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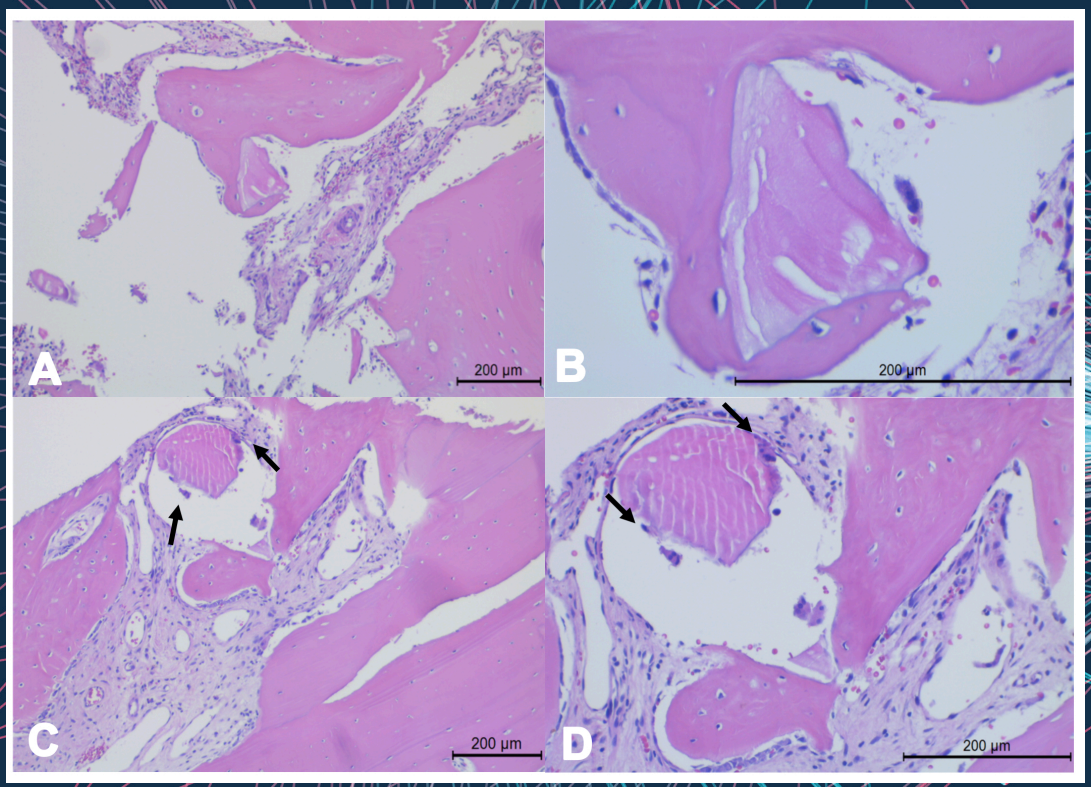

Chiang Mai University's Faculty of Dentistry publishes academic research articles in the newly titled - **Oral Sciences Reports,** which was previously known as *Chiang Mai Dental Journal (CMDJ)*. The journal was originally established for the purposes of publishing academic research articles by the Faculty of Dentistry at Chiang Mai University in 1977. In the current report, editors and experts in their respective fields review articles received from authors prior to being published to ensure that the content of all articles is up-to-date, universal, logical, and in accordace with academic principles so the reader can apply knowledge and cite works in the development of dentistry for the purposes of advancing future research while being beneficial to patients and society.

At present, Oral Sciences Reports openly receives all submissions through an online journal review process system. The new online system also allows reviewers and researchers an ability to read 3 issues each year.

Aim and Scope of the journal

To compile research and content that is up to date and usable to all branches of dentistry and related fields. The articles in Oral Sciences Reports are fundamental research work, including original articles, review articles, case reports/series, short communications, and letters to the editor.

Policy

Accepted articles will be fairly reviewed by the editors and experts with full transparency through the following process.

1. The articles must be correct according to academic principles and not duplicate works that have been previously published.
2. The articles will be considered and reviewed through a non-bias process by concealing the names of authors and related persons in the considered documents while also concealing the names of the experts and reviewers who review the articles (double-blind review).
3. The review process can be tracked online. The article authors can review the status of their article and are able to follow up on the article evaluation through the online process. The duration of each step is closely monitored so that the articles can be published on time.
4. Authors of articles are responsible to review and verify the accuracy of the text, images, tables in the articles before publication.
5. Articles published in Oral Sciences Reports are the copyright of Oral Sciences Reports, which forbids anyone from duplicating published articles for any purpose without explicit permission from Oral Sciences Reports.

Indexing

Thai Journal Citation Index Centre (TCI) Tier 1
Asian Citation Index (ACI)
Google Scholar

Editorial Board

Types of Submission

Oral Sciences Reports invites the following submissions:

1. Original Articles — Original contributions of research reports or unpublished recent academic research to the development and applications in dentistry and related fields. The original article must not exceed 4000 words in length and must contain no more than 10 figures and tables in total.
2. Review Articles — Comprehensive reviews of special areas of focus in dentistry and related fields. Articles that contain important collected data from numerous books or journals and from the writer's experience. Information should be described, reviewed, compared, and analyzed. The review article must not exceed 4000 words in length and must contain no more than 10 figures and tables in total.
3. Systematic Reviews — Clearly formulated reviews that uses systematic and reproducible methods to identify, select and critically appraise all relevant research, and to collect and analyze data from the studies that are included in the review.
4. Case Reports/Series — Original findings that highlight novel technical and/or clinical aspects in dentistry and related fields which include clinical symptoms, diagnosis, patient care, treatment, follow-up, and evaluation. The report must not exceed 2500 words in length and must contain no more than 5 figures.
5. Letters to the Editor — Commentaries on published papers in the journal and other relevant matters that must not exceed 1000 words in length
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Authors should ensure to prepare the following items for submission. Failure to complete the required items may contribute to the delay of publication process. Please check the relevant section in this guideline for more details.

1. Title page — Must include title of the article, author names and affiliations. One author has been designated as the corresponding author with contact details (e-mail address and full postal address) (see 'Title page' section for more information and an example)

2.	CRediT Contribution	Author will be asked to provide CRediT Contributions as well as their degree of contribution at the time of the original submission. CRediT Contribution is a high-level classification of the diverse roles performed in the work leading to a published research output in the sciences. Its purpose to provide transparency in contributions to scholarly published work, to enable improved systems of attribution, credit, and accountability.
3.	Abstract	Must not exceed 250 words. Relevant keywords (up to five keywords) must be included at the end of the abstract. (see the 'Abstract' section for more details)
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Additional considerations the author should confirm before submission:

1. Manuscript must be 'spell-checked', 'grammar-checked', and 'plagiarism-checked'.
2. All figures, tables, and references mentioned in the text should match the files provided.
3. Permission must be obtained for use of copyrighted material from other sources (including the internet).
4. Authors must provide conflicts of interest statement, even if there is no conflict of interests to declare.

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Authors must acknowledge to the following ethical guidelines for publication and research.

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The clinical trial registration number and name of the trial register should be included in Materials and Methods of the manuscript. For epidemiological observational trials, authors of epidemiological human observations studies are required to review and submit a 'strengthening the reporting of observational studies in Epidemiology' (STROBE) checklist and statement. Compliance with this must be detailed in Materials and Methods.

D. Systematic Review

The abstract and main body of the systematic review should be reported using the PRISMA for Abstract and PRISMA guidelines respectively. Authors submitting a systematic review should register the protocol in one of the readily-accessible sources/databases at the time of project inception and not retrospectively (e.g. PROSPERO database, OSF registries). The protocol registration number, name of the database or journal reference should be provided at the submission stage in Materials and Methods. A PRISMA checklist and flow diagram (as a Figure) should also be included in the submission material.

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Submission of an article implies that the work described has not been published previously (except in the form of an abstract, a published lecture or academic thesis), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright- holder. The conference proceedings are allowed to be part of the article if the contents do not exceed 70% of the article.

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All texts in the submitted manuscript are required to be inclusive language throughout that acknowledges diversity, conveys respect to all people, is sensitive to differences, and promotes equal opportunities. Authors should ensure that writing is free from bias, for instance by using 'he or she', 'his/her' instead of 'he' or 'his', and by making use of job titles that are free of stereotyping (for instance by using 'chairperson' instead of 'chairman' and 'flight attendant' instead of 'stewardess'). Articles should make no assumptions about the beliefs or commitments of any reader, should contain nothing which might imply that one individual is superior to another on the grounds of race, sex, religion, culture, or any other characteristic.

A. Title page

The title page will remain separate from the manuscript throughout the peer review process and will not be sent to the reviewers. It should include these following details:

- Title should be concise, information-retrieval, and not exceed 30 words. Please avoid abbreviations and formulae where possible.
- Author names and affiliations. Please clearly indicate the given name(s) and family name(s) of each author are accurately spelled. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript number immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and the e-mail address of each author.
- Corresponding author will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. Please ensure that the e-mail address and contact details given are kept up to date by the corresponding author.

B. Abstract

Abstract must not exceed 250 words with concise and informative explanations about the article. Authors must prepare an abstract separately from the main manuscript using Microsoft Word processing software (.doc or .docx). Please avoid references and uncommon abbreviations, but if essential, abbreviations must be defined at their first mention in the abstract itself. Abstract structure of the original articles must consist of ‘Objectives, Methods, Results, and Conclusions’.

Abstract of other types of submitted articles should be summarized in one paragraph. Up to five keywords relevant to the articles must be provided and arranged in alphabetical order.

C. Manuscript

Oral Sciences Reports adheres to a double-blinded review. The main body of the paper (including the references, figures, tables and any acknowledgements) must not include any identifying information, such as the authors' names. The layout of the manuscript must be as simple as possible with double-spaced, single column format with Sans Serif font and uploaded as an editable Microsoft Word processing file (.doc or .docx). Complex codes or hyphenate options must be avoided, but the emphatic options such as bold face, italics, subscripts, and superscripts, etc. are encouraged.

1. Original article

• *Introduction* should include literature reviews of previous studies, research questions, and the rationale for conducting the study. The Introduction should not be too long and should be easy to read and understand while avoiding a detailed literature survey or a summary of the results.

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• *Results* should show the data gained from the study's design in text, tables and/or illustrations, as appropriate, and be clear and concise.

• *Discussion* is criticism, explanation, and defense of the results from the standpoint of the author, and comparison with other peoples' reports. The discussion can include criticism of materials, methods and study results, problems, and difficulties, pointing out the benefits of adoption and providing feedback where appropriate. Discussions should explore the significance of the results of the work, not repeat them. Avoid extensive citations and discussion of published literature.

• *Conclusions* refers to a summary of the study or research results.

• *Acknowledgments:* Please specify contributors to the article other than the authors accredited. Please also include specifications of the source of funding for the study.

Formatting of funding source:

This work was supported by the 1st organization name [grant numbers xxxx]; the 2nd organization name [grant number yyyy]; and the 3rd organization name [grant number zzzz].

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant or funding from funding agencies in the public, commercial, or not-for-profit sectors.

• *References* should be confined to documents relating to the author's article or study. The number should not exceed 80, placed in order and using numbers which are superscripted and put in parentheses, starting with number 1 in the article and in reference document's name. (see 'References' section for more information regarding reference formatting)

2. Review articles should be divided into Introduction, Review and Conclusions. The Introduction section should be focused to place the subject matter in context and to justify the need for the review. The Review section should be divided into logical sub-sections in order to improve readability and enhance understanding. Search strategies must be described, and the use of state-of-the-art evidence-based systematic approaches is expected. The use of tabulated and illustrative material is encouraged. The Conclusion section should reach clear conclusions and/or recommendations on the basis of the evidence presented.

3. Systematic review

• Introduction should be focused to place the subject matter in context and to justify the need for the review.

• Methods should be divided into logical sub-sections in order to improve readability and enhance understanding (e.g. details of protocol registration, literature search process, inclusion/exclusion criteria, data extraction, quality assessment, outcome(s) of interest, data synthesis and statistical analysis, quality of evidence).

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• Discussion should summarize the results, highlighting completeness and applicability of evidence, quality of evidence, agreements and disagreements with other studies or reviews, strength and limitations, implications for practice and research.

• Conclusion(s) should reach clear conclusions and/or recommendations on the basis of the evidence presented.

4. Case reports/series should be divided into Introduction, Case report, Discussion and Conclusions. They should be well illustrated with clinical images, radiographs and histologic figures and supporting tables where appropriate. However, all illustrations must be of the highest quality.

There are some necessary considerations which should be comprehended and consistent throughout the article:

1. Abbreviations: define abbreviations at their first occurrence in the article: in the abstract and in the main text after it. Please ensure consistency of abbreviations throughout the article.

2. Mathematical expressions: the numbers identifying mathematical expressions should be placed in parentheses after the equation, flush to the right margin; when referring to equations within text, use the following style: Eq. (5), Eqs. (3-10), [see Eq. (4)], etc.

3. Nomenclature: abbreviations and acronyms should be spelled out the first time they are used in the manuscript or spelled out in tables and figures (if necessary). Units of measure and time require no explanation. Dental nomenclature in the manuscript should be complete words, such as maxillary right central incisor. Numbering of teeth from pictures or tables should follow the FDI two-digit system.

4. Units: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

5. Product identification: all products mentioned in the text should be identified with the name of the manufacturer, city, state, and country in parentheses after the first mention of the product, for example, The ceramic crown was cemented on dentin surface with resin cement (RelyX^{TM} U200, 3M ESPE, St. Paul, MN, USA)…

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Figures should be prepared and submitted separately from the main manuscript. Color artworks are encouraged at no additional charge. Regardless of the application used other than Microsoft Office, when the electronic artwork is finalized, please ‘save as’ or ‘export’ or convert the images to **EPS, TIFF, or JPEG format with the minimum resolution of 300 dpi.** Keep the artwork in uniform lettering, sizing, and similar fonts. Please do not submit graphics that are too low in resolution or disproportionately large for the content. Authors must submit each illustration as a separate file.

Please ensure that each illustration has a caption according to their sequence in the text and supply captions separately in editable Microsoft Word processing file (.doc or .docx), not attached to the figure. A caption should comprise a brief title (not on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

E. Tables

Please submit tables as editable Microsoft Word processing files (.doc or .docx), not as images, and avoid using vertical rules and shading in table cells. Each table should be placed on a separate page, not next to the relevant text in the article. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body while ensuring that the data presented in them does not duplicate results described elsewhere in the article.

F. References

Citation in text

Any citations in the text should be placed in order and using numbers which are superscripted and put in parentheses. Please ensure that all citations are also present in the reference list consecutively in accordance with their appearance in the text.

Reference style

All references should be brought together at the end of the paper consecutively in accordance with their appearance in the text and should be in the Vancouver reference format. Please follow these examples of correct reference format below:

1. Journal article

1.1. One to six authors

Author(s) – Family name and initials. Title of article. Abbreviated journal title. Publication year;volume (issue):pages.

Example:

Parvez GM. Pharmacological activities of mango (Mangifera Indica): A review. J Pharmacognosy Phytother. 2016;5(3): 1-7.

Or

Choi YS, Cho IH. An effect of immediate dentin sealing on the shear bond strength of resin cement to porcelain restoration. J Adv Prosthodont. 2010;2(2):39-45.

Or

Firmino RT, Ferreira FM, Martins CC, Granville-Garcia AF, Fraiz FC, Paiva SM. Is parental oral health literacy a predictor of children's oral health outcomes? Systematic review of the literature. Int J Paediatr Dent. 2018;28(5):459-71.

1.2. More than six authors

Author(s) – Family name and initials of the first six authors, et al. Title of article. Abbreviated journal title. Publication year;volume(issue):pages.

Example:

Vera J, Siqueira Jr JF, Ricucci D, Loghin S, Fernández N, Flores B, et al. One-versus two-visit endodontic treatment of teeth with apical periodontitis: a histobacteriologic study. J Endod. 2012;38(8):1040-52.

1.3. Article in press

Authors separated by commas – Family name and initials. Title of article. Abbreviated journal title in italics. Forthcoming - year of expected publication.

Example:

Cho HJ, Shin MS, Song Y, Park SK, Park SM, Kim HD. Severe periodontal disease increases acute myocardial infarction and stroke: a 10-year retrospective follow-up study. J Dent Res. Forthcoming 2021.

2. Books

2.1. Book with author (s)

Author(s) – Family name and initials (no more than 2 initials with no spaces between initials)– Multiple authors separated by a comma. After the 6th author add - "et al". Title of book. Edition of book if later than 1st ed. Place of publication: Publisher name; Year of publication.

Example:

Sherwood IA. Essentials of operative dentistry. Suffolk: Boydell & Brewer Ltd; 2010.

Or

Abrahams PH, Boon JM, Spratt JD. McMinn's clinical atlas of human anatomy. 6th edition. Amsterdam: Elsevier Health Sciences; 2008.

2.2. Book with no author

Title of book. Edition of book if later than 1st ed. Place of publication: Publisher name; Year of publication.

Note: Do not use anonymous. Please begin a reference with the title of the book if there is no person or organization identified as the author and no editors or translators are given.

Example:

A guide for women with early breast cancer. Sydney: National Breast Cancer; 2003.

2.3. Chapter in a book

Author(s) of chapter - Family name and initials, Title of chapter. In: Editor(s) of book - Family name and initials, editors. Title of book. edition (if not first). Place of publication: Publisher name; Year of publication. p. [page numbers of chapter].

Example:

Rowlands TE, Haine LS. Acute limb ischaemia. In: Donnelly R, London NJM, editors. ABC of arterial and venous disease. 2nd ed. West Sussex: Blackwell Publishing; 2009. p. 123-140.

3. Thesis/dissertation

3.1. Thesis in print

Author - family name followed by initials. Thesis title [type of thesis]. Place of publication: Publisher; Year.

Example:

Kay JG. Intracellular cytokine trafficking and phagocytosis in macrophages [dissertation]. St Lucia, Qld: University of Queensland; 2007.

3.2. Thesis retrieved from full text database or internet

Author - family named followed by initials. Thesis title [type of thesis/dissertation on the Internet]. Place of publication: Publisher; Year [cited date – year month day]. Available from: URL

Example:

Pahl KM. Preventing anxiety and promoting social and emotional strength in early childhood: an investigation of risk factors [dissertation on the Internet]. St Lucia, Qld: University of Queensland; 2009 [cited 2017 Nov 22]. Available from: https://espace.library.uq.edu.au/view/UQ:178027

4. Webpage

4.1. Webpage with author

Author/organization's name. Title of the page [Internet]. Place of publication: Publisher's name; Publication date or year [updated date - year month day; cited date - year month day]. Available from: URL

Example:

American Dental Association. COVID-19 and Oral Health Conditions [Internet]. Chicago: American Dental Association; 2021 Feb 12 [updated 2021 Feb 12; cited 2021 Jun 24]. Available from: https://www.ada.org/en/press-room/news-releases/2021-archives/february/covid-19-and-oral-health-conditions

4.2. Webpage with no authors

Title [Internet]. Place of publication (if available): Publisher's name (if available); Publication date or year [updated date (if available); cited date]. Available from: URL

Example:

Dentistry and ADHD [Internet]. 2019 Jan 15 [updated 2019 Jan 15; cited 2020 Apr 8]. Available from: https://snoozedentistry.net/blog/dentistry-and-adhd/

4.3. Image on a webpage

Author/organization. Title [image on the Internet]. Place of publication: Publisher's name; Publication date or year [updated date; cited date]. Available from: URL

Note: If the image does not have a title - give the image a meaningful title in square brackets.

Example:

Poticny DJ. An Implant-Supported Denture Offers a Number of Advantages [image on the Internet]. Texas: Office of Dan Poticny; 2018 Nov 21 [updated 2018 Nov 21; cited 2019 Aug 30]. Available from: https://www.dfwsmiledoc.com/blog/post/an-implant-supported-denture-offers-a-number-of-advantages.html

5. Government publications/reports

5.1. Reports and other government publications

Author(s). Title of report. Place of publication: Publisher; Date of publication – year month (if applicable). Total number of pages (if applicable eg. 24 p.) Report No.: (if applicable)

Example:

Australian Institute of Health and Welfare. Oral health and dental care in Australia: key facts and figures trends 2014. Canberra: AIWH; 2014.

5.2. Government reports available online

Author(s). Title of report. Report No.: (if applicable). [Internet]. Place of publication: Publisher or Institution; Publication date or year [updated date - year month day; cited date - year month day]. Available from: URL

Example:

World Health Organization. WHO mortality database [Internet]. Geneva: World Health Organization; 2019 Dec 31 [updated 2019 Dec 31; cited 2021 Mar 29]. Available from: https://www.who.int/data/mortality/country-profile

6. Tables/Figures/Appendices

Follow the format of book, journal or website in which you found the table/figure/appendix followed by: table/figure/image/appendix number of original source, Title of table/figure/appendix from original source; p. Page number of table/figure/appendix from original source.

Note: each reference to a different table/figure within the same document requires a separate entry in the Reference list. Please provide permission documents from the original sources.

Example:

Smith J, Lipsitch M, Almond JW. Vaccine production, distribution, access, and uptake. Lancet 2011;378(9789):428-438. Table 1, Examples of vaccine classes and associated industrial challenges; p. 429.

7. Journal abbreviation source

Journal names should be abbreviated according to the Web of Science - Journal Title Abbreviations.

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Comparison of Mechanical Properties Between Zirconia-reinforced Lithium Silicate Glass-ceramic and Lithium Disilicate Glass-ceramic: A Literature Review

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Abstract

Lithium disilicate glass-ceramic (LDS) is increasingly being adopted for use in therapeutic restorative procedures. Concurrently, zirconia-reinforced silicate glass-ceramics (ZRS) are becoming broadly utilized in dental applications. The purpose of this study was to evaluate and compare the mechanical properties of zirconia-reinforced lithium silicate glass-ceramics and lithium disilicate-based glass-ceramics, with a focus on their application in CAD/CAM technologies. In this review, the researchers conducted a search of the PubMed (MEDLINE) database to identify studies related to LDS and ZRS. This search was limited to articles published in English over a seven-year period, from January 1, 2015, to December 31, 2022. Additional studies were sourced from Google Scholar and through manual exploration. Key published works were identified and included in the literature review. The findings concluded that ZRS exhibits superior mechanical properties, including higher flexural strength, fracture toughness, and hardness, compared to LDS. Furthermore, ZRS combines desirable esthetic qualities with robust mechanical strength, rendering it an excellent material for single tooth aesthetic restorations such as inlays, onlays, crowns, and veneers, applicable to both tooth and implant supports. Currently, there is a notable scarcity of data concerning the mechanical properties and clinical efficacy of ZRS. Therefore, it is imperative to conduct long-term clinical studies to verify the optical and mechanical properties, clinical applications, limitations, and long-term effectiveness of ZRS.

Keywords: dental ceramic, lithium disilicate glass-ceramic, zirconia-reinforced silicate glass-ceramics

Introduction

Dental ceramics are preferred for restorations needing a natural appearance because they can replicate the natural characteristics of teeth effectively. This preference for all-ceramic restorations has surged in recent times.[1] Lithium disilicate glass-ceramic (LDS) is widely utilized for such all-ceramic restorations, encompassing not only aesthetic veneers, inlays, onlays, and anterior crowns but also for the more demanding applications of load-bearing monolithic posterior crowns and bridges.[2] LDS offers a range of shades and translucency options, making it possible to achieve anatomical contours in monolithic restorations that closely resemble natural teeth. This customization allows LDS to seamlessly blend with the patient's existing dentition. LDS is also employed in dental computer-aided design/computer-aided manufacturing (CAD/CAM) for fabricating inlays, onlays, partial crowns, veneers, anterior and posterior crowns, and single tooth restorations on implant abutments.[3] Despite these advantages, the mechanical properties of LDS may restrict its application in areas subjected to high masticatory forces, such as the molar region.[4]

Zirconia-reinforced silicate glass ceramics (ZRS) have recently been introduced to the field of dentistry. They are utilized by dental CAD/CAM software for fabricating inlays, onlays, partial crowns, veneers, anterior and posterior crowns, and single-tooth restorations on implant abutments. It is claimed that these advanced glass ceramic materials merge the functional and aesthetic advantages of zirconia with those of glass ceramic. The incorporation of zirconia particles within the lithium silicate glass matrix serves to reinforce the ceramic structures by hindering the progression of cracks. Following the crystallization process, the material is expected to exhibit enhanced mechanical properties alongside superior aesthetic qualities. The improved translucency and range of colors enable the creation of anatomically accurate, monolithic restorations.[2-6]

The purpose of this review is to provide a comparative analysis of the mechanical properties between Zirconia-reinforced silicate glass ceramics (ZRS) and Lithium disilicate glass-ceramic (LDS).

Materials and Methods

The PubMed (MEDLINE) database served as the primary source for compiling the most pertinent and up-to-date data on LDS and ZRS. This search was restricted to a span of five years, covering the period from January 1, 2015 to December 31, 2020, and was limited to studies published in English. Additional research was acquired through Google Scholar and direct searches. The most significant article was chosen for inclusion, and it is featured in the reference, along with the selected studies.

Results and Discussion

LDS constitutes a particle-filled glass-ceramic utilized in restorations either through heat-pressing or CAD/CAM processes.[7,8] In 2001, IPS e.max Press® by Ivoclar Vivadent in Schaan, Liechtenstein, was launched as a castable LDS variant that offered enhanced mechanical and optical characteristics.[9] The microstructure of IPS e.max Press is characterized by approximately 70 percent lithium-disilicate crystals ($Li_2Si_2O_5$), set within a glassy matrix.[9] Following this, in 2005, IPS e.max CAD® was introduced by the same manufacturer for CAD/CAM dental restorations.[9] LDS is known for its superior mechanical properties and translucency compared to traditional dental porcelains. Although LDS is more translucent than zirconia, its mechanical properties are somewhat lesser. Nevertheless, LDS has been widely adopted for fabricating monolithic ceramic crowns noted for their aesthetic appeal.[10]

A new generation of ceramic material for dental restorations, Zirconia-reinforced silicate glass ceramics (ZRS), has been introduced to the market. ZRS is characterized by its composition of fine lithium-metasilicate (Li_2SiO_3) and lithium disilicate ($Li_2Si_2O_5$) crystals, with an average size ranging from 0.5 to 0.7 micrometers, embedded within a zirconium dioxide (ZrO_2) matrix that constitutes 10% of its weight.[11] The material undergoes a final crystallization process, leading to the creation of a fine-grained microstructure composed of Li_2O-ZrO_2-SiO_2.[3,4] This structure is noted for its enhanced mechanical properties, boasting a strength range between 370 to 420 MPa, and is designed to meet the highest aesthetic standards, according to the manufacturer's claims.[12]

Presently, two distinct ZRS materials are available for use in dental restorations, each characterized by two crystal phases. One crystalline phase consists of lithium-metasilicate (Li_2SiO_3) crystals, which have a round and slightly elongated form. These crystals are found in larger sizes in Celtra® Duo (up to 1 micrometer). While the other

phase comprises lithium orthophosphate (Li_3PO_4) crystals, presents in a round shape with nanometric dimensions, appearing in a smaller size in Vita Suprinity® PC (approximately 0.5 µm). The variance in grain sizes between these materials can influence their mechanical properties, with larger grain sizes potentially leading to diminished mechanical performance in comparison to materials of the same composition but with smaller grains.[5]

Mechanical Properties

Flexural Strength

The mechanical durability of ceramics, being brittle materials, is primarily influenced by their flexural strength. The findings suggest that ceramics exhibit a markedly higher fragility when subjected to tensile forces compared to compressive stresses.[3]

Numerous studies have been conducted to evaluate the mechanical properties of ZRS (Vita Suprinity® PC) and LDS (IPS e.max CAD). Sen and US examined thirty disk-shaped specimens from each material, measuring 12 millimeters in diameter and 1.2±0.05 millimeters in depth. They employed a biaxial flexure test, utilizing a three-ball setup and a piston in a universal testing machine, with a crosshead speed of 0.5 millimeters per minute until failure.[6] Elsaka and Elnaghy tested thirty bending bars (18×4×1.2 millimeters) of each material using a three-point bending fixture in a universal testing machine, loading the specimens until fracture at a crosshead speed of 0.5 millimeters per minute.[3] The studies found that ZRS (Vita Suprinity® PC) exhibited significantly higher flexural strength compared to LDS (IPS e.max CAD®), a result attributed to the zirconia fillers that reinforce the glassy matrix of the material.[3,6]

Lawson and colleagues conducted a study to evaluate the mechanical properties of LDS (IPS e.max CAD®) and zirconia-reinforced lithium silicate (Celtra® Duo) materials used in CAD/CAM dentistry. They prepared ten bars from each material, measuring 2.5×2.5×16 millimeters, and polished all samples. Both Celtra® Duo (fired group) and IPS e.max CAD® were subjected to firing in a furnace according to the manufacturer's guidelines. The mechanical strength of the specimens was then tested using a three-point bending fixture in a universal testing machine, with a crosshead speed set at 1 millimeter/minute. The results showed that fired Celtra® Duo exhibited superior flexural strength compared to IPS e.max CAD®.[13] Furthermore, it was found that zirconia-reinforced glass-ceramic surpassed LDS (IPS e.max CAD®) in terms of flexural strength, both before and after being subjected to thermo-mechanical load cycling. The remarkable mechanical properties and resistance to ageing of zirconia-based ceramics were noted to prevent any significant impact on their flexural strength from thermo-mechanical load cycling.[13]

Soliman *et al.,* conducted an analysis on the flexural strength of LDS (IPS e.max CAD®) and ZRS (Vita Suprinity® PC) materials used in monolithic dental restorations. The study involved ten rectangular samples for each material, measuring 14×4×1.2 millimeters, which were fabricated from CAD/CAM blocks. These specimens were subjected to a three-point flexural strength test in a universal testing machine, with a crosshead speed of 0.5 millimeters per minute until failure. The results revealed that lithium disilicate-based glass-ceramics demonstrated higher flexural strength compared to their zirconia-reinforced counterparts.[14]

The summary of studies related to flexural strength of ZLS and LDS were shown in Table 1.

Table 1: Comparison flexural strength between lithium disilicate glass-ceramic (LDS) and zirconia-reinforced silicate glass-ceramic (ZLS)

Study	Result	Flexural strength [mean (SD)]
Elsaka and Elnaghy (2016)[3]	ZLS (Vita Suprinity®) had a significantly higher flexural strength than LDS (IPS e.max CAD).	ZLS=443.63 (38.90) MPa LDS=348.33 (28.69) MPa
Lawson *et al.,* (2016)[13]	ZLS (Celtra® Duo (fired)) surpassed the flexural strength of LDS (IPS e.max CAD).	ZLS=451.40 (58.90) MPa LDS=376.90 (76.20) MPa
Sen and Us (2018)[6]	ZLS (Vita Suprinity®) revealed higher biaxial flexural strength compared with LDS (IPS e.max CAD).	ZLS=510.0 (43.0) MPa LDS=415.0 (26.0) MPa
Soliman *et al.,* (2019)[14]	LDS (IPS e.max CAD) showed the higher flexural strength than ZLS (Vita Suprinity®).	LDS=451.35 (9.41) MPa ZLS=383.38 (8.88) MPa

Fracture toughness

Fracture toughness is a critical metric for evaluating the resistance of brittle materials to fracture and their ability to impede crack growth. Restorative materials that exhibit higher fracture toughness are more resistant to fractures and can withstand a higher degree of stress. There are various methods for testing fracture toughness, among which the single-edge-V-notched-beam (SEVNB) method stands out as the benchmark for determining the fracture toughness of ceramics owing to its accuracy and reliability.[1,15-17] In the study conducted by Elsaka and Elnaghy on the mechanical properties of ZRS, ceramic blocks were sectioned into bar-shaped specimens and evaluated using a three-point bending fixture installed in a universal testing machine. These specimens were subjected to loading until fracture occurred, with a cross-head speed set at 0.5 millimeter per minute. The findings from their investigation revealed that ZRS (Vita Suprinity® PC) demonstrated superior fracture resistance compared to lithium disilicate glass-ceramic (IPS e.max CAD®). The enhanced fracture toughness was attributed to the reinforced glass matrix, without dissolved zirconia particles.[3]

Hamza *et al.,* conducted a study to compare the fracture resistance of ZRS (Vita Suprinity® PC) restorations with LDS (IPS e.max CAD®) restorations. The restorations were subjected to a chewing simulator and then loaded until fracture in a universal testing machine. The findings indicated that ZRS restorations exhibited higher fracture resistance compared to LDS restorations.[18] However, the outcome of this study, based on tests conducted with Vita Suprinity® PC, contradicts recent research by Sieper *et al.,* and Gungor and Nemli. These researchers reported that the fracture strength of all-ceramic crowns crafted from LDS exceeded that of those made from ZRS.[19,20]

Mohamed *et al.,* discovered that ZRS (Celtra® Duo) exhibited greater fracture resistance compared to LDS (IPS e.max CAD®), with aging reducing the fracture resistance of both ceramic types.[21] In their study, 40 CAD/CAM crowns were aged, and their fracture resistance was assessed using a universal testing machine. Similarly, Schwindling and Preis observed that ZRS crowns demonstrated a higher average fracture strength than LDS crowns.[22,23]

The summary of studies related to fracture toughness of ZLS and LDS was shown in Table 2.

Hardness

Hardness is a crucial factor in evaluating restorative materials. It refers to a material's ability to resist permanent indentation or penetration.[3]

Several studies have examined the hardness of LDS (IPS e.max CAD®) and ZRS (Vita Suprinity®

Table 2: Comparison fracture toughness/resistances between lithium disilicate glass-ceramic (LDS) and zirconia-reinforced silicate glass-ceramic (ZLS)

Study	Result	Fracture toughness/resistances [mean (SD)]
Preis *et al.,* (2015)[23]	Crowns fabricated ZLS (Celtra® Duo) showed higher mean value of fracture strength than those fabricated from LDS (IPS e.max CAD).	ZLS=2612 (853) N LDS=2528 (668) N
Elasaka & Elnaghy (2016)[3]	ZLS ceramic (Vita Suprinity® PC) revealed higher fracture toughness compared with LDSceramic (IPS e.max CAD).	ZLS=2.31 (0.17) MPa m0.5 LDS=2.01 (0.13) MPa m0.5
Schwindling *et al.,* (2017)[22]	ZLS crown (Celtra® Duo) showed higher fracture resistance than those crown from LDS (IPS e.max CAD).	ZLS=667 (205) N LDS=525 (256) N
Sieper *et al.,* (2017)[19]	LDS ceramic (IPS e.max CAD) was achieved more higher fracture strength than ZLS ceramic (Vita suprinity® PC).	LDS=2499 (167) N ZLS=2015 (270) N
Gungor *et al.,* (2018)[20]	The fracture resistance of all ceramic crowns fabricated from LDS (IPS e.max CAD) was higher than that for ZLS crowns (Vita suprinity® PC).	LDS=2847.64 (108.87) N ZLS=2598.25 (134.77) N
Mohamed *et al.,* (2020)[21]	ZLS ceramic (Celtra® Duo) give rise to higher fracture resistance than LDS ceramic (IPS e.max CAD) and aging decrease fracture resistance of both types of ceramic.	ZLS=1093.96 (120.01) N LDS=1052.16 (282.29) N

PC).[3,13,24] In the research conducted by Elsaka and Elnaghy, thirty specimens of each material, measuring 18×14×5 millimeters, were prepared, and polished. The surface microhardness of these specimens was assessed using a digital microhardness tester. For each material, ten Vickers indentations were made using a diamond indenter under a load of 9.8 newtons for a duration of 20 seconds.[3]

In the investigation by Arthur *et al.,* the hardness was determined using a Vickers microhardness tester and the indentation technique. This assessment was carried out on ten bar-shaped specimens which had been finished to a mirror polish. The surface microhardness of each specimen was measured by conducting five Vickers indentation tests, applying a load of 1.96 newtons for a dwell time of 15 seconds each.[24]

In a separate study by Lawson *et al*., materials were cut into 4-millimeter-thick blocks and embedded in a clear, chemically cured medium. All specimens underwent wet polishing and were then stored. The Vickers microhardness of these specimens was evaluated using a one-kilogram load and a dwell time of 15 seconds. The findings indicated that ZRS exhibited greater hardness compared to LDS.[13]

The findings from hardness testing indicated that ZRS exhibited greater hardness compared to LDS, as documented in Table 3.

Disadvantages

The brittleness and susceptibility to fracture of LDS and ZRS are significant disadvantages. According to Ustun *et al*., 2016, the Vita Suprinity groups exhibited lower bond strength values compared to other glass ceramic groups. Moreover, ZRS groups, containing approximately 10% zirconia by weight, demonstrated lower values than other groups subjected to HF (hydrofluoric acid) etching, leading to both cohesive and adhesive failures. Consequently, silanization could negatively affect the zirconia content in ZRS materials.[25-27]

Clinical applications

The development of clinical practice guidelines for the utilization of Celtra® Duo involved the implementation of two distinct finalization protocols: milling and glaze firing. According to the manufacturer's recommendations, the milled version offers a notable advantage in terms of time efficiency as it eliminates the need for a firing phase, allowing for direct polishing following grinding. This simplifies the process of adhesively luting indirect restorations at the chairside. Although not mandatory, the glaze firing cycle is the preferred method due to its ability to enhance esthetic and flexural strength characteristics. In contrast, Vita Suprinity® PC and IPS e.max CAD® provide the material in a pre-crystallized state, available in amber or opaque purple color variations, necessitating a subsequent crystallization firing after machining.[25]

LDS

Long-term clinical use in patients is being studied in addition to the recommended clinical application procedures, as indicated by the following studies.

Breemer *et al.,* conducted a comprehensive review of long-term clinical data concerning crowns made from single pieces of lithium disilicate glass-ceramic. In this clinical study, they performed 74 repairs on 12 patients. Additionally, they conducted a historical case study where the same clinician replaced the back teeth with full LDS replacements bonded using an adhesive method. The results of this study showed that, after 5, 10, and 15 years, 92%, 85%, and 81.9% of the restorations remained intact. However, thirteen restorations experienced failures: four developed secondary caries, two became dislodged, and seven fractured.[28] Mobilio *et al.,* assessed single LDS

Table 3: Comparison hardness between lithium disilicate glass-ceramic (LDS) and zirconia-reinforced silicate glass-ceramic (ZLS)

Study	Result	Hardness [mean (SD)]
Elsaka and Elnaghy (2016)[3]	ZLS (Vita Suprinity®) had significantly higher hardness than LDS (IPS e.max CAD).	ZLS=6.53 (0.46) GPa LDS=5.45 (0.28) GPa
Lawson *et al.,* (2016)[13]	ZLS (Celtra® Duo) was harder than LDS (IPS e.max CAD).	ZLS=595.10 (37.60) HV LDS=452.90 (16.20) HV
Arthur *et al.*, (2019)[24]	ZLS (Vita Suprinity®) showed the highest hardness values followed by LDS (IPS e.max CAD).	ZLS=692.0 (14.0) HV LDS=596.0 (18.0) HV

restorations on natural teeth, with a mean follow-up period of 51 months involving 43 restorations in 17 individuals. The findings indicated that 97.7% of these restorations survived, with a success rate of 94.2%.[29] Furthermore, crown-retained fixed dental prostheses (FPDs) made from LDS ceramic (IPS e.max Press) were studied over a span of 15 years. In this study, 28 patients received 36 3-unit fixed dental prostheses, which were bonded using either composite resin or glass-ionomer cement. After 10 years, the survival and success rates of monolithic lithium disilicate ceramic FDPs decreased to 48.6% and 30.9%, respectively, after 15 years.[30]

Malamed *et al*., conducted a study that involved the examination of 556 patients with LDS restorations, including single crowns, three-unit fixed partial dentures (FPDs), and cantilevered anterior restorations. The research focused on assessing the 10-year survival of these restorations. The findings from this study revealed that pressed lithium disilicate restorations on molar teeth exhibited a durability of 10.4 years with an overall failure rate of 0.2 percent per year.[31] These long-term survival statistics can be valuable for clinicians in making informed decisions as shown in table 4.

ZRS

The use of ZRS is endorsed for various applications, including veneers, crowns, bridges, implant-supported crowns, inlays, and onlays, as indicated by the manufacturer of the product.[3,32] The clinical reliability of zirconia-reinforced lithium silicate is supported by numerous research studies and observed clinical outcomes.

Zimmermann *et al.,* reported a 96.7 percent success rate for ZRS restorations after a 12-month follow-up period, with clinical failures primarily attributed to bulk fracture, accounting for approximately 3.3 percent.[33] In another study by Rinke *et al*., the success rate for ninety-two ZRS partial crowns (specifically Celtra® Duo) placed on vital or adequately endodontically treated premolars and molars was approximately 98 percent, as assessed over a 3-year follow-up period. The main factor leading to failure in this case was tooth fracture, contributing to a 1.2 percent endodontic complication rate.[34] Rinke *et al.,* also conducted a study with a 2-year follow-up, focusing on sixty-one partial crowns with reduced material thickness (with a minimum material thickness of 1.0 millimeter) fabricated chairside and adhesively cemented on vital premolars and molars. The results showed an overall success rate of approximately 93 percent among the 59 restorations that participated in the 2-year follow-up examinations. Only two restorations were lost due to ceramic fracture.[35]

The durability and success rate of ZLS (zirconia-reinforced lithium silicate) ceramic partial crowns in dental restorations are significantly influenced by the material thickness and the position of the restoration within the mouth.[36] Furthermore, when subject to conditions simulating heavy chewing or bruxism, ZLS dental ceramics are estimated to exhibit a durability that is up to five times less than that of LS2 (lithium disilicate) ceramics. This suggests that while ZLS ceramics offer certain advantages, careful consideration must be given to their application in high-stress areas.[36,37]

Table 4: The success rate of lithium disilicate glass-ceramic (LDS)

Study	Sample	Methods	Result
Breemer *et al.,* (2017)[25] 5, 10 and 15-year follow up	Full crown restorations on premolars and molars.	For a retrospective case series, Full posterior LDS restorations were placed by the same dentist and same dental technician and cemented using an adhesive approach.	From this study, the success rate of restoration after 5, 10 and 15 years was 92%, 85% and 81.9%, respectively. Of the all restoration, 13 of them are failed: 4 because of secondary caries, 2 because of debonding and 7 because of fracture.
Mobilio *et al.,* (2018)[26] 3-year follow up	43 single, partial and total restorations on natural teeth.	For a retrospective study, A total of 43 partial and total restorations in 17 patients were evaluated from a minimum of 36 months follow-up to a maximum of 81 months follow-up.	The cumulative success rate was 97.7%, and the cumulative success rate was 94.2% with only two mechanical complications were observed: fracture of ceramic core and chipping.

Degidi *et al.,* assessed the 2-year performance of definitive implant- or tooth-supported three-unit fixed partial dentures (FPDs) using ZRS material (Celtra® Press). These FPDs were used for repairing premolars and molars with partial edentulism. The findings from this study suggest that both implant-supported and tooth-supported ZRS three-unit FPDs can effectively address posterior partial edentulism.[38] The success rate of ZLS was shown in Table 5.

Nonetheless, it is important to note that there is a deficiency of clinical evidence derived from trials with extended follow-up durations. A more comprehensive and extended long-term study is required to validate the promising results reported in these earlier publications.

Conclusions

ZRS exhibits superior mechanical properties, including higher flexural strength, fracture toughness, and hardness when compared to LDS. Additionally, ZRS offers optimal esthetics while maintaining proper mechanical strength, making it a suitable choice for single-tooth esthetic restorations, such as inlays, onlays, crowns, veneers, both tooth-supported and implant-supported. However, it is important to acknowledge that there is currently a limitation in the available data concerning the mechanical properties and long-term clinical performance of ZRS. Therefore, there is a need for long-term clinical research to thoroughly assess the physical-mechanical properties, clinical indications, limitations, and the long-term performance of such restorations.

Table 5: The success rate of zirconia-reinforced silicate glass-ceramic (ZLS)

Study	Sample	Method	Result
Zimmermann *et al.,* (2017)[30] 12 months follow up	60 indirect ZLS CAD/CAM Restorations.	Indirect restoration was fabricated, using CEREC method and intraoral scanning and adhesive cementation.	In this study, the success rate of indirect ZLS CAD/CAM restoration after 12 months was 96.7%. Clinically failed as a result of bulk fracture about 3.3%
Rinke *et al.,* (2020)[31] 3-year follow up	92 ZLS partial crowns (premolar and molar) on vital or sufficiently endodontically treated teeth.	Monolithic restorations of partial crowns were fabricated chairside from Celtra® Duo and adhesive cementation.	In this study, A success rate of 98% after 3 year was calculated. Apart from tooth fracture leading to failure, which result 1.2% in endodontic complication rate.
Rinke *et al.,* (2020)[32] 2-year follow up	61 ZLS partial crowns on vital premolars and molars.	Partial-crown with reduced material thickness (Minimum material thickness = 1.0 mm.) were fabricated chairside and adhesive cementation.	An overall success rate of 59 restorations participated in the 2-year follow up examinations was about 93%. There are 2 losses due to ceramic fracture.
Degidi *et al.,* (2021)[33] 2-year follow up	100 patients received a Three-unit fixed restoration on implant-supported or tooth supported.	A Three-unit fixed restoration made of monolithic, hot pressed, ZLS (Celtra® Press) was cemented.	From this study, Implant-supported or tooth supported three-unit fixed prostheses made of ZLS can be used to successfully restore cases of posterior partial edentulism.

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Effects of COVID-19 Preoperative Mouthrinses and Different Beverages and on Surface Alteration of Polyetheretherketone (PEEK)

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Abstract

Objectives: to compare the color change and surface roughness of polyetheretherketones (PEEK) immersed in various beverages and mouthrinses for 7 days.

Methods: the specimens were divided into 6 groups, 10 pieces per group, and each group was immersed in different solutions as followed: coffee, cola, red wine, distilled water, 0.5% povidone iodine, and 1% hydrogen peroxide. A color change (ΔE*ab) was measured in each sample before and after 7 days of immersion in different solutions. At a significance level of 0.05, color change data were analyzed using one-way ANOVA and pairwise comparisons with the Games-Howell method, and surface roughness changes were analyzed using the Wilcoxon Sign-Rank test.

Results: immersion of PEEK in 0.5% povidone iodine caused the most color change, followed by red wine when continuously immersed for 7 days. However, immersion in different types of solutions did not affect the surface roughness of PEEK.

Conclusions: After 7 days of immersion, 0.5% povidone iodine and red wine caused color change in PEEK with no change in surface roughness.

Keywords: betadine gargle, COVID-19, discoloration, polyether ether ketone, stain

Introduction

Removable partial dentures (RPDs) have been widely used to replace natural teeth in patients who have lost some teeth. Metal-based RPDs are the most common type and mainly made of cobalt-chromium (CoCr) providing high strength and stiffness, conducting heat and cold for a more natural experience, and being resistant to corrosion.[1] However, it has esthetic limitation due to the gray-colored. Because of its characteristics such as heavy-weight, metallic taste, some patients may develop intolerance to metal. Currently, a new polymer material, polyether ether ketone (PEEK), has been introduced to replace metal in patients with a history of metal allergy. Patients could be more satisfied with this material because of its esthetically tooth-color and lighter weight compared to CoCr.[2-4]

PEEK is a high-performance thermoplastic polymer, consisting of an aromatic backbone molecular chain, interconnected by ketone and ether functional groups. PEEK used in prosthodontics can be divided into two types, pure PEEK and modified PEEK. Pure PEEK is unfilled polymer with 100% of PEEK. The color of pure PEEK or unfilled PEEK is light brown[5] with good biocompatibility, good mechanical properties, high-temperature resistance, and good chemical stability.[6] Modified PEEK is white in color and consisting of either 80% PEEK with 20% titanium dioxide filler or 80% PEEK with 20% nanoceramic filler, with particle sizes of 300-500 nm.[7] Discoloration of dental prostheses can be caused by intrinsic factors such as resin matrix type, percentage and filler size, distribution of incorporated fillers, composition and polymerization mode, chemical reactions within the restorative material, age, and restoration processing mode, or extrinsic factors such as staining from adherent or penetrated by food, beverage, and mouth rinse colorants such as caffeine, anthocyanidins, tannins, and nicotine in smoking.[8] Given the past situation with spreading of SARS-CoV-2, preoperative mouthwash has played an important role in reducing oral viral and bacterial infections and become a routine preoperative procedure. It is recommended to gently gargle for 30 seconds in the oral cavity and 30 seconds in the back of the throat with either one of these following solutions: 1-3% hydrogen peroxide, 0.2-0.5% povidone iodine, 0.12% chlorhexidine.[9] Hydrogen peroxide has of bleaching potential, while providone iodine presents with dark brown color. These two solutions could have effect on the color of dental prosthesis if the patient has to use in a long period of time or routinely use in dental operation.

Color and surface roughness are important factors for the esthetic appearance of removable dental prostheses and patient satisfaction especially in RPDs made of PEEK. Several studies have reported that food and daily consumed beverages could negatively affect these properties. Heimer *et al.,* examined the effect on color stability and stain removal action of different cleaning methods on PEEK material, remaining in different media for 7 days, and revealed that PEEK was the most color stable material compared to polymethyl methacrylate (PMMA) and composite resin,[10] in line with the study of Papathanasiou *et al.,* by immersing the material in red wine, coffee, cola, and distilled water for 30 days, PEEK was the most color stable material compared to polyamide acetal resin and PMMA.[6] In some cases, for example full mouth rehabilitation cases, patients require several dental visits to complete the whole treatment. Most of cases, patients have to receive pre-prosthetic treatment such as periodontal cleaning, caries management, endodontically treatment, and pre-prosthetic surgery prior to the full mouth rehabilitation treatment. Every dental visit, patients have to use preoperative mouth rinse prior to start the treatment. Therefore, they will be facing with mouthrinse for a long period of time. However, the study regarding effect of preoperative mouth rinse on PEEK materials has not yet been clarified and never been compared to the effect of other beverages especially in long-term usage. Therefore, the purpose of this study was to evaluate the effect of preoperative mouth rinse and various beverages on color stability and surface roughness of a newly introduced PEEK polymer.

Materials and Methods

Cylindrical PEEK blanks provided by the manufacturer (Smile PEEK®, Pressing Dental SRL, San Marino, Italy) were prepared in a disc form with a diameter of 12 mm and a thickness of 2 mm for total 60 pieces. All disc-shape specimens were stored in dry conditions until finishing and polishing were done by one investigator at 2 surfaces of the specimens so an overall total surfaces were 120 surfaces. After qualifying the dimensions using a digital caliper (Mitutoyo Vernier Calipers, Mitutoyo, Tokyo, Japan) specimens were ground with 600-grit, 800-

grit, and 1200-grit waterproof silicon carbide paper using a rotary grinding machine (Buehler Metaserve Universal, Buehler Ltd., Lake Bluff, Illinois, USA). After that, they were cleaned with distilled water in an ultrasonic cleaner (Easy 10 Ultrasonic Cleaner, Elma Schmidbauer GmbH, Singen, Germany) and dried with tissue papers.

Ten randomly selected specimens were immersed for 7 days at 37°C and 100% relative humidity in one of the following solutions (n=20 surfaces/solutions): Coca-Cola (Coke®, Coca-Cola (Thai) Trading Co., Ltd., Bangkok, Thailand), black coffee (Birdy Black®, Malee group, Nakhon Pathom, Thailand), red wine (Charles Strong Reserve Classic Bin 991®, Cumulus Estate Wines, New South Wales, Australia), 0.5% Povidone iodine (BETADINE® Gargle, Mundipharma Ltd., Bangkok, Thailand), 1% Hydrogen peroxide (Siribuncha, Siribuncha Ltd., Bangkok, Thailand) and distilled water (Table 1). This period of immersion may correspond to 34 to 67 months of clinical services, based on an average daily exposure of 5 to 10 minutes to coffee or wine.[11] The pH of the solutions was measured using a pH indicator (SevenCompact pH meter S220, Mettler-Toledo (S) Pte Ltd, Singapore). Immersing solutions were renewed every 24 hours. Color and surface roughness measurements were performed before and after immersion. Before any measurement, specimens were rinsed with distilled water in an ultrasonic cleaner and dried with soft tissue paper.

Color measurements were performed using a spectrophotometer (ColorQuest XE, Hunter Associates Laboratory Inc., Virginia, USA). A custom-made black foam holder was fabricated for each specimen to standardize specimen positioning against the spectrophotometer head. The CIE L*a*b* system was used for color assessment. The CIE L*a*b* system represents a three dimensional color space with components of lightness (L), red-green (a), and yellow-blue (b). The average of 3 consecutive measurements in the center of specimens was calculated to yield L*, a*, and b* of each specimen before and after immersion. The total color change (ΔE) obtained was calculated for each specimen using the following equation:

$$\Delta E = [(\Delta L^*)2 + (\Delta a^*)2 + (\Delta b^*)^2]^{1/2}$$

where ΔL*, Δa*, and Δb* are the differences of L*, a*, and b* before and after staining.

Surface roughness determinations were measured by a contact profilometer (Surfcorder SE2300, Kosaka Laboratory Ltd., Tokyo, Japan) The cutoff value for surface roughness was 0.8 mm and the traversing distance of the stylus was 5 mm. The radius of the tracing diamond tip was 5 µm, and the measuring force and speed were 4 mN and 0.5 m/s, respectively. Three random readings at the center of each specimen were performed and the average value was calculated at baseline and after immersion. The changes of surface roughness parameters (Ra) were obtained by the difference between final and baseline values. One-way ANOVA and Games-Howell post hoc tests were used to assess differences in color change parameters among solutions at baseline and after immersion. The Wilcoxon signed rank test was used to assess differences in surface roughness change parameters for each solution at baseline and after immersion. Statistical analyses were performed using IBM SPSS Statistics 22 software at a 0.05 level of significance.

Results

The one-way ANOVA revealed that staining solution significantly affected color change. Games-Howell pairwise comparisons revealed significant differences in a color change of PEEK among solutions after immersion for 7 days. The ΔE value of PEEK after immersion in distilled water, red wine, cola, coffee, 0.5% povidone iodine, and 1% hydrogen peroxide were 0.55, 1.53, 0.42, 0.52, 6.59, and 0.55 respectively. (Table 2) Immersion of PEEK in 0.5% povidone iodine resulted in the significantly highest discoloration of specimens ($p<0.05$), followed by red wine ($p<0.05$). Cola caused the lowest discoloration, however, the color change was not significantly different

Table 1: A list of immersion solutions used in this study and their respective pH

Solution	pH	Brand
Coffee	6.42	Birdy Black, Malee group, Nakhon Pathom, Thailand
Red wine	3.42	Charles Strong Reserve Classic Bin 991, Cumulus Estate Wines, Australia
Coca-Cola	2.49	Coke (Thai) Trading Co., Ltd., Thailand
Povidone-Iodine	3.09	BETADINE® Gargle, Mundipharma Ltd.,Thailand
Hydrogen peroxide	3.49	Siribuncha, Ltd.,Thailand

(p>0.05) when compared with distilled water, coffee, and 1% hydrogen peroxide. (Figure 1)

The Wilcoxon test (α =0.05) was used to test the surface roughness of PEEK after immersion in different solutions for 7 days, and the results showed that the change in surface roughness of all groups of PEEK was not significantly different (p>0.05) (Table 3).

Discussion

This study examined the effect of immersion of PEEK in six challenge solutions on the color change and surface roughness. The first null hypothesis (no differences in color change among different solutions) was rejected for changes in color parameters but the second null hypothesis (no differences in surface roughness among different solutions) was accepted for changes in surface roughness parameters. Immersion of PEEK in various solutions for 7 days significantly affected the color of PEEK, 0.5% povidone iodine exhibited the most color change, followed by red wine, while distilled water, cola, coffee, and 1% hydrogen peroxide showed no significant difference among them. On the other hand, there was no significant difference in surface roughness after immersion in different solutions for 7 days.

Color differences (ΔE) detected by human eyes are normally non-discernible below ΔE values of 1 and only change into an unacceptable color change when ΔE is more than 3.3.[12] In this study, red wine showed a mean value of ΔE*ab at 1.53, which was considered clinically acceptable. whereas 0.5% of povidone iodine possessed the mean ΔE*ab value at 6.59, which was considered clinically unacceptable. However, the data was obtained from a laboratory experiment and the results could be different in clinical circumstances. Staining mechanism of povidone-iodine in PEEK has not been clearly described. These stains, containing not only iodine, but a polymeric complexing agent, are difficult to remove by the usual laundering techniques and currently available detergent products. A study by McNeme *et al.,* reported that immersion of acrylic in iodine caused discoloration. The authors recommend choosing an iodine-free solution to reduce changes in the aesthetics of dentures.[13] In addition, artificial teeth (PMMA) had been immersed in 10% povidone iodine for 2 hours 30 minutes to 10 days. The ΔE*ab result was in the range of 0.042-0.893[14], which was different from the results of this study. Because the materials used in the study were different.

Table 2: Means and standard deviations of ΔE*ab values after 7-day immersion

Solutions	n	ΔE*ab (mean±sd)	Min	Max
Distilled water	20	0.55±0.23^{a}	0.14	1.01
Red wine	20	1.53±0.57^{b}	0.27	2.68
Coca-Cola	20	0.42±0.29^{a}	0.03	0.97
Coffee	20	0.52±0.27^{a}	0.16	1.06
0.5 % Povidone Iodine	20	6.59±1.11^{c}	4.62	8.15
1% Hydrogen peroxide	20	0.55±0.28^{a}	0.21	1.28

Similar superscript lowercase letters represent significant differences among staining solutions

Table 3: Means median and standard deviations of surface roughness after in different solutions

Solutions	Surface roughness Ra (μm)				Wilcoxon Signed Rank test
	Before		After		
	(mean±sd)	median	(mean±sd)	median	Sig. (<0.05)
Distilled water	0.10±0.01	0.1	0.11±0.01	0.1	0.059
Red wine	0.09±0.03	0.1	0.09±0.03	0.1	0.305
Coca-Cola	0.09±0.02	0.1	0.11±0.02	0.1	0.066
Coffee	0.09±0.03	0.1	0.10±0.02	0.1	0.234
0.5 % Povidone Iodine	0.09±0.03	0.1	0.10±0.03	0.1	0.129
1% Hydrogen peroxide	0.09±0.02	0.1	0.11±0.03	0.1	0.059

In red wine, the color change was greater than coffee. Unlike the study of Papathanasiou *et al.,* and Polychronakis *et al.,* their results showed that red wine exhibited less discolor than coffee. Red wine contains natural pigments (anthocyanidin or tannin) in high alcohol concentration and low pH, causing chemical deterioration of the surface of the polymers and increase surface roughness. Thus absorbing stains occurs.[15,16] However, it is noted that color changes in red wines have been influenced by a number of factors, including duration, grape composition, fermentation, and storage conditions.[17] Therefore, it cannot be generalized with all brands of red wine to behave on polymer surface in the same manner. In this study, specimens immersed in red wine showed no difference in surface roughness. Despite cola showed the lowest pH in all solutions, but it caused less staining than red wine.

This study examined the surface roughness of PEEK before and after immersion in various challenge solutions and the results showed no difference in roughness after immersed in all solutions. It was found that the surface roughness of PEEK specimens was below the critical value (0.2 µm). If the surface roughness was above this critical value, it may cause bacterial accumulation.[18] Papathanasiou *et al.,* immersed PEEK in coffee, red wine, and cola for 30 days. The results showed no significant change in surface roughness in all groups. It could be explained that PEEK, used as filler-free, can be polished to a good smooth finish. and no filler particle delamination occurs.[6] In addition, Since PEEK is an inert semi-crystalline polymer, it possessed the resistant to high temperatures, chemically stable, low water solubility and water absorption, low surface energy, and low surface roughness after polishing.[6,8,10] Due to these properties, PEEK has low adsorption and absorption of color stains and is supposed to resist to acidic solutions such as cola and red wine.

This is an *in vitro* study, the result could be different in clinical circumstances. There are more challenges inside the mouth, such as saliva, pH levels, temperature changes, parafunctional habits, food consumption behavior, cleaning which such factors may affect the staining. In addition, the samples were immersed at 37°C, which simulated the oral temperature. However, cola, red wine, and coffee are often consumed in cold or hot condition, which are different from oral temperature. Further *in vivo* studies are needed to determine the staining of PEEK in various solutions that cause staining. Also, the mechanism of iodine staining on PEEK should be further investigated.

Conclusions

Based on the results of the present *in vitro* study, the following conclusions were drawn:

1. povidone iodine (0.5%) caused the highest color changes of PEEK among different immersing solutions, followed by red wine.
2. PEEK surface roughness was not influenced by immersing solutions.

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Conflicts of Interest

The authors declare no conflict of interest.

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Comparison of the Cost Effectiveness of Orthognathic Surgery Treatment Between Orthodontic-first and Surgery-first Approaches in the Surgical Phase in Thammasat University Hospital

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Abstract

Objectives: This retrospective cohort study aims to evaluate the costs and advantages of the surgical phase of the surgery-first approach (SFA) versus the orthodontic-first approach (OFA).

Methods: Orthognathic surgery has been described as having two concepts: an orthodontic-first approach and a surgery-first approach. However, there was no consensus on which group has the best cost effectiveness in the surgical treatment phase. In total, 70 patients were treated; half of the patients were treated via the SFA, and another half were treated via the OFA. The information collected included operation cost, operation time, total hospital cost, and length of hospitalization. Effectiveness was determined by quality of life, which was measured with the Orthognathic Quality of Life Questionnaire Thai Version (OQLQ) before and then 6 months after treatment. The cost effectiveness was assessed with an incremental cost effectiveness ratio (ICER) and an incremental time effectiveness ratio (ITER).

Results: The results indicated the intervention cost and time of SFA were slightly higher but more effective than those of OFA. However, the operation cost (p=0.375), operation time (p=0.556), total hospital cost (p=0.363), and length of hospitalization (p=0.643) and OQLQ scores (p=0.344) of both groups were not significantly different.

Conclusions: The intervention cost and time of SFA were slightly higher but more effective than those of OFA. Depending on the result of this study, SFA treatment planning was a good choice for orthognathic treatment.

Keywords: cost effectiveness, orthodontic-first approach (OFA), orthognathic quality of life questionnaire (OQLQ), quality of life, surgery-first approach (SFA)

Introduction

Dentofacial deformities have created both physiological and psychological problems in those where they are present. The treatment of choice to correct dentofacial deformities is orthognathic surgery.[1] Orthognathic surgery approach has been described as bifurcating into two, competing, concepts: an orthodontic-first approach and a surgery-first approach. The orthodontic-first approach (OFA) is used to correct the worsened occlusion and prepare the appropriate occlusion before orthognathic surgery. This is time-consuming. The risks of this are that teeth and periodontal tissue may be damaged by the amount of time spent. The consequences could include gingival recession and root resorption. Moreover, the presurgical phase can deteriorate the facial profile and oral function. A surgery-first approach (SFA) is performed without a presurgical phase and then followed by regular orthodontic treatment. This is time-saving. One benefit is that it can allow an early response to patient needs. SFA is an alternative treatment plan for orthognathic surgery, the purpose of which is to shorten the overall orthodontic treatment period. Another benefit of this technique is the regional accelerated phenomenon (RAP), which can improve postsurgical orthodontic tooth movement.[2]

A health economic evaluation is performed to analyze the health and health care treatment. This is a set of analytical techniques to compare and decide on which treatment is the best, usually performed in a health care center. Ultimately, health economics is about maximizing social benefits obtained from limited resources.[3] Cost effectiveness analysis is one of the methods of health economic evaluation to compare alternative medical interventions with their cost and outcomes (effectiveness). It is the ratio of the difference in cost to the difference outcomes between the two interventions. Therefore, the cost effectiveness ratio can be interpreted as the additional cost per unit of health benefit gained from one medical intervention to another.[4]

The cost effectiveness ratio is that of the cost (C) to the effectiveness (E) of the medical intervention. The costs of intervention can be expressed in monetary units, such as Thai baht or duration of treatment, while the effectiveness of intervention is expressed by the benefits from the intervention. These benefits include the number of deaths avoided, the survival year, or the quality of life of patients. For example, the C/E ratio can be expressed as dollars/life saved or Thai baht/quality of life gained.[4]

Orthognathic surgery can improve the quality of life (QOL).[5] QOL can be referred to both as the effectiveness in the cost effectiveness ratio (one of the tools to measure the satisfaction of the patient is by questionnaire) and as the quality of life of patients. The most popular questionnaire to evaluate quality of life is "the 22-item Orthognathic Quality of Life Questionnaire (OQLQ)", which concerns both physical and psychological impacts.[6,7]

Although previous studies have shown that the SFA's elimination/shortening of the presurgical phase, coupled with the postoperative accelerated orthodontic tooth movement by RAP, creates shorter treatment times than OFA, some studies have shown that the SFA group's operating time and costs were slightly higher than those of the OFA group.[7,8] However, there is only one research study about the difference in cost effectiveness between SFA and OFA.[8] Furthermore, there is no consensus on which group has the best cost effectiveness in the surgical treatment phase. Moreover, it has not been studied in Thailand before. The aim of this study is to evaluate the cost effectiveness in patients with dentofacial deformities and treatment with orthognathic treatment in the surgical treatment phase, comparing OFA and SFA.

Materials and Methods

This retrospective cohort study recruited 70 patients (SFA=35, OFA=35) who had dentofacial deformities. Sample size is calculated by G*Power 3.1.9.7 software using data from a similar previous study.[8] Power was conducted at 95%. Patients who underwent orthognathic surgery, double jaw surgery without genioplasty, by one surgeon at the Department of Oral and Maxillofacial Surgery, Thammasat University Hospital, a single center. The ethic has been approved by the Human Research Ethic Committee of Thammasat University (Science), Pathum Thani, Thailand, Project Code 141/2565. The date of approval is April 28, 2023.

The inclusion criteria included patients aged between 18-60 years old, which have dentofacial deformity and scheduled for orthognathic surgery, underwent bimaxillary orthognathic surgery including Le Fort I (1 piece) osteotomy for maxilla and bilateral sagittal split osteotomy (BSSO) for mandible. The patients underwent orthognathic surgery at Thammasat University Hospital from 2018 to 2022. The exclusion criteria were patients

with congenital disease or syndrome with maxillofacial deformity such as cleft lip and palate, a mental disease. Patients who had maxillofacial transformation caused by an injury or cancer, temporomandibular joint dysfunction, previous orthognathic surgery, systemic disorders that affect the patient's quality of life.

To determine the two groups were balanced, patient characteristics were compared between groups, including age and quality of life scores. The primary outcome variables are cost, time, and quality of life. The cost effectiveness of the SFA and OFA treatments is the secondary outcome variable.

The cost effectiveness analysis was divided into two parts: including the incremental cost effectiveness ratio (ICER), and the incremental time effectiveness ratio (ITER). The ICER is the ratio of the different costs (C) between SFA and OFA to the different effectiveness (E) of SFA and OFA. Similarly, the ITER is the ratio of the different time spent on treatment between SFA and OFA to the different effectiveness of SFA and OFA.[8] In this study, the costs (C) measured are only direct cost, including intraoperation costs (material costs, billed minutes) and total cost of hospitalization (intraoperation costs and pharmacy/hospital costs). All expenditures are expressed in monetary units (Thai baht).

The time of treatment in this study is composed of operation time (minutes), and length of hospitalization (days). The effectiveness is defined in terms of the change in QOL and will be used to calculate the ICER and ITER. The OQLQ score was assessed before treatment (T_0) and 6 months after orthognathic surgery (T_6). OQLQ data at T_0 and T_6 was available.

The ICER and ITER equations are shown below.[4,9]

$$ICER_{mean} = \frac{mean(C_1)–mean(C_2)}{mean(E_1)–mean(E_2)}$$

C1 = Cost of treatment in SFA in the surgical phase
C2 = Cost of treatment in OFA in the surgical phase
E1 = Effectiveness of SFA (the different OQLQ score between T_0 and T_6 of SFA)
E2 = Effectiveness of OFA (the different OQLQ score between T_0 and T_6 of OFA)

$$ITER_{mean} = \frac{mean(T_1)–mean(T_2)}{mean(E_1)–mean(E_2)}$$

T1 = Time of treatment in SFA in the surgical phase
T2 = Time of treatment in OFA in the surgical phase
E1 = Effectiveness of SFA (the different OQLQ score between T_0 and T_6 of SFA)
E2 = Effectiveness of OFA (the different OQLQ score between T_0 and T_6 of OFA)

The mean of ICER during the surgical phase was reported in terms of the ICER of intraoperation cost and the ICER of total cost of hospitalization. The mean of ITER during the surgical phase was reported in terms of ITER of operation time and ITER of length of hospitalization.

To interpret the data, if the intervention costs were higher and have less effectiveness than the comparator, the intervention was said to be 'dominated', but if the intervention costs were lower and had more effectiveness than the comparator, the intervention was said to be 'dominant'. However, the most common scenario was that a new strategy improves clinical results at increased cost, it was called "trade-off". In trade-off scenarios, the decision-making depends on willingness to pay.[4]

The 22-item Orthognathic Quality of Life Questionnaire (OQLQ)

The OQLQ questionnaire (Thai version) has 22 items that were graded on a four-point scale, with 1 meaning "it bothers you a little" and 4 meaning "it bothers you a lot," and 2 and 3 meaning "it bothers you somewhere in the middle." NA= "indicates that the statement does not apply to you or bothers you". The overall OQLQ scores ranged from 0 to 88. A lower number suggested a better quality of life, while a higher score indicated a worse quality of life. The 22 questions were divided into four groups: awareness of dentofacial esthetics (items 8, 9, 12, 13 scoring 0-16); facial esthetics (items 1, 7, 10, 14 scoring 0-20); oral function (items 2-6 scoring 0-20); and social aspects of dentofacial deformity (items 15-22 scoring 0-32).[6,10] The OQLQ scores were collected at the time of presurgical treatment (T_0) and at 6 months after the surgical treatment (T_6).[6,11]

Statistical analysis

All variables were described as the mean with standard deviation (SD) to compare the different time, cost and OQLQ scores of treatments between SFA and OFA groups. The data were analyzed statistically with Mann-Whitney U test, with *p*-value less than 0.05 considered significant.

To compare the difference in OQLQ scores between before and after treatment of each group, the data were analyzed statistically with an independent *t*-test, with *p*-value less than 0.05 considered significant. All data analysis were conducted by using the IBM SPSS Statistics 22 software.

To compare the cost effectiveness of the two groups: SFA and OFA groups was used ICER and ITER to analyze.

Results

Descriptive statistics

The review of medical records and patient screening was described in Table 1. There were 70 patients (24 men and 46 women); half of the patients were treated via the OFA and another half were treating via the SFA. The patients in these two groups were similar in respect to age (mean 26.29 years in the OFA group, mean 24.77 years in the SFA group) and OQLQ score at baseline (p=0.46). The type of deformity was 7 patients of skeletal II and 28 patients of skeletal III in both groups of SFA and OFA. The two groups were significantly balanced with no differences in terms of ages, OQLQ scores at baseline, or number of samples of deformity type.

Table 1: The demographic data were compared using Pearson's chi-squared test for gender, the independent *t*-test for age, and average OQLQ score before surgery (T_0). The type of deformity is also exhibited in the table

	OFA	SFA	Total	*p*-value
Gender (n,%)				
Male Female	17 (48.6%) 18 (51.4%)	7 (20%) 28 (80%)	24 46	0.012 (Pearson's chi-squared test)
Age (years)				
Mean ±SD	26.29±5.839	24.77±4.959	25.53±5.431	0.246 (Independent *t*-test)
Type of deformity				
Skeletal II (n, %) Skeletal III (n, %)	7 (20%) 28 (80%)	7 (20%) 28 (80%)	14 (20%) 56 (80%)	
Average OQLQ score before surgery (T_0)				
Mean±SD	51.83±2.87	49.34±3.04		0.463 (Mann-Whitney U test)

OQLQ=orthognathic quality of life questionnaire; OFA, orthodontic-first approach; SFA=surgery-first approach
n, number of samples; SD, standard deviation.
The significance level was less than 0.05.

Table 2: Comparisons of cost and time between surgery-first approach (SFA) and orthodontic first approach (OFA), compared using Mann-Whitney U test was used. The quality of life questionnaire (OQLQ) score after 6 months of surgery is also reported in the table

	OFA	SFA	*p*-value
n	35	35	
OQLQ score after surgery 6 months			
Mean±SD	29.54±20.35	24.40±16.67	0.301 (Mann-Whitney U test)
Operation cost (Material costs, billed minutes; Baht)			
Mean±SD	69703.028±8349.08	71420.43±12300.73	0.375 (Mann-Whitney U test)
Hospital cost (Operative cost and pharmacy/hospital costs; Baht)			
Mean±SD	97090.96±9848.57	100052.72±14984.16	0.363 (Mann-Whitney U test)
Operation time (minutes)			
Mean±SD	329.142±76.07	341.971±82.45	0.556 (Mann-Whitney U test)
Length of hospitalization (days)			
Mean±SD	4.09±0.61	4.03±0.86	0.643 (Mann-Whitney U test)

n, number of samples; SD, standard deviation.
The significance level was less than 0.05.

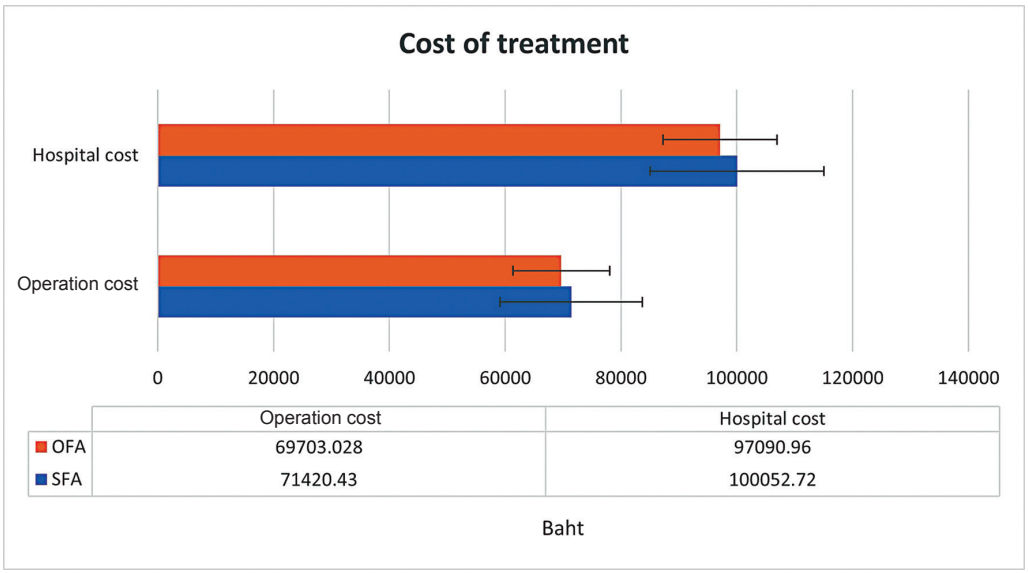

Figure 1: Comparisons of cost between surgery-first approach (SFA) and orthodontic-first approach (OFA)

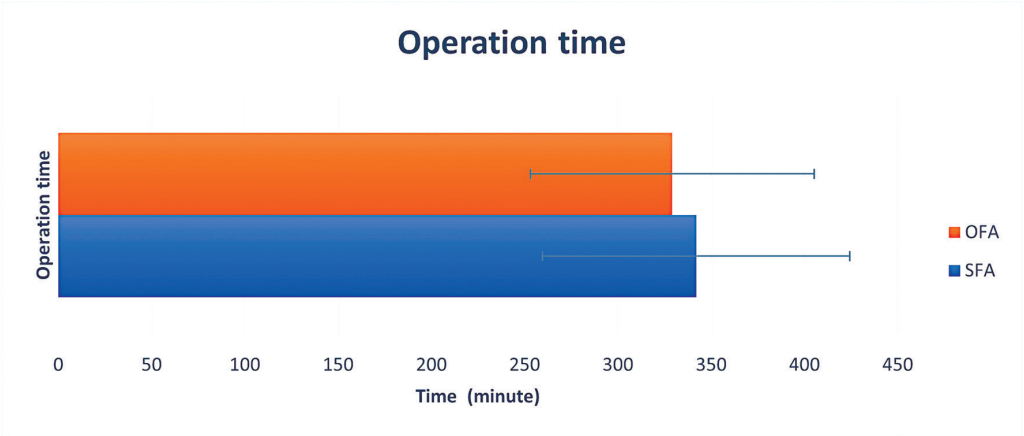

Figure 2: Comparisons of operation time between surgery-first approach (SFA) and orthodontic-first approach (OFA)

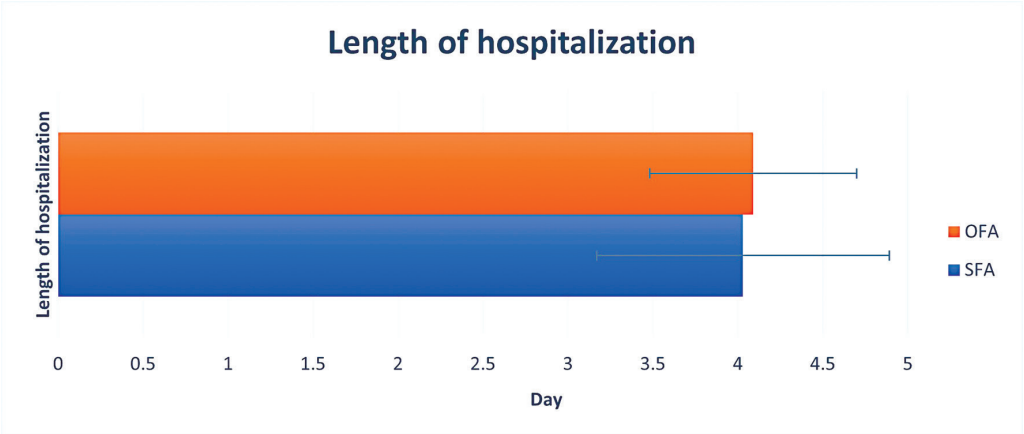

Figure 3: Comparisons the length of hospitalization between surgery-first approach (SFA) and orthodontic-first approach (OFA)

Comparison of time and cost between the SFA and OFA

The cost and time comparison between the SFA and OFA groups was shown in Table 2, Figures 1, 2, and 3. The operation cost, hospital cost, and operation time were slightly higher in the SFA group than the OFA group. However, there were not significant differences between the SFA and OFA groups in terms of operation cost (p=0.375), hospital cost (p=0.363), or operation time (p=0.556). The length of hospitalization was not different between the SFA and OFA groups.

Comparison of OQLQ scores between the SFA and OFA

The changing OQLQ scores of patients in the OFA and SFA groups was described in Table 3 and Figure 4. The mean±SD of change in OQLQ scores were 20.63±14.27 and 25.60±19.74 for patients in the OFA group and the SFA group, respectively. The difference in change in OQLQ score in the SFA more than OFA group, which mean the QOL in SFA group improved more than OFA. However, the difference between the groups was minimal, and there was no significant difference (p=0.344) between the groups. Moreover, there was no significant difference in terms of facial esthetics, oral function, awareness of dentofacial esthetics, or social aspects of dentofacial deformity between patients in the OFA and SFA groups.

Comparison of cost effectiveness between the SFA and OFA

The results of the cost effectiveness analysis were presented in Table 4. The ICER of operation cost in the SFA group compared with the OFA group is 345.55 baht per additional ΔOQLQ point gained, and the ICER of hospital cost is 595.93 baht per additional ΔOQLQ point gained. The ITER of operation time in the SFA group compared with the OFA group was calculated as 2.58 minutes per additional ΔOQLQ point gained, and the ITER of length of hospitalization in the SFA group revealed a reduction in time of 0.012 days per ΔOQLQ point gained when compared to the OFA group. It means the intervention costs and time of the SFA group in the surgical phase result in improved QOL at an increased cost and time compared to the OFA group.

Discussion

Orthognathic surgery is one of the treatments used to correct dentofacial deformities. The OFA and SFA are concepts of orthognathic treatment. Both have advantages and disadvantages, but the SFA is outstanding in terms of time savings. J. Hu *et al.,* showed that the SFA group had a shorter overall treatment duration when compared to the OFA group.[8] Although the SFA uses a shorter total duration than the OFA, the previous study showed the intraoperation time of SFA is significantly longer than OFA.[8] However, in this study, the data showed that the intraoperation time of SFA was slightly longer than OFA but without statistical significance.

A possible explanation for the higher intraoperative duration in SFA might be an unstable occlusion during surgery which might affect the determined occlusion.[8] In OFA, the occlusion and interference were corrected before surgery. In SFA, the occlusion during surgery mainly depends on the occlusal splint[12]; any minor error in the device can affect intraoperation treatment. The expert opinion team in our institute suggested that the minimally higher amount of operation time in SFA may be caused by the occlusal plane's poor alignment, which makes the surgery usually move in 360 degrees of rotation more than in OFA. The OFA usually moves the segment of the jaw following the occlusal plane, which is prepared before surgery. However, the SFA group does not prepare the occlusal plane before surgery; the surgical plan usually moves the occlusal plane with a clockwise or counterclockwise rotation. The rotation of the maxillomandibular complex (MMC) to change the occlusal plane has increased bone management at the surgical site and made the operation more complex. Additionally, predicting the soft tissue esthetic and final occlusion is harder in SFA than in OFA. W. S. Jeong *et al.,* suggests that if a single surgeon performed all approaches with identical techniques and a proper surgical plan, the effect of surgical factors appears to be minimal.[13] Similarly to previous study[8], the terms of duration of hospitalization and postoperative recovery were not different between the two groups.

Cost of treatment in the surgical phase consisted of both operation costs and hospital costs. This study shows that the operation cost in SFA was slightly higher than in OFA due to the slightly longer intraoperation time. The more time spent on general anesthesia, the higher the cost.

Table 3: Comparison of different OQLQ scores (total and subdomain) before surgery and 6 months after surgery, using the independent *t*-test

$\Delta OQLQ_{T1-T6}$			
Domain	**OFA Mean difference±SD**	**SFA Mean difference±SD**	***p*-value**
Social (0-32)	8.26±8.14	8.37±7.77	0.958
Esthetic (0-20)	5.00±5.72	4.03±5.95	0.513
Function (0-20)	2.94±6.46	4.29±5.75	0.413
Awareness (0-16)	5.63±5.13	7.20±5.72	0.176
Total (0-88)	20.63±14.27	25.60±19.74	0.334

OQLQ=orthognathic quality of life questionnaire
The significance level was less than 0.05.

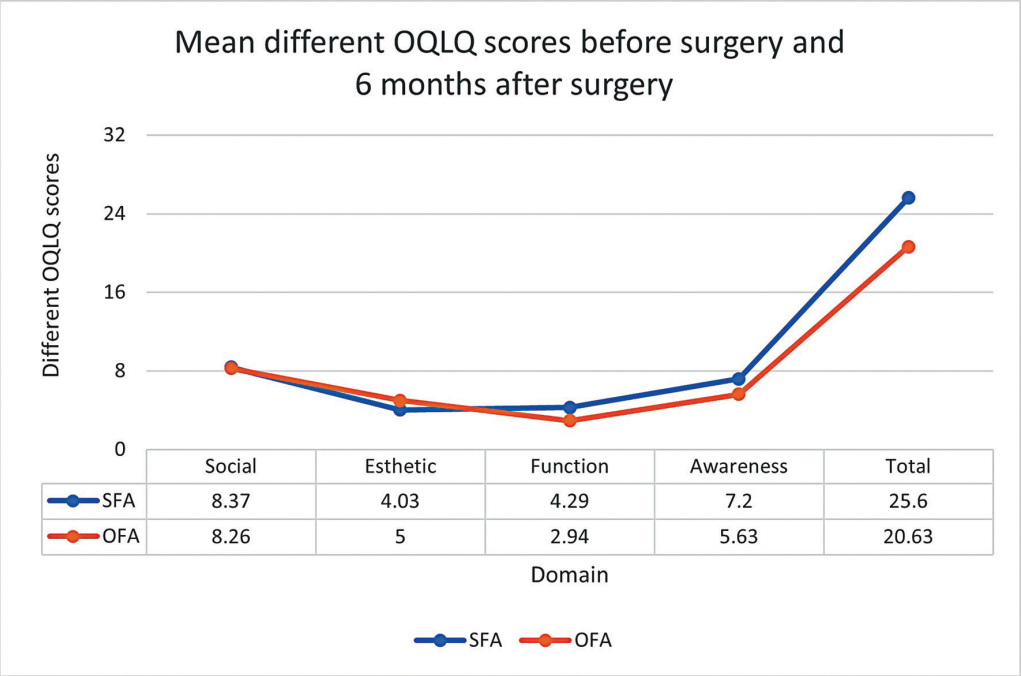

Figure 4: Comparison of different OQLQ scores (total and subdomain) before surgery and 6 months after surgery

Thus, the overall hospital cost was also be increasing. However, there were no significant differences between these two groups. The result was in accordance with the previous study.[8]

In this study, the OQLQ scores at before treatment (T_0) of SFA and OFA were compared and showed no significant difference. After surgery, at 6 months (T_6), the different OQLQ scores compared between before and after surgery show the QOL in the SFA group improved more than that in the OFA group. But the difference in OQLQ scores between the groups were minimal, and there were no significant difference between the groups in each domain.[14] The results were similar to previous.[14,15] While the skeletal classification was mostly based in class I, II, and III patterns, no studies had reported a significant difference in the total OQLQ score between these groups.[16-19] It had been reported that gender affects differences in the outcome of OQLQ between males and females.[16] However, many studies did not find significant variation in QOL associated with gender.[1,17,20,21]

To compare the cost effectiveness between SFA and OFA, the previous study showed that in terms of time spent in the operating room, the time spent in the SFA was slightly more than that of the OFA.[8] This study's findings resemble previous studies; data showed the ICER and ITER of operation costs, hospital costs and operation time of SFA was slightly more than OFA. Although the intervention costs and time of SFA were slightly higher but more effective than the comparator. It means the intervention costs and time of the SFA group in the surgical phase resulted in improved QOL at an increased cost and time compared to the OFA group. This balance of benefits

Table 4: Comparison of cost effectiveness of the surgical first approach (SFA) and the orthodontic first approach (OFA)

Varibles	Mean±SD	Between-treatment increment	Mean±SD different OQLQ score between T_0 and T_6	Between-treatment incremental	ICER or ITER
Cost effectiveness of operation cost					
SFA	71420.43±12300.73	1717.402	25.60±19.74	4.97	345.55 (Baht/ΔOQLQ)
OFA	69703.028±8349.08		20.63±14.27		
Time effectiveness of operation time					
SFA	341.971±82.45	12.829	25.60±19.74	4.97	2.58 (min/ΔOQLQ)
OFA	329.142±76.07		20.63±14.27		
Cost effectiveness of hospital cost					
SFA	100052.72±14984.16	2961.76	25.60±19.74	4.97	595.93 (Baht/ΔOQLQ)
OFA	97090.96±9848.57		20.63±14.27		
Time effectiveness of length of hospitalization					
SFA	4.03±0.86	-0.06	25.60±19.74	4.97	-0.012 (day/ΔOQLQ)
OFA	4.09±0.61		20.63±14.27		

ICER, incremental cost effectiveness ratio; ITER, incremental time effectiveness ratio; SD, standard deviation. The significance level was less than 0.05

and limitations, in terms of economics, was called "trade-off". In trade-off scenarios, the decision-making depends on willingness to pay.[9]

In order to compare the intra- and post-operative risks of SFA with OFA, it was typical for complications from both operations to occur, including bleeding, oronasal communication, perforation of the endotracheal tube, changes in neurosensory changes, periodontal damage, tissue necrosis, and infection.[22] Although there was not much research on SFA complications, all the approaches were able to refer to those technique complications indirectly. SFA-related complications included the existence of an impacted lower third molar, bonding failure, and extensive surgical movements to allow for a post-operative decompensation of the teeth. Because segmental osteotomies were frequently required with this procedure, the SFA group may be slightly more susceptible to complications. However, as surgical skills and knowledge improved, these problems became less prevalent. It had been demonstrated by several authors that, when performed according to basic principles and a meticulous treatment plan, multisegmental surgery may be safe and had only a few minimal problems.[23,24]

There were some limitations concerning the study's findings. The number of patients enrolled here was relatively small, and the data were collected retrospectively, which might lead to bias. The study analysis was conducted in a government-supported tertiary referral dental hospital; it may not represent the data from a private hospital. This study concerns only the surgical phase of orthognathic treatment; it may be better to do a long-term study of total treatment time in the future, which concerns the timing of the pre-surgical phase, the surgical phase, and the post-surgical phase.

Conclusions

In conclusion, the comparison of the cost effectiveness of SFA and OFA in the surgical phase of orthognathic surgery in the study showed that the intervention costs and time of SFA were slightly higher but more effective than those of OFA. However, the cost, time, and OQLQ scores of both groups did not show significant differences. Thus, if the proper criteria are to use both SFA and OFA, the decision to plan treatment depends on the preferences of the patient and clinician. Although the previous study showed significantly more intraoperation time spent in the SFA group, this study shown no significant difference between SFA and OFA. Moreover, the SFA had higher outcomes (QOL score). Depending on the result of this study, SFA treatment planning was a good choice for orthognathic treatment.

Author Contributions

Conceptualization, methodology, formal analysis, original draft preparation were handled by P.C.; project management and review and editing of the writing were handled by S.P., C.O., and N.C. The manuscript's published form was approved by all authors once they had read it.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of Thammasat University (Science), Pathum Thani, Thailand (protocol code 141/2565 and date of approval April 28,2023).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patients to publish this paper.

Data Availability Statement

Not applicable

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Conflicts of Interest

The authors declare no conflict of interest.

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Comparing the Effectiveness and Salivary Levels of TNF-alpha in Patients with Oral Lichen Planus Treated with Topical Clobetasol Propionate and Fluocinolone Acetonide

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Abstract

Objectives: The purpose of this study was to compare the effectiveness and salivary levels of tumor necrosis factor-alpha (TNF-α) in patients with oral lichen planus (OLP) treated with topical clobetasol propionate (CP) and fluocinolone acetonide (FA).

Methods: A total of 26 patients diagnosed with erosive-atrophic OLP were randomly divided into 2 groups: the first group received CP 0.05%, and the other received FA 0.1%. Pain scores, clinical scores, and saliva samples from the patients were collected for analysis both prior to treatment initiation and after 4 weeks. Salivary TNF-α levels were evaluated using an immunology multiplex assay. The Wilcoxon signed-rank test and the Mann-Whitney U test were used for intra-group and inter-group comparisons, respectively.

Results: Both treatments showed significant reductions in pain scores, clinical scores, and salivary TNF-α levels compared with the pre-treatment values ($p<0.05$). After 4 weeks of treatment, CP 0.05% demonstrated a greater reduction in clinical score compared with FA 0.1% ($p<0.05$).

Conclusions: CP 0.05% and FA 0.1% effectively treat OLP. CP 0.05% demonstrated a quicker clinical score reduction than FA 0.1% over four weeks. Additionally, both steroids reduced salivary TNF-α levels, which could indicate the possibility of using disease-related biomarkers for monitoring.

Keywords: clobetasol propionate, fluocinolone acetonide, oral lichen planus, saliva, tumor necrosis factor-alpha

Introduction

Oral lichen planus (OLP) is a chronic inflammatory disease of oral mucosa. Patients typically experience a burning sensation, oral discomfort, and pain.[1-3] The exact etiology and pathogenesis of OLP have not been fully understood; however, several studies revealed an association with a T-cell-mediated immune disease in which cytotoxic CD8+ T cells trigger apoptosis of the oral epithelial basal cells.[1,4]

Topical steroids are commonly used for treating OLP due to their anti-inflammatory and immunosuppressive properties; they provide effective therapy that is cost effective and has minimal side effects.[5-8] Among these steroids, fluocinolone acetonide 0.1% (FA) is a potent medication listed in the Thailand National List of Essential Medicines and has been widely used for treating OLP in Thailand. Studies have shown that FA 0.1% completely heals OLP lesions in 50-73% of cases.[9,10] Recent research has highlighted the potential benefits of using ultrahigh-potency steroids such as clobetasol propionate 0.05% (CP) for OLP treatment; these investigations have demonstrated its success at reducing symptoms and clinical lesions.[8,11,12] CP 0.05% is not readily available in Thailand. Nevertheless, Chiang Mai University's Faculty of Pharmacy has the capability to manufacture it. Moreover, there have been only a limited number of studies directly comparing the effectiveness of FA and CP in treating OLP lesions.

Numerous studies have investigated biomarkers associated with the pathogenesis, progression, diagnosis, and prognosis of OLP, with a specific focus on cytokines as potential tools.[13] Among these cytokines, TNF-α has received considerable attention.[14] Several studies indicate that in patients with OLP, both salivary or serum TNF-α levels and the count of TNF-α-producing cells on tissue biopsy increase compared to healthy controls.[15] However, saliva-based tests can serve as a cost-effective and non-invasive method for measuring TNF-α levels in OLP patients.[13,16] According to Pezelj-Ribaric *et al.,*[17] concentrations of salivary TNF-α vary across different clinical types of OLP, with the heightened production of TNF-α in saliva evidently reflecting clinical changes and correlating with the severity of OLP. Moreover TNF-α levels have been observed decrease following glucocorticoid treatment. This fact suggests that salivary TNF-α levels might serve as a means of monitoring disease progression.[18] Thus, examining potential biomarkers to evaluate treatment responses with topical steroids presents an intriguing. This study sheds light on these critical aspects by comparing the efficacy of CP 0.05% and FA 0.1% in treating erosive-atrophic OLP at reducing pain levels, clinical scores, and TNF-α expression in the saliva for the treatment of OLP.

Materials and Methods

Study design

Patients were recruited from the Oral Medicine Clinic at the Faculty of Dentistry, Chiang Mai University, Thailand, between July 2022 and June 2023. A randomized, double-blind clinical trial was conducted, and the study protocol received approval from the Human Experimentation Committee of the Faculty of Dentistry at Chiang Mai University (No. 46/2021) and the Thai Clinical Trials Registry (TCTR20220705003). Before the study commenced, all patients were fully informed of the study's details and provided written consent to participate.

Participants

The inclusion criteria were as follows: (1) Patients were 18 years of age or older with a definitive diagnosis of OLP based on the 2003 modified WHO criteria,[19] (2) patients had not history of taking drugs that have been reported to cause lichenoid drug reactions, and the OLP lesion was not adjacent to or in contact with a dental restoration, (3) patients had neither other oral mucosal lesions nor a history of lichenoid-related systemic conditions.

The exclusion criteria were as follows: (1) Patients who had been given systemic or topical steroid treatments for oral lesions within the past three months, (2) patients who were pregnant or breast-feeding, (3) patients with a history of smoking or alcohol consumption, (4) patients who had used non-steroidal anti-inflammatory drugs within 14 days prior to the start of the study, (5) Patients who wore removable dentures but refused to remove them at all times during the study period.

The sample size of 12 patients in each group was statistically calculated as the minimum sample size, based on a previous study.[14] This calculation considered a power of 80% ($z\beta=0.84$) and a 95% confidence interval ($z\ \alpha/\ 2=1.96$). Therefore, 26 patients were included to account for any potential dropouts.

Interventions

The patients underwent screening, and their data were recorded. Subsequently, they were randomly assigned to one of two groups using stratified randomization based on sex and age. Each group received either clobetasol propionate gel 0.05% or fluocinolone acetonide in orabase 0.1% topically, four times daily for a duration of 4 weeks. The medications were provided in identical preparations and were placed in blinded containers by the Faculty of the Pharmacy Department at Chiang Mai University. Patients were instructed to apply the medication four times a day: three times after meals and once before bedtime. Additionally, patients were advised to abstain from eating or drinking for 30 minutes after applying the medication. The patients'-maintained diaries were utilized to monitor their treatment.

Assessment of treatment effectiveness

Evaluations were conducted both before and 4 weeks after the treatment. Each visit included a pain assessment, clinical evaluation, and collection of saliva samples. To determine the symptomatology score, a visual analogue scale (VAS) was used. The VAS consisted of a 10-point scale ranging from 0 (no pain) to 10 (most severe pain). During each visit, patients were instructed to indicate the number that corresponded to their pain level. The clinical response of the lesion was assessed using the Thongprasom criteria (TC).[10] The scoring ranged from 0 (no lesion, normal mucosa) to 5 (white striae with erosive area more than 1 cm^2), with various scores for different lesion characteristics. The scoring was performed by one specialist in oral medicine (Thai Board of Oral Diagnostic Sciences Certification) on the most severe site of the lesion throughout the study period. Following treatment completion, we assessed the disease remission (the difference between baseline and endpoint scores numerically indicates clinical and symptomatic improvement) based on the following criteria: (1) Complete remission (CR): no or very mild symptoms; disappearing lesions; or mild white striae, (2) Partial remission (PR): reduced symptoms, mild white striae, and mild erythematous area, (3) No response (NR): symptoms persisted with no improvement or worsening of the lesions.[10]

Saliva collection and cytokine assessment

Whole unstimulated saliva (WUS) was collected between 9:00 and 11:00 A.M. using established procedures.[20] Immediately after collection, the samples were stored at -80ºC until further analysis.[17,21] The tubes containing WUS were then centrifuged at 12,000 rpm for 20 minutes at 4ºC, and the resulting supernatants were utilized for the assays. TNF-α levels in saliva were measured using a Luminex 200 instrument and the MILLIPLEX MAP HCYTOMAG-60K-04 kit (Millipore, Billerica, MA, USA). The immunological multiplex test was conducted at the Merck Thailand Laboratories Service Center, adhering to the manufacturer's instructions, and utilizing MagPix software xPonent/Analyst. A standard curve was generated using the standard solution provided in the kit, and all procedures were performed in accordance with the manufacturer's guidelines. The test was conducted in duplicate, and the results were reported in picograms per milliliter (pg/ml).[22,23]

Statistical analysis

We used the median (first quartile, third quartile) for quantitative variables and presented the qualitative data as frequencies and percentages. VAS, clinical scores, and salivary TNF-α levels had a nonparametric distribution. The Mann-Whitney U-test assessed group differences, and the Wilcoxon signed rank test confirmed pre- and post-treatment significance. SPSS (version 26.0; IBM Corp., Armonk, NY, USA) conducted all statistical analyses. The significance level was $p<0.05$.

Results

Twenty-six patients were screened and analyzed in this study (Figure 1). The majority were women (20 out of 26 patients), The age of the cohort ranged from 21 to 84 years. The most commonly reported symptoms included a burning sensation (69.20%), pain (15.40%), and discomfort (15.40%). The observed OLP lesions were predominantly atrophic (76.90%) and erosive (23.10%). The median VAS was 5.65 (5.00-7.07), the median clinical score was 3.00 (3.00-3.25), and the median salivary level of TNF-α was 37.76 (16.22-48.52) pg/ml. Table 1 lists baseline characteristics for both treatment groups, indicating no significant initial differences ($p>0.05$).

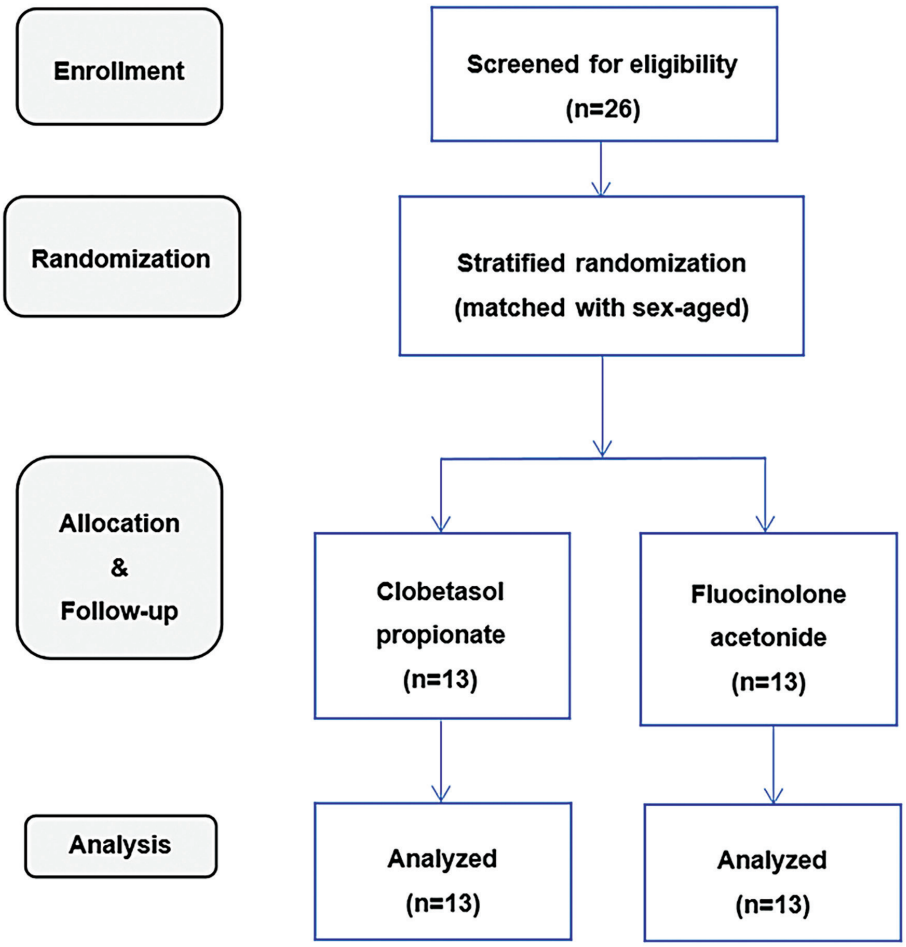

Figure 1: The flow diagram of patients' recruitment and the progress through stages of the study

Table 1: Baseline characteristics for both treatment groups

	Clobetasol propionate (n=13)	Fluocinolone acetonide (n=13)	*p*-value
Age, years[a]	55.00 (46.00-63.50)	57.00 (41.50-68.00)	0.880[c]
Sex[b]			
Female	10 (38.46)	10 (38.46)	1.000[d]
Male	3 (11.54)	3 (11.54)	
Type[b]			
Atrophic	9 (34.62)	11 (42.31)	0.652[d]
Erosive	4 (15.38)	2 (7.69)	
Chief complaint[b]			
Burning	10 (38.46)	8 (30.77)	0.667[d]
Pain/Discomfort	3 (11.54)	5 (19.23)	
Symptoms, VAS[a]	6.60 (5.35-7.45)	5.30 (4.20-6.60)	0.081[c]
Clinical score, TC[a]	3.00 (3.00-4.00)	3.00 (3.00-3.00)	0.418[c]
Salivary TNF-α, pg/ml[a]	29.38 (15.87-44.39)	39.72 (33.26-50.32)	0.235[c]

VAS=Visual analog score
TC=Thongprasom criteria
[a]*Data are presented as median (Q1-Q3)*
[b]*Data are presented as frequency (percentage)*
[c]*Mann-Whitney U Test*
[d]*Fisher's Exact Test*

CP 0.05% and FA 0.1% reduced signs and symptoms of OLP.

The VAS for pain and the clinical score significantly decreased in both groups when comparing values before and after treatment (Figure 2). Moreover, there was no significant difference in the reduction of VAS for pain between CP 0.05% and FA 0.1% groups (Figure 3). However, at the 4-week mark of treatment, CP 0.05% exhibited a significant decrease in the clinical score compared to FA 0.1% (Figure 3). Regarding disease remission, the two study groups exhibited 34.62% (9 out of 26) complete remission, 65.38% (17 out of 26) partial remission, and 0% (0 out of 26) no response to treatment. There was no significant difference in disease remission (p>0.05) between the CP 0.05% and FA 0.1% groups (Table 2). These results highlight that CP 0.05% and FA 0.1% have comparable clinical effects; however, CP 0.05% decreases clinical scores more rapidly than FA 0.1%. Figure 4 shows a patient's bilateral atrophic OLP lesions before CP 0.05% treatment (top panels) and 4 weeks after treatment (bottom panels). The clinical improvement is evident: the lesion is almost completely healed after 4 weeks of treatment. There were no clinical signs of oral candidiasis, atrophy, abnormalities in the taste sense, or allergic reactions detected in the treatment groups after the to the end of the trial.

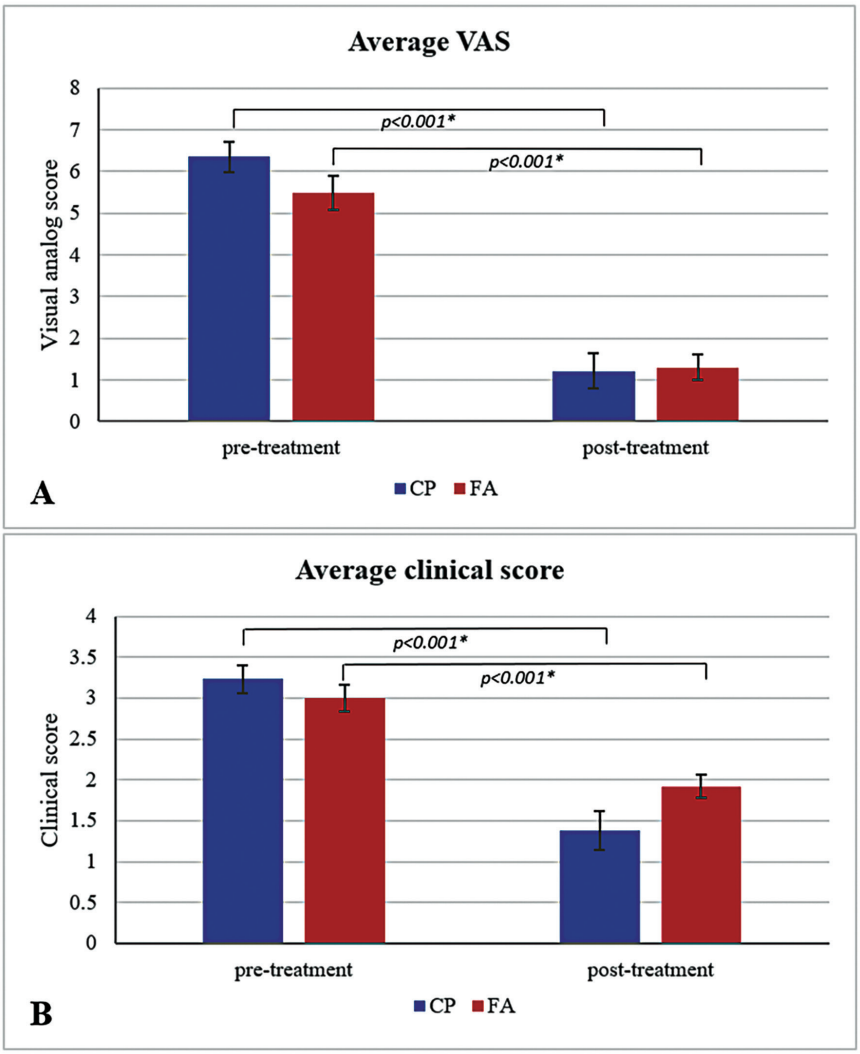

Figure 2: Comparison of clinical parameters pre-treatment and post-treatment. (A) After 4 weeks of treatment, the average pain scores (VAS) for the CP 0.05% and FA 0.1% groups decreased to 1.22±0.42 and 1.30±0.31, respectively. (B) The average clinical scores (Thongprasom scale) for the same groups also diminished to 1.38±0.24 and 1.92±0.14, respectively

CP = Clobetasol propionate, FA = Fluocinolone acetonide

* Statistically significant p<0.05 (Wilcoxon signed rank test)

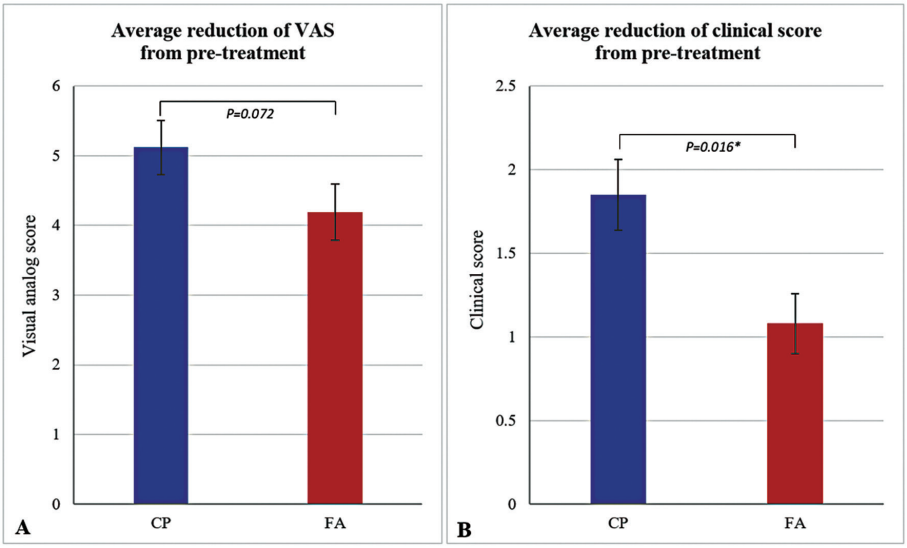

Figure 3: Comparison of the reduction of VAS and clinical scores in the two groups of treatment. (A) After 4 weeks of treatment, the average reduction in VAS for the CP 0.05% and FA 0.1% groups was 5.12 ± 0.40 and 4.19 ± 0.41, respectively. Additionally, (B) the average reduction in clinical scores for the same groups was 1.85±0.22 and 1.08±0.18, respectively

CP = Clobetasol propionate, FA = Fluocinolone acetonide

* Statistically significant $p<0.05$ (Mann–Whitney U test)

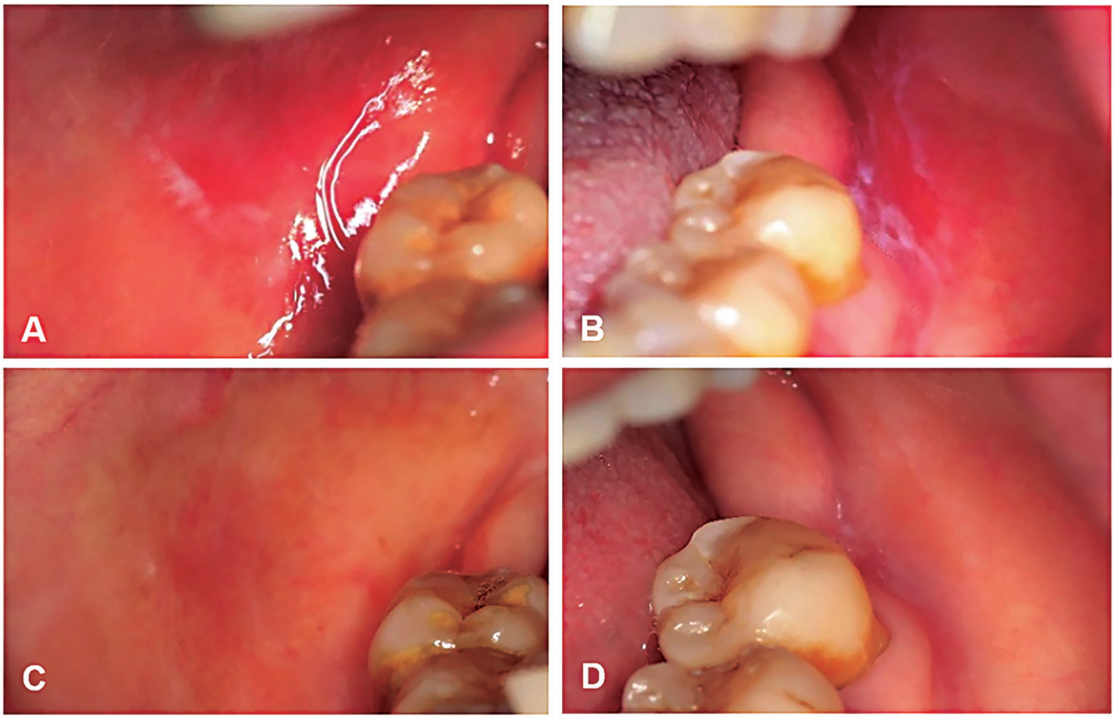

Figure 4: Clinical response of OLP to treatment. (A,B) Bilateral atrophic lesions of the buccal mucosa; following CP 0.05% treatment, clinical improvement was observed. (C,D) Almost complete healing was observed following 4 weeks of treatment

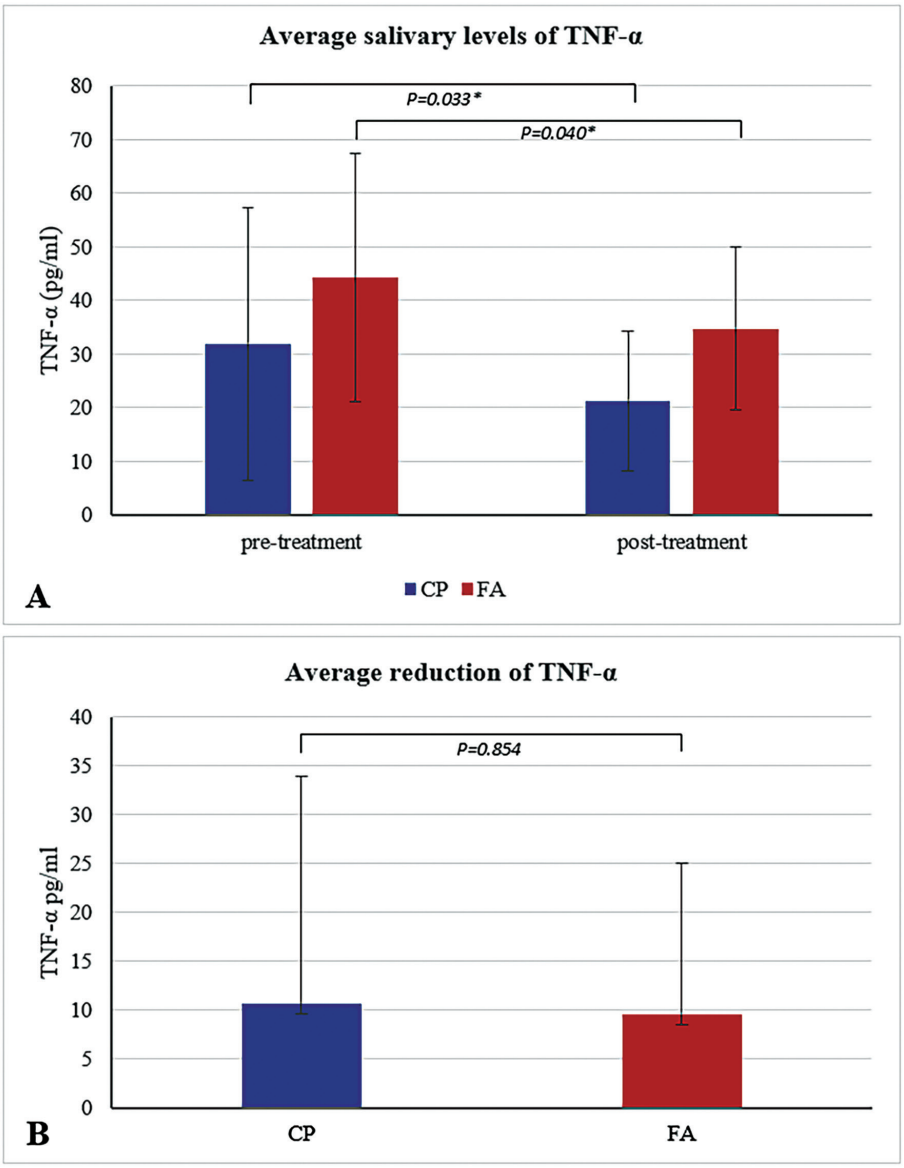

Figure 5: TNF-α in saliva.Following treatment, (A) the average salivary levels of TNF-α in the CP 0.05% and FA 0.1% groups decreased to 21.25±3.78 and 34.71±4.56, respectively. (*Statistically significant $p<0.05$ (Wilcoxon signed rank test)) (B) The average reduction of TNF-α from baseline for these groups was 10.63±23.34 and 9.56±15.47, respectively (No statistically significant $p>0.05$ (Mann-Whitney U test)) CP = Clobetasol propionate, FA = Fluocinolone acetonide

Table 2: Comparison of disease remission between two treatment groups after treatment.

Group	Complete remission	Partial remission
CP	6 (46.15)	7 (53.85)
FA	3 (23.07)	10 (76.93)
p-value	0.411[a]	

CP=Clobetasol propionate 0.05%, FA=Fluocinolone acetonide 0.1%

Data are presented as frequency (percentage)

[a]*Fisher's Exact Test*

The effects of CP 0.05% and FA 0.1% on inflammation were comparable.

TNF-α was detected in all saliva samples obtained from patients with OLP. After 4 weeks of treatment, salivary TNF-α levels in both groups were statistically significantly lower than pre-treatment ($p<0.05$). However, there was no statistically significant difference in the reduction of salivary levels of TNF-α between the CP 0.05% and FA 0.1% treatments (Figure 5). Therefore, this finding suggested that the effects of CP 0.05% and FA 0.1% on inflammation exhibited similarities.

Discussion

OLP is a chronic condition characterized by recurrent flare-ups and symptom-free intervals; achieving remission is challenging.[1,5] The treatment objectives include alleviating painful symptoms, promoting the healing of ulcerative lesions, reducing the risk of malignant transformation, extending symptom-free intervals, maintaining excellent oral hygiene and dental health, and ultimately improving the patient's quality of life.[1,4] Despite numerous guidelines and studies of symptomatic OLP treatment, topical corticosteroids remain the most widely used and effective approach.[6,24] Ultrapotent halogenated corticosteroids such as clobetasol and potent fluorinated corticosteroids like fluocinolone acetonide and fluocinonide have demonstrated success rates ranging from 30-100%.[1,11,24]

This randomized, controlled, double-blind study found that topically applied corticosteroids significantly improved the condition of patients with atrophic-erosive OLP. Both CP 0.05% and FA 0.1% exhibited favorable outcomes; both drugs reduced pain and clinical scores significantly. The effectiveness of CP 0.05% was comparable to that of previous findings.[11,12,25] The efficacy of FA 0.1% was consistent with the findings of Thongprasom *et al.,*[10] and Buajeeb *et al.,*[9] both of whom reported that topical steroids yielded good therapeutic effects and that the drugs were safe and free of serious side effects. After 4 weeks of treatment, we found that CP 0.05% was more effective at reducing the clinical severity of OLP than FA 0.1%. However, the difference between symptom reduction and disease remission was small and did not reach statistical significance, which is consistent with a comparative study of CP 0.05% and FA 0.1% effectiveness on 26 OLP patients in Thailand. The study showed that both medications effectively reduced pain scores, clinical score, and disease remission over a four-week period, with no statistically significant differences observed.[26] In addition, two studies have compared clobetasol with fluocinonide, a potent fluorinated corticosteroid, as well as FA 0.1%. Carbone *et al.,*[27] found that clobetasol was more effective at reducing lesion size and clinical severity than fluocinonide 0.05% after 2 months of treatment, which was consistent with the findings of our study. On the other hand, Lozada-Nur *et al.,*[28] found no difference between the two medications in terms of reducing clinical severity and lesion size. However, those authors found that clobetasol was more effective at reducing pain than fluocinonide. Consistent with previous research, we found that an ultrapotent topical steroid, specifically clobetasol, exhibited superior therapeutic efficacy against OLP compared with a high potent topical steroid (i.e., fluocinolone acetonide). This discrepancy in efficacy can be attributed to the divergent potency profiles of the two medications. Based on our findings and those of other studies, using a super-potent topical steroid like clobetasol to treat oral lichen planus was more effective than using a high-potency topical steroid like fluocinolone acetonide. However, the efficacy gap between the two medications may narrow as treatment progresses. As a result, we recommend that clinicians initiate treatment of an erosive OLP (painful lesion) with a full dose of an ultrapotent corticosteroid, closely monitor a patient's signs and symptoms until noticeable improvement occurs, and then gradually taper the dosage of the drug by reducing the frequency of application. Managing OLP serves as challenges because of its chronic characteristics. It is essential to focus on treating the symptoms. Evidently, the cost of treatment with CP 0.05% is higher compared to FA 0.1%.[29] Although our study couldn't find any adverse effects, candidiasis is commonly associated with the application of topical steroids.[5,10] Therefore, in addition to considering the drug's effectiveness, it is important to take consideration of these factors when tailoring treatment for each patient. Salivary biomarkers are used for diagnosing and monitoring various oral diseases, including OLP. Several studies have revealed abnormal expression patterns of inflammation-related cytokines in saliva, such as interleukins (ILs), transforming growth factor-beta (TGF-β), interferon-gamma (IFN-γ), and TNF-α.[13,18] Specifically, patients with OLP exhibit significantly elevated levels of TNF-α compared with healthy individuals.[16] Ribaric

et al.,[17] noted that symptomatic erosive OLP patients had notably higher salivary TNF-α levels than patients with asymptomatic reticular OLP. These findings suggest that salivary TNF-α has the potential to serve as a biomarker for assessing the severity of OLP.[30]

Our study found that all of the saliva samples collected from patients with OLP contained TNF-α (median value: 37.76 (16.22-48.52) pg/mL). This finding aligns with the results of previous studies.[20,21] After 4 weeks of treatment with CP 0.05% and FA 0.1%, we found a significant decrease in salivary TNF-α levels. However, there was no statistically significant difference in the reduction of TNF-α levels between the CP 0.05% and FA 0.1% treatments; both effectively lowered salivary TNF-α levels. These results are also consistent with our clinical observations-the treatment demonstrated effectiveness at reducing pain and diminishing the severity of the lesions after 4 weeks of administration. Our findings are consistent with the results of several studies that investigated TNF-α levels in OLP patients undergoing corticosteroid treatment. Thongprasom *et al.,*[31] reported a significant reduction in the number of TNF-α-positive mononuclear cells in patients with erosive or atrophic OLP after one month of treatment with FA 0.1%. Rhodus *et al.,*[30] found a statistically significant decrease in salivary levels of proinflammatory cytokines, including TNF-α, IL-1, IL-6, and IL-8, in individuals with erosive OLP who were treated with dexamethasone mouthwash for six weeks. Ghallab *et al.,*[21] demonstrated that systemic prednisone significantly reduced salivary TNF-α levels. Additionally, Othman *et al.,*[14] compared the efficacy of triamcinolone acetonide and laser treatments in OLP and found that triamcinolone acetonide was more effective at reducing TNF-α levels. It is worth noting that TNF-α levels decreased after the application of topical steroids, which can be attributed to the anti-inflammatory and immunosuppressive properties of glucocorticoids. These glucocorticoids are believed to inhibit the expression of cytokine genes, such as TNF-α, IL-1, IL-2, IL-3, IL-6, IL-11, and chemokines[7] by suppressing the transcription factors that control cytokine expression within the cell nuclei.[32] Although our findings support the association between TNF-α and OLP lesions, the use of TNF-α inhibitors like infliximab, etanercept, and adalimumab for the treatment of OLP lesions requires careful consideration: anti-TNF-α therapy has been linked to potential risks, including serious infections, congestive heart failure, malignancy, and autoimmune diseases, when used for treating rheumatoid arthritis.[33] Additionally, paradoxical complications have been observed in three female patients with inflammatory bowel disease who developed OLP-like lesions while receiving TNF-α inhibitors.[34] Therefore, further studies on this topic are necessary; it is crucial that clinicians possess a comprehensive understanding of the physiological effects of cytokines involved in the immunopathogenesis of OLP.

The results of this study add to the body of evidence that suggests using saliva testing for TNF-α to gauge treatment response and track the progression of OLP. TNF-α production in saliva mirrors clinical changes and is closely linked to the severity of OLP.[17,35] If high TNF-α levels persist in saliva over time, they could potentially promote the malignant transformation of OLP lesions.[36] Given the detection of TNF-α in whole saliva, we consider saliva analysis to be a valuable, non-invasive, and worthwhile method for screening, diagnosing, and monitoring OLP.[13,16] However, this study has its limitations, such as a small sample size and a relatively short study duration. Also, because TNFα has some controversial biological effects in the etiopathogenesis of OLP, it's important for future research to focus on looking at and comparing the levels of this cytokine at different stages of the disease and with different treatment plans.

Conclusions

Our study suggests that both CP 0.05% and FA 0.1% had comparable effectiveness in curing OLP. However, CP 0.05% reduced the clinical score more than FA 0.1% over a 4-week timeframe. Furthermore, treatment with these medications resulted in a substantial decrease in salivary TNF-α levels, implying that TNF-α in whole saliva may serve as a useful biomarker of OLP disease monitoring.

Acknowledgments

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Conflicts of interest

The authors declare no conflicts of interest.

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Remineralization Potential of Nano-strontium/Fluoride Hydroxyapatite on Artificial Enamel Caries

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Abstract

Objectives: This study aimed to evaluate the remineralization efficacy of nano-strontium/fluoride hydroxyapatite paste on initial enamel caries in comparison with other remineralization products under a simulated pH-cycling model.

Methods: Following the artificial caries induction, forty enamel specimens with non-cavitated lesion in the same range of lesion depth were selected by mean of micro-CT evaluation. The specimens were block-randomized into four experimental groups regarding remineralizing pastes: 1500 ppm sodium fluoride paste, 10%wt nano-hydroxyapatite paste, 10%wt nano-strontium/fluoride hydroxyapatite paste and 5%wt nano-strontium/fluoride hydroxyapatite paste. Remineralizing effect was evaluated using micro-CT, while SEM/EDS line scan mode facilitated the investigation of remineralization patterns. Changes in lesion depth (ΔLD) and changes in mineral loss (ΔΔZ) were evaluated at 7 and 14 days of treatment under the pH-cycling model. Statistical analyses were performed using 2-way ANOVA and post hoc Tukey's test ($p<0.05$).

Results: The use of 5%wt nano-strontium/fluoride hydroxyapatite paste significantly reduced lesion depth in initial caries under experimental conditions. Meanwhile, the 10%wt nano-strontium/fluoride hydroxyapatite paste yielded the highest mineral gain, though statistically insignificant. EDS graphs indicated an increasing calcium and phosphorus deposition trend over time with nano-strontium/fluoride hydroxyapatite paste, revealing a more uniform mineral distribution compared to both sodium fluoride and nano-hydroxyapatite pastes. Nevertheless, neither fluorine nor strontium was detectable in these graphs.

Conclusions: The study revealed comparable remineralization efficacy with 5%wt and 10%wt nano-strontium/fluoride hydroxyapatite pastes. The treatment durations of 7 and 14 days showed no significant difference in outcomes.

Keywords: initial caries, lesion depth, mineral gain, nano-strontium/fluoride hydroxyapatite, remineralization

Introduction

Dental caries is the outcome of an imbalance between remineralization and demineralization processes. This widespread disease is caused by acid-producing bacteria that ferment carbohydrates. The first sign of dental caries is enamel caries or white spot lesion. The white spot lesion has an intact enamel surface and is reversible as this non-cavitated lesion is caused by subsurface demineralization.[1,2] The movement of calcium and phosphate ions from dissolving enamel, in conjunction with fluoride ions from the oral environment, enhance the acid resistance of enamel surface. As a result, demineralization predominantly affects the subsurface region rather than the superficial enamel.[2] The continuous process of mineral loss led to the structural breakdown of the tooth surface or cavitated carious lesion. This process can be arrested through dietary modifications that balance the acid-base level, and sufficient cleaning with a therapeutic agent.[1] Minimal intervention dentistry is the concept of preserving the tooth structure and preventing further carious experiences.[3] The therapeutic intervention with remineralizing agents enhance remineralization and inhibit the demineralization process.[4] Remineralization of enamel occurs when the concentration of calcium and phosphate ions in saliva and biofilm is supersaturated compared to those of the enamel. This process leads to the inhibition of further mineral loss and the repair of the partially demineralized hydroxyapatite of the enamel.[5,6] Remineralizing agents have been widely classified into fluorides and non-fluoride remineralizing agents.[7] The most common among them is fluoride, typically at concentrations between 1000-1500 ppm.[3,8] There are many fluoride-containing products on the market including toothpaste, mouth rinses, and pastes.

Fluoride is a multifaceted agent against dental caries, functioning through three primary mechanisms, inhibiting demineralization, enhancement of remineralization, and antimicrobial actions.[1,2] After acidic exposures, saliva neutralizes the acids. When the pH surpasses 5.5, the natural remineralization takes place. In this environment, fluoride in the saliva plays a pivotal role in expediting the remineralization process.[1] Fluoride ions adsorbing to the surface of partially demineralized crystals, subsequently attracting calcium ions.[1,9,10] This leads to the formation of modified enamel crystal, fluorapatite, which enhance the enamels resistance to the further acidic challenges.[1,10,11] Additionally, fluoride in the form of hydrogen fluoride infiltrates bacterial cells, it disrupts bacterial glycolytic enzymes, leading to diminished acid production[1,12] and reduced bacterial adherence to teeth.[1,13] However, it is imperative to supervise fluoride consumption in children up to 6 years old as excessive consumption through mouth rinses or toothpaste can lead to acute or chronic fluoride toxicity.[1,13,14]

Non-fluoride remineralizing agents and biomimetic approaches have become outstanding since they have the potential to remineralize teeth using biomaterials such as nano-hydroxyapatite. Recent research has focused on nanohydroxyapatite due to its remarkable similarity to the hydroxyapatite crystals found in enamel, encompassing size, crystal structure, and chemical composition.[15,16] These characteristics confer biocompatibility, referring to the ability of a material to perform with an appropriate host response in a specific situation, and bioactivity, indicating the ability to induce favorable biological interactions.[15] Previous studies confirmed that nano-hydroxyapatite effectively remineralized the initial caries.[4,17-23] Nanohydroxyapatite's mechanism of action includes filling the micropores of demineralized enamel[20], thus forming an apatite-layer over the enamel surface.[21,22] Moreover, nano-hydroxyapatite serves as a reservoir of calcium and phosphate ions, facilitating the remineralization of demineralized enamel.[19] Although nano-hydroxyapatite is associated with a high degree of crystallinity, which tends to increase with concentration, research indicates that the optimum concentration is 10% by weight.[23]

Ionic substitutions of calcium in nano-hydroxyapatite lead to modifications of the physicochemical properties.[24-26] Specifically, strontium substitution induces crystal asymmetry, increases solubility but reduces crystallinity. In contrast, fluoride substitution leads to crystal lattice contraction, enhancing both stability and crystallinity of the nanoparticle. The combined inclusion of strontium and fluoride in nano-strontium/fluoride hydroxyapatite causes slightly distortion and a smaller crystal lattice, resulting in lower solubility compared to both pure nano-hydroxyapatite and nano-strontium hydroxyapatite. Moreover, nano-strontium/fluoride hydroxyapatite also exhibits less crystallinity compared to pure nano-hydroxyapatite. Furthermore, studies suggest that ion-substituted hydroxyapatite exhibited lower

cytotoxicity than pure nano-hydroxyapatite.[26,27]

This study aimed to assess the remineralization efficacy of various remineralizing pastes and to explore the patterns of remineralization under a pH-cycling model. Specifically, the experiment focuses on the comparison of a nano-strontium/fluoride hydroxyapatite paste with a 1500 ppm fluoride paste and a 10%wt nano-hydroxyapatite paste. The hydrothermal synthesis, involving the substitution of strontium and fluoride ions into nano-hydroxyapatite, yields rod-shaped nano-strontium/fluoride hydroxyapatite crystals ranging between 20 to 60 nm. As nano-strontium/fluoride hydroxyapatite exhibits physicochemical properties more prone to remineralization, it is more stable and exhibits less crystallinity compared to nano-hydroxyapatite.[26,27] While nano-hydroxyapatite crystallinity increases with concentration.[23] The concentrations of 5% and 10% nano-strontium/fluoride hydroxyapatite were tested to determine the optimal concentration. Remarkably, as per our knowledge, no previous research has compared these specific pastes using both micro-CT and SEM/EDS analytical techniques. This novel approach promises not only to deepen the understanding of remineralization strategies, but also to pave the way for new avenues in research and potential advancements in dental health practices.

Materials and Methods

Preparation of enamel specimens

Sixty human permanent premolar teeth were extracted due to orthodontic treatment or periodontal disease with the intact crown and no developmental lesion. The study received ethical approval from the Human Experimental Committee of the Faculty of Dentistry at Chiang Mai University, Chiang Mai, Thailand (No. 1/2022). The teeth were cleaned by ultrasonic scaler and stored in 0.1% thymol solution. Sixty cubic specimens, each measuring 4x4x4 (width x length x thickness) cubic millimeters were obtained from the buccal portion of the teeth and subsequently embedded in blocks of acrylic resin. The enamel surface was polished using a grinding/polishing machine (Mopao 160E, LaiZhou Weiyi Experimental Machinery Manufacture, Shandong, China) with silicon-carbide sandpapers at 600-, 1000-, 1500-, and 2000-grit, respectively, with water for 1 minute per each roughness. This process was performed to align the flat enamel surface with the acrylic resin block surface. Post-polishing, all specimens were cleaned using an ultrasonic cleanser (BioSonic UC125, Whaledent Inc, OH, USA) for 10 minutes.

Artificial initial caries formation

Each enamel specimen was divided into three parts, each approximately 1 mm width. The central segment was coated with clear nail varnish to preserve as a sound enamel control. The left and right segments were kept uncoated, serving as the demineralized enamel control and the section undergoing pH-cycling treatment. Following the preparation, specimens were immersed in 5 ml of acetic acid buffer solution with a pH of 4.5 and a temperature of 37°C for a period of seven days as shown in Table 1. In the preparation of the specimens, the method was modified from Vacharangkura A, and Kunawarote S, as detailed in the the proceedings of 6th RSU International

Table 1: The composition of solutions in the experiment

Solutions	Compositions	pH and Temperature
Acetic acid buffer solution	50 mM acetic acid 2.2 mM calcium chloride ($CaCl_2$•$2H_2O$) 2.2 mM potassium dihydrogen phosphate (KH_2PO_4) 0.1 ppm of fluoride	pH 4.5 37°C
Remineralized solution	130 mM potassium chloride (KCl) 1.5 mM calcium chloride ($CaCl_2$•$2H_2O$) 0.9 mM of potassium dihydrogen phosphate (KH_2PO_4) 20 mM of HEPES buffer	pH 7.0 37°C
Demineralized solution	50 mM of acetic acid 2.2 mM calcium chloride ($CaCl_2$•$2H_2O$) 2.2 mM potassium dihydrogen phosphate (KH_2PO_4)	pH 4.5 37°C

Research Conference on Science and Technology (2021), illustrated in Figure 1.[28]

After the formation of artificial initial caries, the specimens were sectioned to obtain a slice of 1 mm thickness cross-sectioned specimen from each specimen using a low-speed precision cutting machine (IsoMet™, BUEHLER, Illinois, USA). Initial evaluations were conducted using micro-CT (microCT35, SCANCO Medical AG, Brüttisellen, Switzerland) to analyze mineral density, which was then used to determine the lesion depth (LD) and mineral loss (ΔZ). Furthermore, the elemental composition and remineralization pattern were examined using the Scanning Electron Microscope and Energy Dispersive X-ray Analysis Systems (SEM/EDS) (Quanta250, FEI company, Oregon, USA) operated in line scan mode.

Remineralizing treatment

After assessment of the artificial initial caries lesions using micro-CT, forty enamel specimens with non-cavitated enamel lesion, and a normalized mean lesion depth were selected. The normalization achieved by excluding the top and bottom deciles of the distribution. To maintain the integrity of the specimens, both the cut surfaces and the demineralized sections were coated with nail varnish. Subsequently, the specimens were systematically allocated into four experimental groups via block-randomization, regarding remineralizing pastes: 1500 ppm sodium fluoride paste (F), 10%wt nano-hydroxyapatite paste (nHA), 10%wt nano-strontium/fluoride hydroxyapatite paste (SrF10), and 5%wt nano-strontium/fluoride hydroxyapatite paste (SrF5), which is rod-shaped, measuring 20-60 nm in length and 10 nm in diameter. The molecular formula of nano-strontium/fluoride hydroxyapatite within the pastes is $Sr_5Ca_5(PO_4)_6F_2$. Within each group, specimens were randomly selected to represent the full range of EDS patterns of that specific group.

For each group, the specimens received identical paste application procedures. A 0.05 ml of the respective paste, with its composition provided in Table 2, was applied onto the moist enamel, emulating oral cavity conditions. The paste was then left on the specimen for five minutes, simulating the effect of paste retention on teeth during periods of non-consumption. Thereafter, the specimens were immersed in remineralizing solutions for an additional 25 minutes. Finally, after a total of 30 minutes of remineralizing paste application, each specimen was thoroughly rinsed with distilled deionized water before being subjected to simulated pH-cycling.

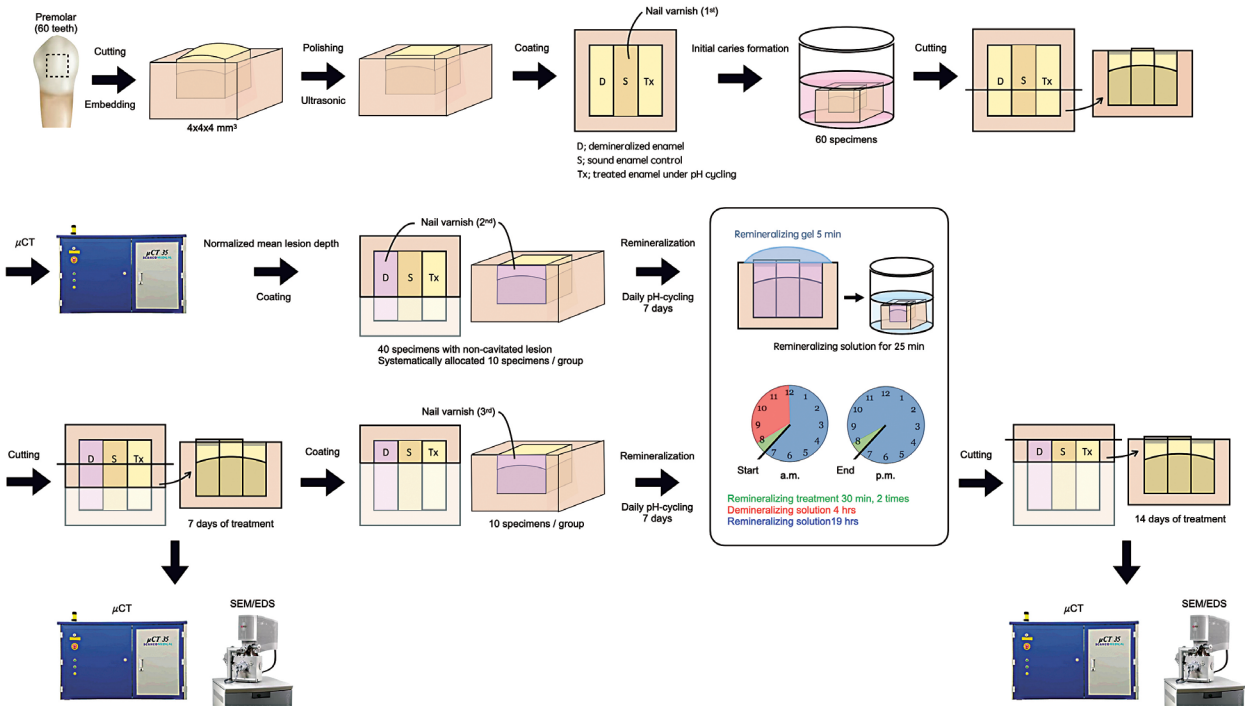

Figure 1: Experimental procedures for specimen preparation and remineralization assessment. The figure illustrates the steps involved in specimen preparation and measurements, including remineralization assessments at 7 days and 14 days using micro-CT and scanning electron microscope and energy dispersive x-ray analysis system (SEM/EDS)

Micro-CT

The cross-sectioned specimens were mounted perpendicularly to the x-ray beam, which was set to 70kV and 114 µA. The scans resulted in 8-bit grayscale TIFF format images, each having a resolution of 1,024 x 1,024 pixels and a voxel size of 5 µm. These images were analyzed using the ImageJ software (NIH, Bethesda, MD, USA). Using the enamel surface as a starting point, the grayscale values were converted to mineral densities for comparison with the sound enamel control. The variables included mineral density profiles, with MD_B representing baseline mineral density and MD_D representing demineralized mineral density. These profiles were used to calculate lesion depth (LD_D as demineralized lesion depth) and mineral loss (ΔZ_D as mineral loss after demineralization). Lesion depth was determined based on the depth of the mineral volume at 95% of the maximum mineral density, and mineral loss was calculated from the area under the graph, which compared the mineral densities of sound and demineralized enamel.[29]

SEM/EDS

The cross-sectioned specimens were desiccated using silica gel to remove moisture prior to examination with the SEM/EDS. The specimens were mounted on the sample holder of the scanning electron microscope (Quanta 250, FEI company, Oregon, USA) for cross-sectional elemental analysis. The settings were adjusted to 20 kV, with a magnification of 500 times. The elemental analysis program (Aztec, Oxford Instruments plc, Abingdon, UK) was used in line scan mode. The origin of the depth axis was referenced from the visible surface of the enamel specimen. The program then processed the elemental intensities and generated a graph showing the relationship

Table 2: The compositions of remineralizing pastes (%wt)

	F	nHA	SrF10	SrF5
Deionized water	58.92	49.25	49.25	54.25
Sorbitol	30.00	30.00	30.00	30.00
Thickening silica	8.00	8.00	8.00	8.00
Carboxymethyl cellulose	1.50	1.50	1.50	1.50
Flavor	0.80	0.80	0.80	0.80
Titanium dioxide	0.20	0.20	0.20	0.20
Sodium benzoate	0.25	0.25	0.25	0.25
Sodium fluoride	0.33	-	-	-
n-HA	-	10.00	-	-
n-Sr/F HA	-	-	10.00	5.00
Total	100.00	100.00	100.00	100.00

n-HA, 10%wt nano-hydroxyapatite paste SrF10; 10%wt nano-strontium/fluoride hydroxyapatite paste; SrF5, 5%wt nano-strontium/fluoride hydroxyapatite paste

Table 3: The variables in this study

Variables	Sound enamel	After demineralization	After Treatment 7 days	Changes in 7 days	After Treatment 14 days	Changes in 14 days
Lesion depth (LD)	-	LD_D	LD_1	ΔLD_1 (LD_1 - LD_D)	LD_2	ΔLD_2 (LD_2 - LD_D)
Mineral loss (ΔZ)	Control (MD_B)	ΔZ_D (MD_D - MD_B)	ΔZ_1 (MD_7 - MD_B)	$\Delta\Delta Z_1$ (ΔZ_1 - ΔZ_D)	ΔZ_2 (MD_{14} - MD_B)	$\Delta\Delta Z_2$ (ΔZ_2 - ΔZ_D)

LD_D is lesion depth after demineralization
MD_B is mineral density of the sound enamel
MD_D is mineral density after demineralization
MD_7 is mineral density at 7 days of remineralized treatment
MD_{14} is mineral density at 14 days of remineralized treatment

between the X-ray signal in counts per second (cps) and the measurement distance in μm.

Simulated pH-cycling

To replicate the natural oral environment, a pH-cycling routine was employed, involving a 19-hour immersion of specimens in a remineralization solution and a 4-hour exposure to an acetic buffer solution with pH 4.5[30] for demineralization, as described in Table 1. The remineralizing pastes were applied twice daily in 30-minute durations: once before the demineralization period, and a second time 12 hours later. The solutions were refreshed daily. Assessments of the remineralization process were then conducted on the 7th and 14th days of the cycle.

Remineralization assessments

After 7 and 14 days of remineralizing treatment along with pH-cycling, the enamel specimens were sectioned into 1 mm thickness. The cross-sectional enamel specimens were evaluated using micro-CT and SEM/EDS. The data of mineral density were gathered at 7 days (MD_7) and 14 days (MD_{14}). The calculation was performed in the term of lesion depth (LD_1 and LD_2) and mineral loss (ΔZ_1 and ΔZ_2). The SEM/EDS concentrated on elemental composition and remineralization patterns across the different groups of enamel specimens treated with various pastes. The assessments were conducted across four stages: sound enamel control, demineralized enamel, 7 days of treatment, and 14 days of treatment. The EDS graphs provides an overview of mineral changes across stages, enhancing the understanding of the remineralization process.

Statistical analysis

The changes in lesion depth (ΔLD_1 and ΔLD_2) and the changes of mineral loss ($\Delta\Delta Z_1$ and $\Delta\Delta Z_2$) were quantitatively analyzed as presented in the Table 3. The data was subjected to statistical analysis using statistics software (SPSS version 28.0, IBM Corporation, Armonk, NY, USA). Normal distribution of the data was evaluated using the Shapiro-Wilk test, while variance homogeneity was analyzed using the Levene statistic. Changes in mineral loss ($\Delta\Delta Z$) and lesion depth (ΔLD) after treatment for 7 and 14 days of treatment across the experimental groups were analyzed using two-way ANOVA, followed by post hoc Tukey's significant difference test. All statistical analyses were performed at a 95% confidence interval with 80% power of the test.

Results

Forty specimens with non cavitated lesion were selected after the formation of artificially demineralized enamel, based on the mean lesion depth. The mean lesion depth after demineralization (LD_D) was 151.2±24.4 μm. The specimens were block randomized into four groups. After the pH-cycling model treatment, the mean changes in lesion depth and mineral loss were evaluated, as shown in Table 4.

Micro-CT imaging in Figure 2 revealed increased radiolucency in demineralized enamel, whereas the outermost layer maintained consistency with normal enamel. The images of the specimens after demineralization displayed enhanced radiopacity. The fluoride paste-treated group exhibited a reduction in the depth of the radiolucent layer and an increase in surface radiopacity. Conversely, groups treated with nHA, SrF10 and SrF5 showed a reduction in the depth of the radiolucent layer and an increase in radiopacity throughout the lesion.

Table 4: The mean and standard deviations of the change in lesion depth (μm) and the change in mineral loss (mgHAP/m^2) of the experimental groups under the simulated pH-cycling model at different timing

Experimental groups	Change in lesion depth on day 7 (ΔLD_1)	Change in lesion depth on day 14 (ΔLD_2)	Change in mineral loss on day 7 ($\Delta\Delta Z_1$)	Change in mineral loss on day 14 ($\Delta\Delta Z_2$)
F group	10.6 (35.3)^{a}	-1.2 (31.9)	-466.6 (9484.3)	-768.5 (11340.5)
nHA group	10.6 (37.9)^{a}	2.0 (32.5)	-35.4 (13735.7)	-363.6 (7760.1)
SrF10 group	-13.9 (39.1)^{ab}	-18.6 (32.6)	-5744.9 (9288.1)	-6534.3 (10880.3)
SrF5 group	-19.0 (25.0)^{b}	-26.8 (21.9)	-4877.8 (5100.0)	-3553.1 (6271.0)

Alphabets that are labeled with a different letter indicate significant differences within the same period across varying treatments ($p<0.05$)

Lesion depth

In the comparison of mean changes in lesion depth between the experimental groups over the period of 7 and 14 days, it was found that the experimental groups showed distinct changes in lesion depth. At 7 days, the SrF5 group showed significantly reduced lesion depth compared with other groups, with the exception of the SrF10 group. This was followed by the fluoride paste group, and the nHA group. Furthermore, all groups demonstrated decreased lesion depths corresponding trends of remineralization at 14 days with no statistically significant difference as shown in Table 4.

Mineral loss

The mean changes in mineral loss between the experimental groups and periods were shown in Table 4. The alteration in negative value indicated the mineral deposition or remineralization on the demineralized enamel. The mean of change in the mineral loss of the SrF10 group demonstrated the most negative values, followed by SrF5 group, and nHA group. Over the usage period, the SrF10 group exhibited the most mineral deposition. However, the data revealed no statistical difference among experimental groups and no difference between the 7 and 14-day periods.

Remineralizing patterns

The SEM/EDS method provided patterns of elemental intensity as qualitative data. The cross-sectional surfaces of sound enamel, demineralized enamel and treated enamel were evaluated. For each experimental group, one specimen was randomly selected to represent the EDS pattern. Following artificial demineralization, the graphs showing the intensity of calcium (Ca) and phosphorus (P) elements demonstrated less uniformity compared to sound enamel. However, after 7 and 14 days of the remineralizing treatment under the pH-cycling model, notable changes in the EDS graphs were observed. The group treated with fluoride paste exhibited an increase in Ca and P elemental intensity compared to demineralized enamel. By the 14th day, the EDS graph reflected intensity levels approximating those of the sound enamel control, though the mineral deposition was disorganized and non-uniform. Notably, an increase in intensity was also observed at the surface. Meanwhile, the groups treated with nHA, SrF10 and SrF5 showed increased Ca and P intensity along the depth of lesion. By the 14th day of treatment, the EDS graphs revealed intensities akin to the sound enamel control, displaying homogeneity in mineral deposition and uniform distribution. Nonetheless, strontium and fluorine were barely detected in the EDS, as shown in Figure 3-6.

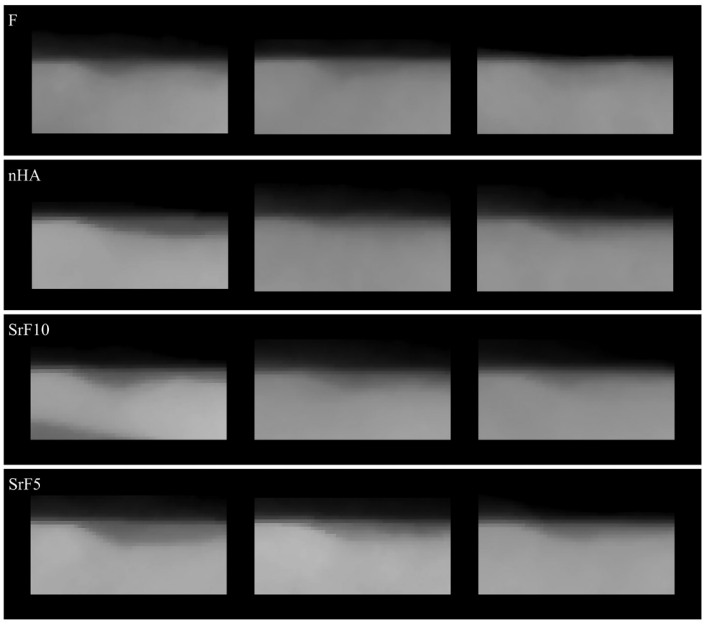

Figure 2: Micro-CT images illustrating the progression of the radiolucency areas in experimental groups. From left to right: artificially demineralized enamel, specimens treated with remineralizing paste under simulated pH-cycling for 7 days, and specimens after 14 days of treatment

SrF10 group

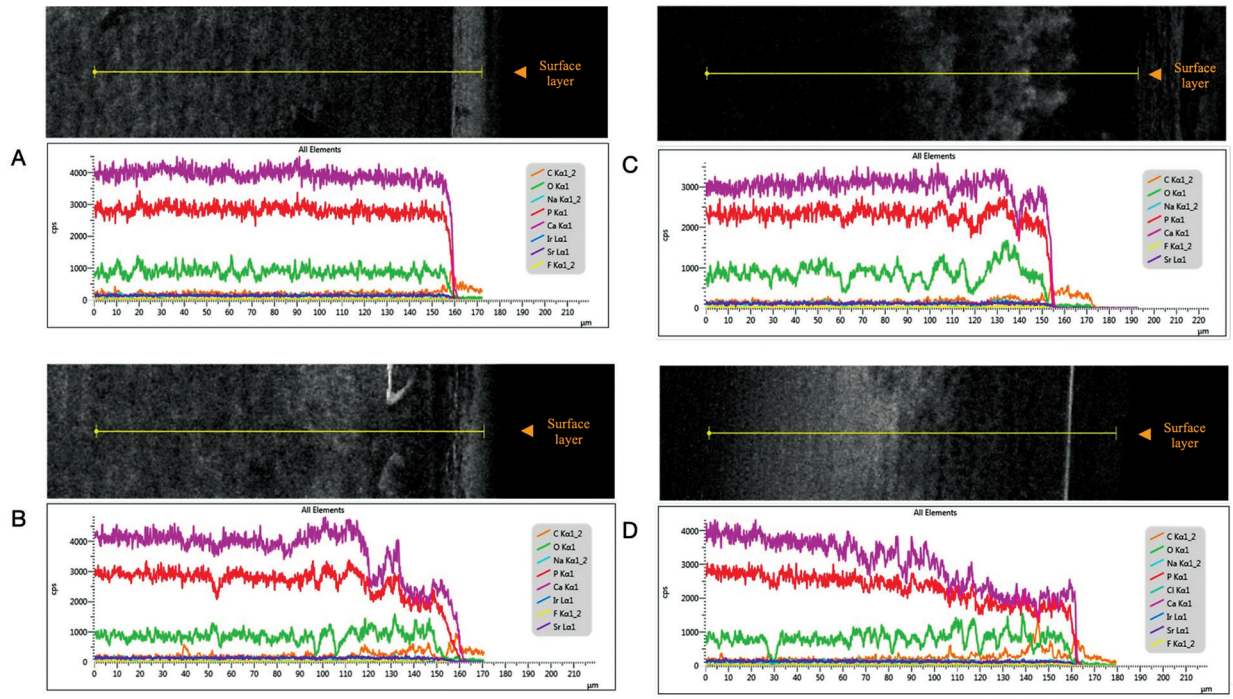

Figure 3: Energy dispersive x-ray analysis systems (EDS) line graphs and images represent element intensity in various enamel conditions, sound enamel control (A), demineralized enamel (B), treated with 1500 ppm sodium fluoride paste under simulated pH-cycling for 7 days (C), and treated with 1500 ppm sodium fluoride paste under simulated pH-cycling for 14 days (D)

SrF5 group

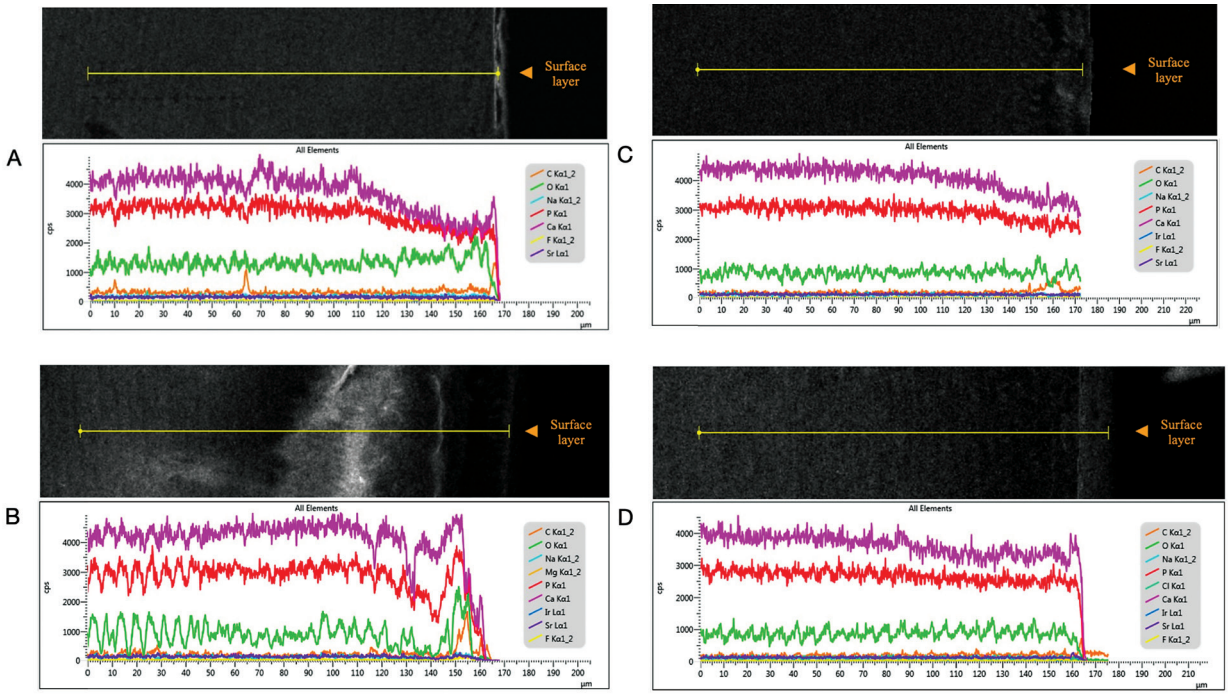

Figure 4: Energy dispersive x-ray analysis systems (EDS) line graphs and images represent element intensity in various enamel conditions, sound enamel control (A), demineralized enamel (B), treated with 10%wt nano-hydroxyapatite paste under simulated pH-cycling for 7 days (C), and treated with 10%wt nano-hydroxyapatite paste under simulated pH-cycling for 14 days (D)

SrF10 group

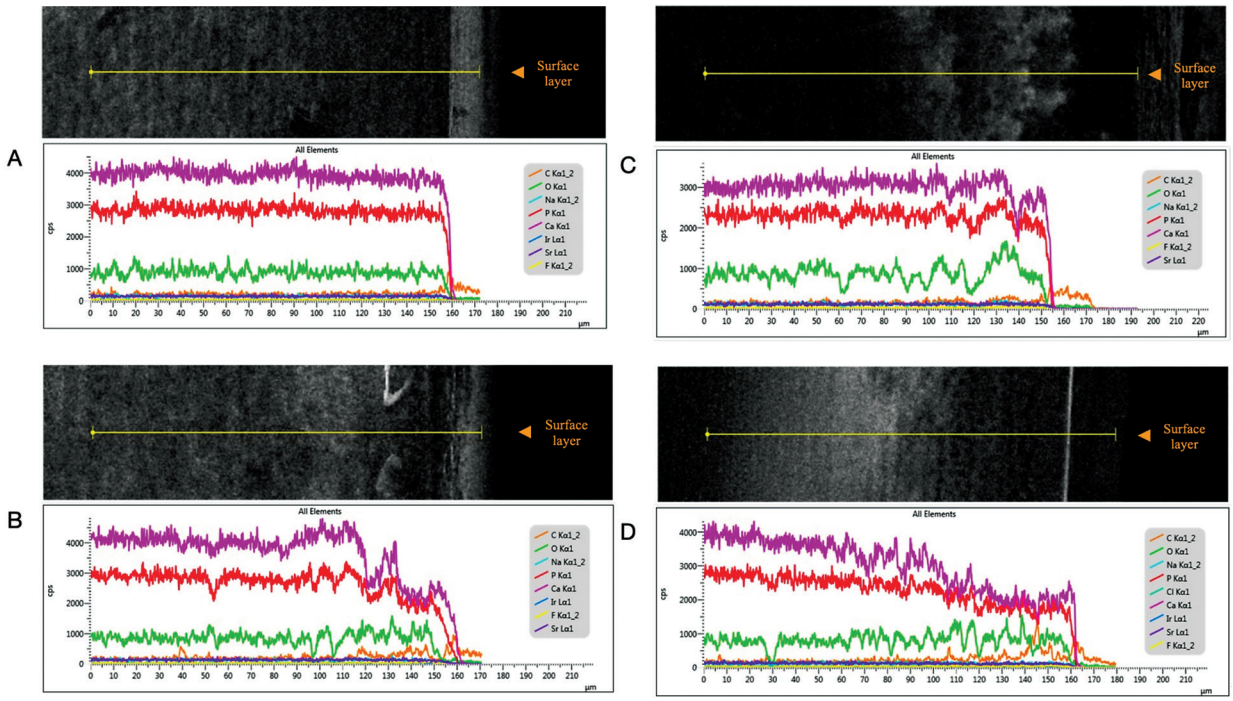

Figure 5: Energy dispersive x-ray analysis systems (EDS) line graphs and images represent element intensity in various enamel conditions, sound enamel control (A), demineralized enamel (B), treated with 10%wt nano-strontium/fluoride hydroxyapatite paste under simulated pH-cycling for 7 days (C), and treated with 10%wt nano-strontium/fluoride hydroxyapatite paste under simulated pH-cycling for 14 days (D)

SrF5 group

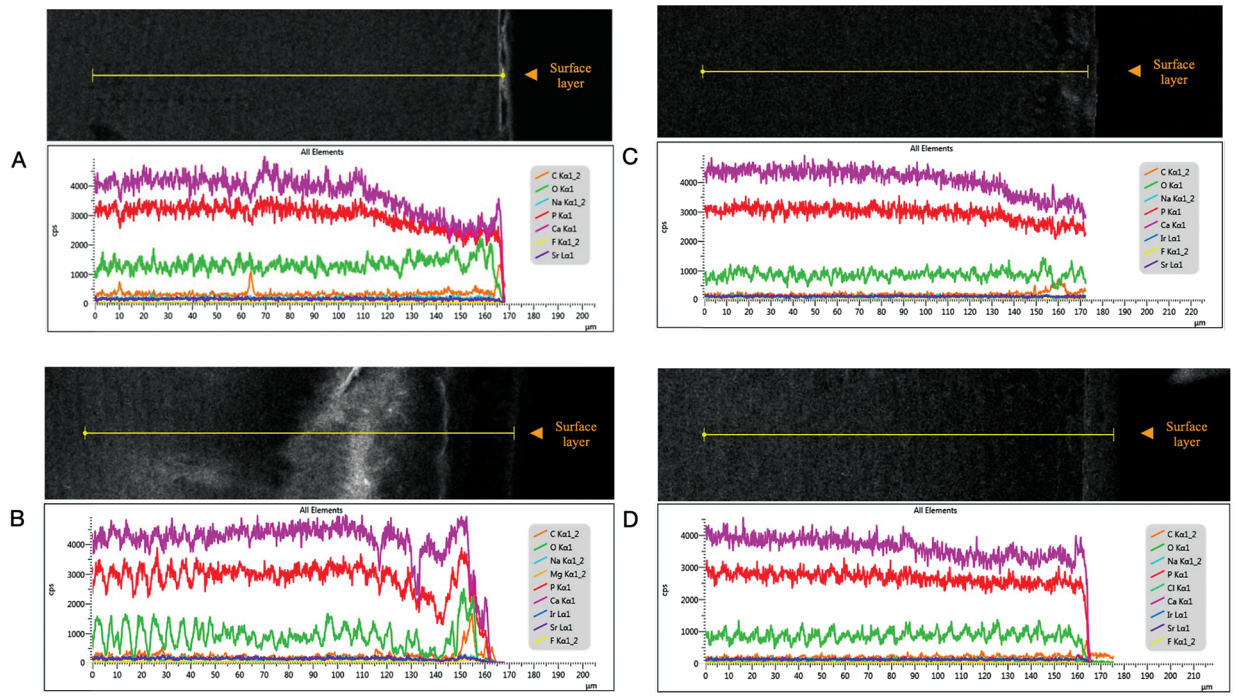

Figure 6: Energy dispersive x-ray analysis systems (EDS) line graphs and images represent element intensity in various enamel conditions, sound enamel control (A), demineralized enamel (B), treated with 5%wt nano-strontium/fluoride hydroxyapatite paste under simulated pH-cycling for 7 days (C), and treated with 5%wt nano-strontium/fluoride hydroxyapatite paste under simulated pH-cycling for 14 days (D)

Discussion

In establishing the experimental design for this study, lesion depth was selected as the baseline parameter to standardize initial lesion severity across all specimens. This ensured that any observed effects could be attributed to the remineralizing pastes being tested. Specimens were then randomized into four groups using block-randomization to maintain balance in group allocation. Although this approach may have introduced variability in initial mineral loss or mineral density among the groups, our analysis confirmed that the distribution of both lesion depth and mineral density remained normally distributed. This is pivotal, as the lesion depth parameter was derived from the calculation of mineral loss, comparing mineral density to that of sound enamel controls. This methodological framework provides a robust basis for the observed significant reductions in lesion depth and indications of mineral loss when using nano-strontium/fluoride hydroxyapatite, underscoring its potential as a viable alternative to traditional fluoride treatments in managing initial enamel caries.

Early demineralized enamel caries or initial enamel caries can be treated with non-invasive treatments such as remineralizing agents. Fluoride with a concentration of 1500 ppm is recognized as an effective remineralizing agent on initial enamel caries. However, recent studies indicate that nano-hydroxyapatite could be a compelling alternative. Nanotechnology biomaterials, especially nano-hydroxyapatite, have gained attention due to their enhanced bioactivity and biocompatibility properties. In our study, the hydrothermal synthesis combined with the strontium and fluoride ions substitution yields rod-shaped nano-strontium/fluoride hydroxyapatite crystals ranging between 20 to 60 nm. This specific morphology is not only safer when compared to other shapes of nano-hydroxyapatite[31], but it also exhibited significantly greater remineralization, along with a significant reduction in both lesion depth and mineral loss, when compared to sodium fluoride and standard nano-hydroxyapatite.

The rod-like shape of the nano-strontium/fluoride hydroxyapatite crystals may play a crucial role in their efficacy for caries prevention. Our data suggest that strontium/fluoride doping not only modifies the shape of nano-hydroxyapatite but also significantly improves its remineralization potential, leading to increased mineral density and reduced lesion depth compared to conventional nano-hydroxyapatite. This indicates that the rod-shaped structure could better facilitate penetration into the micropores of enamel, thereby potentially improving caries prevention. According to previous research, rod-shaped crystals have been found to be less detrimental to rat aortic smooth muscle cells compared to other shapes of nano-hydroxyapatite[31], highlighting their promising safety characteristics for dental applications. Such morphological properties of the crystals are essential when considering their integration with dental enamel and the necessity for minimal tissue-related side effects. Despite promising preliminary evidence, the comprehensive biological implications of these crystals need to be understood better through extensive further studies.

The mechanism under acidic conditions, these rod-shaped nano-strontium/fluoride hydroxyapatite crystals dissolve, releasing strontium, fluoride, calcium, and phosphate ions. These released ions are critical for the remineralization process. The released ions contribute to the remineralization of demineralized enamel, replenishing lost minerals and thus helping to restore the structural integrity and strength of the enamel. Further studies are required to explore the possibility of these ions counteracting the acidification caused by cariogenic bacteria in the oral environment.

In the current study, nano-strontium/fluoride hydroxyapatite pastes exhibit a significant remineralization efficacy on initial caries under experimental conditions. Due to the ions-substitution up to 50 mol% strontium induces lattice distortion and decreases crystal symmetry. In contrast, fluoride substitution causes the lattice contraction and enhances crystallinity. However, the co-doped strontium/fluoride substitution causes slight distortion and smaller lattice parameters. Consequently, the nano-strontium/fluoride hydroxyapatite proves more stable than strontium-substitution hydroxyapatite but displays less crystallinity than fluoride-substitution hydroxyapatite and pure hydroxyapatite.[26,27] The co-doped strontium/fluoride substitution, combined with hydrothermal synthesis, produces nanometer-sized crystals. These modifications increased stability[27], promoting micropore filling, and reduce crystallinity[27], thereby preventing surface aggregation or pore occlusion at the surface. Consequently, there is an expectation of enabling deeper penetration into the initial caries lesion. Moreover, the acid attack process may dissolve the crystals, potentially releasing

ions that serve as a reservoir for the remineralization of partially demineralized enamel. As a result, the groups treated with of nano-strontium/fluoride hydroxyapatite pastes exhibited the lesion depth reduction and increased mineral density. However, the 10%wt nano-strontium/fluoride hydroxyapatite group had a greater opportunity to form a protective layer or outer surface pore filling, increased crystallization in correlation with the concentration. This protective layer could inhibit the direct pore-filling into the subsurface lesion of artificial initial caries. As the result, the lesion depth regained in the 5%wt nano-strontium/fluoride hydroxyapatite group is better but with less opacity than the 10%wt nano-strontium/fluoride hydroxyapatite group. The results indicate that the lesion depth reduction achieved with the 5%wt nano-strontium/fluoride hydroxyapatite group is better, though it exhibits less opacity compared to the 10%wt nano-strontium/fluoride hydroxyapatite group. Nevertheless, no significant difference was observed when compared 5%wt to 10%wt nano-strontium/fluoride hydroxyapatite groups or between treatments lasting 7 and 14 days. Considering the material properties, the study suggests that 5%wt nano-strontium/fluoride hydroxyapatite is more beneficial for remineralization purposes.

In this study, EDS elemental line graphs and images revealed two remineralization patterns: top-down and bottom-up approaches. The sodium fluoride group showed the top-down remineralization pattern, while the nano-hydroxyapatite and nano-strontium/fluoride hydroxyapatite groups followed the bottom-up pattern. In the top-down approach, minerals are deposited from the enamel surface towards the deeper regions of the caries lesion. This pattern, which relies on ion-mediated crystal growth from the surrounding environment, typically results in less organized mineral deposition and non-uniform distribution.[32] Conversely, in the bottom-up pattern, mineral deposition starts from the deeper regions of the caries lesion and progresses towards the enamel surface. This method depends on particle-mediated nano-precursors, where nanoparticles penetrate the deeper sections of the carious lesion, leading to homogeneous mineral deposition and more uniform mineral distribution.[32] Moreover, as confirmed in EDS graphs, the pattern of nano-precursor deposition in the nano-strontium/fluoride hydroxyapatite groups presented more intensity and homogeneity than the 10%wt nano-hydroxyapatite group and 1500 ppm sodium fluoride group. It's important to note that neither fluorine from the sodium fluoride group nor strontium and fluorine from the nano-strontium/fluoride hydroxyapatite groups were detected in EDS graphs. This observation emphasizes the idea that nano-strontium/fluoride hydroxyapatite infiltrated the deeper parts of the caries lesion to fill the micropores, subsequently gradually releasing ions, serving as a reservoir that facilitates deep lesion remineralization. Using 1500 ppm sodium fluoride as a positive control, due to its well-established efficacy in remineralizing early demineralized enamel[8], it's worth noting that nano-hydroxyapatite also demonstrates a remineralizing effect comparable to that of sodium fluoride.[4,15,16,21,22] However, the enamel early lesions treated with nano-strontium/fluoride hydroxyapatite exhibited a statistically significant reduction in lesion depth compared to both sodium fluoride and nano-hydroxyapatite treatments. Although there was a better reduction in mineral loss with nano-strontium/fluoride hydroxyapatite, the difference was not statistically significant. Nano-strontium/fluoride hydroxyapatite may operate via two primary mechanisms that can be summarized as micropore filling and ions releasing. The rod-like nano-strontium/fluoride hydroxyapatite crystals fill the enamel micropores, replacing lost minerals of the partially demineralized enamel. Moreover, when exposed to acidic conditions often present in the oral environment, these crystals dissolve and release ions that aid remineralization. This suggests that nano-strontium/fluoride hydroxyapatite, with its rod-shaped crystal morphology, enhances remineralization efficiency and provides a more structured remineralization process. Essentially, it can replenish minerals from deep layers to the enamel surface while also leveraging ions to restore enamel minerals.

While the *in vitro* findings of this study are encouraging, the true validation will come from clinical trials and applications. Further clinical investigations are essential to validate these results and explore the long-term efficacy of nano-strontium/fluoride hydroxyapatite. As our study sourced the product from a single supplier, future research should aim to compare its effectiveness against other available dental products. Such comprehensive evaluations will establish the foundation for its incorporation into routine dental practice. The potential for nano-strontium/fluoride hydroxyapatite to revolutionize

the non-invasive treatment of early enamel caries is evident. Lastly, our findings suggest significant implications for clinical practice. The adoption of nano-strontium/fluoride hydroxyapatite might offer an effective, non-invasive strategy for managing early enamel caries. Nevertheless, before this treatment becomes a mainstay in dental practice, the practical considerations, including cost, feasibility, patient acceptance, and any associated risks, should be thoroughly assessed through extensive clinical trials.

Conclusions

The use of nano-strontium/fluoride hydroxyapatite paste under the pH-cycling model for 7 days demonstrated superior remineralization capabilities on initial caries lesions when compared to 1500 ppm fluoride paste and nHA. Both 5%wt and 10%wt concentrations of nano-strontium/fluoride hydroxyapatite pastes yielded remineralization outcomes of comparable efficacy. The remineralization assessments measured lesion depth and mineral profile using micro-CT, as well as element analysis using SEM/EDS.

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Conflicts of Interest

The remineralizing agents used in this study were provided by Inno-age Laboratory. The authors declare that there was no financial support or personal relationships that could have appeared to influence the work reported in this paper.

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Validation of a Comprehensive Oral Health Literacy Tool for Thai Older Adults: A Multicenter Cross-sectional Study

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Abstract

Objectives: This study aimed to develop and validate the Oral Health Literacy Assessment for Thai Older Adults (OHLA-OA) tool.

Methods: The study comprised two phases: tool development and data collection. The OHLA-OA consists of three sections: Reading Comprehension, Understanding Directions, and Self-evaluated OHL skills. A cross-sectional survey was conducted with 408 participants from four regions in Thailand. The average age of the participants was 66.8 years (SD=5.6). The descriptive analysis was performed to explore general information, and reliability and validity of OHLA-OA were tested using Kuder-Richardson Formula 20, Cronbach's Alpha, correlation, and logistic regression analyses.

Results: The OHLA-OA showed high reliability with a KR-20 coefficient of 0.79 and Cronbach's Alpha of 0.85. Concurrent validity demonstrated significant correlations between OHLA-OA scores and variables such as age, income, self-assessed literacy ability, and dental service utilization. Convergent validity showed a significant correlation (r=0.319, $p<0.001$) between OHLA-OA and the Thai Rapid Estimate of Adult Literacy in Dentistry (Th-REALD). Predictive validity indicated that higher OHLA-OA scores were associated with better oral health outcomes, including fewer decayed teeth (r= -0.166, $p=0.01$) and more filled teeth (r=0.184, $p<0.01$). The study proposed cut-off scores for 3 levels: Inadequate, Sufficient, and Excellent OHL.

Conclusions: The OHLA-OA tool demonstrated good psychometric properties, making it suitable for assessing oral health literacy among Thai older adults. It highlights the necessity of integrating literacy assessments into dental care and public health interventions to improve oral health outcomes in aging populations.

Keywords: assessment, older adults, oral health literacy, validation

Introduction

Thailand, like many other countries is experiencing a significant demographic shift with an increasing aging population.[1] This demographic change brings forth unique challenges in oral health care, as older adults face a higher prevalence of oral diseases in consequence of decelerating oral health-related quality of life.[2] The oral health prevention and promotion for older adults is required because good oral health affects overall well-being, and it maintains all significance meaning of oral health until the end of the life.[3]

The significance of oral health was previously described in the qualitative study that in older adults concerning only 3 aspects of oral health; comfort, hygiene, and heath, which are very challenging to achieve all in this group.[4] Older adults often encounter unique challenges related to oral health, including increased risk of dental diseases, tooth loss, and impaired oral function. To address these challenges, it is crucial to promote oral health literacy (OHL), in which it means ability to obtain, process, understand, and use health information to make a decision related to oral health[5], in order to strengthen this population's ability in self-care in against the oral health related problems and promote a quality of life.[6]

OHL is associated with good oral health status and oral health behaviours.[7-9] People with adequate OHL will be able to take care of their health, maintain optimal health, leading to happiness in daily life or quality of life. Health literacy in older adults has been studied in many places all over the world.[10-12] In the previous study in Thai older adults, it was found that poor oral health literacy associated with the fewer of number of natural functional teeth, the more teeth with active decay, and the less posterior occluding pairs.[13,14] Therefore, it is essential to promote oral health literacy in older adults to prevent the consequence of the poor oral health.

The Test of Functional Health Literacy in Dentistry in Older Adults (OA-TOFHLiD) was developed in 2019. It presents a good ability to assess oral health literacy in older adults.[15] However, since it is a pilot development, there were some complains about difficulty of the tools that may be too difficult and too complex for rural elderly people. In addition, the tool was pilot studied only one area in Thailand. Therefore, there is a need to further development of an OHL tool, so that it can be used with Thai older adults across the country. The objective of this study was to develop a comprehensive tool to assess oral health literacy for general Thai older adults and to test the validity and reliability of the instrument.

Materials and Methods

The study was divided into 2 phases: The tool development phase and the data collection phase

Phase I: Tool development

A tool was partially modified from the Test of Functional Health Literacy in Dentistry in Older Adults (OA-TOFHLiD).[15] The original OA-TOFHLiD composed of 4 parts of a closed test and 2 parts of a prompt. The newly developed tool was developed according to the suggestions from previous studies[13,16] that the instrument was too long and too difficult for community-living older adults. Researchers also worked together with the experts' comments. Therefore, the meeting for considering the content and further development of the tool was arranged in June 2021, consisting of 5 dental public health specialists from different sectors (University, Ministry of Public Health, and Hospitals). The panel decided to delete some content of the OA-TOFHLiD, but still use the template (a modified closed test and a prompt) and add the new part (subjective assessment of the set of OHL skills) to evaluate OHL in older adults comprehensively.

The Optimized Oral Health Literacy Tool for Thai Older Adults (OHLA-OA)

The newly optimized ***Oral Health Literacy Assessment for Thai Older Adults (OHLA-OA)*** comprises three distinct sections:

Section 1: Reading Comprehension (17 points)

This section includes two subtopics in the final version: 1) Basic knowledge regarding dental caries and its prevention. 2) Knowledge about gum disease and oral hygiene care. In this part, several words within the passages are omitted at intervals of 5-10 words. Respondents must select the appropriate word from four provided alternatives to complete the sentence correctly.

Section 2: Understanding Directions (10 points)

This section involves interpreting a medicine label. Respondents are required to read the provided label and answer questions related to the information on that label (Figure 1).

Section 3: Self-evaluation of Oral Health Literacy Skills (12 points)

This section consists of 12 topics assessing the respondents' ability to obtain, access, and understand oral health information, as well as their capacity to apply this information in daily life or situations related to oral health. The maximum score for the Reading Comprehension section is 17 points (1 point per each item), for the Understanding Directions section is 10 points (2 points per each item), and for the Self-evaluation section is 12 points (Likert scale 0-4).The raw scores in the Self-evaluation have a maximum of 48 points. However, to ensure a balanced representation across all sections, we rescaled these scores to a maximum of 12 in this section. This adjustment was made to prevent an overemphasis on Section 4 relative to Sections 1-3. By dividing the raw scores by 4, we maintained the relative performance of participants while ensuring that no single section disproportionately influenced the overall score.

Additionally, a socio-demographic questionnaire developed in the previous study[15], which includes age, gender, educational level, socio-economic status, oral health care behaviours and dental service utilisation was distributed together with the OHLA-OA to provide data for validity analyses.

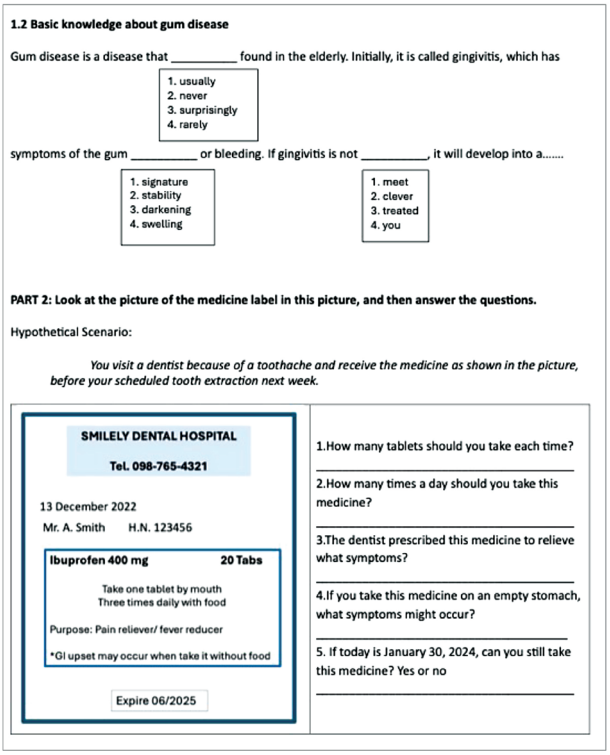

Figure 1: Example of a reading comprehension section and an understanding direction section excerpted from the OHLA-OA and translated to English

Phase II: Data collection

Study design and settings

This study was a cross-sectional survey conducted in April to October 2022, purposively selected a research center from 4 different settings in Thailand including Tak, Nakhon Ratchasima, Yala, Saraburi and Nonthaburi. These centers were the representatives of 4 major regions of Thailand (North, Northeast, South, and Central respectively). The ethical approval for conducting a study was obtained from the ethical committee of Faculty of Dentistry, Chiang Mai University, Thailand (Reference number 37/2021)

Calibration of the examiners

In March 2022, a total of 10 examiners (dentists and dental nurses) and 10 research assistants from 4 centers received training and calibration from the researcher. The training session featured a lecture outlining the data collection procedures and protocol. Additionally, examiners from the 4 centers participated in oral examination training and calibration with the gold standard (PW) on 10 older adults. The inter-rater reliability was found to be 0.81, demonstrating very good consistency.[17]

Sample selection

The sample size was based on a previous validation study of TOFHLiD.[18] In this study, we incorporated a minimum of 100 participants from each of the four centers, aiming for a total participant count of no fewer than 400. Utilizing convenience sampling, we targeted individuals over the age of 55 who were present at the centers on the designated data collection days. To recruit participants, we disseminated infographic advertisements on the social media platform (Line) two weeks prior to the commencement of data collection. Each potential participant was provided with a patient information sheet, which was also verbally explained by a research assistant. Written informed consent was obtained from those who agreed to participate. The study excluded individuals who were unable to read or write in Thai or those with significant medical conditions that would hinder their ability

to independently complete the test (e.g., severe vision impairments or cognitive disabilities).

Questionnaires administration and oral examination

On the data collection day, participants were provided with two self-administered questionnaires: the OHLA-OA and the demographic questionnaire. Upon completion of these questionnaires, participants' pronunciation skills were assessed using the Thai Rapid Estimate of Adult Literacy in Dentistry (Thai REALD-30)[19] which served as the reference oral health literacy (OHL) tool.

The oral examination aimed to assess dental caries status and treatment needs, utilizing only a mouth mirror for the examination. The protocol and diagnostic criteria adhered to adaptations from the 7th Thai National Oral Health Survey.[20] Dental caries were evaluated according to the World Health Organization (WHO) criteria using the Decayed, Missing, and Filled Teeth (DMFT) index.[21] In addition, the prostheses status and prosthesis needs, and the number of natural functional teeth were assessed. Additionally, the examination included an assessment of prosthesis status and needs, as well as the number of natural functional teeth.

Statistical analysis

Descriptive statistics were utilized to depict the characteristics of the respondents in this study, encompassing oral health status, treatment needs, and the scores from the OHLA-OA and Th REALD-30 assessments. For the evaluation of concurrent validity, it was posited that oral health literacy would be associated with age, educational attainment, monthly income, frequency of dental service utilization within the past year, and self-assessed literacy skills. This hypothesis was examined using Spearman's rank correlation.

For the assessment of convergent validity, both Spearman's rank correlation and linear regression analysis were employed to determine the correlation between OHLA-OA scores and Th REALD-30 scores. Predictive validity was assessed by examining the ability of OHLA-OA scores to predict oral health status through Spearman's rank correlation and binary logistic regression.

The internal consistency reliability of the questionnaire was assessed using the Kuder-Richardson-20 (KR-20) coefficient for parts 1 and 2, and Cronbach's Alpha for part 3. The scoring ranges for the new tool were defined based on Sorensen's Health Literacy levels and were categorized into four quartiles: inadequate, marginal, sufficient, and excellent.

Data analysis was conducted using SPSS software for Mac version 23 (IBM Corp, 2015). For multivariate analysis, participants were categorized by age, gender, educational level, residential area, income, dental service usage in the past year, and the number of caries, fillings, or missing teeth. All statistical analyses were two-tailed, with a significance level set at 0.05. To enhance the utility of the new tool for older adults who cannot read or write, a statistical analysis was performed to create a shortened version of OHLA-OA using scores from part 3, which involves a self-rated OHL skill suitable for interview-based administration. This was analyzed alongside the full version.

Results

Descriptive results

The demographic details of the participants in this study are presented in Table 1. A total of 408 individuals participated, with a majority being female. Participants' ages ranged from 55 to 86 years, with a mean age of 66.8 years (SD=5.6). Nearly half (42.6%) of the respondents had an educational level of primary school or lower. Monthly income among participants varied from 0 to 100,000 Thai Baht, with a mean income of 13,282.6 Baht (SD=16,901.5 Baht).

In terms of dental service utilization, only 39.5% of the participants had accessed dental services within the previous year. The majority of these individuals (50.5%) sought dental services for symptomatic reasons, while 27.6% attended for regular check-ups.

The scores for the OHLA-OA full version ranged up to 39, with a mean score of 31.7 (SD=4.5), a maximum score of 39, and a minimum score of 8. In the shortened OHLA-OA, scores ranged from 0 to 12, with a mean score of 7.9 (SD=1.9). For the reference measure, the Thai REALD-30, the scores ranged from 0 to 30, with a mean score of 27.3 (SD=5.4).

Reliability

Two essential metrics were used to evaluate the instrument's reliability. Firstly, the combined parts 1.1, 1.2, and 2, which include a total of 22 items of objective

Table 1: Demographic data

Data		n	%
Gender	Male	115	28.2
	Female	293	71.8
Age	55-65	180	44.1
	Older than 65	228	55.9
Education	Primary school or lower	174	42.6
	Middle to high school	80	19.6
	Diploma, bachelor's degree or higher	154	37.7
Occupation	Current/retired government officer	101	34.1
	Business owner	36	8.8
	Agricultures, or self-employment	73	17.9
	Not working, or others	160	39.2
Utilisation of dental services within 1 year	Use	161	39.5
	Not use	247	60.5
Monthly Income	0-5,000 THB	219	53.7
	More than 5,001THB	189	46.3

measurements, were calculated using the Kuder-Richardson Formula 20 (KR-20). It was discovered that the KR-20 coefficient was 0.79, indicating good reliability. Additionally, Cronbach's Alpha was calculated for part 3, which consists of 12 items. The resulting Cronbach's Alpha was 0.85, signifying very good reliability. These measures show that there is a high degree of internal consistency throughout the instrument's different sections.

Validities

Concurrent validity

Table 2 in Part1 presents the results of concurrent validity. Concurrent validity identified the properties of the newly developed tool is associated with the criterion that it was established the correlation in the previous studies, for example age, income, number of dental services utilizations. The results found that the OHLA-OA scores negatively correlated with age (r=-0.103, p=0.037), positively correlated with monthly income (r=0.336, p<0.001), self-assessment literacy ability (r= 0.430, p<0.001), and the number of dental service utilisation in the previous year (r=0.110, p=0.0026).

For the short form, the correlation was found the same as the full form, except the correlation between the tool and the age.

Convergent validity

This property defines that the ability of the newly developed tool presents correlation with the selected gold standard. In this study, we selected the Th-READ 30 as the gold standard tool. It was found the correlation between the OHLA-OA full and short form were 0.319 (p<0.001) and 0.157 (p<0.001) consecutively.

Predictive validity

It was assessed by examining the ability of oral health literacy scores to predict oral health status. Initially, it was found that the Decayed, Missing, and Filled Teeth (DMFT) index was not significantly correlated with the OHLA-OA scores. However, when analyzing each component of DMFT separately, it was found that the total number of decayed (D) teeth was negatively correlated with oral health literacy scores in both the full and shortened versions (r=-0.166 and r=-0.126, p<0.001, respectively). Conversely, the total number of filled (F) teeth was positively correlated in both the full and shortened versions (r=0.146 and r=0.235, p<0.001). (Table 2.)

To further assess the predictive validity of the Oral Health Literacy Assessment for Older Adults (OHLA-OA), "good oral health status" was defined as a composite variable. This variable comprised two criteria: having no active decay and possessing more than 20 functional teeth. Participants meeting both criteria were categorized

as having "good" oral health status (coded as 1), while those not meeting these criteria were categorized as "not good" (coded as 0). Logistic regression analysis results, as reported in Table 3, demonstrated that both the full and shortened versions of OHLA-OA were significant predictors of good oral health status, with *p*-values of 0.030 and 0.029, respectively. These findings support the utility of OHLA-OA in predicting oral health outcomes among older adults.

Cut-of scores of the Oral Health Literacy Assessment for Older Adults (OHLA-OA)

To measure Oral Health Literacy (OHL) effectively, we employed standard methods to establish index thresholds and create distinct OHL levels. In this study, we proposed cut-off scores for the OHLA-OA, categorized into four groups-Inadequate, Marginal, Adequate, and Excellent-based on the threshold assessment of the HLS-EU indices by Sørensen *et al.*,[22]

Table 2: Results of validity assessment of the Thai OHLA-OA using Spearman correlation

n = 408	OHLA-OA Full version (Score =39)		OHLA-OA Shorten version (Score = 12)	
	r	*p*-value	r	*p*-value
Part 1: Concurrent validity				
Age	-0.103	0.037*	0.010	0.837
Monthly income	0.336	<0.001**	0.205	<0.001**
Self-assessment reading and writing ability scores	0.430	<0.001**	0.313	<0.001**
Number of dental service utilisation in previous year	0.110	0.026*	0.064	0.196
Part 2: Convergent validity				
Th REALD-30 (Reference tool)	0.319	<0.001**	0.157	0.001*
Part 3: Predictive validity				
DMFT	0.056	0.256	0.085	0.088
Number of Decayed teeth (DT)	-0.166	0.001*	-0.126	0.001*
Number of Missing teeth (MT)	0.037	0.460	-0.034	0.495
Number of Filled teeth (FT)	0.184	<0.001**	0.178	<0.001**
Number of functional teeth	0.023	0.640	0.038	0.443
Self-rated overall oral health	0.146	0.003*	0.235	<0.001**

OHLA-OA, Oral Health Literacy Assessment for Thai Older Adults
*Significant value: *p<0.05, ** p<0.001*

Table 3: Using OHLA-OA scores to predict good oral health status by Logistic regression analysis and controlled for confounding factors to determine the predictive validity

	Having good oral health status (Good)							
	OHLA-OA Full version				OHLA-OA Shorten version			
	Exp(B)	*p*-value	95% CI		Exp(B)	*p*-value	95% CI	
			lower	upper			lower	upper
Predictive								
OHLA-OA Scores	1.100	0.030*	1.009	1.198	1.145	0.029*	1.019	1.412
Controlling factors								
Age (years)	0.972	0.279	0.923	1.024	0.968	0.219	0.919	1.019
Monthly Income (THB)	1.000	0.544	1.000	1.000	1.000	0.610	1.000	1.000
Self-assessment reading and writing ability scores (scores 1-5)	1.078	0.716	0.720	1.621	1.022	0.913	0.693	1.506
Number of dental service utilisation in previous year (times/year)	1.007	0.117	0.998	1.015	1.007	0.100	0.999	1.015
Overall percentage	85.1%				85.1%			

OHLA-OA, Oral Health Literacy Assessment for Thai Older Adults
*Significant value: *p<0.05*

The threshold selection was conducted during the questionnaire development in Phase I, with experts unanimously agreeing that the minimum score for the Adequate OHL level should be no less than 50 percent. The expert panel also decided to use quartiles to determine four levels of OHL, with Q1 representing the Inadequate group and Q4 representing the Excellent group consecutively (Table 4).

Subsequently, the four levels of OHL were consolidated into three levels, following Sørensen's suggestion that three levels would be optimal for improving health literacy in vulnerable groups. Therefore, 'Inadequate (Q1)' and 'Problematic (Q2)' were combined into a single category, "Inadequate." Ultimately, the proposed cut-off scores for OHLA-OA are as follows: 1) Inadequate, 2) Adequate, and 3) Excellent.

The final cut-off points for each level of Oral Health Literacy (OHL) are delineated in Table 4, based on the upper and lower limit scores. For the full version of the OHLA-OA, individuals are classified as having Inadequate OHL with scores ranging from 0 to 32.50. Those achieving scores from 32.75 to 34.74 are categorized as having Sufficient OHL, while scores from 34.75 to 39.00 signify Excellent OHL. For the shortened version, the cut-off points are similarly defined: scores from 0 to 8 categorize Inadequate OHL, scores from 8.25 to 8.75 denote Sufficient OHL, and scores between 9 and 12 correspond to Excellent OHL. These thresholds facilitate precise classification of oral health literacy levels, aiding in targeted intervention and assessment.

Discussions

The validation of the Oral Health Literacy Assessment for Thai Older Adults (OHLA-OA) reveals several key findings that significantly contribute to the field of oral health promotion and public health. Firstly, our tool was designed to measure comprehensive oral health literacy skills. It assesses not only word recognition, numeracy skills, and reading abilities as previously developed tools from past decades have done[23], but also evaluates health literacy comprehensively as an outcome of health promotion actions and the perceived abilities of respondents. This approach aligns with contemporary health promotion concepts, empowering individuals to take charge of their health to modify the determinants of health.[6]

The questions in the reading comprehension passages required basic oral health knowledge. For instance, participants were asked about active ingredients in toothpaste that prevent tooth decay. These prompts evaluated participants' comprehension of numbers and label reading skills. Additionally, the self-evaluation of oral health literacy skills, such as the ability to seek, understand, and apply information for oral health care and the use of dental services—was included. This section was added to enhance the tool's properties, addressing a limitation identified in a previous study.[15]

The full version of the OHLA-OA is a comprehensive assessment tool that evaluates older adults' abilities across different dimensions of oral health literacy, including functional, communicative, and critical health literacy. Developed through Delphi methods by experts in dental public health and gerontology, this version requires participants to read, understand, and perform tasks related to oral health, such as comprehending prescribed medications and following directions for their use. This self-administered questionnaire is designed to thoroughly test the respondents' literacy in line with the defined criteria.

Table 4: The proposed cut-off scores of the OHLA-OA

Level		OHLA-OA Full version				OHLA-OA Shorten version			
	Quartile	Lower limit score	Upper limit score	n (408)	%	Lower limit score	Upper limit score	n (408)	%
{ Inadequate	<Q1	0	29.75	96	23.5	0	6.50	98	24.0
{ Problematic/Marginal	Q1-Q2	30.00	32.50	106	26.0	6.75	8.00	119	29.2
Sufficient/Adequate	Q2-Q3	32.75	34.50	104	25.5	8.25	8.75	74	18.1
Excellent	>Q3	34.75	39.00	102	25.0	9.00	12.00	117	28.7

OHLA-OA, Oral Health Literacy Assessment for Thai Older Adults

However, the short version of the OHLA-OA, developed as a supplementary tool, addresses the limitations observed during the validation process of the full version. Specifically, some participants were excluded from the study because they were unable to read and write independently, despite demonstrating adequate oral health knowledge and oral health literacy skills. This limitation was also found in the study using the self-administered tool in older adults.[16] Recognizing this gap, the researchers created the short version to include individuals who might have low literacy levels but possess functional oral health literacy. This version simplifies the assessment process and can be adapted to an interview format, thus making it accessible to a broader range of older adults. While the short form is statistically validated and effective for certain populations, it does not fully replicate the comprehensive evaluation provided by the full version. Further empirical studies are required to validate the short version within broader and more diverse populations.

Furthermore, researchers increased the number of participants from the previous study, despite the prior confirmation that a sample size of one hundred participants suffices for validation studies.[24] This study included four hundred participants from four major regions of Thailand, enhancing the statistical power and ensuring the tool's usability in the general Thai older adult population. The increased sample size is crucial for predictive validity analysis, as it affects clinical outcomes.[25]

The tool demonstrated strong psychometric properties. Concurrent validity was confirmed through correlations between OHL scores and expected variables such as age, educational attainment, monthly income, and self-rated literacy abilities. These findings are consistent with previous studies on Thai older adults[15], and also the studies in the diverse population for example in Iranian[26], Dutch[27], Brazilian[28], Japanese[29] and Canadian adults.[30] This consistency indicates that the tool is robust and can be used confidently across various populations to assess oral health literacy. Additionally, the tool's sensitivity to different educational and socioeconomic levels underscores its utility in identifying at-risk populations, enabling healthcare providers and policymakers to tailor educational programs and resources effectively.

However, Table 2 reveals that age is not correlated with the outcomes of the shortened version of the OHLA-OA. This lack of correlation is attributed to the subjective nature of the shortened version, which primarily assesses self-perceived abilities to access, understand, and use health information for oral health management. As a result, the responses are not dependent on age, and there are no right or wrong answers. In contrast, the full version of the OHLA-OA is designed to objectively measure functional, communicative, and critical OHL, with the first and second sections focusing on these objective metrics. These sections require OHL skills related to functional ability, which the scores may be influenced by cognitive decline associated with aging.[31]

The findings from the convergent validity assessment revealed a significant correlation between OHLA-OA and Thai REALD-30. Although Thai REALD-30 assesses a different aspect of health literacy—serving as a pronunciation test, whereas OHLA-OA is a self-administered questionnaire—both instruments are grounded in similar theoretical frameworks and concepts. These results suggest that OHLA-OA can evaluate OHL to a comparable standard as previously validated instruments. This study aligns with prior research, indicating significant correlations among different OHL measurement tools, although the correlations are not strong ($r<0.5$).[18] The lack of robustness in this correlation may be attributed to the fact that OHLA-OA assesses not only functional OHL, as the REALD-30 does, but also attempts to measure functional, interactive, and critical OHL.

OHLA-OA demonstrated favorable predictive validity. It was negatively correlated with the number of active decayed teeth, suggesting that lower OHLA-OA scores are associated with a higher number of decayed teeth. Conversely, higher OHLA-OA scores correlated with a greater number of filled teeth and better self-rated oral health scores. These results are consistent with previous research highlighting the importance of oral health literacy in maintaining overall oral health. Individuals with higher oral health literacy scores exhibited better oral hygiene practices[32] and had lower incidences of dental caries and periodontal disease.[9] This underscores the critical role of oral health literacy in health outcomes and highlights the necessity of integrating literacy assessments into routine dental care and public health interventions.

Efforts to manage oral diseases and conditions in older adults should be enhanced by providing accessible and affordable oral health services that are tailored to their specific needs, particularly for underprivileged and vulnerable populations.[33] Established cut-off scores of the OHLA-OA are crucial in this context as they enable the identification of individuals most at risk of poor oral health outcomes due to inadequate literacy. These scores facilitate the precise targeting of interventions and efficient allocation of resources, ensuring that those below designated thresholds receive intensive educational programs or preventive measures.[2] Incorporating these cut-off scores into clinical practice and public health research allows for the early detection of at-risk groups, enabling proactive and tailored interventions. This approach not only improves the effectiveness of programs aimed at enhancing oral health literacy but also ensures that interventions are timely and appropriate for each level of oral health literacy. Consequently, it is essential to develop specific interventions tailored to meet the distinct needs of each literacy group in the future studies.

The development of OHLA-OA aimed to address gaps identified in the previous OA-TOFHLiD tool.[15] Utilizing a comprehensive development approach, including expert consensus, pilot testing, and iterative revisions, contributed to the tool's acceptable validity. The inclusion of both objective knowledge-based and skill-based questions and subjective self-assessment items ensured a thorough evaluation of individuals' understanding and attitudes towards oral health. This dual approach not only measures health literacy but also provides insights into behavioral and attitudinal barriers affecting oral health practices. Additionally, the study introduces a shortened version of the tool, which has been optimized for use as an interview questionnaire, complete with established cut-off scores to facilitate future research. To further enhance the utility of the OHLA-OA, it is imperative that the shortened version undergoes separate validation. This rigorous validation process is essential to ensure its accuracy and reliability before its application in broader research contexts.

However, the cross-sectional study design limits the ability to infer causality between oral health literacy and health outcomes. Longitudinal studies are recommended to establish temporal relationships and examine the impact of interventions aimed at improving oral health literacy over time. Additionally, while the tool was tested in a diverse population, further validation in specific subgroups, such as dependent older adults, is recommended. Future research should also explore the integration of this tool into digital platforms.

Conclusions

In conclusion, the Oral Health Literacy Assessment for Thai Older Adults (OHLA-OA) represents a significant advancement in the assessment of oral health literacy. Its reliable and valid measures offer a valuable resource for healthcare professionals, educators, and policymakers. By identifying and addressing oral health literacy gaps, we can enhance oral health prevention and promotion, reduce oral health disparities, and ultimately improve the oral health and quality of life of the older adult population.

Acknowledgment

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Conflicts of Interest

The authors declare no conflict of interest.

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Horizontal Ridge Augmentation Using Sticky Bone with Platelet-Rich Fibrin (PRF) in Anterior Maxilla Clinical and Histologic Evidence: A Case Report

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Abstract

Alveolar ridge deficiency is an unavoidable sequela of tooth extraction and poses major clinical challenges when reconstruction is anticipated. Various surgical approaches have been proposed to address horizontal defects, with autogenous bone grafting considered the current benchmark. However, alternative methods, utilizing tissue engineering principles and bone substitutes, offer reduced patient morbidity. This report presents an alternative case of severe horizontal bone defect augmentation in the anterior maxilla using sticky bone in conjunction with platelet-rich fibrin (PRF), and a Ti-reinforced membrane. Histologic evidence of sticky, deproteinized bovine bone material (DBBM) mixed with PRF without the use of autogenous bone is reported.

Keywords: alveolar ridge augmentation, bone substitutes, guided bone regeneration, platelet-rich fibrin, tissue engineering

Introduction

The current emphasis in dental prosthetics is on positioning implants to enhance both functional and aesthetic outcomes.[1] When assessing implant therapy for tooth replacement, the amount of remaining alveolar ridge significantly influences the ability to place the implant at the optimal site. In many cases, the presence of a resorbed residual bony defect poses challenges in achieving implant and volume stability due to insufficient support from the surrounding bone structure. The bony defect manifests as horizontal, vertical loss, or both, in terms of height and volume. According to Benic and Hämmerle[2], such clinical situations are classified as Class 3 or higher, indicating the necessity of a staged approach for bone augmentation prior to implant placement. A decision tree was proposed based on high-level evidence for scenarios requiring more than 6 mm of bone gain. This tree offers options such as autogenous block grafting, titanium mesh or a titanium-reinforced, non-resorbable, high-density, polytetrafluoroethylene (d-PTFE) membrane with bone substitutes, based on guided bone regeneration (GBR) principle.[3,4]

Autogenous bone is considered the gold standard graft, due to its osteogenic, osteoinductive, and osteoconductive properties. However, limitations, such as increased morbidity, limited availability, and variable resorption rates are recognized.[5] Tissue engineering approaches have been introduced, combining biologically inactive scaffolds with bioactive agents to stimulate bone regeneration. Various bioactive agents and growth factors, such as bone morphogenetic proteins (BMPs), enamel matrix derivative (EMD), or platelet-rich fibrin (PRF), have been utilized to enhance or accelerate bone formation.[6]

Case report

A 57-year-old, systemically healthy, Thai female presented with multiple missing anterior teeth, due to childhood trauma. Both the maxillary right and left canines had been extracted, and socket grafting was performed approximately 6-8 months before the examination. The patient expressed a desire to enhance both aesthetics and functionality with a fixed reconstruction in the upper anterior region. The oral examination of the upper maxilla revealed a partially edentulous condition with severe horizontal defect (Figure 1A). Cone beam computed tomography (CBCT) examination showed a severe horizontal ridge defect with sufficient vertical bone height. The bone graft material placed in regions of both the maxillary right and left canines from the ridge preservation appeared to be well-integrated. The crestal area widths at positions of maxillary right and left central incisors demonstrated a limited bone width of only 2-3 mm.

Following meticulous prosthodontic planning, the anatomical evaluation revealed that the bony defect did not allow for dental implants to be placed in positions compatible with prosthodontically-driven positions. The bone defect, classified as Class 3 by Benic and Hämmerle [2], represents one where sufficient volume stability of the area to be augmented is not provided by the adjacent bone walls (Figure 1B). Therefore, a staged bone augmentation was chosen, with implant placement scheduled for six months later. The surgical approach involved using Ti-reinforced d-PTFE with PRF block. Verbal and written informed consent was obtained prior to the surgery.

After administering local anaesthesia at the surgical site, a full-thickness mucoperiosteal flap was elevated to expose the alveolar crest and extended at least 5 mm beyond the bone defect. The defect was evaluated, confirming a knife-edge ridge with a crest width of 3 mm (Figure 2A). Multiple cortical perforations were created on the recipient sites to expose the medullary space, facilitating the migration of osteogenic cells, and enhancing blood supply[7] (Figure 2B). Prior to surgery, six tubes of blood were collected: five red-topped glass tubes were used to create A-PRF membrane (Figure 2C), and one green-topped plastic tube was used to create S-PRF plasma. The collected blood was centrifuged with the DUO Quattro (Duo Centrifuge, Nice, France), at 1300 rpm, for 14 minutes to obtain membranes and PRF plasma. The membranes were chopped into small pieces and mixed with 0.5 g of deproteinized bovine bone mineral (DBBM) (Bio-Oss®, small particles, Geistlich, Switzerland) at a 50:50 ratio[8] (Figure 2D). PRF plasma was added to enhance the stability of the bone graft, creating a PRF block (Figure 2E).

A Ti-reinforced, non-resorbable, high-density PTFE membrane (Cytoplast™, Biohorizons, USA) was initially secured on the buccal side with titanium tacks. The PRF block was applied, overcorrecting the defect, and obtaining approximately 10 mm of grafting material, specifically at positions of maxillary right and left central incisors (Figure 2F). The membrane was then anchored on the

palatal side and overlaid with a PRF membrane to enhance soft tissue healing and minimize membrane exposure risk.[9] (Figure 2G). After periosteal releasing incisions, a tension-free primary closure was achieved using horizontal mattress and single interrupted sutures (Figure 2H). Patients underwent follow-ups at 1 week, 2 weeks, 3 weeks, 2 months, and 6 months. Complete suture removal was performed at 3 weeks. Special care was taken to avoid the compression of removable dentures on the grafted sites during the initial stage of healing. At the re-entry, after 6 months, implant placements were performed using guided implant surgery.

Results

After 6 months, following the GBR procedure, primary closure was successfully maintained without any instances of wound dehiscence or membrane exposure. A well-rounded augmented ridge was noted, with good soft tissue condition (Figure 3A). Volumetric assessment, comparing pre- and post-augmentation, was performed using Materialise Magics (Materialise, Belgium) which indicated a significant increase in ridge width, approximately ranging from 4 to 6 mm (Figure 3B). A CBCT at 6 months revealed well-integrated bone graft material in the augmented area, resulting in horizontal bone gain of approximately 4 to 6 mm (Figure 3C). The homogeneity of the augmented area, with no irregularities, was noted.

At implant placement surgery, intra-surgical ridge assessment confirmed a horizontal bone gain of approximately 4 to 6 mm. An acceptable contour and curvature with a homogeneous surface and no residual graft particles were noted. (Figure 3D). During the implant osteotomy site preparation at positions of maxillary right and left central incisors, bone samples were collected for assessment using a trephine (Figure 3E). Guided implant placements were successfully performed without additional guided bone regeneration (GBR), at positions of maxillary right and left central incisors. However, simultaneous GBR

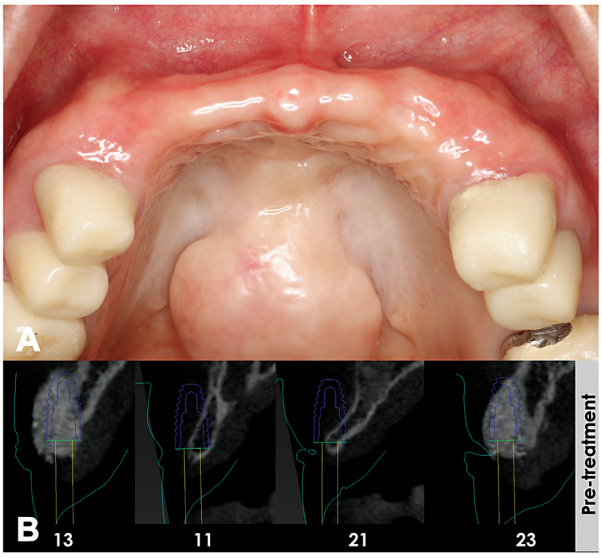

Figure 1: (A) An intra-oral photograph revealed a partially edentulous area from tooth 13 to 23 with a significant horizontal deficiency, but good soft tissue condition was noted (B) Prosthetic implant planning was performed using Co-diagnostix software (version 10.2.0, Dental Wings Inc., Canada). Class IV defects, as classified by Benic and Hämmerle (2014), were particularly notable in the areas of teeth 11 and 21[2]

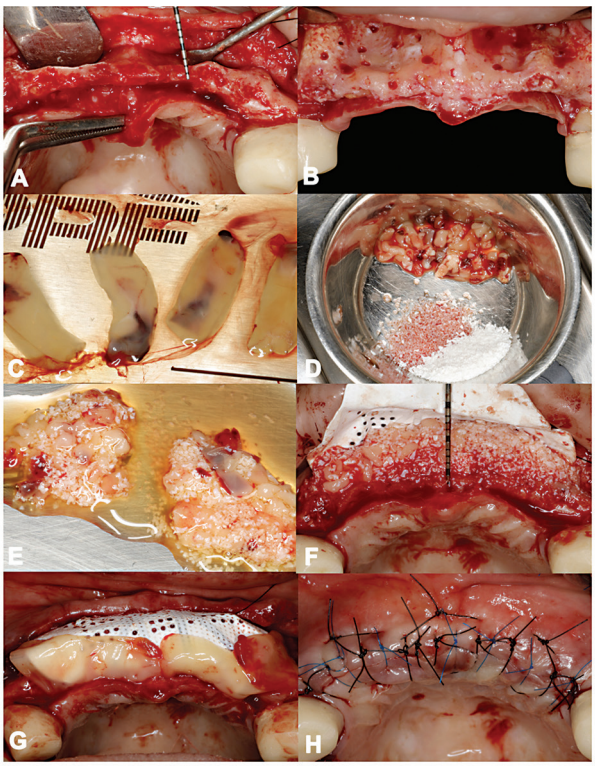

Figure 2: (A) The surgical assessment of the ridge defect. (B) Cortical perforation of the surgical site. (C) Preparation of PRF membranes. (D) Preparation of sticky bone. (E) The addition of liquid fibrinogen. (F) Application of the grafting material and d-PTFE membrane. (G) Application of PRF membranes over the d-PTFE membrane. (H) A primary closure, following periosteal releasing incisions, was performed

procedures were conducted at positions of maxillary right and left canines due to buccal dehiscence. Cover screws were installed, and a submucosal healing period of at least 4 months is planned before proceeding with prosthetic reconstruction (Figure 3F).

Histological analysis

Histological examination through Hematoxylin and Eosin (H&E) staining illustrates the presence of residual bone graft particles enveloped by recently synthesized woven bone with prominent irregular place reversal line (Figure 4A and 4B) Within this region, conspicuous vascularized fibrous connective tissue is observable, accompanied by regions populated by osteoblastic cells and multinucleated osteoclast giant cells (Figure 4C and 4D).

Discussions

The case illustrated that using a tissue engineering approach, with PRF as a bioactive agent, effectively augmented a large horizontal ridge defect in the anterior maxilla. However, success was contingent upon securing other crucial factors, including membrane placement, graft stability, and primary closure during the healing process.[4] To the best of our knowledge, this is the first case report which provided histologic evidence of using PRF mixed with DBBM without the use of autogenous bone.

PRF is produced through centrifugation, without the addition of additives, making it a purely autogenous substance.[10] PRF offers a fibrin-based scaffold enriched with a high concentration of platelets and leukocytes. It facilitates the continuous release of growth factors such as platelet-derived growth factor (PDGF), transforming growth factor beta-1 (TGFβ-1), insulin-like growth factor I (IGF-1), and vascular endothelial growth factor (VEGF) for up to 14 days.[11] Studies have shown that PRF membrane improved revascularization, enhanced soft tissue healing, and reduced the risk of bone or membrane exposure, thus minimizing complications following bone augmentation.[9,12] Despite showing promising clinical outcomes in promoting soft tissue repair and angiogenesis at the injury site, the effect of PRF on bone regeneration during GBR procedures has yet to be fully demonstrated.[13] Its ability to enhance angiogenesis is believed to be a critical factor in promoting bone regeneration during the early stages of healing.[9]

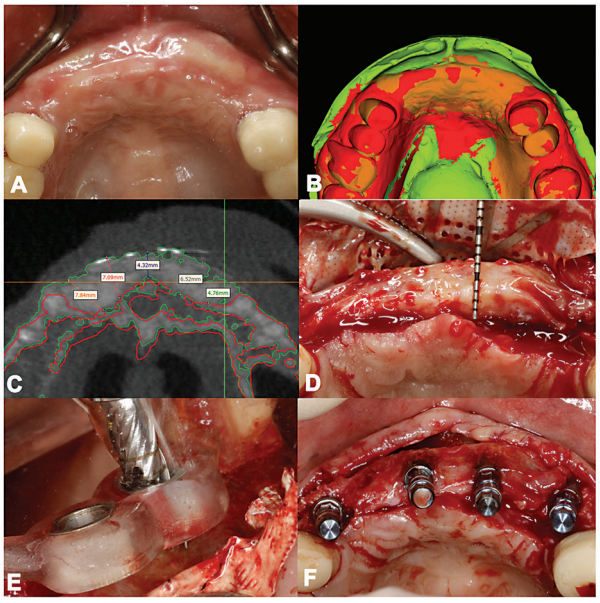

Figure 3: At 6 months following surgery. (A) An intra-oral ridge assessment. (B) The superimposition of intra-oral scans. The red scan represents the condition prior to the surgery, and the green scan represents the condition at 6 months post-surgery. (C) The superimposition of CBCT images. The red outline depicts the pristine condition, and the green outline displays the augmented areas. (D) An intra-surgical ridge assessment. (E) The augmented bone at positions of maxillary right and left central incisors was collected with a trephine for histologic evaluation. (F) Bone-level implants were placed according to prosthodontically planned positions to achieve the correct 3-dimensional position

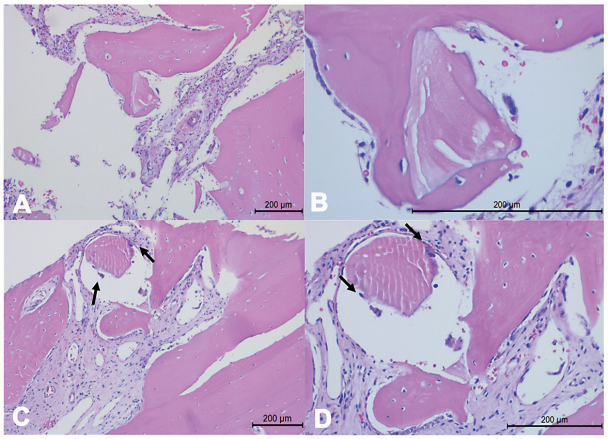

Figure 4: Photomicrographs of histologic samples stained with H&E. Focal areas of bone graft surrounded by new woven bone formation with prominent reverse lines, as seen in (A) at a magnification of x100 and (B) at a magnification of x400. Also, focal areas of bone graft surrounded by seams of osteoblasts and multinucleated osteoclast cells (indicated by black arrows) are depicted in (C) at a magnification of x100 and (D) at a magnification of x400

In this case, a tissue engineering approach that combined a biologically-inactive scaffold, specifically a xenograft material, with a bioactive agent (PRF) is expected to enhance or facilitate new bone formation.[14] A proof-of-concept study by Cortellini *et al.,*[8] showed the effectiveness of a PRF block; consisting of DBBM (xenograft) and PRF in augmenting deficient alveolar ridges. The result was a mean horizontal bone gain of 4.7±2 mm. However, resorbable collagen membranes were used instead of non-resorbable membranes. Similarly, a recent prospective study suggested that utilization of a composite of PRF, in conjunction with particulate xenograft, may effectively promote horizontal bone gain.[14] It is worth noting that only PRF membranes were used, and implants were simultaneously placed. Notably, a recent systematic review indicated a mean horizontal bone gain of 3.45±1.18 mm following staged lateral bone augmentation.[15] Consequently, it can be inferred that PRF block presents a viable alternative approach for horizontal bone augmentation, when compared to other surgical approaches.[16] From a patient perspective, this approach circumvents the need for invasive harvesting surgery and reduces morbidity.

In a clinical scenario, requiring more than 6 mm of horizontal bone gain, several surgical approaches have been proposed, including: block grafting; titanium mesh, combined with bone grafting; or a titanium-reinforced membrane, with bone grafts, based on the guided bone regeneration (GBR) concept.[3] Compared to other surgical approaches, GBR appears to offer greater predictability, reproducibility, and results in fewer surgical complications.[2] In addition, a split-mouth prospective study comparing bone regeneration between the use of d-PTFE and titanium mesh found that both devices could yield similar outcomes. However, higher incidences of membrane exposure with compromised results were noted, possibly due to the stiffness and sharp edges of the titanium mesh.[17] In this case, Ti-reinforced d-PTFE was chosen for to its ability to provide mechanical stability for the particulated graft, create a secluded space, and prevent soft tissue ingrowth.[18] The pores in d-PTFE, measuring less than 0.3 mm,[19] prevented the migration and colonization of bacteria while allowing the diffusion of essential molecules.

DBBM stands as one of the most widely studied bone grafting materials, renowned for its safety, osteoconductive properties, and biocompatibility. While lacking the ability to induce new bone formation, DBBM can maintain volume over time due to its non-resorbable properties. This attribute holds clinical relevance for specific indications, such as in the anterior maxilla.[20] It was observed that the graft resorption rate was approximately 15.6% for the DBBM and PRF approach. In contrast, the cases using allograft and collagen membranes observed results of approximately 50%.[21]

The histological depiction of residual bone graft particles amidst the woven bone matrix signifies the integration and potential incorporation of the bovine graft material into the host tissue. This integration process is facilitated by the surrounding vascularized fibrous connective tissue, which aids in the recruitment of osteogenic cells and supports the bone formation around the graft material. Moreover, the presence of osteoblastic cells and multinucleated osteoclast giant cells indicates active bone remodelling and suggests ongoing tissue regeneration at the graft site. Such observations underscore the dynamic interplay between host tissue and bovine graft material, ultimately contributing to the success of bone grafting procedures in promoting bone regeneration and repair. In some areas, bone grafts were embedded in dense connective tissue (provisional matrix), rich in mesenchymal cells, fibers, and vascular structures. It may be speculated that a longer healing time may be required to facilitate increased new bone formation.[22-23]

This case demonstrates that, prior to augmentation, implant placement was not feasible while considering prosthodontically-driven positions. However, following the augmentation procedure, the planned position lies entirely within the augmented area or the graft site, eliminating any anticipated simultaneously GBR. A systematic review revealed that implant survival rates, when placed in regenerated bone, ranged between 79% and 100%.[24] Moreover, an experimental study indicated that peri-implant tissue, after GBR using DBBM, exhibited a similar degree of bone resorption in an experimental, ligature-induced, peri-implantitis model, compared to that of native bone.[25] Despite the advantages of DBBM mentioned above, it has demonstrated a limited ability to induce bone formation.[26] By being in direct contact with the implant surface, it could adversely affect osseointegration and bone-to-implant contact (BIC). Additionally, a long-term follow-up is imperative to assess the effect

of loading on this augmented area and the survival of dental implants.

Conclusions

The use of sticky bone with PRF and d-PTFE membrane are a promising alternative surgical strategy for the augmentation of a large horizontal defect of the anterior maxilla. The advantages from the patient's perspective are clear, reducing patient morbidity by avoiding a second invasive harvesting surgery to collect autogenous bone. Nevertheless, autogenous bone is still considered the gold standard graft material, and long-term data on the stability of this augmented bone remains to be demonstrated.

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Conflicts of Interest

The authors do not have any financial interests, either directly or indirectly, in the products listed in the study.

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