

SYSTEMATIC REVIEW

Use of bioinformatic strategies as a predictive tool in implant-supported oral rehabilitation: A scoping review

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The growth of population and of increased lifespan has meant that more people are looking for treatments and solutions for lost teeth, resulting in an increased demand for bone regeneration treatments and oral rehabilitation techniques for elderly patients with specific health conditions.^{1,2} Patient-related conditions, such as smoking habits, poor oral hygiene, infectious processes, systemic diseases (osteoporosis, diabetes mellitus), and drugs that affect bone metabolism, might influence the progress of bone regeneration and, consequently, the osseointegration of dental implants.^{3,4} In addition, factors related to the surgical and prosthetic phase, as well as the inherent characteristics of dental implants, such as wettability, porosity, roughness, may influence the osseointegration process.^{5,6}

In the approximately 40 years since the introduction of implants into clinical practice, many complications have been reported, including the loss or fracture of

ABSTRACT

Statement of problem. The use of bioinformatic strategies is growing in dental implant protocols. The current expansion of Omics sciences and artificial intelligence (AI) algorithms in implant dentistry applications have not been documented and analyzed as a predictive tool for the success of dental implants.

Purpose. The purpose of this scoping review was to analyze how artificial intelligence algorithms and Omics technologies are being applied in the field of oral implantology as a predictive tool for dental implant success.

Material and methods. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews checklist was followed. A search strategy was created at PubMed and Web of Science to answer the question “How is bioinformatics being applied in the area of oral implantology as a predictive tool for implant success?”

Results. Thirteen articles were included in this review. Only 3 applied bioinformatic models combining AI algorithms and Omics technologies. These studies highlighted 2 key points for the creation of precision medicine: deep population phenotyping and the integration of Omics sciences in clinical protocols. Most of the studies identified applied AI only in the identification and classification of implant systems, quantification of peri-implant bone loss, and 3-dimensional bone analysis, planning implant placement.

Conclusions. The conventional criteria currently used as a technique for the diagnosis and monitoring of dental implants are insufficient and have low accuracy. Models that apply AI algorithms combined with precision methodologies—biomarkers—are extremely useful in the creation of precision medicine, allowing medical dentists to forecast the success of the implant. Tools that integrate the different types of data, including imaging, molecular, risk factor, and implant characteristics, are needed to make a more accurate and personalized prediction of implant success. (*J Prosthet Dent* 2023;■:■-■)

prosthetic dental screws, fracture of the dental implant, and biologic problems such as peri-implant mucositis or peri-implantitis.⁷⁻⁹ According to Benakatti et al,⁷ “dental implants will need maintenance as long as they remain in the patient’s oral cavity.” Therefore, information about

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Clinical Implications

The combination of both AI algorithms and Omics expertise can provide an extremely powerful tool to support the clinician's opinion, not only in terms of identifying implant systems but also in predicting implant success.

the rehabilitation, including the implant system used, fixation method, and abutment used, is needed. Patient history and radiographic examination provide information that allows the clinician to identify the implant system. However, the patient's history is not always accessible, and the identification of the implant system through radiographic examination requires effort and experience.⁸⁻¹²

The development of methodologies able to integrate all the factors and predictors is possible with the use of artificial intelligence (AI). These strategies support the prognosis of the implant, predicting eventual clinical conditions such as early bone loss, mucositis, or peri-implantitis.^{10,13-15} In addition, when using methods based on advanced neural networks—machine learning—it is possible to foresee the complexity and potential risk involved during the process of oral rehabilitation of the dental implants.¹⁶⁻¹⁷

The scientific evidence, as well as the assessment tools used in contemporary practice, has been based on clinical, analytical, and radiographic parameters which provide the clinician with limited therapeutic guidelines to deal with the multifactorial complexity of the implant-supported rehabilitation procedures.^{18,19} Furthermore, for diagnosing and staging peri-implant disease, such methods can only register the actual tissue destruction rather than current disease activity. Moreover, those conventional strategies do not consider systemic conditions, which may influence the local immunological response, either around a tooth area (periodontitis) or around a dental implant area (peri-implantitis).¹⁸⁻²²

Currently, the role of pathogens and their influence on periodontal and peri-implant diseases have been well described,^{14,20,21,23,24} and it has been reported that oral dysbiotic status is necessary to trigger these pathologies.^{14,20,21,23,24} This understanding has allowed the identification and confirmation of several individual conditions such as risk factors with immunological impact.²³ By considering all these facts, it is possible to create a standard clinical protocol supported by Omics technologies such as proteomics.²³ Omics technologies have emerged as a powerful tool for investigating different molecular mechanisms between health and disease states, for discovering molecules (biomarkers)

Table 1. Research methodology on PubMed (MESH)

#1	"Dental Implants"[MeSH Terms]
#2	"Artificial Intelligence"[MeSH Terms]
#3	"Precision Medicine"[MeSH Terms]
#4	"Computational Biology"[MeSH Terms]
#5	"Biomarkers"[MeSH Terms]
Research combination	#1 AND #2; #1 AND #3; #1 AND #4; #1 AND #5
Total number of articles	241 articles

commonly used in medicine to objectively determine the state of the disease or responses to a therapeutic intervention, and for identifying the targets of new therapies.^{23,25}

The Omics methodology is key to the introduction of precision medicine into dentistry, especially in the field of oral rehabilitation, because it can adapt the procedure to follow in light of the patient's biological, social, and lifestyle characteristics.²⁶ A major goal is to reduce diagnostic mistakes, to develop results, to avoid unnecessary collateral effects, and to clarify why one individual can develop peri-implantitis and others with similar conditions did not.^{23,26}

This scoping review aimed to analyze how bioinformatics have been used to predict the success of dental implants and to determine whether studies in which Omics technology have been integrated as a clinical support tool are available.

MATERIAL AND METHODS

The methodology described in the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist²⁷ was followed, and the research protocol was registered in the Open Science Framework (OSF) under doi: <https://doi.org/10.17605/OSF.IO/XMDHR> reviewed and approved by 2 experienced research professionals (A.C., R.B.). The focal question was "how are bioinformatics being used in the field of oral implantology as a predictive tool to ensure implant success?"

A search was carried out on PubMed and on the Web of Science databases with the search strategy in Tables 1-3. In each database, the search was adapted to its characteristics by combining the Boolean operators (AND, OR) with different mesh terms (PubMed) or natural language (Web of Science). All articles used were stored in a bibliographic reference manager library (Zotero), and duplicate articles were removed.

The selection of studies was based on the selection criteria and focus question (Table 4). After excluding duplicate articles, the remaining articles were selected by reading their titles and abstracts. Lastly, the full text of all imported studies was evaluated in detail by 2 reviewers (A.C., R.B.), who individually screened the articles by considering the inclusion and exclusion criteria. Any

Table 2. Research methodology on PubMed (natural language)

(Dental Implants Survival) and (Biomarkers)	
("dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields] AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields]) AND ("biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields])	
(dental implants success) AND (biomarkers)	
("dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields] AND ("success"[All Fields] OR "successes"[All Fields] OR "successful"[All Fields]) AND ("biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields])	
(dental implants) AND (biomarkers)	
("dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields] AND ("biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields])	
(dental implants) AND (artificial intelligence)	
("dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields] AND ("artificial intelligence"[MeSH Terms] OR "artificial"[All Fields] AND "intelligence"[All Fields]) OR "artificial intelligence"[All Fields])	
(dental implants) AND (bioinformatics)	
("dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields] AND ("bioinformatic"[All Fields] OR "bioinformatically"[All Fields] OR "computational biology"[MeSH Terms] OR ("computational"[All Fields] AND "biology"[All Fields]) OR "computational biology"[All Fields] OR "bioinformatic"[All Fields] OR "bioinformatics"[All Fields])	
Total number of articles	552 articles

Table 3. Research methodology on Web of Science

(Dental Implants) and (Artificial Intelligence)	
(dental implants) AND (computational biology)	
(dental implants) AND (precision medicine)	
(dental implants) AND (biomarkers)	
(dental implants) AND (bioinformatica)	
(dental implants survival) AND (biomarkers)	
(dental implants success) AND (biomarkers)	
Total number of articles	818 articles

differences between them were discussed with a third reviewer (N.R.), who determined the final decision.

The information was gathered from the included articles by 2 independent reviewers (A.C., R.B.), who had developed a methodology to bring together data characterized by the identification of the specific bioinformatic strategy and with regard to the clinical importance and use of that model (Table 5).

RESULTS

A total of 1611 articles were identified on the PubMed and Web of Science databases, and duplicates were removed, leaving 1011 articles. After reading the title and abstract and applying the inclusion and exclusion criteria (Table 4), the total was reduced to 47 articles. After reading the full text, a further 31 were excluded for lack of focus or not answering the focus question, leaving 16 as part of this scoping review (Fig. 1). The Cohen Kappa coefficient defined an achievement level of 84% between investigators.

Figure 1 and Tables 5-7 illustrate the role played by bioinformatics, AI, and Omics as predictive tools in oral implantology during the different phases of oral rehabilitation. Figure 2 shows a word cloud diagram where all the highlighted keywords are differently sized

Table 4. Inclusion and exclusion criteria of articles

Exclusion Criteria	Inclusion Criteria
Comparative microbiological technique studies with no relevance for topic	AI strategies, deep learning, and machine learning
Precision of digital printing techniques or traditional dental implant techniques	Tree model decision tools, support vector machine, or convolutional neural network
Precision in printing 3D surgical guidelines	Studies which apply Omics sciences as predictive tool to ensure success of implant
Studies that do not address Omics strategies that contribute to prediction of implant success	
Comparative and experimental studies with different dental investments/materials/design of dental implant surface or rehabilitation components	
Evaluation procedures to assess biofilm adhesion on dental implant	
Mini orthodontic implants or maxillofacial prosthetics	
Studies using animals or nonoral tissues	

considering their frequency of use in the articles. The words displayed in the largest font were those used most frequently in the 16 articles. The most used words were artificial intelligence, deep learning, machine learning, and convolutional neural networks when combined with other words, including peri-implantitis, dental implant, and biomarkers, showing that studies using bioinformatic models to support clinical decisions in the field of oral implantology are available.

DISCUSSION

During the past 5 years, and especially after 2020, the number of publications on the use of bioinformatic

Table 5. Methodology used in oral implantology: Bioinformatic techniques versus conventional techniques

Article Identification	Bioinformatic Techniques		Conventional Techniques	
	Omics Strategies	AI Strategies	Clinical Exam	X-ray Exam
A deep learning approach for dental implant planning in cone-beam computed tomography images ³¹	–	X	X	X
A pilot study of a deep learning approach to detect marginal bone loss around implants ³²	–	X	X	X
Artificial intelligence applications in implant dentistry: A systematic review ³³	–	X	–	–
Biosensor and lab-on-a-chip biomarker identifying technologies for oral and periodontal diseases ²⁸	X	X	X	X
Deep neural networks for dental implant system classification ⁸	–	X	–	X
Diagnosing peri-implant disease using the tongue as a 24/7 detector ²⁹	X	X	X	X
Diagnostic charting of panoramic radiography using deep-learning artificial intelligence system ³⁴	–	X	X	–
The modern and digital transformation of oral health care: a mini review ³⁵	–	X	X	X
Efficacy of deep convolutional neural network algorithm for the identification and classification of dental implant systems, using panoramic and periapical radiographs ³⁶	–	X	–	X
Identification of dental implants using deep learning-pilot study ³⁷	–	X	–	X
Machine learning-assisted immune profiling stratifies peri-implantitis patients with unique microbial colonization and clinical outcomes ³⁰	X	X	X	X
Multitask deep learning model for classification of dental implant brand and treatment stage using dental panoramic radiograph images ³⁸	–	X	–	X
Osseointegration pharmacology: a systematic mapping using artificial intelligence ³⁹	–	X	–	–
Panoptic segmentation on panoramic radiographs: deep learning-based segmentation of various structures including maxillary sinus and mandibular canal ⁴⁰	–	X	–	X
Peri-implant bone loss measurement using a region-based convolutional neural network on dental periapical radiographs ⁴¹	–	X	X	X
Machine learning for identification of dental implant systems based on shape – A descriptive study ⁷	–	X	–	–

In addition to conventional techniques used in clinical practice (clinical and radiographic examination), studies in *gray* represent combination of AI tools and Omics.

models to assess implant-supported prostheses has increased. All the studies selected used AI algorithms to help clinicians in planning, diagnosis, and follow-up.

Three articles^{28–30} discussed bioinformatic models that integrated AI algorithms into established identification and quantification protocols, which are often used in Omics sciences. A total of 13 articles^{7,8,31–41} underlined the development of different AI algorithms, for example, machine learning, deep learning, and convolutional neural network to support clinical decision and raising precision and accuracy levels of the rehabilitation process. Of these, 6 studies^{8,33,34,36–38} developed AI models for implant type recognition. Most of the articles identified used AI algorithms as a clinical support tool, as opposed to the articles which applied bioinformatic strategies by combining knowledge from AI algorithms with Omics expertise. These findings were expected since the application of strategies based on AI in the field of oral rehabilitation and the importance given to Omics sciences as a complement to a precision diagnosis are very recent.

Comparisons of efficacy were difficult among the different AI models used because of the data input or methods used in the studies reviewed. While each study attempted to standardize the collection of the radiographical images, differences among the studies were identified, including exposure (speed and contrast) and type of radiographic images (2-dimensional [2D] or 3-dimensional [3D]). Furthermore, variations on the radiographic information differed among the reviewed

studies where only the implant (with a cover screw or a healing abutment) was visible on the radiograph or the radiograph also showed the prosthetic component. A comparison of studies that used bioinformatics strategies was also difficult since the methodology was completely different among the 3 included studies.

Most articles used 2D images for implant identification; clinicians generally use these to monitor the condition of a dental implant.^{8,34,36–38} However, studies that used 3D images were also included. The inclusion of cone beam computed tomography (CBCT) images might aid in the development of AI for the recognition of dental implant types.³³

Three recently published studies^{28–30} in which some bioinformatic approaches were considered were identified. The main goal of these studies was to support the clinical decision in terms of the diagnosis and staging of peri-implant diseases.

Ritzer et al²⁹ described a diagnosis mechanism for periodontal disease that could be performed by “anyone, anywhere, anytime.” This model was characterized by embedding sensors in chewing gum that contained peptide bioresponsive sensors consisting of a protease cleavable linker between a bitter substance and a microparticle. Matrix metalloproteinases in the oral cavity, as upregulated in peri-implant disease, specifically targeted the protease cleavable linker while chewing the gum, thereby generating bitterness for detection by the tongue. This line of research had many advantages: it provided a rapid and accurate diagnosis in that the

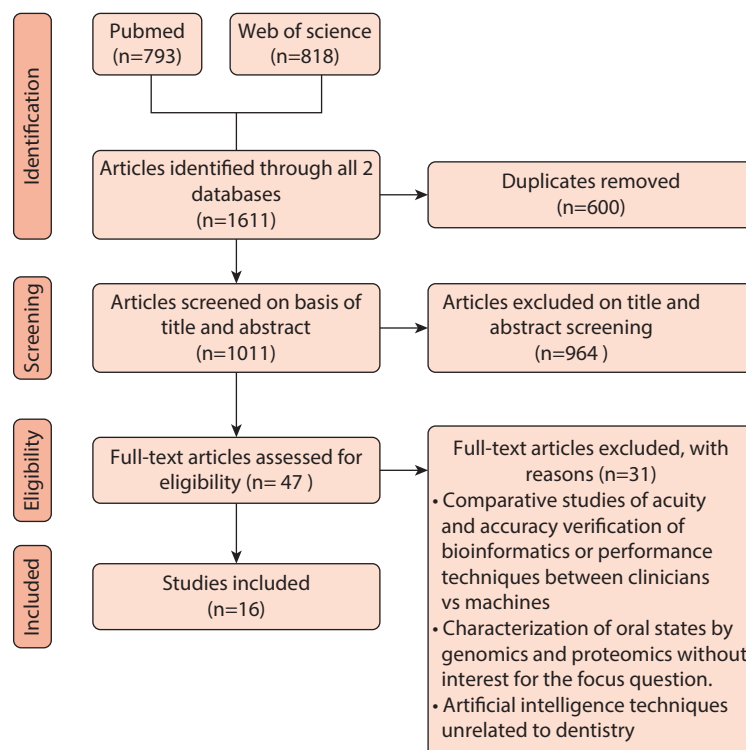


Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) flow diagram for scoping review process.²¹

Table 6. Description of proposed methodology in studies which combined both bioinformatic techniques: artificial intelligence (AI) and Omics

Article	Pub. year	Proposed Methodology	Clinical Improve
Diagnosing peri-implant disease using the tongue as a 24/7 detector ²⁹	2017	<ul style="list-style-type: none"> Developed diagnostic chewing gums "Anyone, anywhere, anytime" diagnostics. Sensors responded to proteins upregulated in peri-implant disease (MMP). 	<ul style="list-style-type: none"> Providing rapid read-out within few minutes. Saliva diagnostic. Accurate diagnosis, even before clinical evidence of disease.
Biosensor and Lab-on-a-chip Biomarker identifying Technologies for Oral and Periodontal Diseases ²⁸	2020	<ul style="list-style-type: none"> Oral biomarkers identification Patient stratification Bioinformatic analysis using artificial intelligence Use of biosensors to oral disease identification and risk assessment. 	<ul style="list-style-type: none"> Data processed in biosensor and AI algorithms applied to establish personal physiological thresholds and out of personal norm trends. Wirelessly transferred output data supports clinical decisions during in-office or tele-dentistry appointments.
Machine learning-assisted immune profiling stratifies peri-implantitis patients with unique microbial colonization and clinical outcomes ³⁰	2021	<ul style="list-style-type: none"> Clinical, immunological, and microbiological characterization of patients diagnosed with peri-implantitis undergoing regenerative therapy. Used artificial intelligence algorithm - machine learning. 	<ul style="list-style-type: none"> Relation of immune and microbiological profile for prognosis of peri-implant states and potential risk analysis tool.

sensor featured a diagnosis from saliva, which removed the need to collect sulcus fluid in sites accessible only to a professional; expert knowledge in interpretation was not required; and the diagnosis could be used anywhere, in the clinic or at home. Therefore, the data provided demonstrated that the complex kits used at present may be complemented or even replaced by more straightforward and reliable chewing gum diagnosis.^{24,29}

Also in 2020,²⁸ a model was created using advances in light-emitting diode (LED) biotechnology which enabled biosensors and microelectromechanical systems (MEMS) suitable for the oral cavity to identify and quantify molecules such as cortisol, proteins, and bacteria, permitting the uninterrupted monitoring of those molecules in human saliva. Knowledge from such testing gives clinicians the opportunity to prevent patients from developing

Table 7. Description of proposed methodology in studies which only used artificial intelligence tools

Article	Pub. year	Proposed Methodology	Clinical Interest/Clinical Improve
A deep learning approach for dental implant planning in cone-beam computed tomography images ³¹	2021	<ul style="list-style-type: none"> Measurement of bone thickness and height in different areas of oral cavity in CBCT images by AI and by clinician 	<ul style="list-style-type: none"> AI results consistent with clinician's measurement in PM/M maxillary and PM mandibular areas
A pilot study of a deep learning approach to detect marginal bone loss around implants ³²	2022	<ul style="list-style-type: none"> Convolutional neural networks prepared by training and validating data set by experienced dentists Creation of AI algorithm 	<ul style="list-style-type: none"> CNN detect peri-implant loss bone by using periapical radiographs.
Artificial intelligence applications in implant dentistry: A systematic review ³³	2021	<p>By using AI algorithms:</p> <ul style="list-style-type: none"> Recognition of dental implant systems Prediction of dental implant success based on risk factors Optimization of dental implant design 	<p>—</p> <ul style="list-style-type: none"> AI models recognize implant system Models to predict osseointegration success/implant success by using different input data AI models to improve design of dental implants
Deep neural networks for dental implant system classification ⁸	2020	<ul style="list-style-type: none"> Recognition of implant system by using CNN 	<ul style="list-style-type: none"> Recognition of 11 different implant systems, despite their implant-treatment stage
Diagnostic charting of panoramic radiography using deep-learning artificial intelligence system ³⁴	2021	<ul style="list-style-type: none"> Recognition of 10 dental states in panoramic radiograph, including dental implants 	<ul style="list-style-type: none"> Allows identification of oral states with no clinician intervention
Efficacy of deep convolutional neural network algorithm for the identification and classification of dental implant systems, using panoramic and periapical radiographs ³⁶	2020	<ul style="list-style-type: none"> Identification and classification of dental implants by deep learning algorithms 	<ul style="list-style-type: none"> Deep CNN architecture useful for identification and classification of dental implant systems using panoramic and periapical radiographs
Identification of dental implants using a deep learning-pilot study ³⁷	2020	<ul style="list-style-type: none"> Identification of dental implant systems using deep learning method 	<ul style="list-style-type: none"> Implants identified from panoramic radiographs
Multi-task deep learning model for classification of dental implant brand and treatment stage using dental panoramic radiograph images ³⁸	2021	<ul style="list-style-type: none"> Multitask deep learning use to investigate classifier that categorizes implant brands and treatment stages from dental panoramic radiographs (implant, implant + abutment and implant + crown) 	<ul style="list-style-type: none"> Classification of implant brands and treatment stages by using CNNs
Osseointegration pharmacology: a systematic mapping using artificial intelligence ³⁹	2021	<ul style="list-style-type: none"> Development of machine learning algorithm to automatically map literature assessing effect of medication on osseointegration 	<ul style="list-style-type: none"> Identification of effects during diagnosis of dental implants by medication that affect homeostasis, inflammation, cell proliferation, and bone remodeling
Panoptic segmentation on panoramic radiographs: deep learning-based segmentation of various structures including maxillary sinus and mandibular canal ⁴⁰	2021	<ul style="list-style-type: none"> State-of-the-art deep neural network model designed for panoptic segmentation trained to segment maxillary sinus, maxilla, mandible, mandibular canal, normal teeth, treated teeth, and dental implants on panoramic radiographs 	<ul style="list-style-type: none"> Automatic machine learning method might assist dental practitioners to treatment plan and diagnose oral and maxillofacial diseases
Peri-implant bone loss measurement using a region-based convolutional neural network on dental periapical radiographs ⁴¹	2021	<ul style="list-style-type: none"> Deep CNN detect marginal bone level, top, and apex of implants on dental periapical radiographs 	<ul style="list-style-type: none"> CNN model can be used to measure radiographic peri-implant bone loss ratio to assess severity of peri-implantitis
The modern and digital transformation of oral health care: a mini review ³⁵	2021	<ul style="list-style-type: none"> Analyses of progress, limitations, challenges, and conceptual theoretical modern approaches in oral health prevention and care, particularly in ensuring quality, efficiency, and strategic dental care in modern era of dentistry 	<ul style="list-style-type: none"> Digital oral scanner Digital oral health records Application of AR/VR and AI Dynamic navigation system (DNS) Static guided systems Additive manufacturing Tele-dentistry with remote consultation
Machine learning for identification of dental implant systems based on shape – A descriptive study ⁷	2021	<ul style="list-style-type: none"> Identification of dental implants in panoramic radiographs by using machine learning algorithms 	<ul style="list-style-type: none"> Machine learning models tested in study proficient enough to identify dental implant systems

AI, artificial intelligence; AR, augmented reality; CBCT, cone beam computed tomography; CNN, convolutional neural networks; MMP, matrix metalloproteinases; M, molar; PM, premolar; VR, virtual reality.

different pathological conditions and enables early identification of mucositis or peri-implantitis. It also allows clinicians to control the different stages of a pre-diagnosed pathology, preventing progression.²⁸

Recently, in addition to the importance given to the accuracy of the diagnosis achieved by using the strategies Ritzer et al²⁹ and Steigman et al,²⁸ emphasis has also been given to the stratification of patients in determining the risk profile of patients and creating a consistent risk

system. Wang et al³⁰ used a robust outlier-resistant machine learning algorithm for immune deconvolution and concluded that the peri-implant immune microenvironment shaped the microbial composition and the regeneration course. Immune signatures have shown the untapped potential in improving the risk-grading for peri-implantitis, as well as the influence of medication during osseointegration. Many patients seeking implant-supported restorations are elderly, polymedicated, or with

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