

3D打印在风湿免疫疾病关节损害中的运用

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摘要

三维打印技术(3D printing)作为一种前沿的增材制造技术,近年来在医疗健康领域中的应用越发广泛。本文主要探讨了3D打印技术在风湿病治疗中的应用及其前景。首先简要介绍了3D打印技术的工作原理及其在医疗领域中的早期应用。随后详细阐述了该技术在风湿病关节置换手术中的应用,包括通过高精度的影像学技术和计算机辅助设计软件,实现了关节的个性化重建和修复。此外本文还探讨了3D打印在药物递送领域的革命性作用,特别是如何通过设计特异性的生物活性材料,实现对风湿病患者的靶向治疗和早期干预。同时3D打印在构建疾病模型方面的应用,为深入理解疾病机制和药物筛选提供了新的工具。尽管存在成本、材料选择、精度和模拟复杂生物环境等挑战,但3D打印技术在医疗领域的潜力仍然巨大。展望未来,随着技术的进一步发展和优化,预计3D打印将在风湿病的个性化治疗和管理中发挥更加关键的作用。

关键词

三维打印, 风湿病治疗, 关节置换, 药物递送系统, 疾病模型构建

The Application of 3D Printing in Joint Damage Caused by Rheumatic Immune Diseases

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Abstract

3D printing technology, as an advanced additive manufacturing technology, has been increasingly utilized in the field of health care in recent years. This article primarily explores the application and prospects of 3D printing technology in the treatment of rheumatic diseases. Firstly, it briefly introduces the working principle of 3D printing technology and its initial applications in the medical field. It then elaborately discusses the application of this technology in joint replacement surgery for rheumatic diseases, including individualized reconstruction and repair of joints through high-precision imaging technology and computer-aided design software. In addition, this paper also explores the revolutionary role of 3D printing in drug delivery, especially how to achieve targeted treatment and early intervention for rheumatic patients by designing specific biologically active materials. Simultaneously, the application of 3D printing in constructing disease models offers new tools for deepening the understanding of disease mechanisms and drug screening. Despite challenges such as cost, material selection, precision, and simulation of complex biological environments, the potential of 3D printing technology in the medical field remains tremendous. With the further development and optimization of technology, 3D printing is expected to play a more critical role in the personalized treatment and management of rheumatic diseases.

Keywords

3D Printing, Rheumatic Disease Treatment, Joint Replacement, Drug Delivery System, Disease Model Construction

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1. 引言

三维打印(three dimensional printing, 3D printing)是一种基于计算机程序快速成型的增材制造技术。通过计算机设计好程序后,按照设定好的路径将原料按照 2D 维度逐层堆积,最终叠加为 3D 实体的技术。跟传统工艺相比,3D 打印更低耗、更快捷,广泛应用于航天航空、汽车制造、医疗健康等领域[1]。在医疗领域中,3D 打印最早在骨科及整形外科领域中得到应用。在骨/关节置换术中,临床医生通过植入假体替换缺损的骨关节,从而达到支持及修复的作用。随着精准医学概念的提出,千篇一律的假体早已不再满足患者的个性化需求。由此,3D 打印应运而生,它通过数字化建模精准设计出不同形状及大小的假体,从而构建出与个体解剖匹配度更高的植入物[2] [3]。2013 年美国 OPM 公司打印出全球首个可应用于临床的头骨假体,成功替换了一位患者的病损骨组织,自此开启了 3D 打印在骨关节领域中的引领时代[4]。在骨/关节置换术的病因中,骨关节炎高居首位[5] [6] [7] [8] [9]。而除了骨关节炎,其他风湿病引起的关节损害及功能障碍也不容小觑。据报道,6.5%~10.5%的类风湿性关节炎患者[10]、1.04%~2.55%的强直性脊柱炎患者[11]、1.16%~2.61%的痛风患者[12]会发展成为终末期关节病需进行关节置换术。因此 3D 打印技术也快速应用于风湿病患者。

2. 关节置换

在进行关节置换的风湿病患者中,3D 打印为手术操作和精准医疗提供了便利。它通过计算机断层扫

描、核磁共振成像等影像学技术获取病变关节的数据, 借助图像处理软件、逆向工程软件及计算机辅助设计软件等反向重建关节的实体模型及修复模型模拟解剖结构及力学性能, 从而协助外科医生进行个体化治疗。王金成研究团队[13]通过 3D 打印技术为一位类风湿性关节炎患者置换了双侧肘关节, 术后患者的 Mayo 肘关节评分从 10 分上升到 90 分, 且随访 3 年过程中并未发生不良反应。Tu 等[14]证实了 3D 打印导板在强直性脊柱炎患者畸形矫形术中有良好的辅助作用。但不同于骨折等物理因素, 已行关节置换的风湿病患者有关节失功、行二次手术的风险[15][16][17]。因为不同于正常骨折修复, 风湿病患者的局部免疫微环境紊乱、炎症持续、成骨细胞与破骨细胞失衡, 假体与周围组织的整合受到阻碍。于是, 3D 打印并不仅限于惰性假体的构建, 还致力于构建活性假体。Zhao Y 等[18]制备了载有英夫利西单抗和干细胞的墨水, 打印出含新型生物活性界面的假体, 提高了惰性金属与骨关节面的整合。无独有偶, 刚芳莉及研究团队[19]也研究出一种高强度多功能的 3D 打印水凝胶, 该水凝胶不仅可以能够支撑称重, 还可以原位缓慢释药抑制炎症、促进关节修复。

3. 药物递送

3D 打印还能对风湿病关节损害患者进行早期治疗, 延缓向终末期关节病的进展[20][21]。3D 打印水凝胶可以作为载体, 向体内递送药物, 从而达到治疗的目的。Collins KH 等[22]制备了一种携带基因工程干细胞的 3D 打印水凝胶, 通过皮下注射, 水凝胶在体内持续缓慢释放 IL-1 受体拮抗剂, 从而治疗类风湿性关节炎。不同于传统的药物递送, 3D 打印水凝胶可以局部递送, 且在释药动力学方面有着无可比拟的优势。通过大分子网络的溶胀、水解作用、酶解作用, 药物可以持续缓慢地释放[23]。Ding 等[24]也制备出同时负载 Kartogenin 和双氯芬酸钠的 3D 打印水凝胶, 在植入膝关节后不仅能够起到良好的支撑作用, 还能够体内持续缓慢释放药物长达 2 周, 很好地预防了继发性骨关节炎。更重要的是, 3D 打印墨水原料大多为细胞外基质, 这些生物来源的大分子还保留部分原有的结构与功能, 模拟细胞生长所需的类组织样物理和空间结构, 从而与体内细胞发生动态交互促进原位再生。Maihemuti A 等[25]就用明胶制备出一种 3D 打印水凝胶, 在置入骨关节炎小鼠后不仅促进了关节的修复, 同时还诱发了软骨组织的再生。

4. 构建模型

3D 打印并不止步于疾病的治疗, 在疾病检测、药物筛选、临床教学中也起到重要作用。通过 3D 打印构建的类器官、微流控芯片等可以模拟细胞微环境, 帮助研究病理生理机制及寻找可能的治疗靶点[26][27][28]。Stephenson W 等[29]通过 3D 打印制备出一种便宜快捷的微流控装置, 通过这个装置他们对 5 个类风湿性关节炎患者的 20387 个细胞进行了单细胞高通量液滴 RNA 测序, 揭示了不同细胞亚群在该病中扮演的角色及相互作用。Lin J 等[30]通过 3D 打印构建了 RA 血管翳病理类组织, 在这个类组织中细胞相互交流, 相较其他的二维培养更好地模拟了人体真实环境, 为药物筛选提供了更有效的平台。3D 模型还可以对患者进行宣教, 让患者更直观地了解疾病。Kleyer A 等[31]构建出了风湿病关节损害 3D 模型, 让患者对疾病有了更直观的认识, 提高了患者对疾病的自我管理意识。

5. 不足与展望

虽然 3D 打印技术优点很多, 但仍有其不足。比如, 打印墨水和设备价格不菲, 限制了该技术的推广; 打印材料有限, 且目前国内缺乏相关标准; 精度不够高, 目前仅限于微米级别; 如何模拟风湿病患者中复杂的免疫微环境, 如何模拟细胞间相互作用、细胞与细胞外基质间相互作用, 如何达到血管化, 如何同时满足墨水的可打印性和成品的力学性能等都是目前需要攻克的难题[32][33]。尽管如此, 3D 打印在医学领域中还是展现了巨大的潜力。随着技术的发展与完善, 从关节置换到靶向免疫治疗 3D 打印都可以实现, 这将为风湿病关节损害患者带来更多福音。

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