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# Biomedical Graft Technologies: An Overview

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## ABSTRACT

**Introduction:** Search for alternatives in the health area, new technologies and concepts help to set up dimensions of the clinical situation, and priorities for investigation. The field of tissue engineering substitutes aims to mimic the extracellular matrix structurally and physiologically to replace or improve functions of the failing organ.

**Objective:** Provide a brief summary of the current achievements of technology in organ transplantation.

**Method:** This is a narrative review based on sources of primary and secondary evidence from a bibliographic survey.

**Results:** In clinical practice, various strategies are available or developed from advantages and disadvantages techniques.

**Conclusion:** Similar to native tissues, sophisticated biomaterial designs are making compliance simpler in a dynamic system, aiming a personalized way.

**Keywords:** Prostheses and implants, Biomedical technology, Bioartificial organs, Biocompatible materials

## INTRODUCTION

According to the World Health Organization (WHO)'s definition, "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [1]. It emphasizes the need for governmental agencies to elaborate on public health policies that responsibility to care about the welfare aspects [1,2]. Based on the foregoing analysis, the worldwide confronted with a shift resulting from globalization and challenges of a new knowledge-driven economy; cultural and community life; religion; morbidity and mortality due to the high prevalence of co-morbidities in a permanently evolving process of society [1-3].

In 2016 the average life expectancy at birth of the global population was 72.0 years [4,5]. Currently, quality of life is an important concern and it will dictate how these people will achieve the 'elderly' [6,7]. Reiterating that the organism has a limit to regenerate itself, loss of functionality through pathological changes or trauma reflects upon high-cost therapy and the population dependence on health services [8-10]. An example is organ transplantation, indicated to diseases sometimes refractory to treatment, which impacts the patients' routine and requires constant changes in their daily life. Nevertheless, the shortage of donors for transplantation therapy is a serious worldwide issue and the number of patients on waiting lists increases [11-14].

The Brazilian Association of Organ Transplants (ABTO), a civil non-profit entity, shows that donation's rate practically stagnated (decrease of 0.6%) compared to the first semester in 2018 [12]. Moreover, some situations that are characterized by key limitations like cold ischemia time and pre-existing physical conditions may affect the survival of the transplanted organ [15].

Considering the biochemical and cellular phenomena to restore the body integrity in a dynamic system [8,16,17]; inter and multidisciplinary intervention correlates the scientific and technological environment by bioengineers supplying cell products that should face a personalized medicine [18-20].

One might hope by several strategies now available to be used for replacing or improve failing organs function (biodegradable or bioresorbable substrate) with specific physical characteristics according to clinical demand [18,20-26]. Attachment cells, growth, proliferation and differentiation in modifiable surface materials by functional reactions establish the bioactivity [22-24,26].

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Others biotechnological tools to fabricate donor tissue or organs are being developed or tested for approval (e.g. tissue-engineered substitutes; molecular diagnosis; genomics, etc.) [21,27-31]. Once, mechanical properties closer to those of natural, as well as attractive cost-effectiveness, safer products, restriction of animal experiments and effective drugs for research are desired [20,24,29,32-34].

Motivated by these considerations, in this narrative review we will provide a brief summary of current achievements in the field of organ transplantation technology, establishing the dimension and priorities for investigation.

## METHOD

This is a narrative review that was based on primary and secondary evidence sources from bibliographic surveys. As Cochrane Library; Web of Science; MEDLINE from the National Library of Medicine of the United States of America via PubMed; databases of Latin American and Caribbean Literature in Health Sciences (Lilacs); SciVerse Scopus and Scientific Electronic Library Online (Scielo) by the Portal of Bases in Health Sciences (VHL).

The Health Sciences Descriptors (DeCS) used in English were: Prostheses and Implants; Biomedical Technology; Bioartificial Organs; Biocompatible Materials. The Boolean Operator "AND" was used. Articles with relevant and current rationale available in full were established as inclusion criteria. Duplicated articles (more than one database searched) and those that did not contemplate the subject matters were excluded.

## RESULTS/DISCUSSION

### Importance of the microenvironment

Difficulty in technical skill, ethical questions, and financing constraints still needed to be overcome [21,31,35,36]. To identify ways to simplify clinical practice through, effective and resolute care, has motivating scientists to achieve functionality model in a highly dynamic entity over the years [9].

The extracellular matrix (ECM) composed by multi-component structural elements (e.g. collagens, laminins, entactin, glycoproteins, elastic fibers, etc.), provide mechanical support to the resident cells, stability, a shape of tissues besides participating in their performance (tissue development, turnover and regeneration) [8].

Herewith, the homeostasis requires constant physical and chemical adaptations from cells residing in living systems [8]. And understanding human physiology as the components, structures and their interactions influence the environment's manufacture [8,26,32,37].

To advance knowledge of sophisticated laboratory-grown, three-dimensional (3D) cultures with specific micro architectural features become a viable alternative to improve the interaction of adhered cells from different transplant techniques [20,27,32,38-41].

The scaffold constitutes in controlled morphologies of interconnected pore networks construction at various scales (nano, micro and macro) and different distribution, which affects the final application at post-injury to physical integrity [32].

Aiming to functional performance to handle the tackle of practical failures such as inadequate vascularization, it is important to select the most suitable material for the guide's supporting substructure. If so, those variables need to be identified in the scaffold because they impact on mechanical properties during cell invasion and remodeling expressed *in vitro* [42-45].

### Tissue engineered

There are valuable tools in tissue restoration for patient survival: I) allografts, also known as allogenic, homologous grafts or homografts; II) xenografts, heterografts or xenogenic grafts; and III) alloplastic grafts or synthetic grafts [20]. Regardless of the case, immunosuppressant medications are needed, even with their side effects [46].

Concerning item III, biomaterials have their compositions explored to act cooperatively or synergistically to the organism [19,20,26]. Confirming the growth of some products in the public and private health care organizations, which were approved by Food and Drug Administration (FDA) [10,23,47-49].

These biomaterials are defined as "a substance that is able, or has been engineered, to take a form which, alone or as part of a complex system, is used to direct, by control of interactions with components of living systems, the course of any therapeutic or diagnostic procedure, in human or veterinary medicine" [19]. However, thus with biological evaluation through material-tissue tests interaction in risk management established by the International Organization for Standardization of the Manufacture of Medical Devices [23], the immune response is one of the determinants of rejection [46].

Research endeavors make worldwide progress with an ingenious structural project that can include many substances and applications in different forms (foams, fibers, membranes, hydrocolloids, and hydrogels) for better settings [27]. Several biomaterials are used with a concept of organotypic models to acquire bottom-up or top-down approaches [30,50,51]. Some of them are discussed below.

**Cells:** The mergers of omics technologies *in vitro* engineered substitutes establish models for research and applications around the world [52,53]. Understanding the multipotent stem cell and its biology behavior, allow us to evolve a noninvasive and accurate method of diagnosis or therapy [54].

Furthermore, the stem cells can proliferate themselves for many generations and differentiating into multi-lineage cells. Readily being used, induced pluripotent stem cells (iPS cells or iPSCs) are reprogrammed from adult cells to create living neo-tissues *in vitro* as a strategy to reproduce biological function [55-57].

Another possibility is mesenchymal stem cells (MSCs) that can differentiate into a variety of cell types. Moreover, the multilineage potential, immunomodulation by express cell surface markers, and anti-inflammatory molecules make it an interesting tool in chronic diseases and clinical trials [54,56,57].

In addition, soft-tissue grafts have shown improvement in clinical outcomes. Abundant adipose tissue-derived stem cells (ADSCs) sources as a form of cell-based therapy are still discussed in regenerative medicine and became a topic of growing interesting [58,59].

**Scaffold:** Temporary to permanent substitutes materials with different characteristics allow for a diversified design [20]. It may consist of natural microstructures (e.g. polysaccharides: chitosan, alginate, cellulose and others; proteins: collagen, gelatin, fibrin and others), polymers (e.g. Polyglycolide (PGA) and its compounds, Polycaprolactone (PCL), Polylactide (PLA) and others) or hybrid approaches [29,43,55,60,61].

The Amniotic Membrane (AM) is a great potential for grafting material [20]. Either directly or following decellularized ECM scaffolds [62], they are used for the treatment of corneal defects, diabetic foot ulcers, severe skin burns and specialties of periodontics and implant surgery [20,63,64].

Another therapeutic possibility is porcine small intestinal submucosa (SIS). This material consists of about 90% collagen, exhibits growth factors and adhesion peptide sequences. Considering an important component of the epithelial basement membrane that facilitates integration with tissue [20,65,66].

**Techniques:** Structuring an integrated and functional graft by association materials, tailored surface, predictable performance for optimizing properties in their final applications makes futuristic technologies even closer to reality [21,32,67,68].

The bioreactor provides strategies for cell seeding of scaffolds [67,69,70] and based on the advantages and disadvantages of the various techniques applied, we have some examples:

- **Fiber-Assisted Molding (FAM):** It establishes a method to fabricate microgrooves and study cells in complex helical and curved structures (e.g. intestine, esophagus, and heart), creating unconventional geometric volumes, which are assembled and remodeled during growth [71].
- **Rotary Jet-Spinning:** By building anisotropic arrays, presenting as advantages reduced commercial cost, high rate of production, and uniaxially aligned nanofiber structures for polymers allow a contributor to fiber formation and its application in tissue engineering [72,73].
- **Bioprinting:** Recently, 'time' is integrated at the evolution of 3D to 4D for complex bioconstructs. One of the possibilities is through 'smart materials' in a dynamic system whereas the external stimuli can change their reshape and function. And others by improving the bio-ink that is manufactured layer-by-layer in a static and inanimate situation, limited by the diameter of the syringe needle and by some polymers of liquid character. Some biomedical applications are transplantation and drug screening [74-77].

**Nanotechnology:** With nano and micro particles, multiple functions became possible [78].

- **Prevention:** To understand the patient-specific basis of disease, the varied practical applications stimulate access to before inaccessible areas. Some characteristics have been observed at the nanoscale like anisotropic properties, concentration polarization, charge exclusion, and streaming current phenomena which are exploring and can contribute in a positive form [78,79].
- **Diagnosis:** Some nanoparticles can serve as imaging agents due to their features contrast. Such as nanoparticles with metallic components used as a biosensor, assisting in image diagnosis and improving the clinical practices [78,79].
- **Treat diseases:** Through targeted drug delivery systems (TTDS) make compliance simpler and can considerably improve therapeutic efficacy with more controlled side effects by harnessing various routes of administration. For example, nanorobots that have the ability to manipulate environments and biological matter [39]. Enable a treatment for cancer, the performance of vitreoretinal microsurgery at ocular sites or on-demand release of specific chemokines at sites of injury [78,79]. Moreover, a nano-fluidic system like biochip is capable of replicating functions of organs from biomarkers with a combination of bioactive agents carrying microparticles [51,80]. And nano-membranes in a sustained delivery system (e.g. alkaloids, flavonoids, essential oils and so on), incorporation of nanosizing with the medicinal plants or into nanostructures that can optimize wound management [78,79,81].

In tissue engineering, nanomaterials are able to enhance cell growth and function. A nanocomposite polymer can include bioactive properties for better results in transplant therapies [30,79].

## TRENDS IN MODERN BIOLOGY

Exceeding the requirements of biocompatibility issues and highlights regenerative and restorative concept of compositional and functional structure, biomimicry, a term in biomaterials science that recently gained traction, can be defined as "new science that studies nature's models and then imitates or takes inspiration from these designs and processes to solve human problems" [82,83].

In an artificial niche inspired by tissue-specific niches, it attempts to provide a high-performance material [51,83,84]. Based on the fact that requires complex design, a multi-layer scaffold bioinspired approach is the alternative most promising guided regeneration [27,85].

## CONCLUSION

The aim of maintaining, enhance or restore tissues and organs into the dynamic landscape – that represents tissue physiology – through advances in synthetic technology and biological science by structural, chemical and physical insights, will yield functional biomaterial designs in the near future upon medical application.

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