



# Is tissue engineering finally ready? The second wave of tissue engineering and its implications for oral and maxillofacial reconstruction surgery

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Tissue engineering has experienced a significant revitalization in recent years across scientific, clinical, and industrial fields. This renewal reflects the convergence of major technological breakthroughs, rising clinical demand, and growing regulatory and investment support. While early tissue engineering faced challenges with inconsistent results and limited clinical application, recent advancements, especially in biomaterials science, immunomodulation technologies, and the digital fabrication of scaffolds, have changed the field as a key driver of next-generation regenerative medicine. This editorial summarizes those second waves of tissue engineering and describes its future application in the field of oral and maxillofacial surgery (OMFS).

Modern tissue engineering was conceptualized in the early 1990s, when Langer and Vacanti<sup>1</sup> first proposed the now-foundational triad of scaffolds, cells, and signaling molecules for tissue regeneration. Conventional tissue engineering approaches in the following 20 years relied on biodegradable scaffolds seeded with cells and growth factors, but translation to routine clinical use was limited due to insufficient vascularization, insufficient mechanical durability, and unpredictable host immune responses<sup>2-4</sup>. Since the 2010s, these limitations were overcoming one by one, the emergence of high-resolution three-dimensional (3D) bioprinting (2013-2016) enabled spatially controlled deposition of biomaterials and living cells, reproducing complex microenvironments

that mimic native tissue structures<sup>5</sup>. Most recently, imaging-guided workflow innovation allows patient-specific scaffold fabrication based on computed tomography (CT) data, particularly relevant in OMFS reconstruction<sup>6</sup>. In parallel, the development of organoids, first demonstrated for intestinal crypts in 2009, and the rise of organ-on-a-chip platforms around 2010-2012, have provided advanced physiologic models for disease simulation, drug evaluation, and preclinical validation prior to clinical translation<sup>7-9</sup>.

Another major recent advancement is the deeper understanding of the immune-biomaterial interface, especially the role of macrophage polarization in wound healing and foreign body reactions<sup>10,11</sup>. This has led to the development of immune-informed scaffolds that actively promote regenerative rather than inflammatory responses, improving graft stability and integration<sup>12,13</sup>. Parallel to scientific progress, global regulatory systems have become increasingly supportive. The U.S. Food and Drug Administration's Regenerative Medicine Advanced Therapy (RMAT) program accelerates approval for regenerative therapies<sup>14</sup>, and Europe's Advanced Therapy Medicinal Products (ATMP) framework provides clear standards for cell- and tissue-based products<sup>15</sup>. In South Korea, the 2019 Advanced Regenerative Medicine and Advanced Biological Products (ARMAB) Act, updated in 2024 to expand patient eligibility from February 2025, strengthened safety monitoring and facilitated application of advanced regenerative technologies. Combined with increasing industry investment and translational funding, these factors create a robust ecosystem for clinical adoption and commercialization of new tissue engineering technologies.

In summary, innovations in biomaterials, immune-responsive scaffold engineering, and patient-specific digital fabrication are propelling the second wave of tissue engineering into clinical relevance. As regulatory systems mature and translational pipelines expand, engineered tissues are expected to

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**Table 1.** Summary of the recent emerging tissue engineering advances and related OMFS-specific innovations

Emerging technology	OMFS-specific innovation (2022-2025 published articles)
Smart, immunomodulatory biomaterials	<ul style="list-style-type: none"> <li>• Anti-inflammatory / M2-polarizing scaffolds for peri-implant bone healing</li> <li>• Infection-responsive hydrogels for GBR and sinus augmentation</li> </ul>
Advanced 3D bioprinting and bioinks	<ul style="list-style-type: none"> <li>• Anti-fibrotic coatings to reduce foreign-body reaction in facial implants</li> <li>• Patient-specific mandibular body/ramus/condyle scaffolds from CT segmentation</li> </ul>
Organoids and organ-on-chip models	<ul style="list-style-type: none"> <li>• Osteochondral printing for mandible, maxilla, including TMJ disc–cartilage interface</li> <li>• Tooth germ organoids for periodontal regeneration research</li> <li>• TMJ joint-on-a-chip for chondrocyte–synovium interaction studies</li> </ul>
Vascularization and perfusion bioengineering	<ul style="list-style-type: none"> <li>• Mucosa-on-chip for oral drug permeation and infection models</li> <li>• Microchannel bioprinting for mandibular reconstruction (fibula-free-flap alternatives)</li> <li>• Perfused bone constructs for irradiated jaw osteonecrosis models</li> </ul>
AI-assisted digital bio-design	<ul style="list-style-type: none"> <li>• AI-guided porosity/topology optimization for mandibular plates &amp; scaffolds</li> <li>• CT-MRI fusion for patient-specific TMJ geometry</li> <li>• Virtual surgical planning integrated with regenerative scaffold design</li> </ul>

(OMFS: oral and maxillofacial surgery, GBR: guided bone regeneration, 3D: three-dimensional, CT: computed tomography, TMJ: temporomandibular joint, AI: artificial intelligence, MRI: magnetic resonance imaging)

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transition from experimental constructs to practical surgical tools—particularly in maxillofacial bone, soft-tissue, and temporomandibular joint regeneration.(Table 1) Sustained progress may ultimately shift OMFS from reconstruction toward true biological restoration, enabling grafts that integrate, remodel, and function as living replacements.

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### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### References

1. Langer R, Vacanti JP. Tissue engineering. *Science* 1993;260:920-6. <https://doi.org/10.1126/science.8493529>
2. Griffith LG, Naughton G. Tissue engineering--current challenges and expanding opportunities. *Science* 2002;295:1009-14. <https://doi.org/10.1126/science.1069210>
3. Jain RK, Au P, Tam J, Duda DG, Fukumura D. Engineering vascularized tissue. *Nat Biotechnol* 2005;23:821-3. <https://doi.org/10.1038/nbt0705-821>
4. Anderson JM, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. *Semin Immunol* 2008;20:86-100. <https://doi.org/10.1016/j.smim.2007.11.004>
5. Murphy SV, Atala A. 3D bioprinting of tissues and organs. *Nat Biotechnol* 2014;32:773-85. <https://doi.org/10.1038/nbt.2958>
6. Sears NA, Seshadri DR, Dhavalikar PS, Cosgriff-Hernandez E. A review of three-dimensional printing in tissue engineering. *Tissue Eng Part B Rev* 2016;22:298-310. <https://doi.org/10.1089/ten.teb.2015.0464>

7. Sato T, Vries RG, Snippert HJ, van de Wetering M, Barker N, Stange DE, et al. Single Lgr5 stem cells build crypt-villus structures in vitro without a mesenchymal niche. *Nature* 2009;459:262-5. <https://doi.org/10.1038/nature07935>
8. Huh DD. A human breathing lung-on-a-chip. *Ann Am Thorac Soc* 2015;12(Suppl 1):S42-4. <https://doi.org/10.1513/annalsats.201410-442mg>
9. Bhatia SN, Ingber DE. Microfluidic organs-on-chips. *Nat Biotechnol* 2014;32:760-72. <https://doi.org/10.1038/nbt.2989>
10. Murray PJ, Wynn TA. Protective and pathogenic functions of macrophage subsets. *Nat Rev Immunol* 2011;11:723-37. <https://doi.org/10.1038/nri3073>
11. Faulk DM, Londono R, Wolf MT, Ranallo CA, Carruthers CA, Wildemann JD, et al. ECM hydrogel coating mitigates the chronic inflammatory response to polypropylene mesh. *Biomaterials* 2014;35:8585-95. <https://doi.org/10.1016/j.biomaterials.2014.06.057>
12. Sadtler K, Estrellas K, Allen BW, Wolf MT, Fan H, Tam AJ, et al. Developing a pro-regenerative biomaterial scaffold microenvironment requires T helper 2 cells. *Science* 2016;352:366-70. <https://doi.org/10.1126/science.aad9272>
13. Salthouse D, Novakovic K, Hilkens CMU, Ferreira AM. Interplay between biomaterials and the immune system: challenges and opportunities in regenerative medicine. *Acta Biomater* 2023;155:1-18. <https://doi.org/10.1016/j.actbio.2022.11.003>
14. U.S. Food and Drug Administration (FDA). Regenerative medicine advanced therapy designation [Internet]. Silver Spring (MD): FDA [cited 2025 Dec 24]. Available from: <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/regenerative-medicine-advanced-therapy-designation>
15. European Medicines Agency (EMA). Advanced therapy medicinal products [Internet]. Amsterdam: EMA [cited 2025 Dec 24]. Available from: <https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview>

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