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Revolutionizing Bone Implants: The Promising Journey of Hyperelastic Bone and 3D Printing in Modern Medicine

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Tóth[1] A., Furka[1] S., Furka[1] D.: Revolutionizing Bone Implants: The Promising Journey of Hyperelastic Bone and 3D Printing in Modern Medicine.

Summary

Introduction: In the rapidly developing world of modern medicine, there is an effort to create innovative materials that are characterized by affordability, quality, and long service life. The main target for the research teams became artificial bone implants produced by 3D printing. Biocompatibility, individualized geometries, and expansiveness of the material during bone growth are basic criteria for simplifying surgical manipulation and simplifying rehabilitation. In the last decade, such materials have mainly included ceramic composites and polyesters containing calcium phosphate. A cutting-edge step was the discovery of a material called hyperelastic bone (HB), which combines hydroxyapatite and biocompatible polymer components. HB is formed by an inorganic-organic composite with a 3D structure, capable of expansion along with growing bone. Due to its biocompatibility, it brings significant advances in the field of bone endoprostheses designed for pediatric patients. HB in combination with suitable 3D printing technology brings the possibility of producing individualized bone replacements of a new generation. This new generation is characterized by a more than 70 % decrease in the need for repeated resections during bone growth in pediatric patients, thereby significantly increasing the patient's quality of life and reducing the demands on rehabilitation.
Aim: Emphasize the importance of hyperelastic bone as a revolutionary material in the field of artificial bone implants, which has the potential to meet the quality of life of pediatric patients after part of the bone transplantation.
Conclusions: The effort to find new materials specifically for pediatric patients with rapidly growing bones has led to the breakthrough discovery of hyperelastic bone developed by the team of Jakus et al. from the Department of Materials Science and Engineering at Northwestern University in Evanston. It is a composite that combines hydroxyapatite, polycaprolactone and polylactic acid. The material improves the physicochemical and mechanical properties of endoprostheses compared to the still commonly used and studied materials based on polyesters and organic-inorganic composites. This material has a significant ability to adapt its geometry during the growth of the child's bone and thus reduce the demands of rehabilitation. In combination with 3D printing, HB offers a reduction in the cost of producing individualized endoprostheses. This groundbreaking material sets new standards for endoprosthesis development, orthopedics, and rehabilitation. Although this is a huge advance in medicine and medical rehabilitation, it is necessary to optimize rehabilitation processes for novel type of endoprostheses.

Key words: rehabilitation, endoprosthesis, 3D printing

Revolution in the 3D print biocompatible bones and endoprostheses

The continuous searching for the novel materials in modern medicine, with the goals of affordability, efficiency, and cost-effectiveness [1, 2], has sparked extensive research across various disciplines, including translational research of artificial bone implants. Fundamental attributes of suitable materials are biocompatibility, the ability to produce the required size and quantity of implants and facilitating ease of handling during surgical procedures [3]. The most advanced materials are composites made of calcium phosphate (CaP), polyesters, and their derivatives [4, 5]. CaP-based ceramic materials reveal high biocompatibility, but their solid porous structure is a challenge during surgical manipulation [4, 5]. This material also significantly limits post-operative medical rehabilitation, in which it is necessary to exert a large force leading to damage to the stressed endoprosthesis. Additionally, when liquid materials are introduced into the target area and subsequently harden, the resulting structure's porosity may cause defects, and limits implant's performance. Furthermore, the exothermic heat generated during the hardening process could have adverse effects on surrounding tissues [6].

The hyperelastic bone

According to the challenges, a breakthrough was achieved by Adam E. Jakus and his team through the development of a revolutionary material named "hyperelastic bone" (HB) [7]. HB comprises a synergistic combination of hydroxyapatite (HA) and either polycaprolactone (PCL) or poly(lactic-glycolic acid) (PLGA) in a precisely balanced 9:1 weight ratio [7]. The incorporation of dibutyl phthalate (DBP), 2-butoxyethanol, and dichloromethane (DCM) completes the formulation, with DBP acting as a plasticizer, 2-butoxyethanol as an active surfactant, and DCM as a volatile agent [7]. Employing cutting-edge 3D printing technology [2, 8], HB can be meticulously crafted into customized structures, and if necessary, further post-print modifications can be provided to cater to specific anatomical requirements [7]. Prior to clinical application, stringent sterilization protocols are employed to eliminate any residual solvents, which might pose potential toxicity risks in the biological environment [8]. Encouraging results from extensive mechanical tests prompted the selection of a material containing PLGA for in vivo testing [7]. Subsequent experiments conducted on female BALB/c mice revealed a positive and promising response to the presence of HB. During the 7-day trial, the initial stages of vascularization and total HB infiltration were readily observed, and after 35 days, complete infiltration of vascular tissues had occurred [7]. After this, comprehensive tests were carried out on rats over an 8-week period, successfully demonstrating HB's capability to induce bone tissue regeneration and growth even without additional modifications using growth factors [7]. Further advances in this cutting-edge material were made through experiments on a Macaca mulatto primate with pre-existing weakened cortical bone tissue in the skull region [7, 8]. During 4-week trial, experiments decisively confirmed HB's ability to stimulate the integration of host bone cells and vascularization into its structure, coupled with its remarkable potential to foster bone growth [7]. This promising outcome paves the way for potential applications of HB in the treatment of human injuries and bone tissue diseases, without eliciting a strong immune response from the recipient's body [7, 8].

However, in some cases, situations arise where the presence of certain modifiers is required for a positive treatment outcome. To ensure the attachment of the artificial bone material and its successful integration into the body, vascularization is necessary, however the natural process of angiogenesis and bone-growth requires long time along with extensive rehabilitation. The larger the surface area of the material, the longer this process takes. Liu et al. investigated this problem and find out that surface of 3D printed hyperelastic bone inoculated with human smooth muscle cells and after 3 weeks with human umbilical vein endothelial cells grew through the artificial bone tissue in a time proportional to the size of this surface [5, 8]. Another result of the experiment was design and preparation of an environment conducive to the growth of microscopic blood vessels [5].

Competing approaches

Due to their desirable properties, e.g. regeneration of tissues (bone, muscle, cartilage), polyurethane (PU) polymers represent another promising option in medicine; however, an obstacle to the use of these materials is the need for surface treatment due to the low amount of functional groups and generally low adhesion to surrounding cells [9, 10]. In a study by Hong et al., isosorbide derivatives were incorporated into the PCL-PU thermoplastic polymer intended for 3D printing. The resulting material was characterized by efficient tissue regeneration (muscle and bone tissue), biocompatibility, absence of cytotoxicity, shape memory properties and significantly enhanced cell adhesion properties [6].

Implementation of 3D print

The implementation of 3D printing technology in the production brings unparalleled level of customization, enabling clinicians to tailor the shape, size, and quantity of the desired implant to suit each patient's unique needs [1]. According to the material's inherent properties and adaptability, ~~it~~

endoprostheses or implants can be manually adjusted during surgical procedures [2, 3], further enhancing utility and versatility in clinical settings. In conclusion, HB emerges as a truly promising material [7], setting new benchmarks in the domain of medical implants, and holding tremendous potential for advancing the field of bone apparatus treatments, as it successfully meets all the necessary criteria for a modern bone implant material. However, the rehabilitation of patients who will have such material implanted requires the proposal, validation and implementation of a new rehabilitation methodology that considers the strength and specific dynamics of HB integration.

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