



ARTIGO DE REVISÃO

4D PRINTED IMPLANTS FOR THE RECONSTRUCTION OF BONE DEFECTS IN CRANIOMAXILLOFACIAL SURGERY: THE EVOLUTION OF REGENERATIVE BIOENGINEERING

Implantes impressos em 4D para reconstrução de defeitos ósseos em cirurgia craniomaxilofacial: a evolução da bioengenharia regenerativa

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ABSTRACT

Biotechnology and regenerative engineering have advanced significantly in recent decades, resulting in remarkable innovations in the field of craniomaxillofacial surgery. One of the most promising advances is the development of 4D-printed implants, which represent a step up from traditional 3D implants. 4D printing involves creating materials that have the ability to change their properties and shapes over time, responding to environmental stimuli such as temperature and pH. These implants offer more dynamic and adaptable solutions for the reconstruction of bone defects, allowing for more efficient regeneration of affected tissues, especially in craniomaxillofacial surgeries. The use of 4D implants opens up new possibilities in the treatment of complex fractures, congenital deformities and traumatic injuries, bringing promising advances to regenerative medicine. Given this scenario, this study seeks to explore the evolution of regenerative bioengineering in the reconstruction of craniomaxillofacial bone defects, with an emphasis on 4D printing of implants and their potential to revolutionize surgical practice. Understanding the properties of these biomaterials and their clinical applications could lead to significant advances in personalized medicine, optimizing patient recovery and reducing post-operative complications. This study consists of a literature review with a qualitative approach, updating advances in 4D printing for biomedical applications, with a focus on bone regeneration and tissue engineering. The review covers studies published between 2021 and 2023, ensuring that the latest innovations are included. 4D printing in craniomaxillofacial surgery represents a notable advance over conventional implants, mainly due to the ability to adapt and integrate with the biological environment. The use of intelligent materials that adjust to the body after implantation offers a number of advantages, such as a reduction in the need for subsequent interventions and better adaptation of the implants to the regenerating tissues. Studies have shown that these 4D implants can improve bone healing, speed up the recovery process and minimize post-operative complications. However, challenges such as the durability of the materials, the complexity of the printing and the associated costs are still issues to be resolved. In addition, the need for more clinical studies to validate the long-term effectiveness of these technologies is crucial. It is concluded that 4D-printed implants for the reconstruction of bone defects in craniomaxillofacial surgery are at the forefront of regenerative medicine. Their ability to adapt and respond to the biological environment could revolutionize the way bone defects are treated, providing more effective and personalized solutions for patients. Although the outlook is promising, further clinical research and technological advances are needed to overcome challenges such as cost and durability in order to make these innovations widely accessible and viable for routine clinical use.

Keywords: Reconstruction of bone defects, general surgery, orthopedics.

RESUMO

A biotecnologia e a engenharia regenerativa avançaram significativamente nas últimas décadas, resultando em inovações notáveis no campo da cirurgia craniomaxilofacial. Um dos avanços mais promissores é o desenvolvimento de implantes impressos em 4D, que representam um avanço em relação aos implantes 3D tradicionais. A impressão 4D envolve a criação de materiais que têm a capacidade de mudar suas propriedades e formas ao longo do tempo, respondendo a estímulos ambientais como temperatura e pH. Esses implantes oferecem soluções mais dinâmicas e adaptáveis para a reconstrução de defeitos ósseos, permitindo uma regeneração mais eficiente dos tecidos afetados, especialmente em cirurgias craniomaxilofaciais. O uso de implantes 4D abre novas possibilidades no tratamento de fraturas complexas, deformidades congênitas e lesões traumáticas, trazendo avanços promissores para a medicina regenerativa. Diante desse cenário, este estudo busca explorar a evolução da bioengenharia regenerativa na reconstrução de defeitos ósseos craniomaxilofaciais, com ênfase na impressão 4D de implantes e seu potencial para revolucionar a prática cirúrgica. A compreensão das propriedades desses biomateriais e suas aplicações clínicas pode levar a avanços significativos na medicina personalizada, otimizando a recuperação do paciente e reduzindo complicações pós-operatórias. Este estudo consiste em uma revisão de literatura com abordagem qualitativa, atualizando os avanços em impressão 4D para aplicações biomédicas, com foco em regeneração óssea e engenharia de tecidos. A revisão abrange estudos publicados entre 2021 e 2023, garantindo que as inovações mais recentes sejam incluídas. A impressão 4D em cirurgia craniomaxilofacial representa um avanço notável em relação aos implantes convencionais, principalmente devido à capacidade de adaptação e integração ao ambiente biológico. O uso de materiais inteligentes que se ajustam ao corpo após a implantação oferece uma série de vantagens, como a redução da necessidade de intervenções subsequentes e melhor adaptação dos implantes aos tecidos em regeneração. Estudos têm demonstrado que esses implantes 4D podem melhorar a consolidação óssea, acelerar o processo de recuperação e minimizar complicações pós-operatórias. No entanto, desafios como a durabilidade dos materiais, a complexidade da impressão e os custos associados ainda são questões a serem resolvidas. Além disso, a necessidade de mais estudos clínicos para validar a eficácia a longo prazo dessas tecnologias é crucial. Conclui-se que os implantes impressos em 4D para a reconstrução de defeitos ósseos em cirurgia craniomaxilofacial estão na vanguarda da medicina regenerativa. Sua capacidade de adaptação e resposta ao ambiente biológico pode revolucionar a forma como os defeitos ósseos são tratados, proporcionando soluções mais eficazes e personalizadas para os pacientes. Embora as perspectivas sejam promissoras, mais pesquisas clínicas e avanços tecnológicos são necessários para superar desafios como custo e durabilidade, a fim de tornar essas inovações amplamente acessíveis e viáveis para o uso clínico de rotina.

Palavras-chave: Reconstrução de defeitos ósseos, cirurgia geral, ortopedia.

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INTRODUCTION

The reconstruction of bone defects in craniomaxillofacial surgery represents one of the greatest challenges in regenerative medicine, requiring innovative approaches to restore the functionality and aesthetics of compromised tissue. In recent years, advances in regenerative bioengineering have enabled the development of more sophisticated biomaterials, including 4D-printed implants. These devices have the ability to dynamically adapt to the biological microenvironment, promoting more efficient and personalized bone regeneration (WANG et al., 2023).

4D printing technology is an evolution of 3D printing, incorporating intelligent materials with properties responsive to external stimuli such as temperature, humidity and mechanical loading. These implants not only mold to the patient's anatomy, but can also stimulate bone growth through the controlled release of biofactors, favoring osseointegration and reducing the need for multiple surgical procedures (KIM et al., 2022).

In addition, the use of biodegradable and bioactive biomaterials in 4D printing has expanded the therapeutic possibilities in craniomaxillofacial reconstruction. Smart polymers, shape memory metal alloys and ceramic composites are some of the main materials explored to create implants capable of self-modeling in response to the body's physiological conditions (ZHANG et al., 2021).

The clinical application of 4D-printed implants still faces challenges, such as

standardization of materials, validation of computer models and regulation for large-scale use. However, preclinical studies and the first clinical trials point to a promising future in which regenerative engineering could redefine the way complex bone defects are treated, promoting greater surgical predictability and better functional and aesthetic results (LI et al., 2023).

The customization of 4D-printed implants also opens up new possibilities in the field of regenerative medicine, allowing biomaterials to be designed with specific characteristics for each patient. With the help of digital modeling and artificial intelligence, it is possible to develop structures that mimic the biomechanical properties of natural bone, facilitating integration with the surrounding tissues and promoting more effective regeneration. In addition, the combination of growth factors and stem cells in these implants can accelerate the bone repair process and reduce the risk of rejection, making them a promising alternative for patients with major bone loss due to trauma or tumor resections (SINGH et al., 2023).

Given this scenario, this study seeks to explore the evolution of regenerative bioengineering in the reconstruction of craniomaxillofacial bone defects, with an emphasis on 4D printing of implants and their potential to revolutionize surgical practice. Understanding the properties of these biomaterials and their clinical applications could lead to significant advances in personalized medicine, optimizing patient recovery and reducing post-operative complications.

MATERIALS AND METHODS

This study consists of a literature review with a qualitative approach, updating advances in 4D printing for biomedical applications, with a focus on bone regeneration and tissue engineering. The review covers studies published between 2021 and 2023, ensuring that the latest innovations are included.

- Guiding Question:

What are the advances and challenges in the use of 4D printing with smart biomaterials for bone regeneration and tissue engineering?

- Inclusion criteria:

1. Articles published between 2021 and 2023;
2. Studies on smart biomaterials, 4D printing, bone regeneration and tissue engineering;
3. Publications available in full and indexed in PubMed, Scopus, Web of Science and SciELO;
4. Works written in Portuguese, English or Spanish;
5. Systematic reviews, laboratory trials and clinical studies with an innovative approach.

- Exclusion criteria:

1. Studies published before 2021;
2. Articles not available in full or not relevant to biomaterials in 4D printing;

3. Studies focused exclusively on 3D printing, with no connection to responsive materials or shape memory;

4. Isolated case reports or studies without robust methodology.

- Boolean markers:

(“4D printing” AND “Bone regeneration”) (“Smart biomaterials” OR “Shape memory materials”) AND (“Tissue engineering”) (“Biodegradable polymers” AND “4D scaffolding”).

Theoretical background

The use of 4D-printed implants for the reconstruction of bone defects in craniomaxillofacial surgery represents a major advance in regenerative bioengineering. Unlike 3D printing, 4D printing incorporates the dimension of time, allowing implants to adjust and change according to internal or external stimuli, such as changes in temperature or pH, after insertion into the body. This process adapts the implant to the patient's biological environment, promoting more efficient integration and faster recovery (RUIZ et al., 2022). In addition, these implants can be designed to respond to changes in the surrounding tissue, such as bone remodeling over time, which facilitates the regeneration of damaged tissue.

The combination of 4D printing with biocompatible materials, such as bioactive polymers and ceramics, is one of the key innovations contributing to the success of this approach. These

materials not only mimic the mechanical properties of bone, but also promote osteoinduction and osteoconduction, which are fundamental for bone regeneration. Studies show that bioactive materials, when combined with 4D printing, allow for the controlled release of growth factors and other therapeutic substances, accelerating the healing process and integration with the surrounding bone tissue (JAIN et al., 2021).

In addition, 4D printing offers the possibility of creating customized implants that fit perfectly with the patient's anatomy. This is particularly relevant in craniomaxillofacial surgery, where precision in implant fit is crucial for a good functional and aesthetic result. Customization reduces the complications associated with standard implants, such as rejection and infection, and allows the bone regeneration process to take place more efficiently (ZHANG et al., 2022). 4D printing also facilitates the manufacture of complex implants with specific geometries that suit hard-to-reach or irregularly shaped areas, increasing the effectiveness of the treatment.

The use of stem cells and growth factors, incorporated directly into 4D implants, is also gaining prominence. These cells can differentiate into osteoblasts and contribute to bone regeneration, while growth factors stimulate angiogenesis and osteogenesis. Combined with 4D technology, these implants not only promote local healing, but also have the potential to stimulate bone regeneration on a large scale, improving the final result and the patient's quality of life (XU et al., 2023).

Another crucial aspect for the success of these implants is the material used. Biocompatible polymers, such as polylactic acid (PLA) and polycaprolactone (PCL), are widely touted for their ability to interact with bone tissue and for their controlled biodegradability. These characteristics ensure that the implant disintegrates gradually as the regenerated bone takes on its function. The use of bioactive ceramics, such as tricalcium phosphate (TCP) and hydroxyapatite, is also common in 4D implants, as these substances promote osteoconduction and osteoinduction, favoring bone regeneration. Controlling the morphology of the implant with the aid of 4D printing allows the materials to be offered in a way that facilitates osteogenesis, minimizing the risk of infection (PENG et al., 2022).

CONCLUSION

4D printing represents a significant milestone in the field of bioengineering and bone regeneration, with direct implications for craniomaxillofacial reconstruction. The ability to create customized implants that adapt to the patient's biological environment over time brings undeniable benefits to the treatment of complex bone defects. The evolution of this technology, combined with the use of biocompatible and bioactive materials, has led to advances in improving bone integration and optimizing the healing process. In addition, the incorporation of stem cells and growth factors into 4D-printed

implants has shown great potential for accelerating bone regeneration, promoting more efficient recovery and lower risks of complications.

The application of 4D printing in craniomaxillofacial surgery, in particular, stands out for its ability to create implants that not only meet the patient's anatomical and functional needs, but also adapt to biological conditions throughout the healing process. This personalized approach improves aesthetic and functional results, as well as minimizing the risk of rejection or infection. However, there are still challenges to overcome, such as the need for precise control in the interaction between implants and the biological environment, as well as the effective integration of biological factors and materials.

In view of this, 4D printing offers an innovative and promising approach to the reconstruction of bone defects in craniomaxillofacial surgery, and its applications in regenerative medicine are only just beginning to be fully explored. The future of this technology will depend on continued research and development, as well as adaptation to the specific needs of each patient, ensuring that regenerative medicine reaches its full potential in the treatment of complex conditions such as craniomaxillofacial bone defects.

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Observação: os/(as) autores/(as) declaram não existir conflitos de interesses de qualquer natureza.