

## Personalised medicine: Applications for dental implant therapy

Our health care system is evolving towards offering more personalised patient care. Personalised medicine uses a patient's genetic profile to guide decision making in regard to disease prevention, early intervention and disease risk assessment. It involves classifying individuals into subpopulations that are uniquely susceptible to a particular condition or responsive to a specific form of treatment.

Dental diseases that contribute to tooth loss, such as dental caries and periodontitis, are examples of cases where personalised medicine has the potential to provide more timely diagnosis and intervention. Rather than adopting a reactive approach after disease progression and tissue destruction, clinicians can address risk assessment, diagnosis and therapy in a more proactive way. When applying personalised medicine to the management of periodontal disease, saliva or gingival crevicular fluid can be collected to identify and measure specific genotypes, phenotypes, pathogens and biomarkers. The clinician can then make more informed decisions about disease susceptibility and treatment interventions. Elevated levels of proinflammatory cytokines such as interleukin-1 (IL-1) can affect host–bacterial interactions in the periodontal tissues. Patients who are genetically positive for the IL-1 gene have shown a higher incidence and increased severity of periodontal disease. A genetic test for IL-1, obtained via a cheek swab, can provide valuable information on risk assessment and subsequent care. One study found that high-risk patients who had two maintenance visits per year rather than one experienced a significant reduction in the number of tooth loss events<sup>1</sup>. The use of these diagnostic tests for early diagnosis may help delay or mitigate the need for replacement of the affected dentition with dental implants.

A history of periodontitis is associated with a higher prevalence of peri-implantitis and risk of implant loss<sup>2</sup>. It would be beneficial to know whether

a patient who lost their teeth due to periodontitis was genetically predisposed to peri-implant disease. The patient could be educated on minimising other risk factors, such as smoking and diabetes, and the importance of oral hygiene and regular professional maintenance to optimising implant longevity. Peri-implantitis lesions typically progress faster than periodontitis and cause greater bone loss; thus, prevention and early diagnosis are a priority. A recent study found that the microRNA content of saliva may be a plausible source for the early diagnosis of peri-implantitis, and that the miR-4484 RNA gene might serve as an encouraging early diagnostic biomarker<sup>3</sup>. There is moderate evidence in the literature to suggest that implants affected by peri-implantitis present higher levels of proinflammatory cytokines in the peri-implant crevicular fluid than healthy implants<sup>4</sup>. In the future, routine maintenance visits for implant patients may involve obtaining crevicular fluid or saliva samples for testing.

Personalised treatment strategies for dental implant therapy may also be tailored to each individual's characteristics and healing profile in future years. Omics technologies are powerful tools that can discover the molecules and signalling pathways involved in bone formation and osseointegration. A recent paper by Refai and Cochran<sup>5</sup> introduced a new concept for osseointegration termed "implantogenomics". Investigating the differences between the molecular mechanisms in health and systemic diseases could help to target future therapeutics. Dental implant therapy may be individualised to unique biomechanistic upregulating genes in favour of osseointegration. Personalised dental implant therapy could provide safer, more effective and reliable treatment that is individualised to a person's unique genome. This could enhance clinical outcomes in patients with compromised healing conditions due to advanced age or systemic disease.

Although not related to use of genetic information, another form of personalised implant dentistry involves customising bone regenerative procedures and implant devices to the individual patient. In patients who have inadequate bone for implant placement, a CBCT scan can be obtained to enable 3D digital planning of the jaw reconstruction relative to the final implant prosthesis. Various personalised scaffolds with optimal fit may then be fabricated using this technology<sup>6</sup>. This could enhance bone graft incorporation and shorten surgical time, which may reduce complications and patient discomfort.

When using CBCT data to create a 3D model of the jaw, a custom scaffold for bone formation can be designed. A contoured, form-stable titanium scaffold can then be printed, providing a customised mesh to fit the individual anatomy of the patient. Another option is to fabricate a customised block bone graft. The bone block is designed virtually to reconstruct the defect and provide a precise fit with the host bone. Ideal sites for fixation of the block are also planned. The block graft may then be milled from allogeneic, xenogeneic or alloplastic materials. For larger defects, combining the use of these custom scaffolds with growth factors and/or cell constructs may offer a more minimally invasive approach compared to harvesting autogenous bone.

In patients with severe jaw atrophy and who are not suitable candidates for bone augmentation procedures, custom dental implants may offer an alternative solution<sup>7</sup>. The CBCT scan data are used to create a 3D virtual bone model. Using modelling software, a subperiosteal implant is then designed to provide a supporting substructure for the dental prosthesis, and the customised design is used to fabricate the implant from titanium by means of direct metal laser sintering. As the implant is designed to distribute load to the atrophic ridge, bone augmentation is avoided.

Embracing the concept of personalised medicine could lead to a paradigm shift in dental implant care. Increased emphasis on disease prevention and precision therapy may allow patients to

maintain their dentition for longer periods and could obviate the need to replace dental implants. A better understanding of the genomics of wound healing will help to identify the precise mechanisms of osseointegration and improve the selection of biomaterials and biologics for compromised conditions or patients with reduced healing capacity. Bone regeneration may also become more predictable with less morbidity and fewer complications, which will allow more patients to receive implant treatment. The era of omics technologies will fuel implant dentistry to reach unprecedented levels of personalised patient care.



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## References

1. Giannobile WV, Braun TM, Caplis AK, Doucette-Stamm L, Duff GW, Kornman KS. Patient stratification for preventive care in dentistry. *J Dent Res* 2013;92:694–701.
2. Sgolastra F, Petrucci A, Severino M, Gatto R, Monaco A. Periodontitis, implant loss and peri-implantitis. A meta-analysis. *Clin Oral Implants Res*. 2015;26:e8–e16.
3. Urvasizoglu G, Kilic A, Barlak N, Gundogdu M, Karatas OF. MiR-4484 acts as a potential saliva biomarker for early detection of peri-implantitis. *Int J Oral Maxillofac Implants* 2021;36:115–121.
4. Duarte PM, Serrão CR, Miranda TS, et al. Could cytokine levels in the peri-implant crevicular fluid be used to distinguish between healthy implants and implants with peri-implantitis? A systematic review. *J Periodontol Res* 2016;51:689–698.
5. Refai AK, Cochran DL. Harnessing omics sciences and biotechnologies in understanding osseointegration - Personalized dental implant therapy. *Int J Oral Maxillofac Implants* 2020;35:e27–e39.
6. Yen HH, Stathopoulou PG. CAD/CAM and 3D-printing applications for alveolar ridge augmentation. *Curr Oral Health Rep* 2018;5:127–132.
7. Jehn P, Spalthoff S, Korn P, et al. Oral health-related quality of life in tumour patients treated with patient-specific dental implants. *Int J Oral Maxillofac Surg* 2020;49:1067–1072.