Advances in Neoteric Modular Tissue Engineering Strategies in Regenerative Dentistry, Systematic Review

Dra. Nathalie Steffy Ponce Reyes Esp[1], Dra. Myrian Margarita Grijalva Palacios Esp[2], Dr.Carlos Mauricio Saeteros Cárdenas Esp[3], Dra. Adriana Katherine Quezada Quiñonez Esp[4]

[1]Docente de la Carrera de Odontología. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra – Ecuador.
Email: ui.nathaliepr73@uniandes.edu.ec
https://orcid.org/0000-0002-1396-1236

[2]Docente de la Carrera de Odontología. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra – Ecuador
Email: ui.miryangp00@uniandes.edu.ec
https://orcid.org/0000-0002-6808-279X

[3]Docente de la Carrera de Odontología. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra – Ecuador
Email: ui.carlossc49@uniandes.edu.ec
https://orcid.org/0000-0001-8209-9814

[4]Docente de la Carrera de Odontología. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra – Ecuador
Email: ui.adrianaqq34@uniandes.edu.ec,
https://orcid.org/0000-0002-1639-3967

Abstract

This research aimed to describe the applications of modular tissue engineering advances in regenerative dentistry and marks a change in the paradigm of endodontic and periodontal therapy from simple pulp capping and root planing to reconstruction of dental tissue. Documentary research was used, data were collected through a descriptive registry and analyzed with the content analysis technique. The bibliometric analysis was performed by searching in three academic databases, which were Scopus, Pubmed and Web of Science. The corpus of the present study consisted of 20 articles (2018- 2022), 9 researches analyzed cell sheets of apical origin for endodontic regeneration, 8 studies included periodontal ligament-derived stem cells for periodontal renewal and 3 studies evaluated cellular spheroids acting on angio/vasculogenesis and resilience. This review compiles strategies for endodontic and periodontal regeneration, emphasizing the commercialization of some cell membrane-based systems. In addition, the synergy between the endo-perio continuum in delayed oral healing and the 3D Bio-fabrication strategy of scaffold-free systems.

Keywords: Regenerative dentistry, dental pulp, periodontium, cellular laminates, 3D Bio-fabrication.

1. Introduction

Oral diseases are one of the main effects on health, imposing serious and prolonged sequelae. The global burden of disease in 2015 estimated that the various oral infections in individuals are permanent dentition caries the most prevalent, contributing to almost half of the global infection rate (1). Nazir et al. (2) note that, dental pulp abscesses, irreversible pulpitis, asymptomatic and advanced apical periodontitis are not detected in about 45-50% of individuals in a population (biotechnological advances in regenerative medicine have transformed translational dentistry to emphasize long-term and prognosis through various scientific findings in biomimetic materials, As are the new postnatal stem cells, postnatal approaches, they are efficient in engineering tissues with scaffolds seeded with growth factors, intracellular signaling mimetics in transcription factors, etc. ; this according to Peres et al. (3).

As indicated by Choudhury et al. (4), forefficient tissue recovery, repair of hard tissue-based dental structures can be challenging, as enamel is incompetent to regenerate and dentin with cementum is partially restricted as self-regenerators. Prolonged pulp infection ends up causing secondary caries, due to the limited blood supply to the pulp tissue of the dentin, thus hindering the repair of the dentin. Due to l

; The unique anatomical boundaries of the tooth, and

doi.org/10.31838/hiv23.03.253 Received: 13.11.22, Revised: 15.12.22, Accepted: 24.01.23.

the deficiencies of partial pulpectomy and endodontic procedures, engineering is a suitable microenvironment that mediates angio/vasculogenesis and innervation is the key requirement. Clinical attempts to regenerate pulp have made sense with the advent of modern tissue engineering systems that explore dental stem cells.

In recent years, the size of the global cell therapy-based market increased exponentially to reach $7.8 billion by 2020, with a compound annual growth rate of 15%, representing regenerative dontology as the fastest and most practical discipline, as noted by Pragya et al. (5). Stem cells derived from dental pulp, gingival periodontal ligament, periapical cysts and other oral tissues with significant therapeutic and differentiation potential, the ability to repair and balance local inflammation holds great promise for regenerative dentistry. The intrinsic matrix and cytokine secretion potential can form constructions analogous to a larger, more unique tissue with analogous constructs, devoid of biomaterials such as "scaffold-free strategies". Despite showing tissue-specific mechanisms, cell-based approaches may experience poor cell localization and retention and low wound site survival rates after transplantation. Several studies have revealed that inoculum survival rates of injected cells are poor at the injection site after transplantation; as described by Hasani-Sadrabadi et al. (6).

To overcome these obstacles, Cunniffe et al. (7) detail that scaffolds combined with stem cells, give signals, and incorporate mechanically stable biodegradable polymers to produce functional analogues of three-dimensional (3D) tissues. 3D scaffolds prevent cell damage from external factors and facilitate a friendly cellular microenvironment for the release of tissue-forming growth factors. Several scaffolds such as hydrogels, sponges, fibers, films, emulsions, etc., have been developed with demonstration of safety, preclinical efficacy and means of cell delivery, but only a few are federally approved specifically for regenerative dentistry. The restricted scientific ambiguity, the costs associated with scalability and the technology of the "laboratory table to the dental chair" require a significantly competent alternative and a reproducible clinical result, which complies with current regulatory frameworks strategies ranging from the arrival of bone to biomimetic scaffolds, custom electrospun matrices to more precise systems, new generation and multifunctional; detailed information by Schüttler et al. (8).

This study aims to analyze, collect, and discuss endodontic and periodontal regeneration (dental pulp and periodontal tissue) using modular tissue engineering scaffolds, such as cell sheets, spheroids, exosomes, and hypoxia emphasizing their clinical application from the laboratory to the dental chair and its commercialization. In addition, the synergy between the continuous endo-perio of delayed oral healing and the consideration of cells as biotubes for the three-dimensional (3D) biofabrication strategy of these systems without scaffolding, their advantages, challenges and perspective have been highlighted today, for which we resort to the systematic review with the different techniques of data collection with content analysis, documentary and bibliometric.

2. Ddevelopment

Materials and Methods

The methodology used was the qualitative modality with the case study (method that allows deepening the approach of the research object), the data collection technique was the documentary analysis and the descriptive bibliometric analysis in the three academic databases that were: Scopus, Pubmed, Web of Science, the data analysis technique used was the content analysis. Search terms were performed using descriptors such as data collection, content analysis, qualitative research. The selection was established from specific criteria, the established year of study was 5 years (2018-2022). The instruments used were descriptive records and content matrices thatallowed the development of the following indicators: articles related to the advances of modular tissue engineering in regenerative dentistry, the type of research, technique and tool for data collection, method of data collection, year of publication were established. The documentary corpus was integrated into 557 articles, based on publications related to the period 2018 to 2022.

Table 1. Search strategy in Pubmed, number of articles found: 198
Search terms in PubMed NCBI. Year 2018 – 2022
Periodontium-supported, Alveolar bone loss.
2. Dentistry, Tissue, Regenerative, pulp.
Periodontium, Regenerative Dentistry, Osseointegration.

Table 2. Search strategy in Scopus, number of articles found: 209
Search terms in Scopus. Year 2018 – 2022
1. Regenerative, Scaffold-free strategies.
2. Endodontic and periodontic regeneration, Scaffold-free tissue, cell sheets.
3. Regeneration of hard tissues, stem cells.

Table 3. Web of Science search strategy, number of articles found: 150
Web of Science search terms. Year 2018 – 2022
1. Three-dimensional (3D) tissue, biomaterials and regenerative engineering.
2. Dentistry, Education, Dental, teeth.
3.Periodontal ligament regeneration, cell sheets, angiogenesis, vasculogenesis.

3. Rresults

The following figure details the results obtained once 557 research articles carried out in different countries and databases have been selected and analyzed, in which they were published in the period 2018-2022.

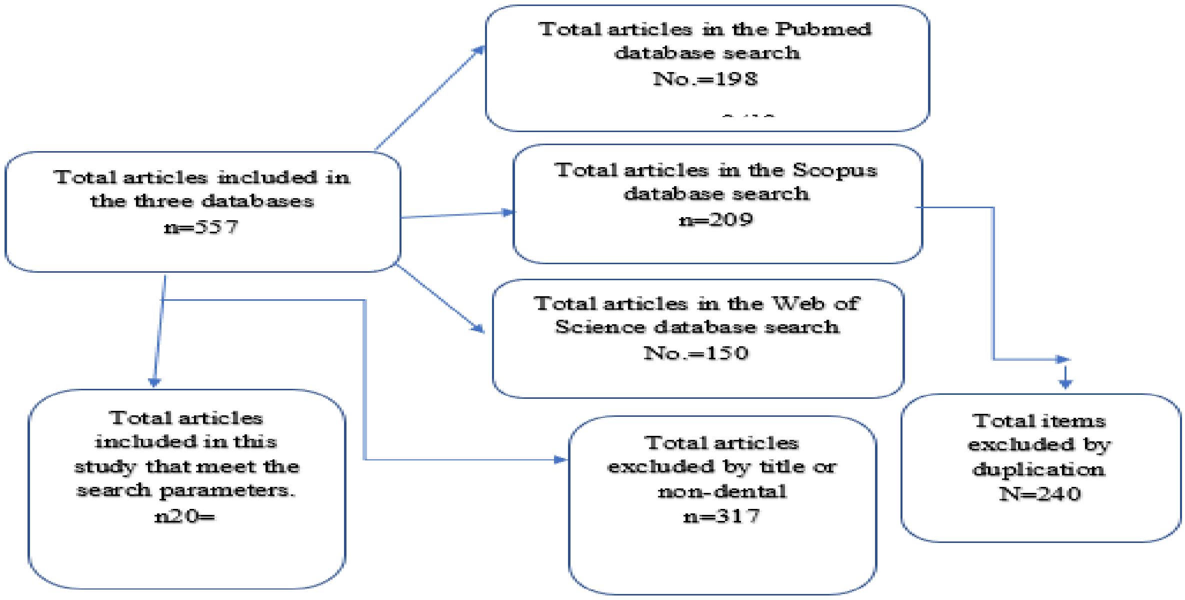

Figure 1. Outline of the search process and results.

As can be seen in Figure 1, what is characterized are the techniques of data collection and analysis, in which predominates in the present study with the search of the three combined databases resulted in 557 articles, of which exclusion criteria were obtained because 240 articles were duplicates. During the search for the header (Neoteric Modular Tissue Engineering in Regenerative Dentistry), another 317 articles were excluded because they did not meet inclusion criteria for this review and covered other different branches such as medicine in its advances of regenerative strategy in the different organs and systems. A total of 20 articles were included in this systematic review for qualitative synthesisa.

Table 1. Distribution of articles found related to advances in neoteric modular tissue engineering in regenerative dentistry.

Number of Articles	Cell sheets (3D) Pulp regeneration (apical)	Cell sheets (3D) Periodontal Regeneration (LP)	Esferoides Cell phones (3D) Periodontal/Endodontic Regeneration	References Bibliographical (2018–2022)
9	X			(Meng, et al. 2020) (Bernabe, et al. 2020) (Peres, et al. 2019) (Purwar, et al. 2021) (Hasani-Sadrabadi, et al. 2020) (Cunniffe, et al. 2019) (De Pieri,et al. 2021 (Liang, et al. 2021) (Dissanayaka et al. 2020)
8		X		(Nazir, et al.2020) (Nikolova, et al.2019) (Baranova, et al.2020) (Yu,et al. 2020) (Raju, et al.2020) (Yelick,et al.2019) (Schüttler, et al. 2020) (Makeeva, et al.2020)
3			X	(G.K. Choudhury, et al. 2021) (Wu, et al. 2021) (Fujii, et al. 2018)

As can be seen in Table 1, which characterizes the technique of collection and analysis of the contents, the result obtained from this research was 20 articles in the corpus, bibliometric analysis and documentary analysis of articles with inclusion criteria both as publication period and title referring to advances in modular tissue engineering in regenerative dentistry, with the distribution of the results as follows: 9 articles that emphasize the cellular sheets obtained at the apical level of human origin for endodontic renewal with a prefabrication of 3D blocks. The stem cells collected in a sample belong to the periodontal ligament and act in the regeneration of the periodontium, 8 articles with research and inclusion criteria and 3 articles that make their study specifically in the cell spheroids with a 3D block execution without scaffolding, for endodontic and periodontal regeneration were included.

4. Discusión

This research aimed to study the systematic review with the different data collection techniques, with content, documentary and bibliometric analysis to develop a general and specific knowledge of the different strategies in the advances of neoteric modular tissue engineering in regenerative dentistry, addressing at the level of approaches without scaffolding which combine different cells to form the complex architecture of tissues. by assembling heterogeneous molecular 3D building blocks these determine various strategies without cell scaffolding evaluated in vitro and in vivo for pulp and periodontal regeneration. The development of teeth begins with embryogenesis and reaches maturation through a series of cellular and tissue processes. The constant epithelial-mesenchymal interrelationship, governed by the signaling of morphogenetic regulators, facilitates tissue and contributes to tooth morphology. The periodontal ligament is an intricate accessory tissue that hides odontogenic stem cells and connects the tooth and alveolar bone (11).

Baranova et al. (12) detail thattherapies for tooth recovery face an important enigma, despite technological advances and existing research. Several methods for its regeneration have been conceptualized, but they are in an incipient experimental phase. The mineralized acellular enamel with high mechanical strength, flexibility fracture resistance and compatibility with tissues, composed of elongated and parallel hydroxyapatite prisms is extremely complex to regenerate anatomically. Although a mucosal barrier imparts a strong immune defense to the tooth, its susceptibility at the microbial and pathological level is the formation of dental caries. Prolonged cariogenic infection can affect the root canal, pulp-dentinal tissue and eventually maxillary bone, altering the physiological function of dentin. In periodontal disease, oral pathogens and a dysregulated immune inflammatory response can cause deterioration of periodontal gingival tissue, cementum, and alveolar bone. It can produce ankylosis, dentinogenesis imperfecta, dental agenesis can negatively influence odontogenesis, tooth eruption and calcification.

Variation of the morphological structures of the crown occlusal surface and tooth root in different types of teeth is a concern when designing a tooth. To maintain a vital tooth requires innervation for its survival. The tooth has continuous structures associated with the pulp and the periodontal ligament. Removing the tooth from the socketcan cause dryness and disrupt cellular, blood vessel and nerve-bone continuity and lose nerve continuity, thus damaging the pulp and periodontal ligament permanently. The degree of regeneration of the periodontal ligament depends on the time of reimplantation of the tooth in the alveolus; this according to Meng et al. (18).

While immediate reimplantation in the alveolus can allow partial recovery of the periodontal ligament, a delay can affect viability and cause several problems such as ankylosis after reimplantation, after resorption of the tooth root at the level of the bone. The dental pulp is innervated by sympathetic nerve axons protruding from the apical foramen into the root pulp with an intricate network of nerves and blood vessels acting on the constriction of vessels inside the pulp. An unusual gap in the apical foramen affects the resilience of the blood/nerve supply leading to necrosis. In addition, tooth extraction can also cut off the supply of pulp tissues (20). The number of publications that use cell sheets or 3D stem cells of the pulp at the level of the human dental apex, for endodontic regeneration is investigated from 2018 to 2022, which in the present study had the inclusion criteria of 9 articles.

The cell sheet paradigm is beneficial in endodontic and periodontal applications. Recently, implantable devices based on human cells have proven effective in terms of safety and accessibility to a diverse range of clinical outcomes, such as the use of stem cells from human dental pulp to cure bone defects experimentally in mice. Stem cells grown with an osteogenic derivative of helioxanthine in plates at an appropriate temperature showed that cell differentiation induced compared to control plates after 8 weeks. Stem cells derived from the apical portion were used to develop 3D cell sheets for the renewal of the dental-pulp/dentin complex, dental/dentin complex renewal that showed high secretion and odontogenic potential as evidenced by alkaline phosphatase, bone sialoproteins and rRNA expression levels of the Runt-related gene (RUNX2). After in vivo transplantation, granules combined with dentin matrix fragments showed vascular tissue formation; this was described by Yu et al. (13).

Cell sheets, according to Raju et al. (19) requiresubstantial repair of periodontal tissue at the destination transplant. Cell sheets derived from human periodontal ligament tissue grown in heat-resistant plates with a medium replaced by autologous serum showed greater cell adhesion, increase in radiographic bone height, and decreased periodontal probing depth in affected patients after transplantation. Complex 3D multicellular cell sheets were fabricated from layers of cells originating from the periodontal ligament and osteoblast-like cells to form bone-ligamentous tissue structures in ectopic tissues.

The present study includes publications using cellular laminae derived from human periodontal ligament tissue for applications in regenerative dentistry. Thereare a total of 8 articles in this research. Scaffold-free tissue engineering approaches generate cohesive 3D multicell-based functional constructions using prefabricated building blocks, and intercede cell cell/matrix communication to mimic the tissue microenvironment through self-assembly.

As initial cell density is considerably low in systems without scaffolding, cell proliferation and migration are not limiting factors, while tissue formation is achieved in a short timeframe. Tissue regeneration using scaffold-free approaches allows direct cellular interaction without any exogenous intrusion, thus creating the necessary and effective microenvironment. The engineering of tissues with cellular sheets, in addition to possessing an enormous medicinal and healing potential, cells have superior tissue-specific biochemical characteristics and mechanical characteristics. A variety of therapeutically competent cells such as mesenchymal stem cells, adult cells, and induced pluripotent stem cells, explored for preclinical and clinical cell transplantation, cell transplantation has shown promising results (15).

Liang et al. (11) state that the success of cell transplantation depends on cell efficacy, a good survival rate and appreciable cellular integration with little or no adverse effect on the host. Transplantation techniques so far, whether they use intravenous/intra-arterial infusion or direct injection into tissue, have limitations. The development and regeneration of oral tissues through biocellular processes have led to the emergence of new regenerative approaches based on hypoxic response, such as preconditioning and pharmacological hypoxic stimulation. The success of these techniques has opened avenues for cellular oxygen sensors to help cells subsist and balance tissues, as noted by De Pier et al. (9). Clinical research on hypoxia-based healing responses to regenerative dentistry has been very prevalent over the past decade.

Dissanayaka et al. (16), state that cell spheroids are possibly the most widely used building blocks in tissue engineering without scaffolding due to their high accessibility and ease of handling, spontaneous self-assembly and cell aggregation. Manufactured by means of droplet culture, granule and rotation culture, liquid superposition, magnetic levitation microfluidics, centrifugation, non-adhesive cell surfaces, etc. The gradient diffusion of the cell growth medium determines the size of the spheroids in cultures. Spheroids show prominent angio/vasculogenesis and regenerative capacity, which is credited to cells and resemble the biological configuration of 3D tissue structure. In this research, cell spheroids are emphasized the most used in modular tissue regeneration, and which is projected in the future the use with automated robotic systems to improve cell renewal capacity including 3 articles in current research.

Exosomes are extracellular vesicles attached to the membrane and enclosed within the phospholipid layer of the endosomal lumen of cells comprising DNA, RNA and proteins. Vitally, exosomes regulate paracrine functions that show the cell/cell-ECM interaction that affects the functionality of the recipient cell. In oral and dental tissues, exosomes act as a odont/osteogenic differentiation and influence innate and acquired immune responses (16).

Stem cell-derived exosomes can activate several endogenous repair pathways to maintain homeostatic balance, immunomodulation within recipient cells, and initiate tissue repair. The latest inclusion of building blocks without scaffolding is weaving. The cells acclimatize to self-aggregate and form mini-blocks of tissue without scaffolding that accumulate into multiple cell constructs for the formation of complex tissues and organs. Weaving yarns have so far been the most promising candidate for the rapid manufacture of biomimetic constructed fabrics. Large-scale imitable tissue strands derived solely from tissues or organs and grown in a liquid or near-solid medium to form tissue patches have been used for tissue engineering and as tissue models for drug design; Fujii et al. (17).

Recent advances in neoteric modular tissue engineering strategies have shown great promise for regenerative dentistry. Researchers have been exploring new methods to engineer dental tissues by using modular approaches that can help repair damaged or lost teeth. Several studies have been conducted to evaluate the level of knowledge of dental students on various aspects of dentistry, such as oral cancer, use of antibiotics, dental emergencies, halitosis, and diagnosis of dental caries(21,22,23). These studies have used neutrosophic sets and systems, linguistic neutrosophic scales, and image segmentation techniques, among others, to assess the students' knowledge and skills(24, 25, 26). Additionally, some studies have investigated the application of artificial intelligence and intellectual property in dentistry. Overall, these studies highlight the importance of continuous education and training of dental professionals to keep up with the latest advances and provide the best care to their patients (27).

5. Conclusions

Modular tissue engineering has emerged as a promising manufacturing strategy for multifaceted cohesive tissue regeneration. Scaffold-free approaches combine different cells to form the complex architecture of tissues by assembling heterogeneous molecular building blocks these determine various strategies without cell scaffolding evaluated in vitro and in vivo for pulp and periodontal regeneration, however, the consequence of such regeneration depends on several aspects, such as the durability of implantation cells, the level of inflammation of the place and the appropriate stimuli in the surrounding microenvironment. Lack of oxygen and nutrients at the implantation site can compromise the survival of stem cells in vivo, and an inflammatory microenvironment around the infectious pulp/periodontium can reduce stem cell proliferation and renewal.

Non-scaffolding approaches such as those based on complementary scaffolds at variable points stabilize the pulp/periodontium, pulp/periodontal inflammation, and its regeneration along with enamel maturation. Although there have been substantial advances in tissues, its scope of commercialization has not yet been reached and it is not yet used in clinical practice.

Given the volatility of the long-term efficacy and safety of regenerative dentistry, financial models are needed to help facilitate patient access to these therapies. The impediments that arise are also during the manufacture of cellular products and approved regulatory establishments.

References

(1) Bernabe E, Marcenes W, Hernandez C, Bailey J, Abreu L, Alipour V. Global, regional, and national levels and trends in burden of oral conditions from 1990 to 2017: a systematic analysis for the global burden of disease study, J. Dent. Res. 2020. 362-373.

(2) Nazir M, Al-Ansari A, Al-Khalifa K, Alhareky M, Gaffar B, Almas K. Global prevalence of periodontal disease and lack of its surveillance, Sci. World J. 2020.

(3) Peres M, Macpherson L, Weyant R, Daly B, Venturelli R, Mathur M, Listl S, Celeste R, Guarnizo-Herre~no C, Kearns C, Benzian H, Allison P, Watt R. Oral diseases: a global public health challenge, Lancet 394. 2019. 249-260.

(4) Choudhury G, Panda S, Garahnayak M. Possible pathways of disease communication of the endo-perio lesions and their management. 2021. https://doi.org/10.37506/ijfmt.v14i4.13010.

(5) Pragya A. Effect of Different Root Canal Filling Materials in Endo-Perio Lesions: Design and Computational Analysis. 2021. 485-494.

(6) Hasani-Sadrabadi M, Sarrion P, Pouraghaei S, Chau Y, Ansari S, Li S, Aghaloo T, Moshaverinia A. An engineered cell-laden adhesive hidrogel promotes craniofacial bone tissue regeneration in rats, Sci. Transl. Med. 2020. 12.

(7) Cunniffe G, Díaz-Payno P, Sheehy E, Critchley S, Almeida H, Pitacco P, Carroll S, Mahon O, Dunne A, Levingstone T, Moran C, Brady R, O'Brien F, Brama P, Kelly D. Tissue-specific extracellular matrix scaffolds for the regeneration of spatially complex musculoskeletal tissues, Biomaterials. 2019. 188: 63 -73.

(8) Schu̇ttler K, Bauhofer M, Ketter V, Giese K, Eschbach D, Yenigu̇n M, Fuchs-Winkelmann S, Paletta J. Direct incorporation of mesenchymal stem cells into a Nanofiber scaffold-in vitro and in vivo analysis, Sci. Rep. 2020. 10.

(9) De Pieri A, Rochev Y, Zeugolis D. Scaffold-free cell-based tissue engineering therapies: advances, shortfalls and forecast, Npj Regen. Med. 2021. 6.

(10) Nikolova M, Chavali M. Recent advances in biomaterials for 3D scaffolds: a review, Bioact. Mater. 2019. 4. 271-292.

(11) Liang C, Liao L, W. Tian, Stem cell-based dental pulp regeneration: insights from signaling pathways, Stem Cell Rev. Rep. 17 (2021) 1251-1263.

(12) Baranova J, Bu̇chner D, G€otz W, Schulze M, Tobiasch E. Tooth formation: are the hardest tissues of human body hard to regenerate? Int. J. Mol. Sci. 2020. 21.

(13) Yu T, Klein O. Molecular and cellular mechanisms of tooth development, homeostasis and repair, Development 147. 2020.

(14) Makeeva M, Daurova F, Byakova S, Turkina A. Treatment of an endo-perio lesion with ozone gas in a patient with aggressive periodontitis: a clinical case report and literature review, Clin. Cosmet. Invest. Dent. 2020. 12. 447-464.

(15) Yelick P, Sharpe P. Tooth bioengineering and regenerative dentistry. J. Dent. Res. 2019. 1173-1182.

(16) Dissanayaka W, Zhang C. Scaffold-based and scaffold-free strategies in dental pulp Regeneration, J. Endod. 46 (2020) S81eS89.

(17) Fujii Y, Kawase-Koga Y, Hojo H, Yano F, Sato M, Il Chung U, Ohba S, Chikazu D. Bone regeneration by human dental pulp stem cells using a helioxanthin derivative and cell-sheet technology, Stem Cell Res. Ther. 2018. 1-12.

(18) Meng H, Hu K, Zhou Y, Ge Z, Wang H, Wu C, Jin J. A sandwich structure of human dental pulp stem cell sheet, treated dentin matrix, and matrigel for tooth root regeneration, Stem Cell. Dev. 2020. 29. 521-532.

(19) Raju R, Oshima M, Inoue M, Morita T, Huijiao Y, Waskitho A, Baba O, Inoue M, Matsuka Y. Three-dimensional periodontal tissue regeneration using a bone-ligament complex cell sheet, Sci. Rep. 2020. 10.

(20) Wu M, Liu X, Li Z, Huang X, Guo H, Guo X, Yang X, Li B, Xuan K, Jin Y. SHED aggregate exosomes shuttled miR-26a promote angiogenesis in Pulp regeneration via TGF-b/SMAD2/3 signaling, Cell Prolif. 2021. 1-20.

(21)Veliz Gutiérrez ON, Gutiérrez Ponce M, González Benítez N, Lozada López FR, Villacreses Medina ME, Villacis Lascano EC. Measure of Knowledge in Students at Uniandes, Ecuador, on the Manifestations of Oral Cancer. Neutrosophic Sets and Systems. 2020;37:151-159. doi: 10.5281/zenodo.4122086

(22) Morales Cobos JD, Guallpa Paguay AM, Troya Roa SB. Escala lingüística neutrosófica para la valoración del conocimiento sobre uso de antibiótico de mayor frecuencia en infecciones odontológicas. Neutrosophic Computing and Machine Learning.

2023;26:40-47. doi: 10.5281/zenodo.7604146
(23) Ricardo JE, Vázquez MYL, Palacios AJP, Ojeda YEA. Inteligencia artificial y propiedad intelectual. Universidad y Sociedad. 2021;13(S3):362-368.
(24) Ricardo JE, Vázquez ML, Fernández AR. Assessment of project-based learning. Investigacion Operacional. 2022;43(3):409-419.
(25) Romero Fernández A, Labrada González E, Loyola Carrasco D. Study on the Level of Knowledge in Dental Medical Emergencies of Dentistry Students through Neutrosophic Values. Neutrosophic Sets and Systems. 2020;37:99-107. doi: 10.5281/zenodo.4122035
(26) Morales Cobos JD, Enríquez Suarez SM. Estudio neutrosófico sobre el conocimiento de los tratamientos para el control de la halitosis en la odontología. Neutrosophic Computing and Machine Learning. 2023;26:48-56. doi: 10.5281/zenodo.7604149
(27) Cevallos-Torres LJ, Contreras-Puco SF, Ortiz-Zambrano MC, Torres-Martínez DE. Image Segmentation Techniques Application for the Diagnosis of Dental Caries. In: Advances in Emerging Trends and Technologies: Volume 1. 2019;1066:312.

Author's details

1.Dr. Nathalie Steffy Ponce Reyes Esp.
ui.nathaliepr73@uniandes.edu.ec, Professor of Dentistry. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra –Ecuador
https://orcid.org/0000-0002-1396-1236
2.Dr. Myrian Margarita Grijalva Palacios Esp.
ui.miryangp00@uniandes.edu.ec, Professor of Dentistry. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra – Ecuador
https://orcid.org/0000-0002-6808-279X
3.Dr.Carlos Mauricio Saeteros Cárdenas Esp.
ui.carlossc49@uniandes.edu.ec, Professor of Dentistry. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra – Ecuador
https://orcid.org/0000-0001-8209-9814
4.Dr. Adriana Katherine Quezada Quiñonez Esp.4
ui.adrianaqq34@uniandes.edu.ec, Professor of the Dentistry Career. Universidad Regional Autónoma de los Andes UNIANDES, Ibarra – Ecuador
https://orcid.org/0000-0002-1639-3967