(Online) ISSN 2744-1636
Bioengineering Studies *Review Article*
Vol. 6, No. 2, 2025, pp.52-66
https://doi.org/10.37868/bes.v6i2.id335

Bioengineering in medicine - a review

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Received Oct. 3, 2025
Revised Oct. 29, 2025
Accepted Dec.8, 2025
Online Dec. 31, 2025

Abstract

Bioengineering in medicine is a field that connects engineering, biology, and medicine in order to provide better therapeutic and regenerative solutions. Stem cells, biomaterials, and 3D bioprinting play a crucial role in this field. In this paper, regenerative medicine is highlighted as a transformative approach for restoring and replacing damaged tissues. In addition, advances in organ bioengineering and transplantation are discussed as a solution for the global shortage of donor organs. Primary focus was given to artificial blood vessels, their design, fabrication techniques, and current challenges such as thrombosis, biocompatibility, and long-term patency. This paper explores the broad application of bioengineering in medicine, including tissue engineering, regenerative medicine, nanotechnology, and organ biotechnology. Future development in bioengineering in medicine will be based on multidisciplinary collaboration and integration of different cells and materials to improve healthcare delivery and create a long-lasting biological replacement.

Keywords: Regenerative medicine. Artificial blood vessels, Tissue engineering, Biomaterials, 3D bioprinting, Gene therapy and Stem cells.

1. Introduction

The new field of research in medicine and biology known as biomedical engineering (BME) aims to improve health care and eradicate numerous diseases. It is based on biomedical research designs, concepts, and principles for diagnostic and therapeutic purposes [1]. Tissue engineering, stem cell engineering, genetic, neural, clinical, and chemical engineering are all examples of biomedical engineering, which uses skills from engineering, medicine, and biology to improve human or animal health care [2]. Regenerative medicine, cell and tissue growth, brain-imaging equipment like MRI and EEGs, artificial limbs and organs, and pharmaceutical drugs and therapeutic developments are all included in this application. It also includes the development of biocompatible prostheses, therapeutic devices, and several medical diagnostics. Modern tools for molecular cloning and transformation are used in genetic engineering to alter the structure and characteristics of target genes for disease treatment. Neural engineering is a field that uses biomedical engineering techniques to fix, replace, or improve neural cells or neurons in a patient's brain or body. Medical technologies and equipment are examples of medical devices. Diseases are diagnosed, treated, or prevented with these tools. Biomedical engineering can use bionics techniques to replace damaged or injured body parts using human spare parts. Tissue engineering, on the other hand, combines cells, biochemical and physico-chemical factors, engineering materials, and tissue synthesis to enhance, repair, or replace human body tissues for biomedical purposes [3].

Tissue engineering is synonymous with regenerative medicine; however, umbilical cord blood cells, also known as stem or progenitor cells, are utilized in the process of producing essential human tissues [4].

As previously stated, biomedical engineering plays a crucial role in the diagnosis, treatment, prevention, and treatment of numerous human diseases. It is also capable of producing artificial cells, tissues, or organs that are required for the treatment of numerous human diseases or damaged organs. Many hardware's and methods are extremely valuable for human wellbeing, as well as innovative work. The technology that uses stem cells to make cells for the pancreas, liver, neurons, heart muscle, and blood vessels is the future of biomedical engineering. To control human diseases, additional research is required on the synthesis of blood cells, tissues, and organs.

To meet health requirements, biomedical engineering provides interfaces between the human body and electronic devices. The intricate structure of traditional appliances causes some issues. With the recent advancements in nanotechnology, composite nanomaterials are becoming increasingly important in biomedical devices. Nanotechnology is important because, as is well known, it is relatively inexpensive, safe, and clean. It is an innovation, as well as science region orientated toward various applications in compound industry, energy industry, gadgets, and biomedical fields. Biomedical designing address one of the huge and quickly developing exploration part of nanotechnology [5]. This kind of engineering tackles health-related issues using techniques and knowledge from all engineering fields [2]. Techniques from biomedical engineering will make it easier to improve older devices, such as pacemakers, pumps, imaging technologies, medical implants, and advanced prosthetics [6]. Numerous clinical products made with nanomaterials and new healthcare opportunities are provided by Nanobiomedicine. The ability to produce the desired biological response in a natural setting is known as biocompatibility, and the materials used in biomedical applications should be nontoxic and highly biocompatible [7]. Numerous enzymes have been immobilized by either adsorption or covalent binding on a variety of supports in a wide range of practical medical applications, particularly in biomaterials, bioreactors, and biosensors [8]. Composite nanomaterials can be used in diagnostic and therapeutic procedures for a variety of diseases by combining biomedical engineering. Nanomaterials that are being developed ought to be safe for clinical translation and biocompatible. It is still challenging to use nanomaterials and nanocomposites in medical implants[9].

2. Regenerative medicine

The process of replacing or regenerating human cells, tissues, or organs to restore or establish normal function is referred to as regenerative medicine [10]. This suggests that the body can heal damaged tissues and organs by either replacing damaged tissue or stimulating the body's own repair mechanisms [11]. It can empower researchers to develop tissues and organs in the lab and securely embed them when the body can't fix itself.

Human cells are the focus of regenerative medicine. Cells can be somatic, adult stem, or embryo-derived, and there are now embryo-derived versions of the latter that have been reprogrammed from adult cells, allowing them to be conveniently grouped under the term "pluripotent cells" [12]. Through this sequence, there appears to be a progression in interest. It is driven by the heterogeneity of adult stem cells derived from sources like bone marrow and the limitations on the expansion of the majority of specialist somatic cells. Regenerative medicine and gene therapy may become more closely related as a result of this progression, which necessitates the transfer of genes to human cells [13]. Even though the early stages of regenerative medicine have had some failures, new products have come out, like for knee cartilage injuries from sports [14]. The treatment of patients with bladder dysfunction [15] is also experiencing significant advancement. These treatments make use of autologous somatic cells, and the products, especially those for the bladder and skin, contain biomaterials. Although the outcome of adult stem cell therapy is currently less clear, their significance will be demonstrated in the future [16]. However, there are philosophical differences regarding some cases. The interest in nanotechnology has influenced some biomaterials scientists, who may be drawn to those who anticipate a future in which man-made nanodevices will play a significant role in medical care [17]. On the other hand, those who focus on cells tend to focus more on mimicking nature's capabilities with as little artificial material as possible. When looking at medicine, it won't want to reject cell-based regenerative therapy in favor of other molecular

medicine options or new technologies like nanomedicine; rather, it will want to find the best combination. Human cell therapy, biomaterials, molecular medicines, and gene-based approaches will all be integrated into a so-called "regen" industry [18]. In the medium term, many medical conditions, including heart failure, Parkinson's and possibly Alzheimer's, insulin-dependent diabetes, and spinal cord injury, appear to be treatable with cell-based therapies. There are also a lot more that don't affect many people, have terrible effects, can't be treated, and should be sensitive to approaches based on human cells.

Although human cell-based therapies have received a lot of attention from scientists, the growing and significant connection between gene therapy and regenerative medicine deserves even more attention. The process of inserting genes into cells, determining whether the result is safe, and then implanting the cells into patients is known as cell therapy [19]. Genetic manipulation makes it harder to control things, and when cells and genes are linked together, new options for regenerative medicine are possible. The application of activator molecules, whether once or a few times, can influence the outcome to cause regeneration, but their placement is more challenging. Different from antibiotic doses, which are restorative of health but not regenerative, there are numerous examples of molecular pharmaceuticals whose effect can be regenerative. Human cells are the primary focus of regenerative medicine, which uses human cells to treat patients. In humans, the term "regeneration" refers to the process by which unharmed specialized cells multiply to replace the damaged tissue that has been lost. In people, it is by and by restricted to only a couple of tissues (liver) leaving to the side typical substitution of individual cells in epidermis and digestive mucosa [20]. Because of this, the goal of regenerative medicine is to help people regenerate more fundamentally by providing them with cells, particularly stem cells that can encourage more extensive regeneration. Repair is an adaptation to the loss of normal organ mass and results in the synthesis of scar tissue to restore interrupted continuity without restoring normal tissue. On the other hand, recovery re-establishes the interfered with coherence by combination of the missing organ mass at the first physical site, yielding a recover. The organ's normal structure and function are reestablished through regeneration; repair cannot be [21]. Regenerative medicine's goal is to get a patient back to full health for a particular condition, while traditional medicine, like surgery, focuses on fixing problems. Based on Greenwood et al., "Regenerative Medicine is an emerging interdisciplinary field of research and clinical applications focused on the repair, replacement, or regeneration of cells, tissues, or organs in order to restore impaired function resulting from any cause, including congenital defects, disease, trauma, or aging," [22]. It utilizes a blend of various mechanical methodologies that move it past conventional transplantation and substitution treatments. The use of soluble molecules, stem cell transplantation, the reprogramming of various cell and tissue types, and gene therapy are all examples of this kind of approaches [22].

A number of tissues and organs, including the skin, kidney, heart, and liver, have shown promising results in regenerative medicine, and it has the potential to correct some defects that are present at birth [23]. For regenerative medication systems to find actual success, the material utilized, for the most part mixes of platforms, undeveloped cells and development factors, should have the option to supplant the harmed tissue and have the option to work as the first tissue or have the option to animate recovery of the first tissue [24]. Regeneration can be sparked by materials and biomimetics on their own, but they can also be used to present biomolecules as growth factors to encourage cell growth [25]. Biomaterial or scaffold can now incorporate biological signals to encourage tissue regeneration and function as a physical support for cells. 3D bioprinting is one of the most impressive technological developments of recent decades [24]. The method of printing biological material directly onto scaffolds that could be seeded with cells is the most important. Material science, cell biology, and tissue engineering are all involved in 3D bioprinting. The placement of biological components and biomolecules as growth factors is essential for successful bioprinting. Each required tissue's vascular and nervous systems must be replicated using bioprinting [26].

To enable the translation of promising regenerative medicine strategies, 3D bio-printed models of human diseases and conditions must continue to improve. Scientists and clinicians must be able to "mimic nature" or "work with nature" when developing novel biomaterials and technologies like nanotechnology to advance regenerative medicine and tissue engineering [24].

3. Organ Bioengineering and Transplantation

Bioengineering and transplantation have emerged as promising fields to revolutionize modern medicine. Bioengineering refers to the application of engineering knowledge and principles to design and develop biological products, while transplantation involves the transfer or replacement of organs, tissues, or cells from one individual to another. Bioengineering and transplantation have revolutionized the field of medicine by providing innovative solutions to previously incurable diseases. The convergence of these two fields has provided new and innovative approaches to tissue engineering, organ replacement, and regenerative medicine. One of the most promising applications of bioengineering in transplantation is the creation of artificial organs. With a severe shortage of donor organs worldwide, researchers are developing functional, man-made organs to replace damaged or diseased ones [27].

The field of regenerative medicine focuses on repairing and regenerating malfunctioning organs. One key goal in this area is to reach a state where immunosuppressive drugs are no longer needed since this would improve quality of life, reduce toxicities, and cut down on costs. Several innovative approaches are being explored to achieve this, such as using acellular scaffolds created through decellularization, three-dimensional printing, and interspecies blastocyst complementation. Another significant advance is the development of induced pluripotent stem cells, which offer a way to sidestep the ethical issues and other limitations associated with embryonic stem cells and other types of progenitor cells that lack pluripotency [28]. The potential of regenerative medicine technologies is immense, with applications spanning diverse fields. These technologies can facilitate the regeneration of indigenous cell lines, generate new tissue or organs, replicate disease states for better understanding, and enhance the effectiveness of ex vivo transplanted organs. Over the years, significant advances have been made in tissue engineering, with the creation of viable organs like the heart, lung, kidney, and liver, among others. These organs have been developed using scaffold-based approaches or utilizing de-acellularized organs and decellularizing them. By utilizing autologous cells, bioengineered organs could be produced without the necessity of immunosuppression and its corresponding negative effects.

Bioengineering methods are not restricted by the shortage of donated organs, providing a further advantage [29]. Another area where bioengineering has shown great promise in transplantation is the development of biomaterials. Biomaterials refer to synthetic or natural materials that are designed to interface with biological systems. These materials may be used to create implantable devices, which replace or enhance the function of other organs or tissues. For instance, engineers have designed biomimetic pancreases, which helps to maintain blood glucose levels in diabetic patients efficiently. Similarly, implantable devices like heart valves or stents have been developed to reduce the risk of complications after procedures such as coronary angioplasty [30].

In the field of whole-organ bioengineering, a scaffold is needed for cells to develop and function properly.

This role is performed by the extracellular matrix (ECM) in living organisms. To create a bioengineered organ construct, current methods involve using a support structure produced by decellularization of human or animal tissues or organs. The next step is to repopulate the scaffold with cells, followed by organ-specific culture, to create a functional organ for transplantation. Much effort has been devoted to developing reliable and effective protocols for each of these steps, resulting in the successful creation of functional organ products [31].

A significant milestone in the progress toward creating a bioengineered organ was accomplished through the successful creation of a feasible decellularized heart scaffold. In 2008, Ott and the team created an appropriate heart scaffold from a rat heart, followed by the process of reseeding and maturing the matrix to develop a structure that could contract and react to medications. This was the first procedure that resulted in a functional, decellularized organ scaffold [32]. Liver bioengineering involves the fabrication of functional liver tissue using various tissue engineering techniques. This approach has the potential to address the current shortage of donor livers for transplantation and to provide an alternative treatment for liver diseases. Liver bioengineering involves the use of biomaterials, cells, and growth factors to create a three-dimensional structure that mimics the architecture and function of native liver tissue.

The goal is to create functional liver tissue that can perform essential metabolic and detoxification functions. The development of liver bioengineering techniques is still in its early stages, but promising results have been

obtained in animal models. Continued research in this field may lead to the development of functional liver tissue for clinical applications in the future.

In conclusion, Organ bioengineering and transplantation hold immense potential in revolutionizing the field of medicine by addressing the persistent shortage of viable donor organs. The advancements in stem cell research and tissue engineering have enabled the creation of functional, lab-grown organs that can be transplanted into patients suffering from various diseases. However, despite the promise of this technology, there are still several challenges that need to be addressed before it can be widely implemented. These challenges include the cost of the procedure, ethical concerns, and the need for further research to ensure the safety and efficacy of the process. Despite these challenges, the potential benefit of organ bioengineering and transplantation cannot be ignored. It has the potential to drastically reduce the waiting time for donor organs and save the lives of countless individuals around the world. Thus, more investment and research in this field are needed to ensure that this technology becomes a viable solution soon [33].

4. Tooth Bioengineering

Tooth bioengineering is a branch of regenerative medicine that focuses on the development and restoration of damaged or missing teeth. The ultimate goal of this field is to provide patients with functional, aesthetic, and long-lasting replacement teeth that integrate seamlessly into their existing dentition [34]. Several approaches have been tested in the research and clinical setting to achieve this goal, including dental pulp regeneration, tooth germ development, and 3D printing of teeth.

Dental pulp regeneration is an emerging field in tooth bioengineering that focuses on regenerating the dental pulp, which is the soft tissue inside the tooth. The goal is to restore the tooth to its natural function while avoiding the need for root canal treatment or tooth extraction [35]. Several techniques have been used to regenerate dental pulp, including the use of stem cells, growth factors, and tissue engineering approaches. Stem cells have been used to regenerate dental pulp by differentiating them into odontoblasts, which are cells that produce dentin, the hard tissue that surrounds the dental pulp. Growth factors, such as BMP-2 and BMP-7, have been used to stimulate the formation of new tissue in the tooth pulp. Tissue engineering methods have also shown promise in the regeneration of dental pulp. Using a combination of scaffolds, growth factors, and cells, researchers have been able to create a microenvironment that stimulates the growth of new tissue in the tooth. These tissue-engineered pulp-like tissues have been shown to maintain the structural and functional characteristics of native dental pulp. Overall, dental pulp regeneration is a promising field in tooth bioengineering that has the potential to revolutionize the way we treat dental problems such as tooth decay and root canal infections. With further research and development, dental pulp regeneration could become an effective and safe alternative to traditional dental treatments [36].

Tooth bioengineering is an innovative field that involves the development of functional teeth through the use of biological processes and engineering techniques. One of the key components of tooth bioengineering is the understanding of tooth germ development. Tooth germ development is a complex process that begins during embryonic development. At around six weeks' gestation, the first signs of tooth bud formation appear in the developing oral cavity. The tooth buds originate from the dental lamina, which is a thickened epithelium that forms along the developing jaw [37]. Tooth germ development can be divided into several stages.

The first stage is the initiation stage, in which the mesenchymal cells in the dental papilla interact with the dental epithelium to form a growth center. The cells in this growth center undergo mitosis and differentiation to form the various cell types that make up the teeth.

The next stage is the bud stage, in which the tooth bud grows and develops into a recognizable tooth shape. During this stage, the cells in the dental epithelium and dental papilla continue to proliferate and differentiate into the different cell types required for tooth formation.

The cap stage follows the bud stage, during which the tooth bud undergoes morphological changes to form a cap-like structure. At this stage, the enamel epithelium and dental papilla differentiate into the ameloblasts and odontoblasts respectively, which are responsible for the formation of the enamel and dentin layers.

The bell stage is the final stage of tooth germ development, during which the tooth assumes its final shape and the different cell types involved in its formation become fully differentiated. At this stage, the ameloblasts and odontoblasts begin secretion of the enamel and dentin layers respectively, and the tooth crown and root begin to form [38]. In tooth bioengineering, the knowledge of tooth germ development is used in the creation of functional teeth through tissue engineering and regenerative medicine techniques. Scientists aim to replicate each stage of tooth germ development in the lab to produce functional teeth that can be used for dental restorations or replacements. In conclusion, tooth germ development is a crucial component of tooth bioengineering, which seeks to create functional teeth using biological processes and engineering techniques. Understanding the different stages of tooth germ development is essential for developing effective tissue engineering and regenerative medicine techniques in the field of dental restoration and replacement.

5. Artificial blood vessels

Rapid social development, lifestyle and diet changes have left society with an increased number of patients with a higher tendency for cardiovascular diseases and arteriosclerosis. As the aging population is increasing as well, a focus on promoting health and longevity has led to the swift development of the biomedical industry. Most of the materials used in the biomedical industry were created in the last century, during the period of the 1940s and 1950s, but were established for use in industry in the 1980s. Among many artificial organs like kidneys or ligament bones, artificial blood vessel prevention is likely to be the most effective.

One of the leading causes of mortality worldwide is cardiovascular disease, which has led scientists to work to sustain the need for artificial vascular grafts in medical procedures. One of the first recorded uses of vascular prostheses in humans was a magnesium absorbable tube used in surgery that was performed by a German-Austrian surgeon in the 1900s. Unfortunately, the patient passed away three days after the surgery due to the development of fibrotic tissue caused by magnesium. Over the past twenty years, major improvements have been made in the biomedical field, creating numerous tissue-engineered vascular replacements.

New methods are used to produce tissue-engineered vascular grafts (TEVGs) for clinical applications, like 3D bioprinting that enables use of various sizes of artificial blood vessels. "The idea was to add independent mechanical properties to 3D structures that can mimic the body's natural tissue," stated Xiaobo Yin, an associate professor in the mechanical engineering department at CU Boulder [39]. However, only a tiny number of thorough studies have been done on artificial small-caliber vascular grafts that show long-term patency in vivo [40]. A perfect tissue-engineered vascular graft has also not yet been made clinically accessible. It is still very difficult to evaluate the next generation of grafts since it requires combining the fields of mechanical engineering, vascular biology, and immunoregulation to address complicated and diverse problems [41]. "There's even a particular size range that has better benefits when it comes to the kind of cardiovascular effects that were seen with previous generations of this material." explains the research's main author, a PhD candidate in chemical and biomolecular engineering at Ohio State [42].

Vascular blood arteries composed of synthetic polymers are commonly used in the treatment of cardiovascular disease. However, problems persist, and the inability to mimic important components of the natural vasculature as well as the mismatch of biomechanical qualities may lead to additional issues [43], [44]. To promote advances in the materials' design, it is crucial to comprehend the most typical failure types. Failures of vessel grafts are almost invariably brought on by restenosis and thrombus formation, and almost always follow the development of atherosclerotic disease or intimal hyperplasia [45]. Furthermore, infection is the main factor in the late failure of grafts because the inflammatory response to infection might lead to restenosis [46].

Grafts could keep their patency for a considerable amount of time if endothelial hyperplasia-related vascular graft occlusion was avoided. Intimal hyperplasia has three main causes: extracellular matrix (ECM) deposition, hyperproliferation of fibroblasts, and migration of intravascular SMCs from the media to the intima [47]. There are other additional causes as well, including mismatched artery diameter, stress after surgery, and inadequate blood flow [48].

5.1. Biomaterials used for production

Since the graft will be replaced by tissue ingrowth through the graft's pores, biodegradable materials are thought to be a wise candidate for use as artificial blood arteries. This type of reconstruction, however, is dependent on a delicate balance between the host cells' invasion, the destruction of the materials, and the replacement of the materials by host tissue [49], [50]. Chemically synthesized polymers are used to create synthetic biomaterials. They may be managed to provide good mechanical qualities thanks to their precise chemical structures. Polymer-based synthetic vascular grafts have emerged as a desirable choice due to their ease of polymer synthesis, mass repeatability, and quick availability [51], [52]. Vascular grafts made of biodegradable materials may be more suitable for use in clinical settings, particularly for the development of blood vessels with tiny diameters. When the grafts disintegrate, regenerated vascular tissue ensures the same function as autologous blood vessels [53], [54]. In particular, its nanofiber form created by electrospinning, polycaprolactone (PCL), a biodegradable polymer that has been licensed by the US Food and Drug Administration (FDA), has been widely used to create tissue engineering scaffolds [55]. A biomaterial gains strength thanks to synthetic polymers. However, most of the breakdown products have been demonstrated to incite unfavourable immunological reactions in vivo, indicating poor cellular compatibility. They also have a weak resistance to the surface thrombus development that causes graft blockage [56]. To increase their potency and the potential of synthetic polymers, the strategic plan must be implemented to change the surface of the synthetic polymers. Organic biomaterials are also frequently employed for vascular grafts in addition to the synthetic materials. They typically consist of proteins, polysaccharides, and proteoglycans that are taken from plants or animals. Traditionally used materials for artificial blood vessels include non-mammalian macromolecules like silk, cellulose, and chitosan as well as traditional mammalian ECM components like collagen and elastin [56], [57], [58]. The previously mentioned biomaterials are more biocompatible than synthetic materials, and when developed using the right production procedures, some have even been discovered to have advantageous qualities for vascular applications [59], [60]. With the improvement of manufacturing procedures, physical characteristics of polymers have been improved as well, making it desirable to use them exclusively.

Because of its unique biodegradability and biocompatibility, silk fibroin, which is produced from natural silk, is widely used in the field of biomedicine. Furthermore, compared to ePTFE, it has been shown to encourage vascular graft reendothelialization more quickly [61].The most abundant protein in higher animals is collagen, which is readily available in vast quantities from pigs, sheep, and fish. Gelatine can also be purchased for a low cost because it can be made from hydrolysed collagen. Elastin, another important component of the vascular ECM, is also derived from animals, albeit in smaller amounts [62]. Artificial polymers, despite having great mechanical qualities, have drawbacks when used in grafts because they frequently lead to thrombosis, intimal hyperplasia, calcification, and they have low hemocompatibility and regenerative capacity [63]. The mechanical characteristics of most natural materials are insufficient for usage as independent materials. Although they offer great biocompatibility, natural materials are susceptible to tumours and vascular graft dilatation [64], [65], [66], [67]. In these circumstances, demand for hybrid materials has grown because of enhanced durability when mixed with synthetic polymers.

5.2. Production of blood vessels

Thanks to biomedicine and progressive advances, structure and structure of artificial blood vessels and their manufacturing has been significantly improved. Some of techniques used for manufacturing artificial blood vessels are 3D printing and waving technology.

Stretch moulding is a time-tested method of producing ePTFE artificial blood vessels that has found widespread commercial use. In this method, polytetrafluoroethylene resin used as the raw material is extruded to create a preform that is longitudinally arranged into a fibrous shape, stretched at a high speed, and then chilled to produce a formed product [68]. The structure and mechanical characteristics of ePTFE are significantly influenced by each link's manufacturing process. The mechanical strength and biocompatibility of ePTFE artificial blood arteries can be impacted by porosity, which is crucial to ePTFE's performance [69]. A high-voltage electric field is utilized in the electrospinning process to spin a tiny jet of polymer created from a polymer solution or melt.

The direct and continuous preparation of polymer microfibers is made possible by electrospinning [70]. The following are some of the technical benefits of electrospinning: (1) it can increase blood vessel permeability to meet cell growth specifications; (2) it has a significant amount of surface area, which is beneficial to cell attachment and development; (3) the length of the generated fibbers is identical to the size of natural extracellular matrix or cells, so it can most closely resemble the framework of human extracellular matrix; and (4) it can carry growth factors and trigger cell proliferation [71]. To produce artificial blood arteries, numerous filaments are weaved in a precise pattern during the braiding process [72].

To expand blood vessels elasticity, conformity, and insusceptibility the braiding technique is used. Biomedical application has been notably relieved with braided grafts edge. The focus was on inner layer material and strength, the inner layer stays elastic, and strength of anastomosis is applied through the braiding technique.

The 3D printing industry first emerged in the middle of the 1990s and is based on digital model files, layer-by-layer printing, and powdered metal or plastic components [73]. Few studies have concentrated on the direct fabrication of artificial blood arteries by 3D printing, despite it having an adjustable shape characteristic. In particular, the synthesis of in vitro vascular abrasives to help in the production of inner layer materials of artificial blood arteries and the fabrication of organ chips to support the investigation of material patency has received the majority of research attention [74].

Beside mentioned techniques, other important techniques are composed of gas foaming, freezing- casting and usage of hydrogel technology. Most of the time, it’s impossible to use one technique in the production of artificial blood vessels, usually process is a combination of numerous methods. Combining them should result in a greater performance and achieving the best result in making artificial blood vessels. One of the most common combining techniques are weaving and electrospinning. Weaving strengthens the conformity of the vascular system while the electrospinning has a task to develop filaments that adjust growth and movement of the cells.

5.3. The various artificial blood vessels and their primary uses

The treatment of large, medium, and small pulses has evolved with the development of surgical techniques. Vascular transplantation is required when a disease or injury causes the body's blood vessels to stop functioning [75]. Now, composite vessels, synthetic blood vessels, and biological blood vessels are the main sources of vascular substitutes. Autologous, homologous, and xenogeneic vascular are examples of biological blood arteries. Due to their low patency rates, the latter two types of biological blood vessels are currently used in few uses in medicine and are susceptible to degradation and significant rejection. Although the source is smaller, the diameter and length are likewise constrained, autologous blood vessels can be employed as a small calibre vascular good substitute in peripheral vascular reconstruction. Since artificial blood vessels and composite vessels have features of vascular convergence similar to those of the human body and can maintain long-term patency and more steady performance, they are the perfect vascular substitutes that are most frequently used in clinical settings [76-78].

Artificial vascular systems come in a variety of shapes and sizes, including straight, Y-shaped, and multi-branch bifurcation. They can treat a variety of illnesses, including venous and arterial diseases, arteriovenous fistulas, and other conditions. For example, a straight type is frequently used to treat coronary artery stenosis during heart bypass surgery, a Y type is primarily used to implement abdominal aortic aneurysm endovascular exclusion, and a multi branch type is primarily used to manage heart aortic stenosis rebuilding efforts. Artificial blood vessels can be created using either the nonwoven technique or the textile approach. In the production of textiles, organic weaving and knitting predominate. Warp knitting vascular prosthesis, which combined the benefits of knitted and woven artificial blood vessels, are currently the type most frequently employed in clinical settings [79]. Nonwoven materials are made in two main steps: electrostatic spinning and injection moulding. Even though artificial blood vessels are made of nonwoven materials that still doesn’t guarantee that characteristics like biocompatibility or antithrombotic state are ideal. Biomaterials like elastin and collagen beside flexibility have a great quality to be main materials of human artery walls. In general, artificial vascular materials should meet three fundamental criteria, including long-lasting strength, adequate pore size, and high

compliance. The three primary areas in which research has advanced are the choice of novel materials, the alteration of blood vessels and coatings, and the creation of synthetic vascular endothelium [78].

5.4. Approaching future challenges

As was previously mentioned, there is a high need for acceptable vascular grafts because to the increase in patients with cardiovascular disease who need replacement therapy. Much progress has lately been made, from an initial simple synthetic blood artery substitute to tissue-engineered vascular grafts, and tissue engineering techniques offer prospective solutions for overcoming the obstacles of replacing vascular prostheses and addressing future regeneration of organs [47].

Many scientific research work has been focused on improvement of performance and material upgrading using tissue engineering to create the artificial blood vessels.

Three structural layers make up the normal human artery. The intimate fit of the intima, media, and adventitia, which transport blood flow, is related to the physiological function of blood vessels. Researchers have enhanced the production process and utilized cutting-edge technologies including electrospinning, thermal-induced phase separation, microfluidics, stretch forming, and weaving technology to mimic the multi-layered structure of real blood arteries as closely as possible [80], [81].Research is very interested in finding the best fabrication methods that can be used to solve problems associated with the failure of artificial blood arteries. With the help of 3D bioprinting technology, it is possible to rotate and print along a rod template to create complicated three-dimensional structures of various orders of magnitude [47], [82].The structure of artificial blood vessels can be made in such a fashion as to mimic the structure of the human body, such as through microenvironment changes that lead to optimizing the quality of the blood vessels. The selection of the right biomaterials can significantly enhance tissue mechanics and contribute to better biocompatibility. Researchers work on improving biomaterials mostly by combining and matching a few materials together. Right now, there are a lot of promising systems made through organic layering on synthetic materials. Probably in the future, organic or hybrid materials will be exchanged for synthetic materials, which will lead to a better acceptance rate and biocompatibility, which are the main factors in creating artificial blood vessels.

In fact, many artificial blood vessels have already been shown to possess adequate performance, however, they are still unable to meet usage requirements in terms of long-term patency rate and thus require optimization. Current commonly-used optimization methods are mainly related to certain biological technologies, such as gene editing and exosomes [47].

Future development should go in the direction in which cells and materials work together to build artificial blood vessels. Essentially, in order to develop a successful, long-lasting artificial blood vessel that satisfies the growing demand, a strong collaborative effort among various forms of expertise in fields involving material science, engineering, mechanics, and biology is needed [83].

6. Conclusion

Combining the concepts and blueprints from biomedical research, engineering and biology, biomedical engineering makes an infusion of all of them as a new branch that intends to promote better healthcare and eliminate diseases. The domain of biomedical engineering involves the use of tissue engineering, stem cell engineering, genetic engineering, neural engineering, clinical engineering, and chemical engineering to boost human health. Biomedical engineering is necessary for diagnosing, preventing, and treating human diseases. Recently, nanotechnology brought a new perspective to biomedical engineering and, since then, it plays a big role in new healthcare options. Another important branch of this study is regenerative medicine, which targets restoring human cells, tissues, or organs to restore homeostasis. Regardless of theoretical differences between biomedical and regenerative medicine, they both have remarkable positions in medicine and improving healthcare in the future. The shortage of organ donors that are suitable for patients, has inspired and pushed further development of bioengineering. Progressive techniques in organ replacement, regenerative medicine, and tissue engineering are built by the conjunction of these disciplines. Thanks to the improvement of tissue engineering and stem cell research, lab grown organs can be successfully transplanted into patients through

collection of alliances. Adapting this new technology and its approaches raises questions like cost of the operation and ethical issues, which both require further study to secure effectiveness and safety. It's out of the question to disregard probable advantages of organ bioengineering and transplantation, and more investment and research are necessary for this technology to become an achievable treatment. Lastly, tooth engineering is an area of regenerative medicine that centers on producing and replacing teeth. The intention of tooth engineering is to give patients practical, nice looking and long-lasting teeth that mimic natural odontiasis. The use of various biomaterials and constructing techniques has considerably proceeded with the designing of artificial blood vessels. Thankfully, biocompatibility and the ability to recover or replaced by host tissue, have become engaged in choosing bio gradable materials like bio polymers, especially for tiny diameter blood arteries. Nevertheless, with their exceptional mechanical characteristics and mass reproducibility, synthetic polymers remain to play a notable role. Some of the preferable organic biomaterials are silk, collagen and elastin, but lately hybrid materials are becoming preferred as well thanks to their heightened durability. Artificial blood arteries are created by composing the process of 3D printing, electrospinning, and weaving, which creates wanted features like permeability, surface area, and cell development. Using the braiding process, artificial blood vessels enhanced elasticity, conformity and flexibility have been successfully achieved. The chances for clinical settings have generally been significantly accelerated by the expansion of artificial blood vessel creation.

Declaration of competing interest

The authors declare that they have no known financial or non-financial competing interests in any material discussed in this paper.

Funding information

No funding was received from any financial organization to conduct this research.

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