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Organ printing is essentially based on 3D printing, or additive manufacturing, which is the automated computer-aided deposition of living cells, together with matrix materials and biochemical factors, at specified positions with adequate numbers and in the right combination for the development of three-dimensional (3D) tissue/organ constructs \([1, 2]\). Charles W Hull first described a 3D printing method in 1986, which he named ‘stereolithography’ \([3]\). In this process, thin layers of a material are printed sequentially in layers and subsequently cured with ultraviolet light to form a solid 3D structure. However, this process was used to create sacrificial resin molds, which were then used for making 3D scaffolds from biological materials. Direct printing of biological materials into 3D scaffolds was made possible after the development of solvent-free, aqueous-based systems, and these scaffolds were used for transplantation with or without seeded cells \([4]\). True 3D cell printing, where living cells are included in the printing process itself, was made possible by more recent advances in 3D organ printing technology, cell biology and materials science \([5]\).

In organ printing, layer-by-layer precise positioning of living cells, matrix materials, biochemicals, and bioactive factors at a deliberately targeted location with a resolution similar to that found in biological tissues is used to fabricate 3D structures \([6]\). Researchers are trying to print living tissues with biological and mechanical properties suitable for the clinical restoration of tissue and organ function \([2]\). However, the key challenge is to replicate the intricate micro-architecture of the extracellular matrix (ECM) components and the organization of multiple cell types at a sufficient resolution to develop functional tissues or organs \([7]\).

Despite the initial challenges, organ printing has experienced rapid growth in the last few years, due to the development of novel tools and technologies. Although whole organ development is still at an early stage, this technique has the potential to deliver a long-term clinical solution to the tissue and organ shortage \([8]\). Implants with anatomical shapes and sizes can be made using computer-aided design (CAD) combined with medical imaging techniques, such as computed tomography (CT)
and magnetic resonance imaging (MRI) [9]. In recent years there has been increasing interest in applying this technology to various applications in biology and medicine. The development of diverse 3D organ printing technologies has also enabled the inclusion of highly sensitive stem cells. This can be seen from the use of various kinds of stem cells, such as human bone marrow stem cells (BMSCs), adipose-derived stem cells (ASCs), and even highly sensitive embryonic stem cells (ESCs) [10–12]. Interestingly, 3D organ printing can be advantageous for controlling microenvironments within a structure through the generation of spatial gradients of immobilized macromolecules to direct the fate of stem cells [13–15].

Based on the working principle, organ printing systems can be primarily classified as stereolithography-based, inkjet-based, and dispensing-based. Inkjet-based organ printing is one of the primary and the most promising biofabrication approaches currently available [16]. Inkjet printing is a non-contact technique that works by depositing ink drops in successive layers, at times with the support of a biopaper, to produce biological tissues or organs [4, 17, 18]. Laser-assisted bioprinting (LaB) uses a pulsed laser source, an absorption layer and a substrate to directly position multiple cells and biological components onto arbitrary surfaces to fabricate living tissues or organs [19]. Although inkjet- and stereolithography-based organ printing technologies offer great potential for printing living cells onto target-specific positions, the printing of clinically relevant 3D tissues or organs is hard to achieve with these technologies [20]. Dispensing-based organ printing technologies, using a syringe, micronozzle and pressure system, seem to be the most promising approach for producing clinically relevant-sized 3D tissue or organ constructs [21].

Several kinds of biomaterials are used for the 3D organ printing of tissue and organ constructs. Biopolymers are widely used biomaterials for the organ printing of scaffolds as well as living tissue/organ constructs. They offer distinct advantages in terms of biocompatibility, versatility of chemistry and the biological properties that are important in tissue engineering and regenerative medicine [22]. Biopolymers can be classified into several categories with respect to their structural, chemical and biological characteristics, and based on their origin (e.g., naturally occurring, synthetic or semi-synthetic) [22]. Synthetic biopolymers such as polycaprolactone (PCL), polylactic acid (PLA) and poly(lactic-co-glycolic acid) (PLGA) are used for printing structurally stable 3D scaffolds for implantation with or without seeded cells [23–25]. To impart light sensitivity, biopolymers of both natural and synthetic origin have been modified to attach chemical groups that induce crosslinking upon exposure to light [26]. Acrylated biopolymers, such as polyethylene (glycol) diacrylate (PEGDA) [27] and gelatin methacrylate [28], have been used for printing 3D constructs using stereolithography-based 3D printers. Hydrogels are popular for encapsulating cells because they provide an aqueous gel environment. Cells encapsulated in hydrogels (often called ‘bioink’) are generally fed into the dispensing-based 3D printer to make cell-laden constructs [29]. These are solidified through thermal processes or post-print crosslinking and used to produce diverse tissues ranging from liver to bone using materials such as gelatin [30], gelatin/chitosan [31], gelatin/alginate [32], gelatin/fibrinogen [33], Lutrol F127/alginate [34] and alginate [20]. However, these materials do not represent the complexity of natural ECMs and are
thus inadequate to recreate tissue-specific microenvironments. Consequently, the cells within these hydrogels do not exhibit the intrinsic morphologies and functions of living tissues in vivo. Recently, Cho’s group developed bioink from decellularized extracellular matrices and used it to organ print 3D tissue analogs [8]. The decellularized extracellular matrix (dECM) provides a natural chemical milieu for the embedded cells because, to date, no other natural or man-made material has been found to fully recapitulate all the features of natural ECM [35].

There are several application areas where bioprinted tissues/organs are valuable, such as tissue engineering [36, 37], cell-based sensors [38], drug/toxicity screening [39] and tissue and tumor models [40]. An example of the application of 3D organ printing to produce medical devices for use in the clinic is the bioresorbable airway splint [41]. In vitro models of human physiology and pathology can also be developed using bioprinted tissues/organs and can convincingly and accurately predict the outcome of in vivo drug administration and potential toxic exposure in human-specific models [39]. Furthermore, cancer models can be developed with organ printing, recreating the microenvironmental characteristics representative of tumors in vivo [40].

In this book, we describe the principles and processes of several tissue/organ printing methods. We also discuss various synthetic materials and hydrogels used for organ printing, together with their processing conditions. We review the applications of 3D organ printing in tissue and organ engineering and develop in vitro models for drug discovery and cancer models. Organ printing’s achievements, challenges and future directions are also discussed.

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