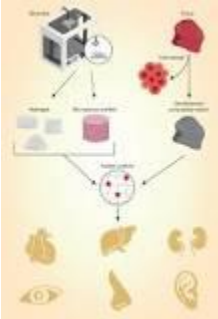
ARTIFICIAL ORGAN

INTRODUCTION:

Artificial Organ, any machine, device, or other material that is used to replace the functions of a faulty or missing organ or other part of the human body. Artificial organs include the artificial heart and pacemaker (*qq.v.*), the use of dialysis (*q.v.*) to perform kidney functions, and the use of artificial substitutes for missing limbs (*see*prosthesis).

What are artificial body parts called?
A prosthesis is an artificial replacement body part.

What are the three types of artificial organs?



Mechanical artificial organs are made exclusively of inanimate polymers such as plastics and metals; biomechanical organs involve both living materials such as cells and inanimate materials; and biological or bioartificial organs can be made of living cells and biodegradable polymers.

What are the benefits of artificial organs?

Artificial organs are needed for cardiac assist devices, orthopedic devices, neuroprostheses and neurological support, urological support, visual support, blood cell and tissue replacement, and autoimmune and metabolic therapy treatments.

Who is the father of artificial organs?

KOLFF, WILLEM J., "Pim," (14 February 1911-11 February 2009) was a prominent medical surgeon and inventor whose work on the artificial kidney, lung, and heart earned him the title "The Father of Artificial Organs." Kolff served as the founding president of the American Society for Artificial Internal Organs from 1955.

Who makes artificial organs?

Global Artificial Organs and Bionics Companies - Top Company List. **Cyberonics Inc.**Ekso Bionics Holdings Inc.

What are the disadvantages of artificial organs?

Possible organ failure is a negative aspect, too. While all organs have the potential to fail, artificial organs could have an even higher chance. Patients must be aware of the risk that many man-made organs have. People make mistakes and could easily make an error while constructing an organ.

What are the disadvantages of artificial body parts?

The potential disadvantages include **increased risk of infection, increased risk of allergic reactions, increased risk of rejection of the implants, and potential over-reliance on the technology**. Additionally, synthetic body parts may be more expensive than natural body parts and may be difficult to replace or repair.

What is the future of artificial organs?

3D bioprinting, which can produce tissues and organs with customized shapes, sizes and functions, has also made it possible to create complex structures with high precision and accuracy, including livers, kidneys, hearts, ears and skin grafts.

When were artificial organs used?

1967 --- The first clinical use of the capillary fiber kidney occurs, developed by R. Stewart, and thereafter becomes universally used for long-term hemodialysis. 1967 --- The double-leaflet prosthetic cardiac valve described by Lillehei and Kaster at ASAIO.

Can artificial organs extend life?

Adds Nigel Lovell, professor of biomedical engineering at the University of New South Wales in Australia, “In the coming years, artificial organs will blur the lines between technology and biology. **They will improve and extend lifespans**. They are the next step in humans becoming more like cyborgs.”

How do artificial organs work?

The cells grow on the scaffolds in a bioreactor. The scaffold provides the required three-dimensional shape for the cellular growth and, with time, the material dissolves and the cells form a living tissue. This is then implanted into the patient to replace the diseased or damaged tissues.

Who was the first organ?

The world's first successful organ transplant was kidney transplantation which was undertaken by **David Hume and Joseph Kelly** at the Peter Brigham Hospital in Boston in 1954. The first

kidney transplant in India was performed on 1st December, 1971 at the Christian Medical College, Vellore (Tamil Nadu).

What is the function of the artificial organs?

Generally, an artificial organ is an engineered device that can be implanted or integrated into a human body—interfacing with living tissue—**to replace a natural organ, to duplicate or augment a specific function or functions so the patient may return to a normal life as soon as possible**

Material Basis of Organ Manufacturing

All complicated living phenomena in the world, including organs, are the outcome of physical, chemical or biophysical, biochemical changes. Small organic and inorganic molecules polymerize or combine to form large polymers or compounds. Large polymers and compounds then aggregate to form cells with organelles inside the cell membrane. The cell is the basic unit of life. It is also the basic structural and functional unit of the human body. Tissues are made of homogeneous cells/ECMs, while organs are made of heterogeneous cell/ECM types. Cells, tissues, and organs are different forms (degrees or levels) of materials existing in human body.

For example, an artery can be regarded as a special organ since it is generally comprised of three layers in its tubular wall with three major cell/tissue types (Fig 2): (1) the innermost thin tunica intimal layer made of endothelial cells (i.e., endothelium) and basal lamina, consisting of mainly type IV collagen and laminin, with the main functions of anticoagulant of the blood, and anti-infection/anti-inflammation of the surrounding tissues; (2) the middle thick tunica medial layer made of smooth muscle cells (i.e., muscular layer) arranged circumferentially around the vessel (i.e., vascular wall), type I, III collagen, elastin and proteoglycan, with the main function of mechanical support, such as anti-pulse or anti-stress; (3) the outermost loose tunica adventitial (or external) layer made of fibroblasts, longitudinal collagens, and elastic fibers, with the main function of anchoring the blood vessel to the surrounding tissues and provision of additional mechanical support[39]. Each of these layers plays an important role in transporting nutrients, oxygen, and metabolic wastes, and in maintenance of homeostasis

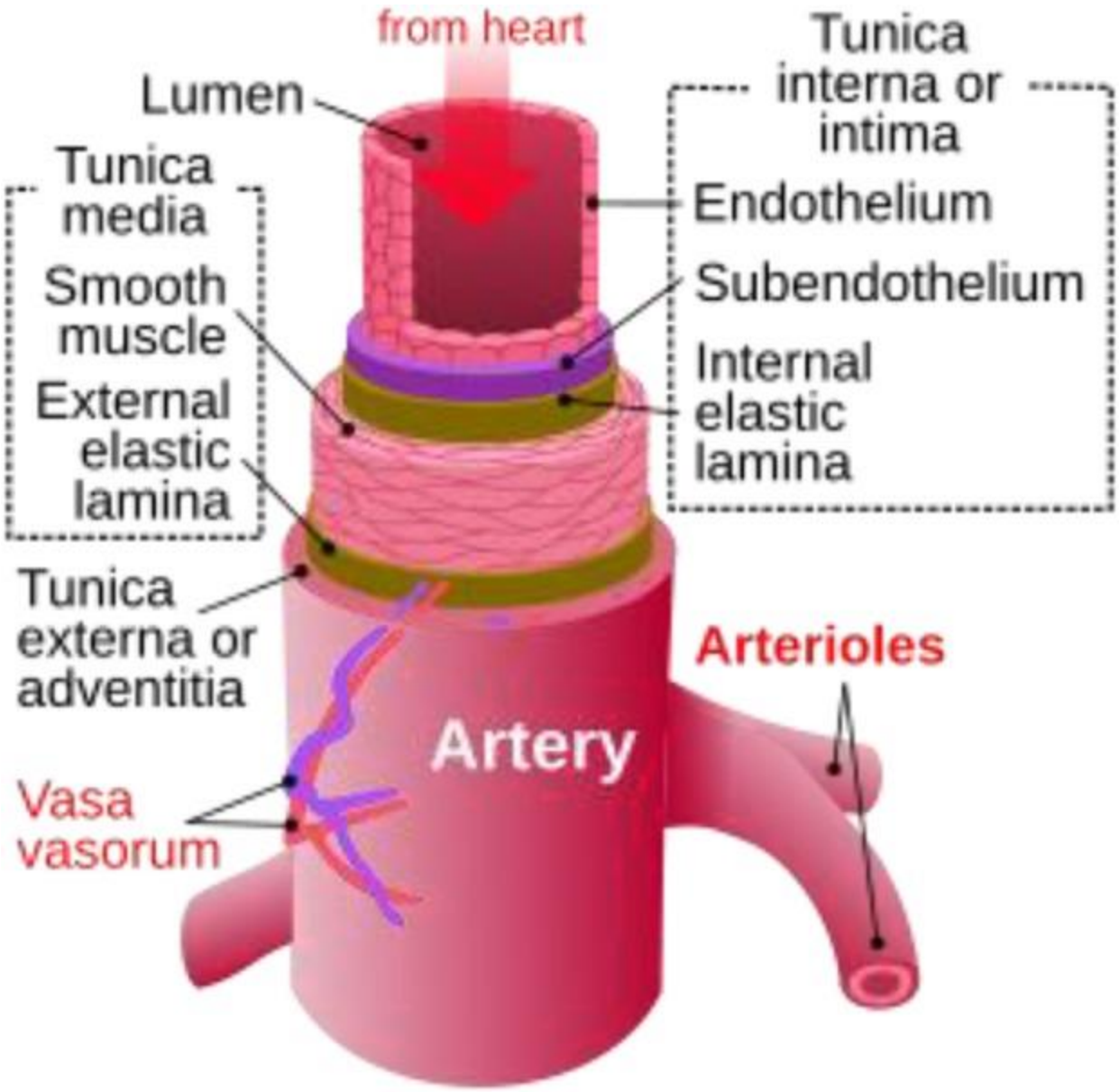


Fig 2.

Diagram of an artery[39].

The anatomical structures and compositions of artery tissues correspond closely to their biochemical and physiological functions. Unlike tunica adventitia, all the ECMs of the tunica intima and media, such as collagen, laminin, elastin, and proteoglycan, are synthesized by smooth muscle cells. The topological arrangement of the thick type I and III collagen in the tunica media make the middle layer strong enough to withstand blood flow and pressure. In a healthy artery, once the old terminal differentiated cells, such as the endothelial cells, smooth muscle cells, and fibroblasts, in the three tubular layers die, new cells coming from blood stem

cells or mesenchymal stem cells (MSCs) will replenish them and fill in each of the three layers. The complexity of the cell/tissue types, ECM components, and topological arrangements of the constituents in the organ determine the difficulty level of organ manufacturing technologies.

During the development stages of a human body, the great variety of human cell types develops from a single fertilized egg, a process that is governed by regulatory networks controlling the required genetic programs. Different tissues combine to form organs. For a typical tissue, the cell and ECM types are the same. In an typical organ, the cell and ECM types are very different. An organ consists of at least two or three different cell/ECM types with certain morphological characteristics and physiological functions. The differences of tissues and organs are summarized into Table 1. With the help of enzymes biochemical reactions in the human body are so quick and mild that we cannot sense them in most cases. Though cells, tissues, organs, and systems in the human body are at different complexity degrees (or levels), they are all based on the combinations of organic and inorganic materials. In particular, organs can be manufactured through assembling different cell types or stem cells/growth factors along with other biomaterials[1–6]. Stem cells need to be controlled as they differentiate into different cell types before the formation of heterogeneous tissues. Two stem cell engagement strategies have been developed in our former studies. One of them is to mix growth factors in the cell-laden polymeric hydrogels before three-dimensional (3D) printing. The other is to add growth factors in the culture medium after 3D printing. The later is termed as “cocktail stem cell engagement”, in which different growth factor combinations are added into the culture medium in chronological order[28–38]. Homogeneous tissue forms with the same growth factor incorporation, while heterogeneous tissue forms with different growth factor combinations. Temporal and spatial effects are necessary for multiple tissue formation in a specific 3D construct. Both natural and synthetic polymers are essential for producing branched vascular, neural and/or lymphatic networks with anti-suture capabilities.

Table 1.

The Differences Between Tissues and Organs.

Differences	Content	Ref.
From concepts	A tissue is an ensemble of similar cells from the same origin that together carry out one or more specific biological functions; An organ is a collection of multiple tissues joined in a structural unit to serve one or more common physiological functions. The concepts of tissues and organs are different.	Liu and Wang[6]
From cell/ECM types	A tissue consists of only one homogeneous cell type with the same shapes and ECMs; An organ consists of at least two different cell types with different shapes and ECMs. The cell and ECM types of an organ is more than that of a tissue.	Wang[19]

Differences	Content	Ref.
From the evolution degree	Tissues are at cellular organizational level; Organs are at tissue organizational level. The evolution degree of organ is higher than that of tissue.	Wang[33]
From formation approaches	A tissue can be made by the division, growth and differentiation of one type of cells; An organ can only be made by assembling multiple cell types using special approaches. The formation approaches of tissues and organs are different.	Wang[35]
From manufacture tools	It is easy to construct tissues with simple material processing tools; It is difficult to construct organs with the existing material processing tools. The complexity of organ manufacturing tools is much higher than that of the tissue.	Yan et al.[23]
From functions	A tissue normally performs only one or few functions; An organ normally performs multiple functions. The functions of an organ is much more complex than that of a tissue.	Wang [19]

Organ Manufacturing Process

Ordinarily, there are four basic steps for an organ manufacturing process (Fig 3): (1) architectural predesign; (2) preparation of materials and construction tools; (3) homogeneous/heterogeneous cell assembling (or integration); (4) post multi-tissue maturation. For the fully automated MNRP and partially automated additive combined molding technologies, computer-aided design (CAD) modeling can be used for the architectural predesign to create a blueprint, while for manual cell seeding and perfusable decellularized organ regeneration technologies, the architectural predesign stages can be omitted when the organ's original architecture is used. During the construction or building stages, the construction tools play a key role in recapitulating the micro, meso, and macro (i.e., multi-scale) cell survival environments, the integration of homogeneous and heterogeneous cell types, and the realization of multi-tissue functionalities[1–6].

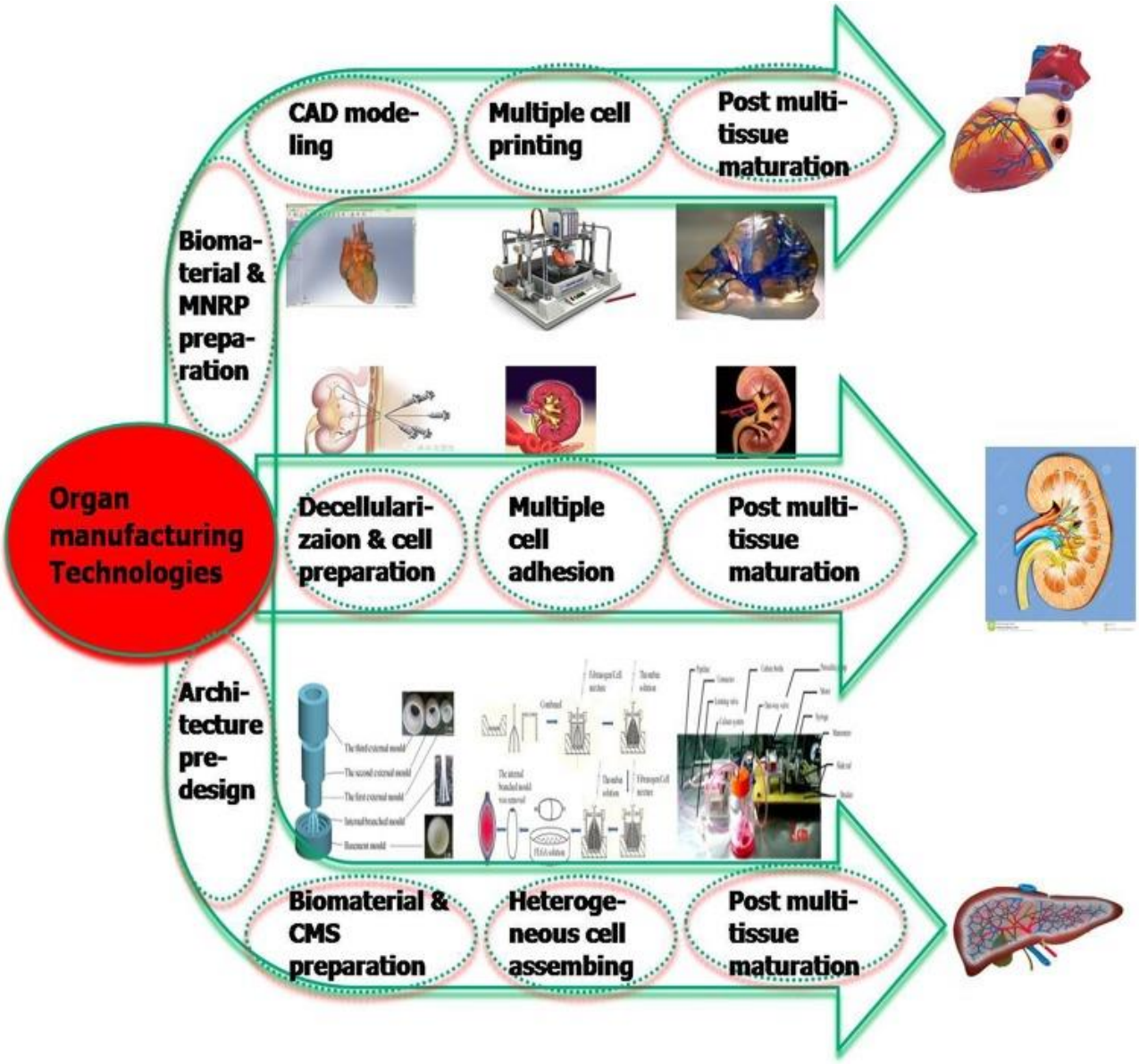


Fig 3.

Typical processes for organ manufacturing technologies: multi-nozzle rapid prototyping (MNRP), additive combined molding, and decellularization matrix regeneration.

As with building a nuclear power plant, a blueprint is necessary during the architectural predesign stage. Materials, such as different types of cells or stem cells with different growth factors, and construction tools are essential for the material/tool preparation stage. Cells from the individual patient, including adult cells and stem cells, are preferred to overcome immune rejection issues. Stem cell/ECM/growth factor assembling is a promising approach during the third homogeneous/heterogeneous cell assembling stage. Some MSCs, such as the adipose-derived stem cells (ADSCs), bone marrow mesenchymal stem cells (BMSCs), and umbilical

cord blood stem cells (UBSCs), have become more and more popular in the organ manufacturing fields. Growth factors, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (b-FGF), are essential for vascular endothelium formation, while hepatocyte growth factor (HGF), human platelet-derived growth factor (PDGF-BB), and transforming growth factor β1 (TGF-β1) are essential for tunica media generation. These growth factors are therefore very important for any complex organ manufacturing involving incorporation of a branched vascular/neural/lymphatic network incorporation. Among all the effective enabling organ manufacturing technologies, MNRP and additive combined molding have offered great benefit in the following homogeneous/heterogeneous cell arrangement and hierarchical vascular/neural/lymphatic network integration stage.

Emphasis should be given to the post multi-tissue maturation stage. During the post multi-tissue maturation stage, the assembled 3D constructs containing homogeneous/heterogeneous living cells need to be stable for *in vitro* culture or *in vivo* implantation. Physical, chemical and/or biochemical crosslinking of the supportive polymers are usually necessary to immobilize the living cells and to improve the structural stability[28–38]. Within the 3D construct, homogeneous and heterogeneous cell aggregation takes place to form homocellular and heterocellular tissues with the spatially and temporarily mechanical support of the crosslinked polymers. Thus, post multi-tissue maturation is a self-finishing process in which homogeneous or heterogeneous cell populations contact and coalesce to form coherent functional tissues. It is a continuous, materially changing, process that can provide living cells with multi-directional environmental signal, including biophysical (e.g., mechanical)/biochemical (e.g., enzymic) even physiological (e.g., potential of hydrogen, PH)/pathological (e.g., viral), stimulation. Only through multiple tissue formation, maturation and coordination, can a bioartificial organ with a whole spectrum of physiological functions be realized. For a solid organ with more than three cell types, such as the liver, heart or kidney, multiple gradient time and space factors need to be considered sufficiently.

During the multi-tissue maturation stage, stem cells can also be engaged into different cell/tissue types using a cocktail induction procedure. For example, ADSCs in a 3D printed construct have been induced effectively into various cell/tissue types, such as endothelial cells/tissues, adipose cells/tissues, smooth muscle cells/tissues and fibrocytes/tissues, under the guidance of sequential growth factor signals applied to the culture medium[28–38].

Thus, a typical organ manufacturing process can be described as follows: (1) like building a nuclear power plant, the manufacturing process is a dynamic transformation process, but in this case, containing the basic characteristics of life, with a series of changes in the physical/chemical/physiological properties of the starting materials; (2) advance processing technologies play a key role in the architectural predesign, homogeneous/heterogeneous cell integration, and multi-tissue formation, maturation and coordination stages; (3) stem cell engagement is benefitial for multi-tissue formation, maturation and coordination with respect to the limited cell resource, amount, and type; (4) both natural and synthetic polymers are useful in producing a branched vascular/neural/lymphatic network with anti-suture capabilities; (5) the generation of a hierarchical multi-scale vascular/neural/lymphatic network is critical to successful vascularized bioartificial organ manufacture with a whole spectrum of physiological functions.

Classification of Organ Manufacturing Technologies

Traditionally, there are several different types of artificial organs. According to the materials used, these artificial organs can be divided into three classes: mechanical, biomechanical, and biological. To date, the former two classes can only partially and temporarily replace and repair failed organs in the body, while biological artificial (i.e., bioartificial) organs can totally and permanently replace and cure failed organs.

According to the traditional manufacturing processes, bioartificial organ manufacturing technologies can be sorted into three basic classes: (1) fully automated, such as AM, RP, or 3D bioprinting[51–55]; (2) semi-automated, such as rotational combined mold system, involving mechanical handling (i.e., mechanized operation) steps[26,36]; (3) hand-manipulated, such as the layered biomaterial casting, cell sheet overlapping, and decellularized organ regeneration[29,30].

Depending on the processing mechanism, bioartificial organ manufacturing technologies can also be classified into several patterns: (1) bottom-up engineering technologies capable of integrating multiple homogeneous/heterogeneous cells in a bottom-up layer-by-layer deposition manner[56–59], e.g., MNRP is a typical fully automated bottom-up engineering approach employing sophisticated 3D printing. (2) Inside-out engineering technologies capable of integrating multiple homogeneous/heterogeneous cells in an inside-out, layer-by-layer increasing manner. Additive combined molding is a typical semi-automated inside-out engineering technique regarding to the predefined scale-up molds[26,36]. (3) Outside-in engineering technologies capable of integrating homogeneous/heterogeneous cells in an outside-in layer-by-layer attachment manner; decellularized organ regeneration is a typical hand-manipulated outside-in engineering protocol involving heterocellular adhesion on the preserved vascular networks[60–63].

During the last decade, all three classes (i.e. automated, semi-automated, and hand manipulated) of organ manufacturing technologies have developed very quickly. Some specific MNRP, additive combined molding and decellularized organ regeneration techniques have been extended rapidly, with substantial progress in the field of manufacturing certain complicated organs, such as the liver, heart, lung, and bone. Theoretically, these technologies hold extraordinary versatility in creating any organ in the human body, especially for those complex organs containing more than three cell types and multi-scale hierarchical vascular/neural/lymphatic and nerve networks. Currently, each of the fully automated, semi-automated, and hand-manipulated organ manufacturing technologies has its own limitations in creating bioartificial organs mimicking native counterparts in both physical structures and physiological functions. The advantages and disadvantages of MNRP, additive combined molding and decellularized matrix in producing organ substitutes are summarized in Table 2. Despite the great benefits and flexibility of these technologies in creating complex organs, these technologies currently still face some obvious limitations in producing organ substitutes with a whole spectrum of native organ functions.