PROSTHODONTIC APPLICATION OF INTRAORAL SCANNING SYSTEMS

Ph.D. Thesis

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Budapest
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"Life is a board game where the players must learn the rules while playing it."

Viktória Vitai

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1. LIST OF ABBREVIATIONS

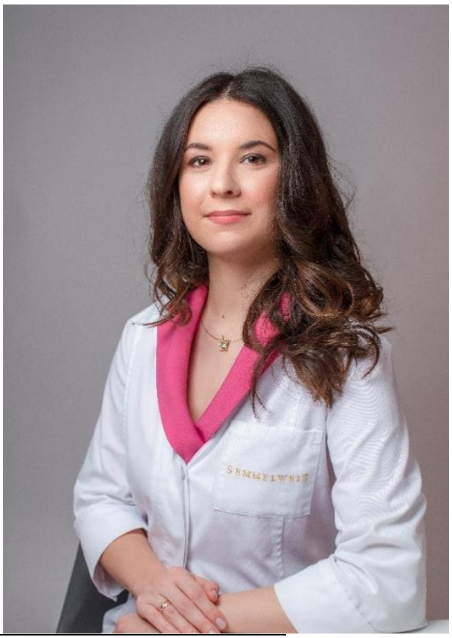
3D	3D-Master (Shade Guide System)
AT	Acceptability threshold
Blu	CEREC Bluecam
CAD/CAM	Computer-aided design/ computer-aided manufacturing
CI	Confidence Interval
CS35	Carestream 3500
CS36	Carestream 3600
CS37	Carestream 3700
DWIO	Straumann DWIO
E4D	Nevo E4D
Eme	Planmeca Emerald
Eme S	Planmeca Emerald S
ES	Vita Easyshade
ESA	Vita Easyshade Advance
ESV	Vita Easyshade V
Fast	Fastscan
GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
i500	Medit i500
IOS	Intraoral scanner

ISO	International Organization for Standardization
iT1	iTero Element 1
iT2	iTero Element 2
iTC	iTero Cadent
JBI	Joanna Briggs Institute (Critical Appraisal Checklist)
Lau	Launca DL-206
Lava	3M Lava COS
LED	Light-emitting diode
MA	Meta-analysis
MAD	Mean absolute deviation
NMA	Network meta-analysis
Omn	CEREC Omnicam
Plan	Planmeca Planscan
PMMA	Polymethyl methacrylate
Pri	CEREC Primescan
PT	Perceptibility threshold
RGB	red, green, blue
RMS	Root Mean Square
Run	Runyes Quickscan
SG	Shade guide tab

SP	spectrophotometer
SS	SpectroShade
SSM	SpectroShade Micro
STL	Standard Tesselation Language
TR1	3Shape TRIOS (standard)
TR2	3Shape TRIOS 2 (color)
TR3	3Shape TRIOS 3
TR4	3Shape TRIOS 4
TRU	3M True Definition
V	Visual shade selection
VC	Vita Classical (Shade Guide System)
Vir	Straumann Virtuo Vivo
Zfx	Zfx IntraScan

2. STUDENT PROFILE

2.1. Vision and mission statement, specific goals



My vision is to make high-end digital prosthodontics available to all patients.

My mission is to implement intraoral scanning systems in prosthodontic workflows.

My specific goals include evaluating the accuracy of intraoral scanners (IOSs) for complete-arch scanning and comparing the shade matching between the IOS and the spectrophotometer (SP).

2.2. Scientometrics

Number of all publications:	7
Cumulative IF:	21.34
Av IF/publication:	3,05
Ranking (Sci Mago):	D1: 4, Q1: 3, Q2: 0
Number of publications related to the subject of the thesis:	2
Cumulative IF:	8
Av IF/publication:	4
Ranking (Sci Mago):	D1: 2, Q1:0, Q2: 0
Number of citations on Google Scholar:	182
Number of citations on MTMT (independent):	97
H-index:	4

2.3. Future plans

My plans involve research, education, treating patients, and networking.

In the research field, I want to investigate the effect of scan number images, heat, and depth on the accuracy of IOSs. I want to guide dental and TDK students to learn how to do high quality research. I also want to continue with the research work I have been involved in for six years about validating IOSs to provide up-to-date information on the newest devices for dentists.

In the education part, I want to bring digital dentistry closer to dental students in predoctoral education. In the Department of Prosthodontics, we have several courses available for postdoctoral education, and I want to continue participating in the digital dentistry courses as a lecturer. I want to provide Moodle educational materials and videos on the topic for students.

I also aim to enhance my skills in patient care. I want to apply the knowledge I've gained from my research on IOS to my dental practice and eagerly await my patients' benefits. I also want to do photo documentation and case reports so I can present real-life translational medicine to dentists at conferences.

During the Ph.D. program, I learned that networking is one key point to be effective and successful, so I am excited and motivated to keep in touch with the researchers I met and build a good relationship with. Professor Vygandas Rutkunas, from the University of Vilnius, offered me the opportunity to join one of his studies and initiated a postdoctoral course with our Department. Another significant project, expanding the validation study of IOSs, is associated with Professor Francesco Mangano, President of the Digital Dentistry Society.

3. SUMMARY OF THE PH.D.

In the prosthodontic application of intraoral scanners (IOS), their accuracy and additional features, such as shade determination, are crucial.

Two meta-analyses (MAs) were conducted to compare the complete-arch scanning accuracy of different IOSs to that of reference Standard Tesselation Language (STL) files and the accuracy of IOSs tooth shade determination to that of reference spectrophotometers (SPs) in determining tooth shade.

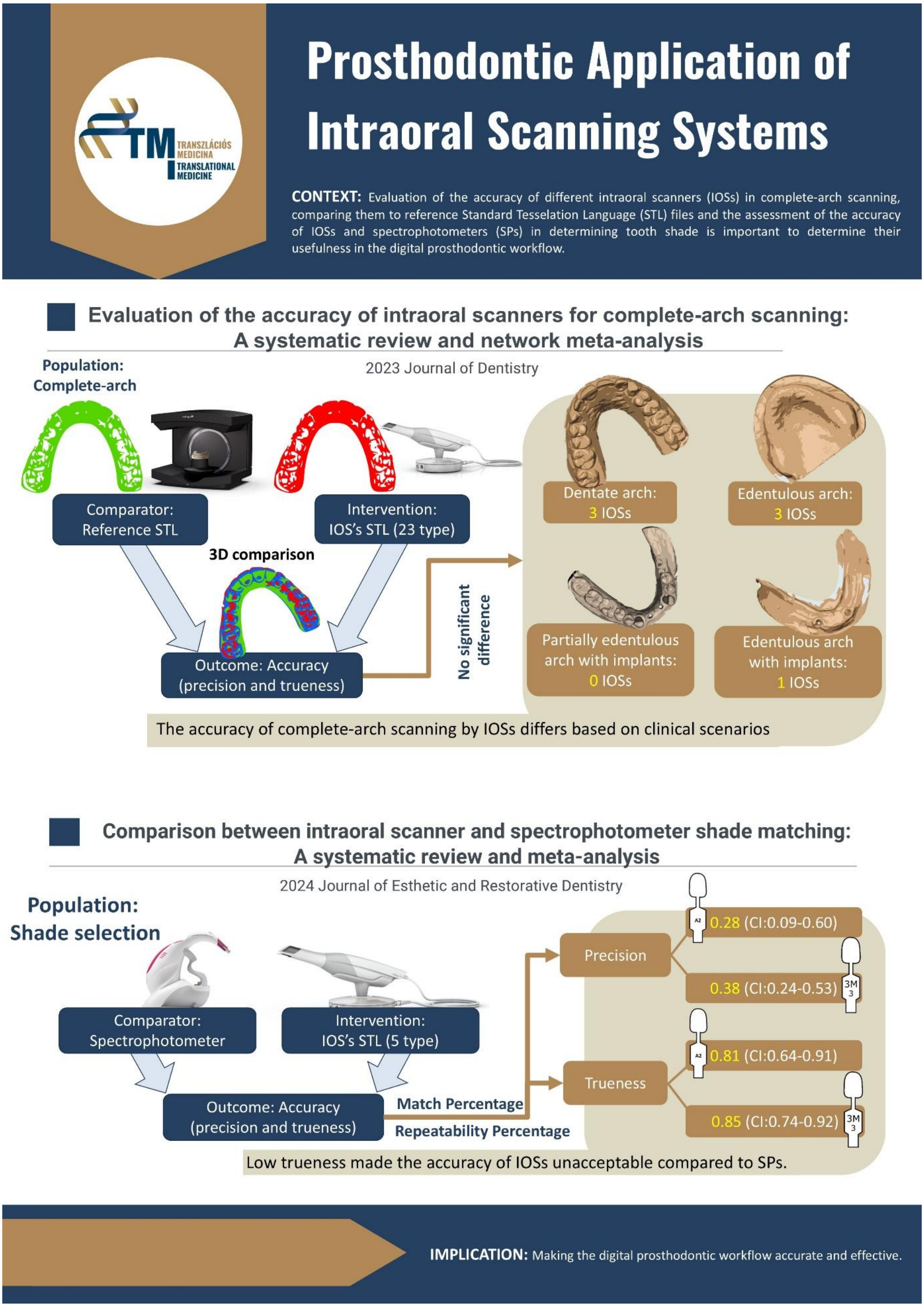
For Study I, in vivo and in vitro diagnostic test accuracy studies were included. A network meta-analysis (NMA) was performed to define the scanning accuracy for four arch subgroups using four outcomes (trueness and precision expressed as mean absolute deviation and root mean square values). The accuracy of IOS scans was similar to the reference scans for dentate arches (three IOSs), edentulous arches (three IOSs), and completely edentulous arches with implants (one IOS). The accuracy of the IOSs was significantly different from the reference scans for partially edentulous arches with implants. Significant accuracy differences were found between the IOSs, regardless of clinical scenarios.

For Study II, quasi-experimental studies were included. Quantitative analysis was performed to determine the accuracy of the IOS in subgroups using four outcomes: trueness and precision in 3D Master (3D) and Vita Classical (VC) shade guide system coding with different measurement locations. The shade determination trueness with IOS was 0.28 (CI: 0.09– 0.60) in VC and 0.38 (CI: 0.24– 0.53) in 3D shade guide codes. Repeatability was 0.81 (CI: 0.64– 0.91) in VC and 0.85 (CI: 0.74– 0.92) in 3D shade guide codes. Significant differences were found between the IOSs and SPs shade determination.

Study I found that the accuracy of complete-arch scanning by IOSs differed based on clinical scenarios.

In Study II, the accuracy of shade matching with IOSs was lower than that of SPs, though the precision is high and comparable to that of SPs.

4. GRAPHICAL ABSTRACT



5. INTRODUCTION

5.1. Overview of the topic

5.1.1. What is the topic?

The topic is the prosthodontic application of intraoral scanning systems, focusing on their complete-arch accuracy and the additional feature of tooth shade determination.

5.1.2. What is the problem to solve?

Dentistry is digitalizing, and the modern digital workflow begins with intraoral scanning. The number of new IOSs introduced in the market is proliferating; however, scientific knowledge and evidence often need to be improved, and the changes cannot be followed as quickly as rapid advancements. The biggest expectation against IOSs is accuracy, as, without an accurate impression, the fabrication of orthodontic appliances and prostheses is impossible. IOSs are not just impression machines; they also have additional features that can be used during the workflows. These devices can even determine the tooth color, which is essential for achieving an aesthetic result. The literature agrees that both visual and digital methods should be used for accurate color determination. The accuracy of shade determination with IOSs still needs to be investigated.

5.1.3. What is the importance of the topic?

More and more dental prostheses are manufactured with computer-aided design/computer-aided manufacturing (CAD/CAM) technology, where digital data generated from the upper and lower jaw is used to design the restoration digitally. Digital data can be generated by laboratory scanners or by IOSs. IOS can make the digital workflow and patient treatment faster and easier. One of the most critical factors determining patient satisfaction is tooth color. Due to human vision, the visual method is subjective and unreliable, so both digital and visual methods should be used together. If the scanner is capable of digital determination, there is no need to invest in a separate device or require additional time to determine the tooth color.

5.1.4. What would be the impact of our research results?

Our research aims to assist dentists in effectively using IOSs, particularly for prosthodontic procedures. We seek to determine whether they are fully equipped for all types of digital prosthetic treatments or if there are limitations in their usage. The accuracy of these devices is a critical factor. While they are considered sufficiently accurate for single restorations (1), the accuracy for full-arch scans remains uncertain, with both acceptable and unacceptable results reported in both clinical practice and the literature. Besides accuracy, manufacturers often try to convince dentists to purchase their products by offering special features such as caries detection, smile design, patient-specific movements, and shade selection. If these features are accurate and valuable, they can help make the treatment process more effective. However, dentists should be cautious if their performance is lacking and recognize that such claims may be more about marketing than evidence-based dentistry.

5.2. Background of the topic

5.2.1. Growing popularity of IOSs

The COVID-19 pandemic has significantly accelerated digital dental technology development and wide distribution. One example of the wide distribution is the expanding market for IOSs, which was valued at $382.52 million globally in 2020 and is expected to grow to $875.60 million by 2030, showing a compound annual growth rate of 18.6% from 2021 to 2030 (2). The rise of digital dentistry is primarily driven by its ability to enhance diagnostic accuracy, improve treatment planning, and streamline the creation of orthodontic appliances and prosthetics (3). In digital workflows, an IOS generates an STL file when creating a restoration or orthodontic appliance. This 3-dimensional file is usually used by the dentist or dental technician to design and manufacture the restoration with CAD/CAM technology. Therefore, obtaining a highly accurate virtual 3-dimensional model is essential for producing high-quality dental restorations and appliances.

5.2.2. Validation of IOSs

Along with the increasing number of IOSs on the market, dentists have encountered a new challenge: which is the best choice for their practice? To address this, the Department of Prosthodontics Digital Dentistry working group developed a unified set of criteria for comparing IOSs available in Hungary. In 2018, a validation protocol was introduced, and the results were published in 2022 (4). To make it accessible to practicing dentists and assist them in their decision-making, the comparative system and the processed data of

IOSs available on the Hungarian market were made accessible to dentists via the website https://semmelweis.hu/dentalszkenner/en/ (5).

The protocol evaluates IOSs based on both objective and subjective parameters.

A summary chart overviews the key factors influencing dentists when selecting an IOS that best suits their needs. This chart includes 21 distinct features, such as remote control, configuration, file types, system compatibility, application, and special functions (e.g., tooth-shade selection, jaw movement detection, pre-preparation scans, dowel core scans, impression scans, denture workflows, smile design, caries detection, and varying sizes of scanning tips). It also considers support, service, and training opportunities (4, 5).

One of the key evaluation points is accuracy; a polymethyl methacrylate (PMMA) model (featuring crown, bridge, and inlay preparations) was scanned ten times per dental student. The observed parameters were complete arch accuracy, abutment accuracy, inlay cavity accuracy, 4-unit bridge distance accuracy (distance between 14 and 17 abutments), and complete arch distance accuracy (distance between 17 and 27 distobuccal cusps). Accuracy results are expressed in precision and trueness in micrometers. The accuracy results are translated to scores so dentists can quickly conclude the accuracy of the different IOSs.

Ergonomic factors such as head circumference, scanner weight, and scanning time are also assessed (4, 5).

The study revealed that the accuracy of IOSs, particularly full-arch accuracy, was a crucial factor. Additionally, shade selection was also found to significantly impact the clinical usefulness of the IOS (5). As a result, our following research focused on these aspects.

5.2.3. Accuracy measurements of IOSs

IOSs are considered sufficiently accurate for producing single restorations (1). The introduction of newer generations of IOS devices has resulted in variations in their accuracy, especially regarding full-arch optical impressions (6). The accuracy of these devices can be assessed using various methods, as they generate STL files containing virtual 3-dimensional coordinates (7). According to ISO 5725–1 from the International Organization for Standardization (ISO), accuracy consists of precision and trueness.

Trueness refers to how close the average value is to an accepted reference value, while precision pertains to the consistency of results under defined conditions (8). Accuracy is usually measured using the mean absolute deviation (MAD) metric, but a more recent approach, the root mean square (RMS), is also used. RMS evaluates the absolute distance of all virtual points in the scanned area, showing trueness and precision in more detail (9, 10). Both metrics are used in the literature; however, the clinical significance of their differences remains uncertain. A comparative review of IOS accuracy metrics—MAD versus RMS—could clarify the metric most suitable for future research. To evaluate the accuracy of IOSs, we used STL files produced by laboratory or industrial scanners as references. Laboratory scanners provide wider coverage and offer high accuracy, similar to that of industrial scanners (11-14).

5.2.4. Clinical acceptability and influencing factors of the accuracy of IOSs

Measuring the accuracy of various IOSs is vital, but it is also essential to translate their clinical acceptability for different indications. Unfortunately, there is no consensus on an acceptable accuracy threshold for dental impressions or digital models. Instead, most studies suggest that the clinically acceptable misfit for fixed restorations ranges from 50 to 200 μm (15-17). The marginal film thickness of spark-eroded titanium copings is reported to be less than 120 μm (90 ± 44 μm) (18). In contrast, for Procera AllCeram crowns, the median maximal marginal gap width ranges from 80 to 180 μm in anterior teeth and from 115 to 245 μm in posterior teeth (19). Furthermore, based on McLean and Fraunhofer's original study, many studies consider 120 μm to be the clinically acceptable misfit (20). Factors influencing IOS accuracy include hardware and software characteristics (21-24), scan object properties such as material and span length (25-29), and clinical conditions (11, 30-32). These factors can be categorized into four main subgroups where the most significant accuracy differences occur: dentate arches, edentulous arches, completely edentulous arches with implants, and partially edentulous arches with implants. Other contributing variables include operator experience (33), scanning technique (34, 35), environmental conditions such as light, temperature, and humidity (36), and the presence of saliva or wet conditions (37).

5.2.5. Previous studies on IOS's accuracy

Numerous research are published connected to IOSs, with approximately 300 articles published every year since 2008 and the numbers are growing (38). With great numbers comes great heterogeneity due to the wide variety of methods used in these studies, making it difficult to draw definitive conclusions regarding the accuracy of different IOSs. A systematic review and MA comparing digital and conventional implant impressions confirmed the high heterogeneity across studies, which hindered the ability to perform a simultaneous MA in many cases (21, 39, 40). Before, no systematic review or NMA has directly compared IOSs. Given the growing market for IOSs, clinicians must consider all available data when evaluating the accuracy of different devices, and an NMA offers a valuable tool to estimate the relative ranking of various IOSs.

5.2.6. Shade determination in dentistry

In recent decades, aesthetic standards have significantly increased. Ensuring that the patient is pleased with the final result's function and appearance is crucial when creating a dental restoration. Zirconia and lithium disilicate are among the most commonly used materials. Selecting the appropriate color for the patient is often considered one of the most challenging aspects of achieving the desired aesthetic outcome (41, 42).

Tooth color can be assessed using various methods. One of the most widely used techniques, visual shade matching, has been practiced for many years. Various shade guide systems, such as the VC and the Vita 3D-Master systems, are commonly employed in the subjective process of visual shade assessment (43, 44). Although the Vita Toothguide 3D-Master tabs are often criticized for not accurately reflecting darker tooth shades, their system offers more precise results than the VC system, supported by scientific research (45-48). While dentists tend to favor visual shade matching, the accuracy of this method is influenced by several factors, including the operator, lighting conditions, and background (49-52).

The market has seen the introduction of digital objective methods to reduce the subjective part of shade matching. Devices like digital cameras, SPs, and colorimeters have been developed (53-55). While these tools may have slight differences, they offer greater accuracy in measuring tooth shade compared to traditional visual techniques. As a result, they are becoming increasingly popular among dentists for their ability to simplify procedures and save time (49, 56-58).

SPs transform the reflected light's intensity and spectral composition into tristimulus data (54, 59). Typically, measurements are taken at a single point on the tooth surface, where the light strikes perpendicularly (60). Due to their excellent repeatability, extensive research, and their status as gold standards in tooth-color measurement studies, SPs are regarded as highly dependable instruments (61).

Numerous IOS manufacturers offer a range of models, including tooth shade detection, caries identification, and smile design. While not all devices currently support tooth shade determination, there is a noticeable trend toward incorporating this capability, typically using a light-emitting diode (LED) as the light source. The IOS captures multiple images from various angles to create a 3-dimensional representation of the dental arch, and through the use of VC and 3D shade guide coding, the software can determine the tooth shade from the generated file. However, existing literature presents conflicting views on using IOSs for shade determination in routine dental treatments, as their accuracy has not been sufficiently validated.

5.2.7. Shade determination accuracy measurements

Various methods can be employed to assess the accuracy of shade matching. The trueness and precision (repeatability and reliability) of shade determination techniques can be demonstrated through percentage agreement or by quantifying color differences (62).

Precision refers to the extent to which independent test results agree when conducted under defined conditions. It also describes the overall variability observed in repeated measurements. There are two specific types of precision based on variability: repeatability, which involves fixed variables, and reproducibility, which consists of changing variables (63, 64).

Reliability refers to the connection between the size of measurement errors in observed data and the inherent variability in the "true" or underlying value of a quantity across different subjects. Repeatability is the variation between repeated measurements on the same subject taken under identical conditions. This implies that the same operator uses the same tool or method within a short time frame, where the underlying value is assumed to remain unchanged. Reproducibility describes how subject measurements can vary under different conditions (65).

There are various formulas for calculating color difference (ΔE). The CIELab color scale, where the L axis represents brightness, the axis represents red-green chromaticity, and the b axis displays yellow-blue chromaticity, can be used to calculate and measure ΔE between two measurements. CIEDE2000 (ΔE00) formula is the most recent, widely accepted to calculate ΔE and recommended by the International Commission on Illumination (CIE) (64). The results of color difference can be applied in clinical practice using the 50:50% perceptibility threshold (PT) and the 50:50% acceptability threshold (AT). According to the CIEDE2000 formula, the color difference thresholds are as follows: PT ΔE00 = 0.8 and AT ΔE00 = 1.8 (66). Unfortunately, IOSs cannot display the CIELab values directly; converting charts are needed to translate the 3D or VC shade guide codes to CIEALab values to calculate ΔE with the formula.

5.2.8. Previous studies on IOS's shade-determination accuracy

The shade-determination accuracy of IOSs is contradictory to that of the existing literature. Most studies have focused on their accuracy in both in vitro and in vivo settings, while more recent systematic reviews have also addressed the topic (62, 67). Some articles argue against using IOSs, while others strongly recommend their use due to their high precision results. Studies exploring various shade-determination methods suggest combining digital and traditional visual techniques for the most accurate outcomes (53). However, whether IOSs can be fully relied upon as consistent and reliable digital methods for shade determination remains unclear.

6. OBJECTIVES

6.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

This NMA aimed to investigate the accuracy, precision, and trueness of complete-arch intraoral scanning with different IOSs to that of reference STL files and to provide dentists with guidance on choosing the suitable device for complete-arch scanning through an NMA (68).

1. The first null hypothesis is that there was no statistical difference between the IOS STL scans and the reference STL scans.
2. The second null hypothesis is that there was no statistically significant difference in IOS devices' accuracy (precision and trueness).
3. Thirdly, we hypothesized that the accuracy of the 95% confidence interval (CI) of the IOSs was within the clinically acceptable threshold of 120 μm.

6.2. Study II. - Color comparison between intraoral scanner and spectrophotometer shade matching

This systematic review and MA aimed to compare IOSs' accuracy, trueness, and precision (repeatability) to SPs in determining tooth shade (69).

The research hypothesis is that there was no significant difference in the accuracy of shade selection between IOSs and SPs.

1. The null hypothesis is that there was no significant difference in shade selection between IOSs and SPs when trueness was expressed in match percentages.
2. The alternative hypothesis was that the repeatability of IOSs is high with a clinically acceptable match percentage.

7. METHODS

7.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

7.1.1. Protocol and registration

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 Statement and its extension for network analysis (70) were followed when reporting the systematic review and NMA. We used the Cochrane Handbook's Version 6.4 (71) criteria for Systematic Reviews of Interventions, and the review protocol (Study I: *CRD42021281989*) was registered on PROSPERO. The protocol was altered by switching from MA to NMA because of the large number of multi-arm studies.

7.1.2. Literature search and eligibility criteria

The systematic literature search was performed in five databases: MEDLINE (via PubMed), Cochrane Library (CENTRAL), EMBASE, Web of Science, and Scopus. The original articles provide the dates for the search and the query utilized (68).

We used multiple- or two-arm studies on primary diagnostic test accuracy published in English that reported on complete-arch scanning with IOSs as index tests and used reference standard STL files to compare accuracy. Maxillary and mandibular edentulous or dentate arches and arches with implants were included. Dentate arches included those with natural dentition with or without partial edentulism and with or without tooth preparation. Reference STL files could be generated by industrial or laboratory scanners. Studies determining accuracy (precision and trueness) by superimposition of data were included. The study included both in vitro and clinical studies (68).

7.1.3. Study selection and data collection

We used EndNote X21 (Clarivate Analytics, Philadelphia, PA, USA) to select articles. Two authors independently extracted the data using a standardized preconstructed data extraction form. A third author resolved disagreements between the data collectors.

Information about the article (first author, title, year of publication, study design), information about participants or dental models, information about IOS (type, software version), information about the operators, information about the sample size, information about the reference standard and information about outcomes (all possible data of the investigated outcomes were collected) were gathered from each eligible article. Automation tools were not used in this process.

If data were available as median and interquartile range (IQR) values with a normal distribution, they were used for the statistical analysis. Non-Normally Distributed Data were collected only for systematic review. If different complete arch types or environmental conditions (light source, presence of saliva, and different scanning strategies, among others) were compared within an article, all results were collected for quantitative analysis; however, for the qualitative synthesis, information on the following was used to reduce inconsistencies across the reports: normal dentition without crowding, prepared teeth, implant impressions made only with scan bodies, scanning strategy of the manufacturer, dry surfaces, room light conditions, and experienced operator (68).

7.1.4. Quality assessment

The risk of bias was assessed using the Cochrane Risk of Bias Tool for Primary Diagnostic Accuracy Studies (QUADAS-2) for each outcome (68, 72). A third reviewer resolved disagreements.

We used the GRADEPro Guideline Development Tool for visualization. We adhered to the advice of the "Grades of Recommendation, Assessment, Development, and Evaluation (GRADE)" workgroup to evaluate the quality of the evidence for each outcome (73).

7.1.5. Data synthesis and analysis

R (R Core Team 2022, v4.1.3) was used for the statistical analyses (74). The results were graphically summarized using forest plots. A network plot was created for each subgroup to determine if the resulting network was fully connected. Subgroup analysis was performed according to the different complete arch types, namely dentate, edentulous, completely edentulous with implants, and partially edentulous with implants. The RMS and MAD values were also investigated for precision and trueness in different subgroups. Based on these network plots, all subgroups were eligible for the NMA. The basic characteristics of each analysis were reported using network and study characteristic tables containing the most important statistics from each NMA. R software was supplemented with the BUGSnet package (74) for the statistical analysis. The detailed statistics are available in the original publication in Supplementary Material 2 (68).

7.2. Study II. Color comparison between intraoral scanner and spectrophotometer shade matching

7.2.1. Protocol and registration

The systematic review and MA followed the PRISMA 2020 guidelines and the Cochrane Handbook (71, 75). The study protocol was registered on PROSPERO (registration number CRD42022330109) and fully complied with it. The main research question of the MA was, "What is the accuracy of shade selection using IOSs?"

7.2.2. Literature search and eligibility criteria

An electronic search was performed on May 5, 2022, and updated on October 19, 2023, using the PubMed, Scopus, Embase, CENTRAL, and Web of Science databases. The search had no restrictions. A citation chaser tool (https://estech.shinyapps.io/citationchaser/) (76) was utilized to identify further articles cited or referenced in the included studies.

We included both in vivo and in vitro quasi-experimental studies that investigated shade matching with IOSs compared to SPs. Outcomes were accuracy measured in match percentage or color difference in ΔE and repeatability measured in match percentage in VC and 3D shade guide systems. Articles using shade selection on natural teeth or other specimens such as blocks, shade tabs, and crowns were included. In clinical studies where shade selection was done on patients' natural teeth, the inclusion criteria were subjects without any restorations (fillings, crowns, bridges) of the shade determination area. Discoloration and plaque, if present, should be removed. Exclusion criteria were bleaching and any restoration discoloration or caries in the area of shade selection. In the in vitro studies, shade determination with known tooth shade of the specimens was involved, as well as those where a reference measured the original shade (69).

7.2.3. Study selection and data collection

We used EndNote X21 (Clarivate Analytics, Philadelphia, PA, USA) to select articles. Two authors independently extracted the data using a standardized preconstructed data extraction form. A third author resolved disagreements between the data collectors.

The following information was retrieved by data extraction from relevant studies: author(s), year of publication, title, location, center, period, study design (in vivo, in vitro), population, shade subjects (patients, known colors of block or shade tabs), patient demographics (age, gender, inclusion criteria, exclusion criteria), number of measurements performed at a single location, measurement locations (cervical, central, and incisal region), type and number of teeth, sample size, operators (number, experience, inter- operator agreement), shade measurement methods, type of IOS, software version, type of SP, outcome type, and value. If data in the articles needed to be more sufficient, the authors were contacted by email to request clarification and any missing data (69).

7.2.4. Quality assessment

Two authors independently assessed the risk of bias using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Quasi-Experimental Studies (77). A third author (J.B.) decided if there was any disagreement. The overall risk of bias was determined based on responses to nine questions, and the percentage of each risk type was calculated.

The certainty of evidence for each subgroup was assessed using GRADE Pro (78).

7.2.5. Data synthesis and analysis

R (R Core Team 2022, v4.1.3) was used for the statistical analyses (74). The results were graphically summarized using forest plots.

Subgroups were formed based on various outcomes, measurement locations, and types of IOS. The initial division was made between groups based on trueness and precision. If sufficient data were available, these groups were further divided by tooth locations (incisal, central, cervical, or all locations) and IOS type. Given the expected considerable heterogeneity across studies, a random-effects model was used to pool the effect sizes. Study proportions were calculated using the total number of patients and the number of patients with the event of interest from each study. The pooled proportion and its 95% CI were used to determine the effect size. Statistical significance was set at p-values < 0.05. The findings of the MA were presented in forest plots. Where applicable, if the study number was sufficiently large and not overly heterogeneous, prediction intervals (indicating the expected range of effects in future studies) were also reported. Between-study heterogeneity was assessed using Higgins & Thompson's I statistics (79). A potential slight study bias was assumed if the p-value was less than 10%. However, it was noted that this test had limited diagnostic utility when fewer than 10 studies were included. The detailed statistics are available in the original publication (69).

8. RESULTS

8.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

8.1.1. Search and selection, characteristics of the included studies

A total of 3,815 studies were identified through the search keywords. Of these, 2,121 were screened, and 114 diagnostic test accuracy studies were included in this review, with 53 contributing to the NMA. The list of excluded studies and the reasons for their exclusion are provided in Supplementary Material 3 of the original publication. Cohen's kappa coefficient for title and abstract selection was 0.88, and for full-text selection, it was κ = 0.9, indicating nearly perfect agreement. A summary of the selection process is presented in **Figure 1**.

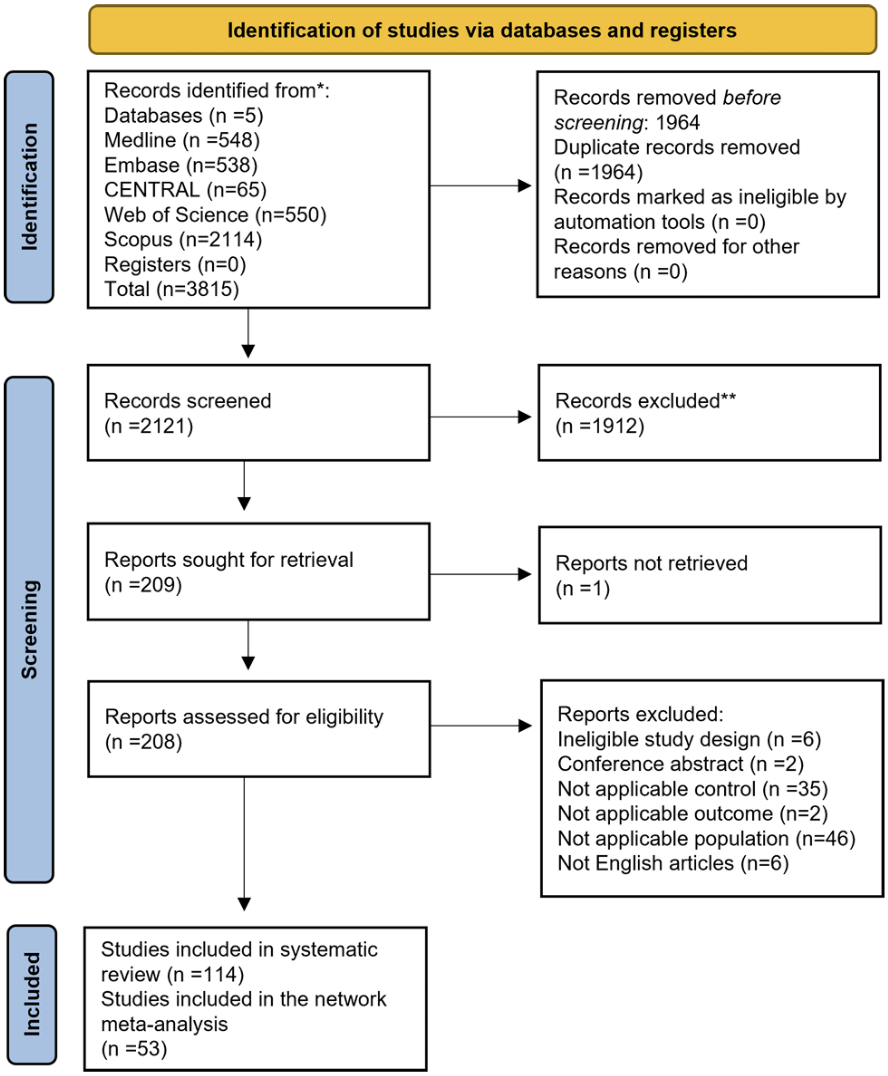


Figure 1. PRISMA flow program for study selection (68).

*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

All the studies included in this review were published in English between 2012 and 2022. A total of 26 IOSs were used across the studies. The details of the articles are provided in **Table 1**. For complete dental arches, five out of 21 IOSs were evaluated for trueness, and five out of 18 IOSs for precision, with each being mentioned in a single article. For edentulous arches, the ratio was two out of nine IOSs for trueness and three out of nine IOSs for precision. In the case of edentulous arches with implants, nine out of 17 IOSs were assessed for trueness, and six out of 12 for precision, each being investigated only once. For partially edentulous arches with implants, seven out of 12 IOSs were studied for trueness, and five out of 10 for precision.

Table 1. Basic characteristics of included studies in the final NMA (n=56) for Study I (68).

Author (year)	Type of full-arch	Operator	Scanner software	Scan strategy	Sample size	Intraoral scanner	Reference	Evaluation method
Zarone et al. 2020(80)	edentulous maxilla model	1 prosthodontist	unkown	along the ridge of the arch, starting from the right maxillary tuberosity and ending at the left one and then continuing on the buccal side and finally on the palatal vault with a clockwise movement	10	TR3	industrial scanner (ATOS Core, GOM)	trueness and precision mean
Li et al. 2020(81)	2 edentulous maxilla and 1 mandible model	unkown	unkown	for the maxillary typodonts, the U-shaped alveolar ridge portion was first scanned from the left side of the arch. Subsequently, the buccal or labial aspect of the alveolar ridge was scanned, after which, the palatal portion was scanned	12	TR3 i500	industrial scanner (ATOS Triple Scan)	trueness and precision mean and SD
Patzelt et al 2013(82)	edentulous maxilla model	5	CEREC 3D Service Pack V3.85 (Sirona, Bensheim Germany); Lava software 3.0 (3M ESPE, St. Paul, Minn.); iTero software version 4.0 (Align Technology, San Jose, Calif.); Zfx IntraScan software version 0.9 RC33 2.8 (manufactured by MHT Italy, Negrar, Italy/MHT	starting at the distobuccal areas, following the crest to the opposite side and finally closing the palatal gaps by moving the scanner head in a zigzag fashion over the palate	5	Blu iT1 Lava Zfx	laboratory scanner (Activity 101, smart optics Sensortechnik)	trueness mean and SD

			Optic Research, Niederhasli, Switzerland; distributed by Zfx, Dachau, Germany)					
Gutmacher et al. 2021(83)	edentulous human cadaver maxilla	unkown	iTero software version 1.9.3.7; CEREC software version 5.0; 3Shape software version 1.6.9.1; Medit software version 1.2.0.3	manufacturer's recommendations	8	TR3 TR4 iT2 Pri i500	industrial scanner (ATOS Capsule scanner, GOM GmbH)	trueness and precision mean and SD, median and IQR
Elbashti et al. 2017(84)	polyurethan edentulous maxilla models (defect types: half/quarter maxillectomy)	unkown	unkown	zig-zag	10+10	TRU	CBCT (ProMax 3D Mid, Planmeca Oy)	trueness mean and SD
Schimmel et al. 2021(85)	4 models: completely edentulous mandible and maxilla, partially edentulous maxilla and mandible	1 experienced	Primescan; Sirona, Bensheim, Germany with the software version 5.0	manufacturer's recommendations	10	Pri	industrial scanner (ATOS Capsule 200MV120; GOM GmbH)	trueness min, max, median, IQR
Tasaka et al. 2019(86)	2 models: completely edentulous maxillary model and partially edentulous mandibular model	5	unkown	zig-zag	5	TR2	dental laboratory scanner (D900, 3Shape A/S, Copenhagen, Denmark)	trueness mean and SD

Vandeweghe et al. 2017(87)	edentulous acrylic mandible model with 6 implants	unkown	unkown	manufacturer's recommendations	15	TR2 Omn Lava	laboratoray scanner (104i, Imetric, Courgenay, Switzerland)	trueness and precision mean and SD
Çakmak et al. 2021(88)	PMMA edentulous mandibular model with 6 implants and a partially edentulous mandibular model with single implant	1 experienced	unkown	manufacturer's recommendations	10	TR3 Vir	industrial scanner (ATOS Core 80 5MP; GOM GmbH)	trueness and precision mean and SD
Çakmak et al. 2020(89)	PMMA edentulous maxillary model with 4 implants	~~1~~ unkown	unkown	standardized scan path, which started from the occlusal surface, followed by the buccal and palatal surfaces as recommended by other IOS manufacturer (TRIOS 3, 3Shape)	10	TR3 Vir	industrial scanner (ATOS Core 80 5MP, GOM GmbH)	trueness and precision mean and SD
Bilmenoglu et al. 2020(90)	edentulous scannable Type 4 gypsum mandibular model with six implant analogs	unkown	Omnicam, Bluecam Cerec SW4, Planscan Romexis 3.6.0.R, Mono color cart, Color pod, color cart 3Shape TRIOS, lythos Ormco 1.9.10398, E4D Tech Design Center 2.0.0.19	unkown	10	E4D TR1 TR2 Plan Blu Omn	industrial scanner (ATOS Core-80; GOM GmbH)	trueness mean and SD
Mangano et al. 2020(91)	type IV gypsum edentolous	1 experienced	latest version	zig-zag	5	Eme S CS37	laboratory scanner (desktop	trueness mean and SD

	maxillary model with 8 implant scanbodies and analogues						scanner, 7Series)	
Albayrak et al. 2020(92)	polyurethane edentulous mandibular model with 8 implants with different angulations	1 trained operator	unkown	manufacturer's recommendations	10	TR3 CS35	laboratory scanner (Activity 885 Mark 2 Scanner, Smart Optics)	trueness mean and SD
Imburgia et al. 2017(93)	2 gypsum models: a partially edentulous maxilla, with three implant analogues in positions #23, #24 and #26 , and a fully edentulous maxilla with implant analogues in positions #11, #14, #16, #21, #24 and #26	1 experienced	unkown	randomized	5	TR3 Omn CS36 TRU	industrial scanner (ScanRider, VGER srl)	trueness and precision mean and SD
Mangano et al. 2019(94)	2 models: totally edentulous maxillary model, with implant analogs in position #11, #14, #16, #21, #24 and #26 and partially edentulous maxillary model restoring a single implant crown and	1 experienced	Planmeca Romexis 5.1.0 software, DWIO version 2.1.0.421, CEREC Connect 4.4.4 version, 1.6.4 (Trios on Dental Desktop)	zig-zag	10	TR3 Eme Omn CS36 DWIO	laboratory scanner (desktop scanner)	trueness and precision mean and SD

	a partial implant prosthesis and with scanbodies							
Mangano et al 2016(30)	2 stone models: edentulous maxilla with six implants analogues, and a partially edentuous maxillary model with three implant analogues	unkown	Trios release 1.3.3.1	unkown	5	TR3 Plan CS35 Zfx	industrial scanner (IScan D104I)	trueness and precision mean and SD
Favero et al. 2019(95)	resin model of all the natural teeth of an upper dental arch	1 experienced	unkown	Scanning started at element #27 continuing along the entire arch up to element #17	10	CS36 Zfx	laboratory scanners (Zfx Evolution, Zimmer Biomet)	trueness mean and SD
Feng et al. 2021(96)	dentated maxillary and mandibular model	1 experienced	unkown	linear	10	TR3	laboratory scanner (E4 Dental Scanner; 3 shape)	trueness mean and SD
Chun et al. 2017(97)	dentated mandibular models	unkown	iTero1 iTero Orthodontic ver. 5.2.1.290 (Align Technology Inc., Santa Clara, CA, USA), Trios2 3Shape Trios ver. 1.3.2.1 (3shape Dental Systems, Copenhagen, Denmark)	manufacturer’s recommendations	10	TR2 iT1	laboratory scanner (Sensable S3, Solution X Inc.)	trueness mean and SD

Nulty et al. 2021(98)	fully dentated maxilla model with geometries	1 experienced	Omnicam with 4.6 Software, Omnicam with 5.1 Software, and Primescan—Dentsply Sirona	manufacturer's recommendations	10	Omn Pri Lau Tr3 TR4 CS36 i500 Run	laboratory scanner (Ineos X5 Lab Scanner)	trueness and precision mean and SD
Anh et al. 2016(32)	maxillary model with crowded dentition	1 sufficient	unkown	manufacturer's recommendations	6	TR1 iT1	-	precision mean and SD
Vág et al. 2019(99)	maxillary and mandibular dentated model	unkown	PlanScan, with PlanCAD Easy v. 5.9.2 software; Planmeca, Helsinki, Finland	4 different scanning patterns (linear, and saddle technique combinations)	40	Plan	industrial scanner (ATOS Core 135, GOM GmbH)	trueness mean and SD
Oh et al. 2020(100)	maxillary and mandibular printed models (total 10 models)	unkown	TRIOS 3 (version 18.1.2, 3Shape, Copenhagen), i500 (version 1.1.1, Medit, Seoul, Korea)	3 different scanning strategies (CH, CV, S groups)	3	TR3 i500	industrial scanner (ATOS Triple Scan; GOM GmbH)	trueness and precision mean and SD
Kwon et al. 2021(101)	maxilla and mandible of healthy participants with a complete permanent dentition with geometries (6 maxilla 3 mandible)	3 experienced	Medit i500 1.1.1.2, Carestream CS3600, 3 Trios3 1.3.4.5, iTero 4, Omnicam 4.4	continuous method, starting from the right molar	5	i500 CS36 TR3 iTC Omn	industrial scanner (Solutionix C500)	trueness and precision mean and SD
Müller et al. 2016(102)	maxillary cobalt-chromium alloy dentated model	1 experienced	unkown	3 different scan strategies (A, B, C)	15	TR3	industrial scanner (Infinite focus standard)	trueness and precision mean and SD

Stefanelli et al. 2021(103)	Ten type IV stone casts (5 maxillary and 5 mandibular) of dentated patients	1 experienced	unkown	2 different scanning strategies with old tip and new tip	10	i500	laboratory scanner (Medit T710, Seoul, South Korea)	trueness and precision mean and SD
Michelinakis et al. 2020(104)	Thirty-eight Type IV stone casts acquired from completely dentate adult patients	2 experienced	Medit i500 Medit Link version 2.0.3 build 376 Revision 27 520, 3Shape A/S TRIOS 3 Dental Desktop 1.6.9.1 (insane mode), Planmeca Emerald Romexis 5.3.2.13	1 continuous stroke of the occlusal surface, followed by the buccal surface, and then the palatal surface	38	TR3 Eme i500	laboratory scanner (E3; 3Shape A/S)	trueness mean and SD, precision SD
Patzelt et al. 2014(105)	polyurethan maxillary model with all teeth prepared	1 experienced	CEREC AC Bluecam, CEREC 3D Service Pack V3.85 Sirona, Bensheim, Germany; Lava C.O.S., Lava software 3.0, 3M ESPE, St. Paul, USA; iTero, software version 4.0, Cadent Inc., Carlstadt, USA; Zfx IntraScan, software version 0.9 RC33 2.8, MHT S.p.A., Arbizzano di Negrar, Italy/MHT Optic Research AG, Niederhasli, Switzerland	manufacturer's recommendations	5	iTC Blu Zfx Lava	industrial scanner (IScan D101, Imetric 3D GmbH)	trueness and precision mean and SD

Su et al. 2015(106)	maxillary dentated model with all teeth prepared	unkown	unkown	unkown	10	TR1	laboratory scanner (D800 3D scanner, 3Shape)	trueness mean and SD
Zhang et al. 2021(107)	Model with all of the maxillary teeth prepared as abutments.	1 experienced	unkown	manufacturer's recommendations	10	TR1 iTC Omn	laboratory scanner (D1000 scanner)	trueness mean and SD
Reich et al. 2021(108)	dentated maxillary model with 13, 14, 15, 16, 17 crown preparation	unkown	Cerec Omnicam (software v4.6; Dentsply Sirona) TRIOS 3 (software v1.18.1.3; 3Shape A/S) Cerec Primescan (software v5.0.1; Dentsply Sirona)	manufacturer's recommendations	10	TR3 Omn Pri	industrial scanner (ATOS Compact Scan 5M; GOM, GmbH)	trueness and precision mean and SD
Park et al 2016(109)	dentated mandibular and maxillary model with prepared abutments: Dental models with various preparation designs. Right maxillary incisor and canine (#11, 13); 3-unit fixed dental prosthesis, right maxillary second molar (#17); MO inlay, and right mandibular	unkown	unkown	manufacturer's recommendations	4	E4D TR2 iTC Fast Zfx	laboratory scanner (7 Series; Dental Wings Inc.)	trueness and precision mean and SD

	second molar (#47); crown							
Yatmaz et al. 2021(110)	dentated maxillary model with 17-14 3 unit bridge prep, 24 inlay prep, 26 crown prep	1 experienced	Cerec Primescan, software v5.1, Dentsply Sirona, Bensheim, Germany	manufacturer's recommendations	15	Pri	industrial scanner (ATOS Compact Scan 5 M, GOM GmbH)	trueness mean and SD
Diker et al. 2021 (1)(111)	maxillary complete-arch model (the canine and first molar teeth on the reference model were prepared for bilateral 4-unit FPDs)	1 unkown	unkown	manufacturer's recommendations	10	Vir Pri Omn Eme TR3 iT2	industrial scanner (ATOS Core 80; GOM GmbH)	trueness and precision median and IQR
Diker et al. 2021 (2)(112)	maxillary complete-arch model (Kennedy Class I and Class IV models)	1 unkown	Trios 3 version 1.4.7.5 (3Shape), iTero Element 2 version 1.9.3.3. (Align Technologies), CEREC Omnicam 4.6.1. (Dentsply Sirona), Emerald version 6.0 (Planmeca), CEREC Primescan version 5.0 (Dentsply Sirona Dental Systems), Virtuo Vivo version 3.0 (Dental Wings)	2 scan strategies (right and left)	10	Vir Pri Omn Eme TR3 iT2	industrial scanner (ATOS Core 80; GOM GmbH)	trueness and precision mean and SD

Ender et al. 2015(26)	steel reference model fabricated from a patient's upper jaw impression with two full crown and one inlay preparation	unkown	unkown	manufacturer's instructions (ITE, LAV) or using self-developed scanning strategies (CER, OC).	5	iTC Blu Omn Lava	industrial scanner (Infinite Focus Standard, Alicona Imaging)	trueness and precision mean and SD
Passos et al. 2019(113)	dentated maxillary model with 16, 26, crown preparation	1 experienced	Cerec Omnicam 5.1.0. Primescan 5.0.2	manufacturer's recommendations	10	Omn Pri	industrial scanner (ATOS Triple Scan; GOM GmbH)	trueness and precision mean and SD
Mennito et al. 2019(114)	human cadaver maxilla with crown preparations on teeth 16, 11, 24	1 experienced	unkown	manufacturer's recommendations	5	TR3 Plan Eme iT1 iT2 CS36	industrial scanners (ATOS III Triple Scan 3D and ATOS Capsule; GOM GmbH)	trueness and precision mean and SD
Medina-Sotomayor et al. 2019(115)	epoxy resin maxillary dental arch model with abutments (crown, FPD, veneer, onlay) and with implant analoges	unkown	TRIOS (software v1.4.5.3, 3Shape Dental Systems), iTero (software OrthoCAD 5.7.0.301 CadentLTD), Cerec AC Omnicam (software CEREC SW 4.4.4; Dentsply Sirona), and the True Definition (softwarev4.2; 3M ESPE Dental Products)	unkown	40	TR1 iTC Omn TRU	industrial scanner (ATOS II TripleScan, GOM Technologies)	trueness and precision mean and SD

Medina-Sotomayor et al 2018 (1)(116)	maxillary master cast with several dental preparations for onlay, abutment tooth, fixed dental prosthesis (FDP), veneer and Straumann RN anti-rotational Core3D scanbody	1 experienced	Trios (software version 1.4.5.3, 3Shape Dental Systems, Copenhagen, Denmark), iTero (software version OrthoCAD 5.7.0.301 Cadent LTD, Align Technology Inc., San Jose, CA, USA), Cerec AC Omnicam (software version CEREC SW 4.4.4; Sirona, Bensheim, Germany); and True Definition (software version 4.2; 3M ESPE Dental Products, Seefeld, Germany)	4 scanning strategies: (A) Exterior-Interior, (B) Quadrants, (C) Sextants, (D) Sequential.	10	TR1 iTC Omn TRU	industrial scanner (ATOS II Triple Scan, GOM Technology)	trueness and precision mean and SD
Medina-Sotomayor et al. 2018 (2)(117)	maxillary model with different dental preparations and four implant analogs	unkown	unkown	unkown	40	TR1 iTC Omn TRU	industrial scanner (ATOS II Triple Scan, GOM Techology)	trueness and precision mean and SD
Resende et al 2021(33)	3D printed typodont maxillary model with 2 prepared teeth (first maxillary right premolar and first	3 operator with different level of experience	CEREC Omnicam v4.5.1, TRIOS 3 Dental Desktop v1.6.4.1; 3Shape A/S	Scanning the occlusal surface, scanning the buccal surface by inclining the scanner wand toward the buccal surface while moving the reference model, and scanning the	10	TR3 Omn	laboratory scanner (D2000; 3Shape).	trueness and precision mean and SD

	maxillary right molar) and 3 implants (from first maxillary left premolar to first maxillary left molar)			lingual surface by inclining the scanner wand toward the lingual surface and scanning the lingual surface.				
Michelinakis et al. 2022(118)	partially dentated maxillary model with different substrates and 2 scan bodies	3 experienced	Trios 3 Dental Desktop 1.6.10.1 (insane mode), CS 3600 CS ScanFlow 1.0.1.402, Emerald S Romexis 5.3.4.39	manufacturer's recommendations	10	TR3 Eme S CS36	laboratory scanner (7series, Dental Wings)	trueness mean and SD
Osnes et al. 2021(119)	stone maxillary model	1 experienced	Primescan, CEREC 5.0.0; Omnicam, CEREC 4.6	manufacturer's recommendations	10	Omn Pri	laboratory scanner (Rexcan DS2, Solutionix)	trueness mean and SD
Revilla-León et al. 2020(120)	mandibular model with missing second right premolar	1 experienced	unkown	unkown	10	TR3 iT1 Omn	industrial scanner ((L2 Scanner; Imetric)	trueness and precision mean and SD
Jeong et al. 2016(121)	dentated maxillary model	experienced	unkown	manufacturer's recommendations	8	Blu Omn	industrial scanner (SmartSCAN R5; Breuckmann GmbH)	trueness and precision in RMS mean and SD
Kang et al. 2020(122)	dentated maxillary model	experienced	unkown	manufacturer's recommendations	20	TR2 TR3 CS35 CS36 i500	industrial scanner (Solutionix C500, MEDIT, Seoul, Korea)	trueness in RMS mean and SD
Gao et al. 2021(123)	maxillary and mandibular jaw typodonts with	unkown	unkown	unkown	10	TR3	laboratory scanner	trueness in RMS mean and SD; precision

	prepared abutment (all)						(D2000; 3Shape A/S)	in RMS median and IQR
Oh et al. 2019(10)	a maxillary typodont with prepared teeth	1 experienced	unkown	manufacturer's recommendations	10	CS36	industrial scanner (ATOS Triple Scan; GOM GmbH, Braunschweig, Germany)	trueness in RMS mean and SD; precision in RMS median and IQR
Emara et al. 2020(124)	five pairs of dentated maxillary and mandibular plaster dental models were randomly chosen	1 experienced	unkown	manufacturer's recommendations	3	TR3	laboratory scanner (IScan L series LI70910, Imetric 3D SA, Courgenay, Switzerland)	trueness in RMS median and IQR; precision in RMS mean and SD
Cho et al. 2015(125)	maxillary model with with prepared teeth	1 experienced	unkown	unkown	5	Lava	industrial scanner (Flex 3A; Otto Vision Technology GmbH)	trueness and precision in RMS mean and SD
Park et al. 2019(12)	dental stone dentated maxillary model	1 experienced	unkown	The scan was initiated from the occlusal surface of the left second molar, and a complete-arch scan was performed in the counterclockwise direction	20	TR2 TR3 CS35 CS36	industrial scanner (Solutionix C500; MEDIT)	trueness in RMS mean and SD
Son et al. 2021(9)	dental stone dentated maxillary model	1 experienced	unkown	Different scanning strategies	15	TR2 TR3 CS35 CS36 Pri	industrial scanner (Solutionix C500; MEDIT)	trueness in RMS mean and SD

						i500		
Chen et al. 2021(37)	mandibular jaw model with three standard abutment tooth models	1 experienced	19.2.5, 3Shape; 5.1.1.207230, Dentsply-Sirona Primescan	manufacturer’s recommendations	10	TR3 Pri	industrial scanner (Zeiss Metrotom 800, Zeiss, Gottingen)	trueness and precision in RMS mean and SD
Kim et al. 2018(126)	fully dentated mandibular model with 36 crown preparation	1 experienced	unkown	unkown	10	TR3 Plan CS35	laboratory scanner (Identica Hybrid; Medit)	trueness and precision in RMS mean and SD
Al-Rimawi et al. 2019(127)	dry human mandible with a full set of intact teeth	1 experienced	unkown	manufacturer’s recommendations	7	TR3	CBCT	trueness RMS mean and SD

8.1.2. Results of the quantitative analysis

8.1.2.1. Trueness for dentate arches (MAD)

The trueness analysis for the complete dentate arch encompassed 24 studies (26, 85, 95-106, 108-114, 119, 120, 128) along with 31 arches and 21 IOSs. Scans from six of the 21 IOSs showed no significant difference when compared to the reference scans: 3Shape Trios 2 (TR2), iTero Element 1 (iT1), FastScan (Fast), 3Shape Trios 4 (TR4), 3M Lava (Lava), and Runyes Quickscan (Run). **Figure 2** illustrates that the 95% CIs for these six IOSs fell within the clinically acceptable threshold of 120 µm: CEREC Primescan (Pri), TR2, iT1, 3Shape TRIOS 3(TR3), Medit i500 (i500), and iTero Cadent (iTC). While earlier generations of CEREC IOSs, such as CEREC Bluecam (Blu) and CEREC Omnicam (Omn), showed poor trueness, Pri achieved the best results for complete dentate arches. The iTero IOSs also performed well, with no significant differences between their generations. As for the 3Shape IOSs, the newer models, TR4 and TR3, did not show superior trueness compared to the older TR2. The i500 IOS also exhibited acceptable trueness.

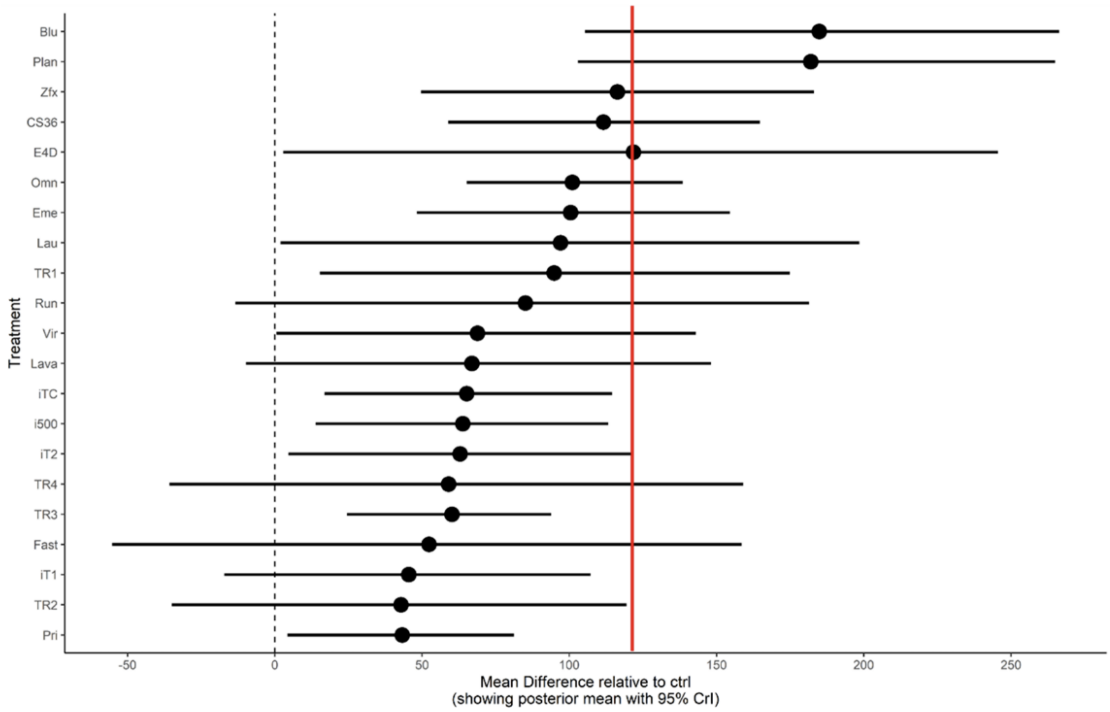


Figure 2. A forest plot illustrating the trueness of various IOSs and their mean difference compared to the control, along with the 95% CIs for the dentate arch group. The null-effect line (X-axis = 0) represents the control group's value (reference STL file), which

is set to 0, as the trueness of the gold-standard STL files should be 0. The X-axis shows the performance of each IOS (mean and CI) in relation to the reference scanner group. The further the CI deviates from the null-effect line, the poorer the performance of the index test. The Y-axis displays the different index tests ordered by performance, with a red line indicating the 120 µm threshold (68).

8.1.2.2. Precision for dentate arches (MAD)

The precision analysis of complete dentate arches included 14 studies (10, 26, 32, 101-103, 105, 108, 109, 111-114, 120) involving 17 arches and 18 IOSs **(Figure 3a)**. Scans from 13 of the 18 IOSs showed no significant difference when compared to reference scans, with the exceptions being Omn, Carestream 3600 (CS36), Planmeca Emerald (Eme), Zfx IntraScan (Zfx), and iT1 **(Figure 3b)**. No significant differences were found between the IOSs. The 95% CIs of the Fast, i500, TR3, Pri, iTC, and iTero Element 2 (iT2) IOSs fell within the clinically acceptable threshold of 120 µm. Both the Fast and i500 IOSs demonstrated very good precision in the dentate models. The 3Shape IOSs displayed acceptable precision, while the Pri from CEREC IOSs outperformed previous-generation IOSs (Blu and Omn) in terms of precision. The newer generation iTero IOS (iT2) exhibited significantly improved precision compared to the older iT1.

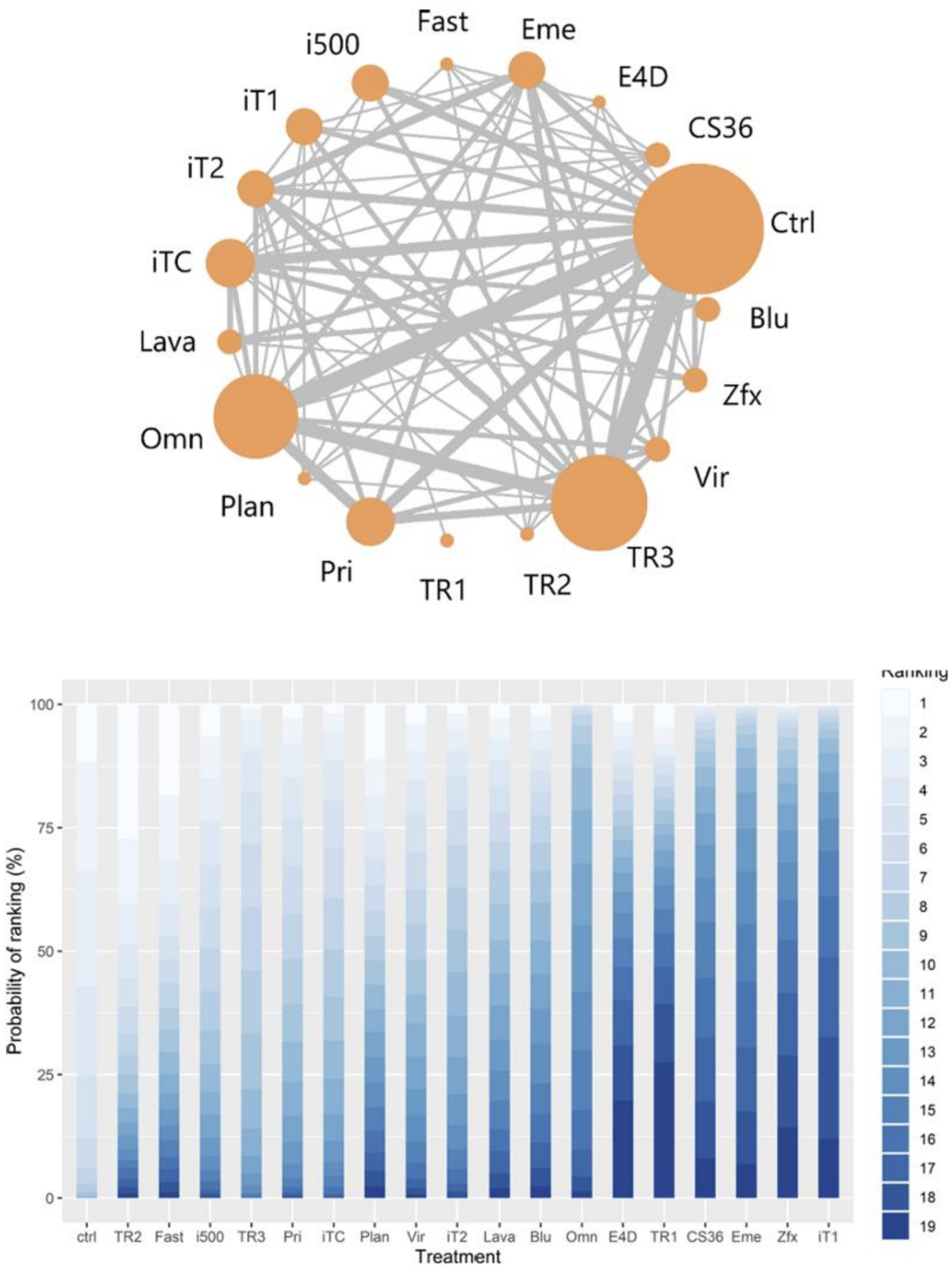


Figure 3. Precision of dentate arch a) Network plot containing 14 studies and 18 IOS. b) Rankogram showing the ranking probability of 18 IOS (68).

8.1.2.3. Trueness for dentate arches (RMS)

The RMS trueness analysis for dentate and prepared models encompassed 11 studies (9, 10, 12, 37, 121-127), 13 arches, and 10 IOSs. The ranking probabilities revealed that scans from two of the 10 IOSs showed no significant difference when compared to the reference scans (Lava and Pri). The IOS ranking aligned closely with the MAD values for dentate arch trueness. Newer models of 3M, CEREC, 3Shape, and Carestream IOSs demonstrated better trueness than their older counterparts.

8.1.2.4. Precision for dentate arches (RMS)

The RMS precision analysis for both dentate and prepared models involved seven studies (10, 37, 121, 123-125, 129), nine arches, and eight IOSs. Scans from seven of the eight IOSs showed no significant difference when compared to the reference scans, with the exception of the Planmeca Planscan (Plan). No significant differences were found among the IOSs, except for the Plan IOS, whose precision differed notably from all the other IOSs.

8.1.2.5. Trueness for edentulous arches (MAD)

The trueness analysis for completely edentulous arches included five studies (80-83, 85, 130), covering eight arches and nine IOSs. Scans from four of the nine IOSs showed no significant difference when compared to the reference scans (Lava, Pri, iT2, TR4). Only the Lava and Pri IOSs met the clinically acceptable trueness threshold of 120 μm. While the results suggest that intraoral scanning of edentulous arches can be challenging, the Pri and Lava IOSs demonstrated clinically acceptable trueness. Additionally, the precision results for iTero and 3Shape IOSs were also promising, showing no statistically significant differences between them.

8.1.2.6. Precision for edentulous arches (MAD)

The precision analysis for fully edentulous arches involved four studies (80-83), six arches, and nine IOSs. Scans from five of the nine IOSs (Pri, iT2, TR3, Lava, and i500) showed no significant differences compared to the reference scans. The 95% CIs for Pri, iT2, TR3, Lava, and i500 IOSs were within the clinically acceptable limit of 120 μm. The latest generations of CEREC (Pri) and iTero (iT2) IOSs delivered the most accurate results for edentulous arches, while the 3Shape, 3M, and Medit IOSs also demonstrated clinically acceptable precision.

8.1.2.7. Trueness for edentulous arches with implants (MAD)

The trueness analysis of complete edentulous arches with implants involved nine studies (30, 87, 89-94), nine arches, and 17 IOSs. Nine out of the 17 IOSs demonstrated no significant difference when compared to the reference scans: TR2, 3Shape Trios 1 (TR1), Carestream 3700 (CS37), Blu, CS36, Planmeca Emerald S (Eme S), Carestream 3500 (CS35), Eme, and Nevo E4D (E4D). Only the TR1 IOS had a trueness within the clinically acceptable range of 120 µm, while TR2, CS36, Omn, and TR3 were near this threshold. The newer generation 3Shape IOS models did not show better trueness than the older versions, although the difference was not statistically significant. In contrast, the newer Carestream and Planmeca IOS models performed better than the older ones.

8.1.2.8. Precision for edentulous arches with implants (MAD)

The precision analysis for edentulous arches with implants involved seven studies (30, 87, 89, 93, 94, 131), seven arches, and 12 IOSs. Four of the 12 IOSs demonstrated no significant difference when compared to the reference scans: Straumann Virtuo Vivo (Vir), TR3, TR1, and 3M True Definition (TRU). The precision of nine IOSs fell within the clinically acceptable limit of 120 µm, with Zfx, Straumann DWIO (DWIO), and Plan being exceptions. The newer generation of 3Shape (TR3), Straumann (Vir), Carestream (CS36), and 3M (TRU) showed better precision than the older models (TR1, DWIO, CS35, Lava).

8.1.2.9. Trueness for partially edentulous arches with implants (MAD)

The trueness analysis of partially edentulous arches involved seven studies (30, 33, 88, 115-118), seven arches, and 12 IOSs. All IOS scans showed a notable difference when compared to the reference scans. The trueness of the TRU, CS35, TR1, and TR3 IOSs fell within the clinically acceptable limit of 120 µm, while the trueness of the Vir was very close to this threshold. Both the newer generation 3M (TRU) and the older generation Carestream (CS35) and 3Shape (TR1, TR3) IOSs demonstrated clinically acceptable trueness.

8.1.2.10. Precision for partially edentulous arches with implants (MAD)

The precision analysis for partially edentulous arches involved six studies (30, 33, 88, 115-117), six arches, and 10 IOSs. Among the 10 IOSs, scans from six showed no significant difference when compared to the reference scans (TRU, CS35, TR3, Vir, Pri, and Zfx). However, none of the IOSs met the clinically acceptable precision threshold of 120 µm.

The mean MAD values for all IOSs and subgroups varied from 35.37 µm to 581.43 µm for trueness and from 4.72 µm to 355.51 µm for precision. IOSs with a CI below the clinically acceptable limit of 120 µm had average trueness values between 42 µm and 76.28 µm, and average precision values ranging from 5.48 µm to 60.75 µm. The mean RMS values ranged from 27.55 µm to 389.02 µm for trueness and from 39.5 µm to 561.45 µm for precision. The accuracy results for all IOSs are shown in **Table 2**.

Table 2. Accuracy (trueness and precision) of IOSs in different clinical scenarios (68).

IOS	dentate arches (MAD)		edentulous arches (MAD)		partially edentulous arches with implants (MAD)		fully edentulous arches with implants (MAD)	
	Trueness	Precision	Trueness	Precision	Trueness	Precision	Trueness	Precision
iTC	**64.85** (14.3, 116.62)	34.76 (−28.69, 101.39)			**102.01** (76.91, 127.04)	**193.71** (99.39, 288.03)		
iT1	45.66 (−16.35, 109.12)	**103.81** (21.3, 185.58)	**147.44** (63,09; 230,41)	**172.46** (93.66, 250.75)				
iT2	**62.5** (3.0, 122.51)	44.13 (−25.88, 116.04)	73.11 (−12.81, 160.87)	6.99 (−58.35, 74.8)				
TR1	**93.44** (14.61, 175.16)	99.64 (−63.65, 254.6)			**65.15** (41.07, 89.72)	**142.95** (59.69, 226.48)	47.88 (−22.53, 116.3)	27.76 (−14.24, 71.99)
TR2	42 (−38.12, 122.81)	4,72 (−114.52, 129.88)					35.37 (−56.08, 132.15)	
TR3	**60.41** (26.49, 97.71)	31.5 (−16.24, 77.24)	**87.57** (31.9, 145.02)	9.86 (−33.94, 53.04)	**76.28** (55.72, 97.31)	68.36 (−17.71, 152.95)	**76.99** (33.12, 120.3)	13.33 (−6.43, 33.5)
TR4	59.47 (−36.47, 155.52)		72.98 (−14.10, 161.29)	**78.81** (12.55, 147.46)				
Plan	**182,63** (98.95–265.64)	37.96 (−77.37, 147.54)			**235.89** (168.97, 303.79)	**222.24** (83.34, 367.88)	**303.88** (233.42, 377.13)	**181.49** (135.73, 224.11)
Eme	**99.86** (47.46, 153.7)	**89.30** (20.72, 159.32)					78.62 (−13.56, 170.41)	**42.74** (1.91, 83.32)
Eme S					**100.39** (63.09, 138.82)		53.25 (−55.23, 161.89)	
CS35					**50.17** (13.27, 89.31)	43.75 (−93.41, 185.61)	65.54 (−8.34, 137.12)	**42.3** (10.41, 73.61)
CS36	**111.43** (59.43, 165.4)	**89.17** (7.65, 171.25)			**92.19** (55.61, 130.8)		57.35 (−10.96, 126.02)	**29.72** (0.91, 60.27)
CS37							42.42 (−67.6, 153.01)	
Zfx	**115.85** (49.05, 180.77)	**97.16** (4.13, 192.97)	**264.4** (146.98, 383.59)	**324.98** (210.14, 437.36)	**118.79** (72.4, 163.01)	128.97 (−9.59, 272.97)	**116.68** (18.8, 211.43)	**90.37** (44.04, 133.56)
Blu	**185.15** (105.69, 268.87)	56.65 (−33.17, 144.42)	**581.43** (279.53, 859.16)	**355.51** (185.52, 521.6)			49.77 (−44.45, 142.2)	
Omn	**101,27** (64,36; 138,91)	**72.75** (23.78, 126.16)			**107.94** (88.01, 128.4)	**157.4** (83.99, 229.42)	**74.96** (25.94, 125.15)	**55.5** (31.84, 80.91)
Pri	**43.03** (3.33, 81.39)	33.17 (−27.94, 97.9)	53.29 (−4.49, 110.38)	5.48 (−63.85, 77.19)	**104.8** (58.41, 150.69)	70.35 (−61.05, 200.88)		
Lava	66.31 (−11.45, 146.28)	50.51 (−37.7, 142.05)	48.21 (−25.26, 120.12)	11.04 (−42.76, 63.93)			**132.28** (36.98, 226.77)	**60.75** (18.06, 104.72)
TRU					**42.93** (20.83, 65.37)	44.35 (−38.15, 127.54)	**78.03** (10.9, 149.77)	**33.71** (0.88, 70.62)
DWIO							**104** (9.59, 197.67)	**92.19** (52.24, 134.12)
Vir	68.28 (−3.39, 140.09)	39.92 (−40.05, 121.8)			**84.34** (43.29, 125.98)	67.22 (−60.77, 193.04)	**84.63** (9.26, 158.76)	10.59 (−19.82, 40.92)
i500	**63.66** (14.25, 113.08)	27.58 (−41.88, 97.91)	**104.19** (39.92, 172.2)	23.98 (−27.88, 77.28)				
Fast	52.14 (−54.32, 160.57)	16.82 (−102.44, 136.69)						
Lau	96.38 (−2.04, 196.92)							
Run	84 (−15.43, 182.34)							
E4D	**121.97** (3.44, 243.27)	87.79 (−54.46, 227.96)					87.58 (−4.7, 181.71)	

Mean (CI) in µm.
** ** showing CI is statistically significant from the reference.

Considering both trueness and precision, the accuracy of the IOSs did not show significant differences when compared to the reference scans in dentate arches (three IOSs), edentulous arches (three IOSs), and fully edentulous arches with implants (one IOS). However, for partially edentulous arches, the accuracy of all IOSs differed significantly. There were notable differences between the IOSs themselves.

Out of the 18 IOSs tested for accuracy in dentate arches (MAD), only four (Pri, TR3, i500, iTC) demonstrated clinically acceptable accuracy, with the CI for trueness and precision below 120 µm. Only one of the nine IOSs (Pri) met clinically acceptable accuracy in edentulous arches. For completely edentulous arches with implants, only one of the 12 IOSs (TR2) was clinically acceptable. No IOSs were clinically acceptable for partially edentulous arches (see Supplementary Material 9 of the original publication).

8.1.3. Qualitative analysis

The findings from the studies not included in the quantitative analyses are discussed in detail in the discussion and systematic review sections of the original publication (68).

8.1.4. Quality assessment

Out of the 53 studies, 33 were categorized as having an unclear risk, while 11 were deemed high-risk due to insufficient information regarding the IOS software version, scanning strategy, operator, sample size, and lighting conditions. The results of the risk-of-bias assessment can be found in the Supplementary Material 7 of the original publication (68).

As for the accuracy outcomes of the included studies, the confidence ratings for IOSs, determined using GRADEPRO, were of low certainty; however, the outcome was critical in every outcome (Supplementary Material 11 of the original publication). The quality of evidence was downgraded due to significant inconsistencies and indirectness. Major inconsistencies arose from the varying measurement methods used across studies, with most focusing on dental models rather than patients. The wide range of CI also contributed to the downgrade. As a result, no direct conclusions could be drawn regarding the trueness and precision of IOSs for intraoral use.

8.2. Study II. Color comparison between intraoral scanner and spectrophotometer shade matching

8.2.1. Search and selection, characteristics of the included studies

A total of 163 studies were identified through the search. After screening, 23 studies were retained for data extraction. The agreement between the two investigators for screening titles and abstracts was κ = 1, and for full-text articles, the agreement was also κ = 1. The selection process is summarized in **Figure 4**.

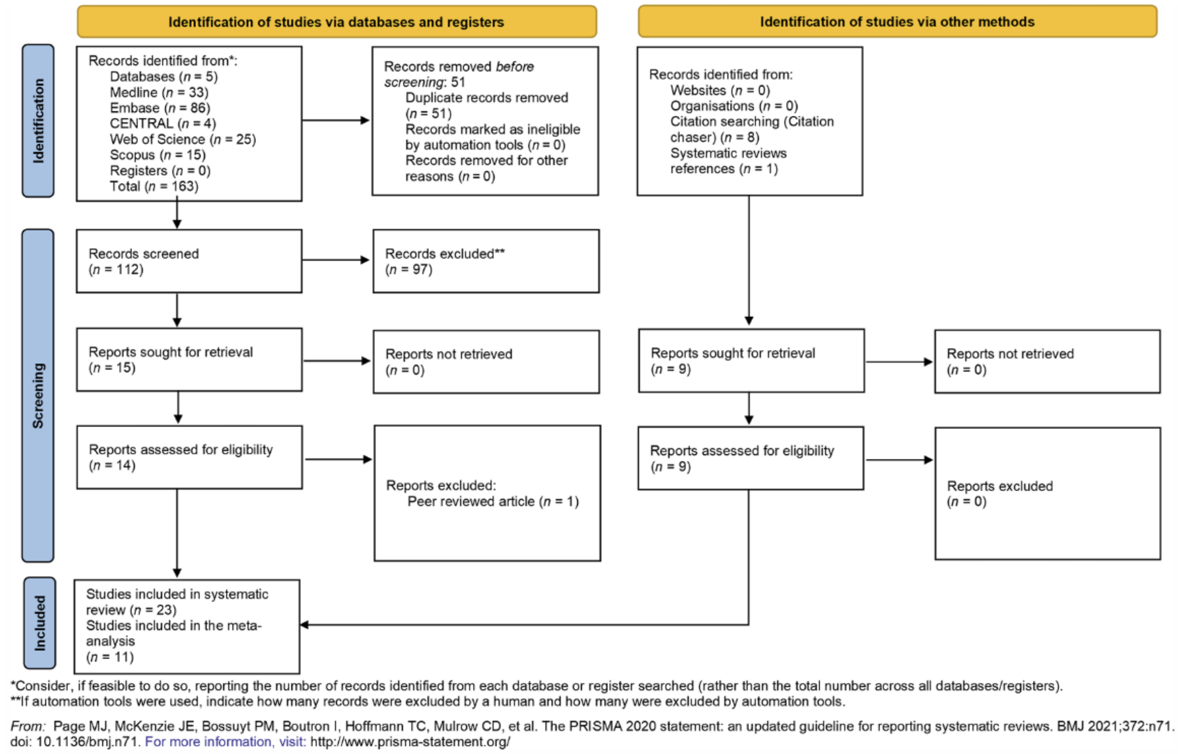


Figure 4. PRISMA 2020 flowchart representing the study selection process (69).

The baseline characteristics of the analyses included are detailed in **Table 3**.

Table 3. Basic characteristics of studies included for Study II (69).

Reference	**Intraoral scanner**	**Spectrophotometer**	**Visual method**	**Sample Size**	**Shade Guide Code**	**Type of Specimens**	**Type of Experiment**	**Measured area**	**Trueness**	**Precision**
Gotfredsen et al., 2015(132)	3Shape TRIOS Color	SpectroShade	Vita 3D-Master Vitapan	29 patients (87 teeth), eight patients (24 teeth for repeatability)	Vita 3D-Master	maxillary incisors and canine	in vivo	middle	(TR2-SS) Weighted Kappa:0.8	Value Weighted Kappa value:0.8
Brandt et al., 2017(133)	3Shape TRIOS Color	Vita Easyshade Advanced 4.0	Vita Toothguide 3D-Master + dentist (V1), Vita Toothguide 3D-Master + dental technician (V2)	107 patients	Vita 3D-Master	maxillary middle incisors	in vivo	middle	(TR2-ES) 43.9% ΔE mean = 5.0 ΔE SD=2.7, (TR2-V1) 25.2% ΔE mean=4.0, ΔE SD= 2.7, (TR2-V2) 33.6% ΔE mean=3.7, ΔE SD= 3.2; threshold ΔE =6.8 ACCEPTABLE	TR2= 78.3%
Mehl et al., 2017(134)	3Shape TRIOS Color	1) Vitai Easyshade 2) Vita Easyshade Advanced 3) SpectroShade 4)SpectroShade Micro	Vita Toothguide 3D-Master + 2 dentist (V1), Vita Toothguide 3D-Master + 2 dental technician (V2)	20 patients (40 teeth)	Vita 3D-Master	maxillary middle incisors and canine	in vivo	cervical, middle, incisial	(TR2-ES) ΔE mean= 7.0, ΔE SD= 5.0, (TR2-ESA) ΔE mean=6.8, ΔE SD= 4.4, (TR2-SS) ΔE mean= 3.7, ΔE SD= 1.9, (TR2-SSM) ΔE mean=3.4 , ΔE SD=2.2 (TR2 relative match=61.2%	TR2=66.7%

Yoon et al., 2018(135)	3Shape TRIOS Color	ShadeEye	none	Five shade tabs (repetition ten times on each shade tab)	Vita Classical	Vitapan Classical Shade guide	in vitro	middle	(TR2-SE) ΔE mean A1=7.0, (TR2-SE) ΔE mean A2=13.6, (TR2-SE) ΔE mean A3=12.1, (TR2-SE) ΔE mean A3.5=11.6, (TR2-SE) ΔE mean A4=10.5	(TR2-SE) ΔE SD A1=1.2, (TR2-SE) ΔE SD A2=0.8, (TR2-SE) ΔE SD A3=0.5, (TR2-SE) ΔE SD A3.5=0.7, (TR2-SE) ΔE SD A4=0.5
Culic et al., 2018(136)	CEREC Omnicam (SW: 4.5.2)	Vita Easyshade Advanced	none	Four patients (80 teeth)	Vita Classical, Vita 3D-Master	maxillary and mandibular teeth (10)	in vivo	cervical, middle, incisial	(TR2-ESA) VC+3D=15%, (TR2-ESA) VC all=17.5%, (TR2-ESA) 3D all=12.9%, (TR2-ESA) VC cervical=21.5%, (TR2-ESA) 3D cervical=20%, (TR2-ESA) VC middle=22%, (TR2-ESA) 3D middle=19%, (TR2-ESA) VC incisal=10%, (TR2-ESA) 3D incisal=8%	no data
Liberato et al., 2019(137)	3Shape TRIOS Color	Vita Easyshade Advanced 4.0	Vita Toothguide 3D-Master (V1), Vita Classical (V2)	28 patients	Vita Classical, Vita	maxillary middle incisors	in vivo	middle	Weighted kappa agreement (TR2) 3D=0.9,	no data

					3D-Master				Weighted kappa agreement (TR2) VC=0.6, Weighted kappa agreement (TR2-ESA) VC=0.6, Weighted kappa agreement (TR2-ESA) 3D=0.2	
Reyes et al., 2019(138)	3Shape TRIOS Color	none	Vita Toothguide 3D-Master + 10 prosthodontists	Ten patients	Vita 3D-Master	maxillary middle incisors	in vivo	middle	no data	TR2 mean=86.7%, TR2 SD=11.5%
Liu et al., 2019(139)	3Shape TRIOS 3	ColorEye 7000A (colorimeter)	none	120 blocks	none	color patches, blocks	in vitro	center	TR3 Quadratic polynomial mean ΔE_{ab}=4.4, TR3 Cubic polynomial ΔE_{ab}=3.8	no data
Yilmaz et al., 2019(140)	3Shape TRIOS 3	Vita Easyshade Compact	Vita 3D-Master shade guide	Five patients	Vita 3D-Master	maxillary middle incisors	in vivo	cervical, middle, incisial	(TR3-ESC) no significant difference	no data
Revilla-León et al., 2020(141)	3Shape TRIOS 3	Vita Easyshade V	none	One patient (6 teeth), ten repetition	Vita Classical, Vita 3D-Master	maxillary middle incisor, lateral incisor, canine	in vivo	middle	(TR3-ESV) significant difference	no data
Rutkunas et al., 2020(60)	3Shape TRIOS 3	SpectroShade	none	20 patients (120 teeth)	Vita Classical, Vita	maxillary middle incisor,	in vivo	middle	(TR3-SS) 3D=53.3%, (TR3-SS) VC=27.5%,	(TR3) 3D=90.3%, (TR3) VC=87.2%

					3D-Master	lateral incisor, canine			(TR3 ΔE 3D<3.7 = 51.7%, (TR3) ΔE VC<3.7 = 21.7% NOT AN EXACT MATCH	
Hampé-Kautz et al., 2020(142)	1) 3Shape TRIOS 3 2) CEREC Omnicam	1)Vita Easyshade V 2) Rayplicker	Vita 3-D Master Linearguide+novice practicioner (V1), Vita 3-D Master Linearguide+expert practicioner (V2),	40 patients	Vita 3D-Master	maxillary middle incisor	in vivo	middle	(IOSs-SPs) statistically different color	(TR3) ΔE median=3.4, (Omn) ΔE median=2.9 (2.45 ΔE acceptibility threshold)
Ebeid et al., 2021(59)	1) CEREC Omnicam (SW:4.6.) 2) CEREC Primescan (SW:5.5.1.) 3) 3Shape TRIOS 3	Vita Easyshade V	none	Ten blocks, ten repetitions per block	Vita Classical	Vita Mark II blocks	in vitro	center	(TR3-Block) =66%, (Pri-Block) =63%, (Omn-Block) =57%	TR3=51.7%, Omn=51.9%, Pri=48.4%
Fattouh et al., 2021(143)	3Shape TRIOS 3	Vita Easyshade Advance	Vita 3D-Master shade guide (V)	50 patients	Vita 3D-Master	maxillary middle incisor	in vivo	middle	(TR3-V) agreement =68%	no data

Czigola et al., 2021(144)	3Shape TRIOS 3	Vita Easyshade	Vita 3D-Master Linearguide + dental students (V1), Vita Classical + dental students (V2)	Ten patients (3 teeth per patient)	Vita Classical, Vita 3D-Master	maxillary middle incisors, premolars, and molars	in vivo	cervical, middle, incisial	(TR3-best match) 21.6%	TR3 cervical= 100%, TR3 middle= 75%, TR3 incisal 40%
Antony et al., 2021(145)	3Shape TRIOS Color	SpectroShade Micro	Vita Classical+clinician (V)	Ten patients	Vita Classical	maxillary middle incisors	in vivo	middle	(TR2) mean rank= 19.8 IOS is as accurate as the visual method	no data
Sirintawat et al., 2021(146)	3Shape TRIOS 3 (SW: 1.3.2.0)	Vita Easyshade Advance 5.0	none	resin model with 30 milled restorations	Vita 3D-Master	Restoration on milled from Vita Mark II blocks	in vitro	middle	(TR3-Block) ΔE mean=6.0, (ΔE threshold: 6.8) statistically significant difference	TR3 ΔE SD=1.8
Ebeid et al., 2022(147)	1) CEREC Omnicam (SW:4.6.) 2) CEREC Primescan (SW:5.5.1.) 3)3Shape TRIOS 3	Vita Easyshade V	Vita Classical+observer (V)	20 patients	Vita Classical	maxillary middle incisor	in vivo	middle	(TR-V) =75%, (TR4-V) = 76%, (Omn-V) =55%, (Pri-V) =69%	TR3=79%, TR4-V= 82%, Omn-V=77%, Pri-V=82%

	4) 3Shape TRIOS 4									
Huang et al., 2022 (148)	1) 3Shape TRIOS 3 2) 3Shape TRIOS 4	Vita Easyshade V	Vita 3D-Master shade guide system+experienced prosthodontist (V1), Vita Classical+experienced prosthodontist (V2)	23 patients (130 teeth)	Vita Classical, Vita 3D-Master	maxillary middle incisor	in vivo	cervical, middle, incisial	(TR3-ESV) VC=43%, (TR4-ESV) VC=6%, (TR3-ESV) 3D=27%, (TR4-ESV) 3D=3%,	TR3 VC=75%, TR4 VC=72%, TR3 3D=76%, TR4 3D=64%,
Huang et al., 2023(149)	1) CEREC Omnicam (SW:4.5.2.) 2) 3Shape TRIOS 3 3) 3Shape TRIOS 4	Vita Easyshade V	none	16 shade tabs	Vita Classical	Vita Classical shade guide tabs	in vitro	center	(TR3-SG) =72.5%, (TR4-SG) =35%, (Omn-SG) =15%	TR3 Fleiss' kappa=0.9, TR4 Fleiss' kappa=0.9, Omn Fleiss' kappa=0.8
Abu-Hossin et al., 2022(150)	1) 3Shape TRIOS 3 2)CEREC Omnicam	none	Vita Classical+experinced dentist(V)	31 patients	Vita Classical	maxillary middle incisor, canine, and first molar	in vivo	middle	(TR3-V) Cohens' kappa= 0.2, (Omn-V) Cohens' kappa=0.1	TR3 Fleiss' kappa= 0.6, Omn Fleiss' kappa=0.5

Vavřičková et al., 2023(151)	3Shape TRIOS 3	Vita Easyshade Compact Advance	Vita 3D-Master Vitapan	23 patients	Vita 3D-Master	referential tooth	in vivo	middle	(TR3-V) =42.9%	no data
Jagtap et al., 2022(152)	3Shape TRIOS Color	Vita Easyshade	Vita 3D-Master Vitapan	20 patients	Vita 3D-Master	adjacent tooth	in vivo	middle	(TR2-ES) = 70%	TR3 variablity=70%

8.2.2. Results of the quantitative analysis

8.2.2.1. Trueness by VITA 3D- Master

A total of six articles were included in the statistical analysis of the trueness outcome, as represented by the 3D shade guide system **(Figure 5)** (60, 133, 136, 151-153). The average trueness of IOSs was found to be clinically significant at 0.38 (CI: 0.24–0.53), with a statistically significant difference (p < 0.001). The average trueness for the TR3 subgroup was 0.4 (CI: 0.24–0.59).

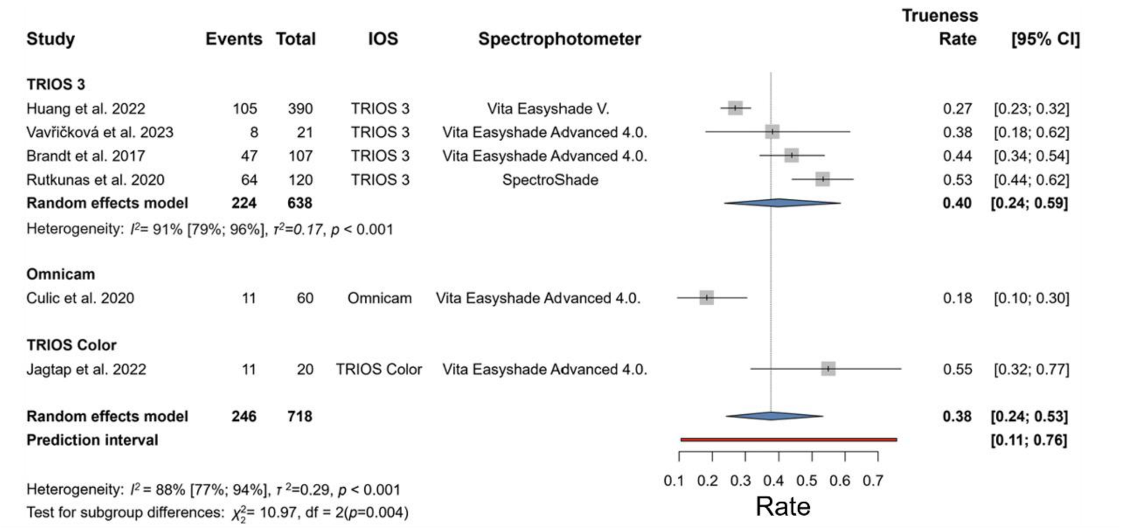


Figure 5. Forest plot representing trueness in VITA 3D- Master (69). The trueness rate is 0.40 (CI: 0.24-0.59) with TR3 and 0.38 (CI: 0.24-0.53) with multiple IOSs.

8.2.2.2. Trueness by VITA Classical

Three studies were included in the statistical analysis of the trueness outcome, which was measured using the VC shade guide system **(Figure 6)** (60, 136, 153). The average trueness of IOSs was found to be clinically significant at 0.28 (CI: 0.09–0.60), with a statistically significant difference (p < 0.001).

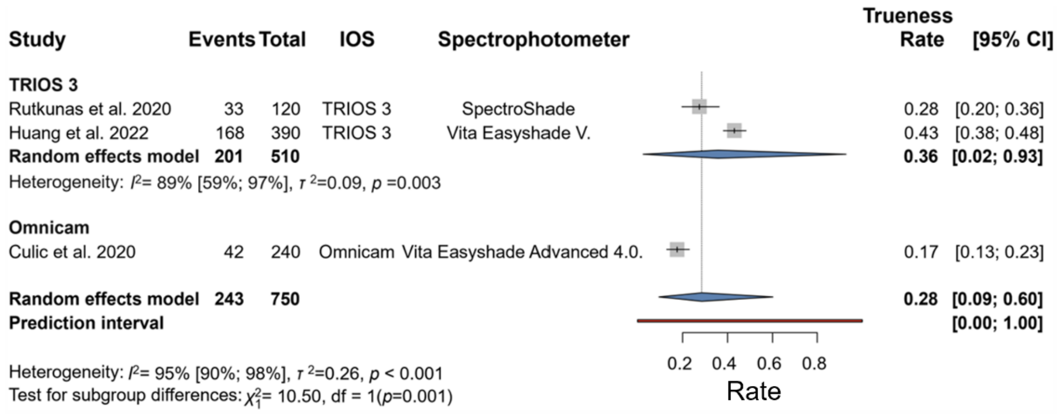


Figure 6. Forest plot representing trueness in VITA Classical (69). The trueness rate is 0.36 (CI: 0.02-0.93) with TR3 and 0.28 (CI: 0.09-0.60) with multiple IOSs.

8.2.2.3. Precision (Repeatability) by VITA 3D-Master, Measurement Location: Central

Six articles were included in the statistical analysis of the repeatability results, which were assessed using the 3D shade guide system and measured at the middle third of the reference teeth **(Figure 7)** (60, 133, 143, 144, 152, 154). The average trueness of the IOSs was 0.85 (CI: 0.74–0.92), showing a statistically significant difference ($p < 0.001$).

8.2.2.4. Precision (Repeatability) by VITA 3D-Master, Measurement Location: Cervical, Central, and Incisal Third,

Three studies were part of the statistical analysis for the repeatability outcome, which was evaluated using the 3D shade guide system at the cervical, middle, and incisal third of the reference teeth **(Figure 7)** (134, 144, 153). The average trueness of the IOSs was clinically acceptable, at 0.73 (CI: 0.59–0.84), with no statistically significant difference ($p < 0.070$).

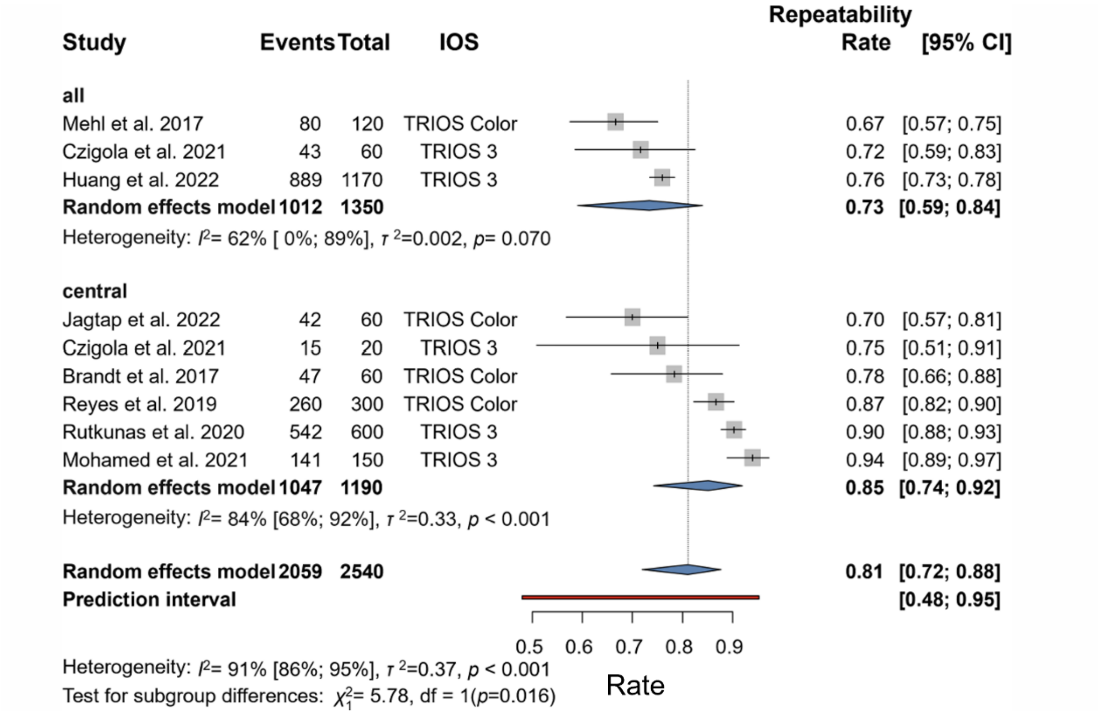


Figure 7. Forest plot representing precision (repeatability) in VITA 3D- Master with measurement location: cervical, central, incisal third (all), and central only (69). The precision rate is 0.73 (CI: 0.59-0.84) with all measurement areas and 0.85 (CI: 0.74-0.92) with central areas.

8.2.2.5. Precision (Repeatability) by VITA Classical

Three studies were incorporated into the statistical analysis of the repeatability results for the VC system using the TR3 **(Figure 8)** (60, 153, 155). The average trueness of the IOSs was clinically acceptable, measuring 0.81 (CI: 0.64–0.91), with a statistically significant difference (p < 0.001).

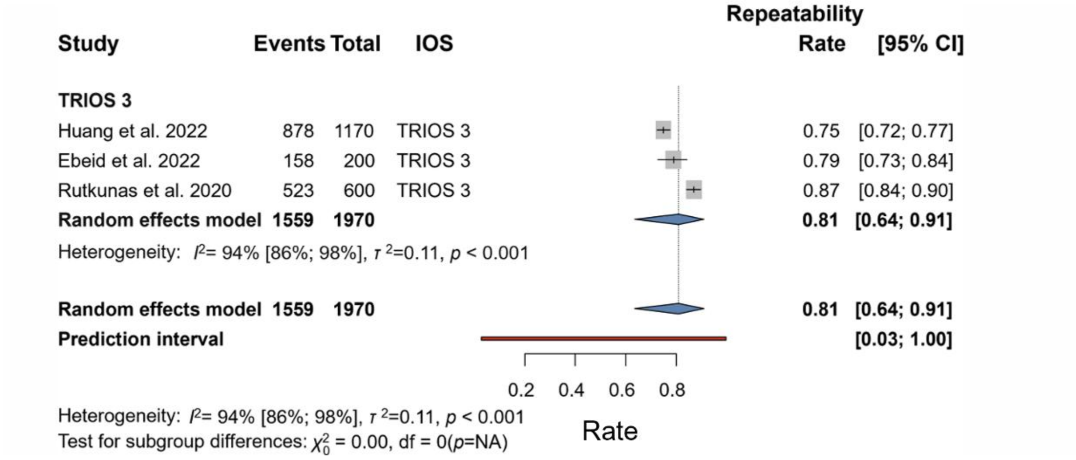


Figure 8. Forest plot representing precision (repeatability) in VITA Classical (69). The precision rate is 0.81 (CI: 0.64-0.91).

8.2.3. Qualitative analysis

The findings from the studies that were not included in the quantitative analyses are discussed in detail in the discussion and systematic review sections of the original publication (69).

8.2.4. Quality assessment

Our study had a risk at 78% (as shown in Table 2 of the original publication). Therefore, the results across all studies were consistent, indicating a low risk of bias (Data S4 of the original publication) (69).

Publication bias was evaluated using Peters' modified Egger's test, with the results for publication bias in various subgroups provided in Data S5 of the original publication. Heterogeneity among the subgroups ranged from 62% to 94% (69).

The certainty of the evidence was assessed using GRADE Pro, and the findings are presented in Data S6 of the original publication. Very low certainty of evidence was observed in the accuracy groups of critical importance due to the use of different IOS systems and SP types. Additionally, SPs used as gold standards do not detect tooth color with 100% accuracy, meaning there is no absolute confirmation of the original tooth color. The certainty of evidence in the repeatability groups was moderate, which is crucial due to the variation in the IOS systems used (69).

9. DISCUSSION

9.1. Summary of findings international comparisons

9.1.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

This NMA and systematic review assessed the accuracy, precision, and trueness of different IOSs for complete-arch scanning. Our findings revealed notable differences between the reference and IOS STL files and between various IOSs in complete-arch scanning. The IOS STL files exceeded the clinically acceptable threshold of 120 µm, leading to the rejection of our hypothesis. Additionally, the results suggest that the accuracy of IOS may be affected by factors such as dentulism, edentulism, complete edentulism with implants, and partial edentulism with implants.

The forest plots displaying the absolute mean results represent the statistically significant impact of sample sizes. The null-effect line (X-axis) marks the control group's value, which is 0 in this case, as the accuracy and precision of the gold-standard STL files should be close to 0. If the CI intersects the null-effect line, the difference from the reference is deemed statistically significant. As the sample size increases, the CI narrows. In some instances, a broad CI may suggest clinical unacceptability. Consequently, data from a limited number of studies should be interpreted cautiously.

Dentate arches are the most extensively studied among dental arches. The findings indicate that IOSs such as Pri, TR3, i500, and iTC were clinically acceptable for scanning a full dentate arch. Additionally, scans from TR2, Lava, Vir, and Fast showed no significant differences from reference scans in terms of trueness or precision based on MAD outcomes. Similar results were observed in the RMS dentate subgroup, where no statistical differences were found between Lava and Pri. These results suggest that while some IOSs can produce accurate digital impressions of complete dentate arches, not all are suitable. A systematic review and MA comparing conventional and digital impressions of complete dentate arches revealed that the trueness of IOS was comparable to conventional impressions, and their precision was high (156). Another MA concluded that digital impressions were on par with conventional ones regarding the marginal fit of complete-coverage, fixed-tooth-supported prostheses (157).

There was a lack of sufficient studies on the RMS group using clinical scenarios other than dentate arches for statistical analysis. Out of the six articles excluded from the statistical analyses, one focused on edentulous arches (158), three examined edentulous arches with implants (159-161), and two used dentate models (162, 163). These studies exhibited greater variation in their research methodologies. Another issue was the differing outcomes in RMS, which could not be combined into a single, unified result. In three articles, RMS medians were reported (160, 161, 163), while one article did not present absolute values for the results (162).

The data indicate that it is difficult for IOSs to accurately capture edentulous areas, as scans from only one IOS (Pri) showed no significant clinical or statistical differences compared to the reference scans. While scans from Lava and iT2 were not significantly different from the reference scans, their accuracy was not clinically acceptable. Although no systematic review has been conducted on the accuracy of digital impressions in edentulous arches, it is evident that improvements are needed in digital scans for edentulous areas (29, 158).

A similar issue arises when scanning implants in both completely and partially edentulous arches. Only one IOS (TR2) showed no significant clinical or statistical differences from the reference scans in the completely edentulous arch with implants. In contrast, none of the IOS STL files from the partially edentulous arch were clinically acceptable, and all showed statistically significant differences compared to the reference scans. A systematic review and MA published in 2020 found that the accuracy of digital impressions from IOSs was comparable to that of conventional implant impressions. However, they recommended further research before IOSs could be routinely used in clinical practice (39). Another systematic review concluded that several factors influence the accuracy of scanning completely edentulous arches with implants, including the type of IOS, scan pattern, environmental conditions, distances between implants, implant angles, and material (164). A systematic review of full-arch implant impressions also found that full-arch digital implant impressions using IOSs were not accurate enough for clinical use (40).

9.1.2. Study II. - Color comparison between intraoral scanner and spectrophotometer shade matching

The research hypothesis was dismissed due to the discovery of significant differences in shade matching between IOSs and SPs. The shade-matching accuracy of IOSs was evaluated separately in terms of trueness and precision.

Our results show that IOSs have a clinically acceptable repeatability of 81%, comparable to SPs' precision. However, they are not clinically acceptable due to their low trueness (28%-38%). High precision is ineffective if the trueness is poor because it allows for the repeated measurement of an inaccurate shade.

Similarly, the accuracy of RGB devices, including photo-based shade matching, is questionable, as they capture the color properties of an image rather than measure the instrument's reading (165, 166). This type of systematic error may be corrected with new software algorithms. A further limitation of IOS software is its inability to display CIELab values, meaning color difference values cannot be generated without a conversion chart. Therefore, great bias can occur if ΔE needs to be calculated due to the different conversion charts used for the calculation of Lab values.

The literature indicates that SPs are more precise than other shade-taking tools (150, 151). They are considered the most reliable for tooth-color measurements, with a reliability rate exceeding 96% (57, 167, 168). One study found that Easyshade and SpectroShade Micro yielded higher b* and a* values, respectively. Other studies (169, 170) showed that Easyshade Advance 4.0 and V provided comparable color measurements for premolars and incisors, demonstrating both accuracy and precision. While SpectroShade is more accurate than Easyshade in vivo, the accuracy and precision of Easyshade may be notably affected in freehand situations (168).

Our study revealed significant variation in the precision of the articles that reported data on the SP used. Low precision was observed in an in vivo study involving dental students using the Vita Easyshade (32%) (144), and in an in vitro study measuring blocks (44.3%) (59)]. In contrast, higher precision was observed in in vivo studies conducted by expert operators using Vita Easyshade, with results ranging from 68.3% to 93.5% (60, 133, 134, 155). Similar results were seen with SpectroShade SPs, showing precision rates of 61.7% and 71.7%, respectively (134).

The translucency of teeth increases from the cervical to the incisal area, allowing light to pass through more effectively (69). However, the IOS may detect the darker background of the oral cavity in the incisal region, resulting in a shade that appears darker than the actual color. This effect is also visible in the IOS software, where a dark incisal edge is followed by a lighter middle and cervical area.

We encountered an additional issue when we attempted to replicate the measured shade. Unfortunately, not all dental materials match the 3D or VC shade guide coding colors (49). We found considerable differences when comparing shade guides and different material block colors (171). As a result, replicating the exact color of a tooth remains challenging, even if the correct color is identified within the shade guidance system.

9.2. Strengths

9.2.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

Study I is the first systematic review and NMA on the accuracy of IOSs. The number of indirect and direct comparisons in the NMA subgroups was significant, which provides strong evidence. The network analysis made simultaneous comparisons with a wide range of IOSs possible. Evaluation of the trueness, precision, and accuracy made it possible to determine the relative ranking of the IOSs, indicating their superiority (72). This study gathered data on multiple anatomical areas of the intraoral cavity and demonstrated the accuracy of IOSs for various complete arch types. As a result, guidelines can be developed based on the accuracy of IOSs in different anatomical contexts for their appropriate use.

9.2.2. Study II. - Color comparison between intraoral scanner and spectrophotometer shade matching

In terms of the strengths of the MA, we adhered to our pre-registered protocol. For the quantitative synthesis, we included only in vivo studies. Efforts were made to minimize heterogeneity by organizing the data into subgroups. This study gathered data on multiple shade measurement locations of the reference tooth and demonstrated the accuracy of IOSs in both 3D and VC shade guide codings. With the help of the results, guidelines can be developed based on the accuracy of IOSs in different measurement locations. It is also important to highlight that all the outcomes in the study were crucial, and the overall risk of bias was low, at 78%.

9.3. Limitations

9.3.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

Due to the limitations of the studies, not all subgroups had enough data on a broad range of IOSs.

More data is needed for all IOSs available on the market, and this should be taken into account. Some IOSs are only mentioned in a single article, meaning the data available offers less evidence than IOSs discussed in multiple articles.

In the NMA, most studies used models instead of patients, which means the accuracy may vary when IOSs are used on patients.

Relying on different devices as references can result in inconsistency. Although studies referred to these references as gold standards in the literature, the accuracy of various industrial and laboratory scanners may differ (14).

Another limitation is that the 120 µm value isn't a gold standard or recommendation; it pertains to the "marginal fit" of the prosthesis, making it difficult to use this threshold to evaluate IOS accuracy (20). Typically, but not always, if IOS accuracy is within 120 µm, the prosthesis fit would be less than 120 µm. This represents a clear limitation, as various factors in prosthesis production could introduce errors. The interpretation of the results would depend on how one defines an acceptable clinical value. Currently, there is no established consensus or guideline regarding the acceptable accuracy range or value for IOSs.

9.3.2. Study II. - Color comparison between intraoral scanner and spectrophotometer shade matching

Given the constraints of the MA, we observed considerable heterogeneity across all groups, stemming from factors such as variations of the original tooth shades of the reference, measurement locations, types of shade guide systems used, different IOS and SP types, diverse operators, varying light conditions, and inconsistent measurement setups.

The reference tooth shade can influence measurements' accuracy and consistency (172). While maxillary central incisors were the most studied, teeth of various types—including lateral incisors, canines, premolars, and molars—were chosen for shade selection. Different measurement areas, such as the cervical, central, and incisal regions, can significantly impact the trueness and repeatability of IOSs, as these regions vary in translucency levels (144). Additionally, the thickness of the labial enamel has a more significant effect on the tooth's color (173).

Numerous studies have explored the differences between VC and 3D shade guide matching when using IOSs. A systematic review concluded that 3D shades provided more accurate color measurements than VC (67).

While SPs are generally considered reliable for reference, they can vary, and various factors can influence their accuracy. Key factors that can impact spectrophotometric measurements include the measured surface's size, the probe's correct positioning, its angle and alignment, the device's color analysis software, and the shade guide's mode (49, 67).

While the fundamental principles of shade measurement are consistent across IOS software, there may be variations between devices (68). These differences can occur due to the shade-calculating algorithm or hardware variations, but our study didn't evaluate these factors. Furthermore, not all IOS devices that can measure tooth shade have been examined.

10. CONCLUSIONS

10.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

1. Statistically significant differences were found between IOS STL scans and the reference STL scans (precision and trueness).
2. Statistically significant differences were found between the various IOS devices' accuracy (precision and trueness).
3. Additionally, the accuracy of the 95% CI of some IOSs was within the clinically acceptable threshold of 120 µm.

In conclusion, with some exceptions, IOS systems are sufficiently accurate for generating clinically acceptable complete-arch digital impressions. The accuracy of IOSs for complete arches can differ under various clinical scenarios. IOSs do not provide accurate complete-arch digital impressions in cases with implants. The newer generation IOSs are not always the most accurate devices, but there is a visible tendency for an increase in accuracy over time with advances in IOS technology.

10.2. Study II. - Color comparison between intraoral scanner and spectrophotometer shade matching

There was a significant difference in the accuracy of shade selection between IOSs and SPs.

1. There was a significant difference in shade selection between IOSs and SPs when trueness was expressed in match percentages.
2. The repeatability of IOSs is high, with a clinically acceptable match percentage.

In conclusion, while the precision is regarded as high and comparable to SPs, the trueness of shade matching with IOSs is lower than with SPs. The low trueness made the accuracy of IOSs unacceptable compared to SPs.

11. IMPLEMENTATION FOR PRACTICE

11.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

As Hegyi and his colleagues have stated, scientific results must be incorporated into clinical practice as quickly as possible. (174).

Dentists should select an IOS that is most appropriate for the specific indication (Prosthodontics, Orthodontics, Implantology) when scanning a full arch. The biggest challenge for IOSs is the field of implantology in full-arch, where dentists need additional tools to improve the accuracy of full-arch scans, such as using stereophotogrammetry, splints, or special scan bodies (175).

Supplementary Material 9 of the original publication provides the probability rankings for various complete arch types based on clinical situations (68). IOS devices such as Pri, TR2, TR3, i500, iTC, iT2, Lava, Vir, and Fast are all suitable for scanning complete arches. On the other hand, Plan, Blu, Zfx, E4D, Launca DL-206 (Lau), and DWIO IOSs are not recommended due to limited data or inadequate accuracy. Plan, Zfx, and Blu IOSs are designed for quadrant scans, and their manufacturers do not recommend them for complete-arch scanning, which aligns with our findings on IOS accuracy.

11.2. Study II. - Color comparison between intraoral scanner and spectrophotometer shade matching

Based on our findings, we advise against using IOSs for determining tooth shade, as no evidence supports their reliability in routine dental practice. Since we don't have information on all available IOSs, additional research is needed to explore other devices. This recommendation may change with future software updates that could enhance the IOSs examined and the release of new generations and types of IOSs for tooth shade matching.

The best shade determination method is still the digital method combined with visual methods, especially in 3D shade guide coding. IOS is not recommended for the digital method, so SPs such as the Easyshade are still the gold standard for that purpose.

To reconstruct the determined tooth color, choosing the material that matches the shade coding selected system is essential.

12. IMPLEMENTATION FOR RESEARCH

12.1. Study I. - Evaluation of the accuracy of intraoral scanners for complete-arch scanning

Based on our findings, we recommend using a standardized accuracy assessment protocol for IOS, including methods such as calipers, conventional impressions and coordinate measuring machines. Future research should adopt a standardized reporting protocol for scanning parameters, such as lighting conditions and scanning sequence. Additionally, multi-arm clinical trials with standardized methodologies are necessary for evaluating various IOS devices. In 2021, a guideline was published outlining the fundamental accuracy terms in digital dentistry, incorporating ISO standards and extending them to cover specific aspects of 3-dimensional data acquisition, particularly for surface meshes (65). Similar guidelines are needed for future publications, and it is also important to standardize the reference scanners used in the studies. In agreement with the research by Borbola and colleagues, it is recommended that laboratory scanners be validated before their use in IOS evaluation studies (14).

Additional research is necessary to evaluate the performance of other IOSs on the market to create current guidelines for choosing the best IOS for full-arch intraoral scanning. More in vivo studies are needed to provide evidence in dental practice. The notable variances among IOSs should be considered by researchers comparing digital impressions and digital technology with traditional impressions and methodologies, as these discrepancies might significantly affect the outcomes.

12.2. Study II. - Color comparison between intraoral scanner and spectrophotometer shade matching

Since we don't have information on all IOSs that are capable of tooth determination, additional data collection is required to explore other available devices.

It could be beneficial to examine the translucency error and how the background colors—black, gray, and white—impact the accuracy of IOSs.

Since the papers used various measurement techniques that weren't always comparable, future research should utilize more consistent results. Critical results, such as $\Delta E00$ determined using the CIEDE2000 formula, should be investigated in future studies. A more accurate depiction of color variations and perceptibility is possible with ΔE00, and ATs can be used to assess clinical relevance. Using consistent conversion charts when calculating color differences is crucial, as IOS software does not provide lab values.

In future research, it's essential to acknowledge that the accuracy of measurements can be influenced by the location where they are recorded. As a result, it is suggested that data be collected from various locations and shared for more comprehensive comparisons.

Since the original color of the tooth is often unknown in clinical studies, it would be valuable to explore how accurate IOS is when compared to other methods, like visual assessment. It might also be beneficial to use the same study design applied to determine PT and ATs (66). Data on IOS accuracy from various references could serve as the foundation for network analysis, offering more reliable information on the precision of IOS in determining tooth shade.

13. IMPLEMENTATION FOR POLICYMAKERS

It is becoming more and more crucial for legislators to guarantee the proper and moral use of IOSs as they grow in popularity among dentists and patients. These scanners have many advantages, such as the possibility of better patient experiences and more precise and effective treatment planning. However, their increasing adoption also brings forth critical concerns regarding accuracy, data privacy, and ethical implications that must be addressed at the regulatory level.

Depending on the clinical scenario, IOSs can produce adequate full-arch scans, although their accuracy varies. Furthermore, the accuracy of the various IOS models differs from one another. This emphasizes the importance of choosing devices carefully, especially in increasingly complicated clinical settings. Before releasing IOSs onto the market, policymakers should ensure they are validated through research to support their claims.

Manufacturers often use marketing tactics to highlight features such as shade determination, but without proper validation, these claims can be misleading. If a feature like shade matching is inaccurate, it can undermine the overall utility of the IOS in clinical practice.

When using an IOS, there is a possibility for identity theft and the use of sensitive patient data because IOSs generate STL files, which can provide specific detailed anatomical information, including the tooth setup and even the palatal area of the patient's oral cavity. These files can be used for patient identification, raising important questions about data ownership and privacy (176-179). Guidelines should be kept strictly in accessing these 3-dimensional files to authorized personnel only, and any third-party use should be closely monitored.

In conclusion, while IOSs have the potential to transform dental practice, policymakers must ensure that their regulation is robust, evidence-based, and sensitive to patient privacy concerns. By establishing clear guidelines around accuracy, data use, and security, policymakers can help ensure that these technologies are implemented wisely and ethically, benefiting both patients and practitioners.

14. FUTURE PERSPECTIVES

IOSs have a bright future since continued technical developments are expected to broaden their uses in dentistry and improve their capabilities. Broader usage across various treatment contexts, from simple solutions to more complex cases, is anticipated as these devices' accuracy and speed improve.

The development of artificial intelligence and machine learning algorithms could enable IOSs to provide more precise diagnostics, such as detecting early signs of oral diseases or improving treatment predictions.

Regulations about the distribution and storage of STL files will also change due to the growing emphasis on patient privacy and data security, guaranteeing the moral and responsible use of new technologies.

As IOSs become more accessible and versatile, they can revolutionize the dental field, offering better precision, improved patient experiences, predictable results, and more efficient workflows.

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16.2. Publications not related to the thesis

Németh, A., **Vitai, V.**, Czumbel, M. L., Szabó, B., Varga, G., Kerémi, B., Hegyi, P., Hermann, P., & Borbély, J. (2023). Clear guidance to select the most accurate technologies for 3D printing dental models - A network meta-analysis. **Journal of Dentistry**, 134, 104532. https://doi.org/10.1016/j.jdent.2023.104532

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