INPLASY PROTOCOL

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INTRODUCTION

Review question / Objective: What is the diagnostic test accuracy of emerging technologies for non-cavitated dentin caries detection, considering in vivo and in vitro studies that reported results regarding the occlusal and proximal surfaces, over the last 10 years?

Emerging Technologies for Dentin Caries Detection. A Systematic Review and Meta-Analysis

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Review question / Objective: What is the diagnostic test accuracy of emerging technologies for non-cavitated dentin caries detection, considering in vivo and in vitro studies that reported results regarding the occlusal and proximal surfaces, over the last 10 years?

Information sources: Electronic databases of Medline, Embase, and PubMed were searched for articles published within the last decade (January 2011 to August 2021).in the period mentioned above. Medline and Embase databases were searched concomitantly using the Ovid interface. To find articles potentially missed by the search, Google Scholar was queried for diagnostic validity studies pertaining to technologies for dentin caries diagnosis.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 January 2022 and was last updated on 18 January 2022 (registration number INPLASY202210097).

> **Rationale:** Due to the declining caries trends worldwide as a result of fluoride introduction and emphasis on oral hygiene maintenance, there is an increased demand for effective methods of detecting caries lesions. Throughout the past decades, various new and innovative tools for caries detection have been developed, steadily progressing towards the contemporary clinical practice. Emerging methods for caries detection include non-ionizing

technologies based on fluorescence, light transillumination, light-emitting diode devices, fiber-optic transillumination, optical coherence tomography, alternating current impedance spectroscopy, optical coherence tomography and photothermal radiometry and modulated luminescence. Previous studies have evaluated the performance of caries detection methods in detecting and quantifying carious lesions, but results from in vivo and in vitro studies are heterogeneous and there is ambiguity regarding their overall effectiveness as diagnostic methods. Recent systematic reviews have investigated the most commonly used caries detection methods for occlusal and proximal studies, but they either overlooked less studied or reported methods, such as near-infrared light transillumination and alternating current impedance spectroscopy or included only in vivo studies. In order to gain a comprehensive view and address the risk of bias in both in vitro and in vivo studies, data from both clinical and laboratory settings were used in the present metaanalysis.

Condition being studied: The condition being studied are non-cavitated dentin caries lesions. These are caries lesions that have progressed further than the tooth enamel and have penetrated into the dentin level of the tooth. The review will consider what emerging diagnostic test can best detect these types of caries.

METHODS

Search strategy: The search was divided into three categories. The first category was associated with finding studies related to the clinical situation under investigation so the term "dental caries" was employed. The second category aimed to capture articles related to caries detection technologies, therefore the following terms were used: "lasers" OR "fluorescence" OR fiber optics" OR "optical coherence to m o g r a p h y" O R "light" O R "transillumination" OR "electrical conductivity". The third category aimed to capture diagnostic validity studies and the following terms were used: "diagnosis" OR "detection" OR "validity". Each category was connected to the others through the Boolean tool "AND" and the search was limited to the last decade.

Participant or population: Non-cavitated dentin caries.

Intervention: Diagnostic tests using emerging technologies for caries detection.

Comparator: Gold standard techniques.

Study designs to be included: In vitro and in vivo settings.

Eligibility criteria: Studies eligible for inclusion in the review examined the validity of one or more caries detection technology for diagnosis of dentin-level primary caries. Both in vitro and in vivo studies were accepted. Any sample size was accepted. There was no limit on the age of the population under in vivo conditions. Studies analyzing smooth, proximal, or occlusal surfaces of human permanent teeth were accepted. The following index tests were accepted: laser fluorescence (LF; DIAGNOdent 2095 or 2190, i.e. "DDpen", KaVo, Biberach, Germany), fluorescence camera (FC; VistaProof or VistaCam iX, Durr Dental, Bietigheim-Bissingen, Germany), nearinfrared light transillumination (NIR-LIT; DI-AGNOcam, KaVo, Biberach, Germany), light-emitting diode-based device (LED; Midwest Caries I.D.), OCT, fiber-optic transillumination (FOTI; Electro-Optical Science Inc., Irvington, NY, USA), quantitative light-induced fluorescence (QLF; Inspektor Research Systems BV, Amsterdam, The Netherlands), lightinduced fluorescence (LIF; SoproLife, SOPRO, ACTEON Group, La Ciotat, France), alternating current impedance spectroscopy (ACIS; CarieScan PRO, CarieScan LTD, Dundee, Scotland), as well as photothermal radiometry and modulated luminescence (PTR-LUM; Canary System, Quantum Dental Technologies, Toronto, Canada). Accepted reference standard tests were histology, micro-computed tomography (CT), operative validation, and

cone-beam computed tomography (CBCT). As radiography is commonly used in clinical settings, all types of conventional and digital bitewing radiographs used in conjunction with visual examination were considered an acceptable reference standard test for in-vivo studies.

Information sources: Electronic databases of Medline, Embase, and PubMed were searched for articles published within the last decade (January 2011 to August 2021).in the period mentioned above. Medline and Embase databases were searched concomitantly using the Ovid interface. To find articles potentially missed by the search, Google Scholar was queried for diagnostic validity studies pertaining to technologies for dentin caries diagnosis.

Main outcome(s): Outcomes of the quantitative analysis comprised: (a) descriptive statistics for sensitivity, specificity, and summary receiver operating characteristic (sROC); (b) estimation of decision odds ratios (DOR) applying the random-effects model of DerSimonian and Laird; (c) bivariate aggregated statistics for sROC and area under the curve (AUC).

Data management: RevMan 5 was used for primary data management. Data were later transferred to an Excel spreadsheet. The meta-analysis was performed with the R 4.0.5 language and environment for statistical processing, including packages "mada" (version 0.5.8), "meta" (version 4.18-2), "metafor" (version 3.0-2), and "mvmeta" (version 1.0.3).

Quality assessment / Risk of bias analysis:

A risk of bias (RoB) assessment tool for caries diagnostic studies, developed by Kuhnisch et al. was used to assess the included studies' quality. The tool is based on existing assessment methods such as QUADAS-2 and Joanna Briggs Institute Reviewers' Manual, but the signaling questions are tailored for the specific methodology of caries diagnostic studies. The tool consists of four domains: (1) selection and spectrum bias, (2) index test, (3) reference test, (4) study flow and data analysis. Within the four domains, there are a total of 16 signalling questions. Two reviewers independently evaluated the studies; any doubts or disagreements were resolved by consensus.

Strategy of data synthesis: Each caries detection and diagnosis technology was put in a separate review sub-group. Based on the number of included studies in each group, there were three types of analyses potentially carried out: (a) descriptive, (b) univariate, and (c) bivariate. For review groups with one study report, only descriptive analysis was performed. For groups with two reports, only descriptive and univariate analyses were performed. For groups with at least three reports, all three types of analyses were conducted (partially for three-study groups and comprehensively for the others).

Subgroup analysis: Meta-analysis was separately conducted for each technology, and each index test, tooth surface and study setting. In order to gain a comprehensive view and address RoB in both in vitro and in vivo studies, data from both clinical and laboratory settings were used in the present meta-analysis. The inclusion of all emerging detection methods into one comprehensive metaanalysis and systematic review and the analysis of these methods on different tooth surfaces allowed for a full assessment of the technologies and comparison.

Sensitivity analysis: Sensitivity analysis according to the One Study Removed Method was considered. It could be partially carried out, and only for the univariate analysis. For the bivariate analysis, at this stage, there were insufficient number of studies regarding the emerging technologies for such a sensitivity analysis approach.

Country(ies) involved: Romania.

Keywords: dental caries; dentin caries; diagnosis; occlusal caries; proximal caries; permanent teeth; laser fluorescence; optical coherence tomography (OCT); sensitivity; specificity. **Dissemination plans:** Publication of a research article in an open access medical journal.

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