun* 2019;10:4087.
- [175] Yu J, Xing Y, Li X, Shao L. Dual-stimuli responsive carbon nanotube sponge-PDMS amphibious actuator. *Nanomaterials* 2019;9(12):1704.
- [176] Wang Y, Guo Q, Su G, Cao J, Liu J, Zhang X. Hierarchically structured self-healing actuators with superfast light- and magnetic-response. *Adv Funct Mater* 2019;29(50):1906198.
- [177] Liu JAC, Gillen JH, Mishra SR, Evans BA, Tracy JB. Photothermally and magnetically controlled reconfiguration of polymer composites for soft robotics. *Sci Adv* 2019;5(8):eaaw2897.
- [178] Tang J, Yin Q, Qiao Y, Wang T. Shape morphing of hydrogels in alternating magnetic field. *ACS Appl Mater Interfaces* 2019;11(23):21194–200.
- [179] Li M, Wang Y, Chen A, Naidu A, Napier BS, Li W, et al. Flexible magnetic composites for light-controlled actuation and interfaces. *Proc Natl Acad Sci USA* 2018;115(32):8119–24.
- [180] da Cunha MP, Foelen Y, van Raak RJH, Murphy JN, Engelas TAP, Debye MG, et al. An untethered magnetic- and light-responsive rotary gripper: shedding light on photoresponsive liquid crystal actuators. *Adv Opt Mater* 2019;7(7):1801643.
- [181] Ma C, Lu W, Yang X, He J, Le X, Wang L, et al. Bioinspired anisotropic hydrogel actuators with on-off switchable and color-tunable fluorescence behaviors. *Adv Funct Mater* 2018;28(7):1704568.
- [182] Wang J, Wang Z, Song Z, Ren L, Liu Q, Ren L. Biomimetic shape-color double-responsive 4D printing. *Adv Mater Tech* 2019;4(9):1900293.
- [183] Ionescu E, Kleebe HJ, Riedel R. Silicon-containing polymer-derived ceramic nanocomposites (PDC-NCs): preparative approaches and properties. *Chem Soc Rev* 2012;41(15):5032–52.
- [184] Holzapfel GA. Biomechanics of soft tissue. In: Lemaitre J, editor. *Handbook of materials behavior models*. Pittsburgh: Academic Press; 2001. p. 1057–71.
- [185] Orlovskii VP, Komlev VS, Barinov SM. Hydroxyapatite and hydroxyapatite-based ceramics. *Inorg Mater* 2002;38(10):973–84.
- [186] Weaver JC, Milliron GW, Miserez A, Evans-Lutterodt K, Herrera S, Gallana I, et al. The stomatopod dactyl club: a formidable damage-tolerant biological hammer. *Science* 2012;336(6086):1275–80.
- [187] Munch E, Launey ME, Alsen DH, Saiz E, Tomsia AP, Ritchie RO. Tough, bio-inspired hybrid materials. *Science* 2008;322(5907):1516–20.
- [188] Mao LB, Gao H, Yao H, Liu L, Colfen H, Liu G, et al. Synthetic nacre by pre-designed matrix-directed mineralization. *Science* 2016;354(6308):107–10.
- [189] Chen SM, Gao H, Sun X, Ma Z, Ma T, Xia J, et al. Superior biomimetic nacreous bulk nanocomposites by a multiscale soft-rigid dual-network interfacial design strategy. *Matter* 2019;1(2):412–27.
- [190] Chen J, Chen B, Han K, Tang W, Wang Z. A triboelectric nanogenerator as a self-powered sensor for a soft-rigid hybrid actuator. *Adv Mater Tech* 2019;4(9):1900337.
- [191] MacCurdy R, Katzschmann R, Kim Y, Rus D. Printable hydraulics: a method for fabricating robots by 3D co-printing solids and liquids. In: Okamura A, Menciassi A, Ude A, Burschka D, Lee D, Arrichiello F, editors. *Proceeding of IEEE International Conference on Robotics and Automation (ICRA)*; 2016 May 16–21; Stockholm, Sweden. New York: IEEE; 2016. p. 3878–85.
- [192] Paterno L, Tortora G, Menciassi A. Hybrid soft-rigid actuators for minimally invasive surgery. *Soft Robot* 2018;5(6):783–99.
- [193] Tong WP, Tao NR, Wang ZB, Lu J, Lu K. Nitriding iron at lower temperatures. *Science* 2003;299(5607):686–8.
- [194] Sun HQ, Shi YN, Zhang MA, Lu K. Plastic strain-induced grain refinement in the nanometer scale in a Mg alloy. *Acta Mater* 2007;55(3):975–82.
- [195] Yan X, Yin S, Chen C, Jenkins R, Lupoi R, Bolot R, et al. Fatigue strength improvement of selective laser melted Ti<sub>6</sub>Al<sub>4</sub>V using ultrasonic surface mechanical attrition. *Mater Res Lett* 2019;7(8):327–33.