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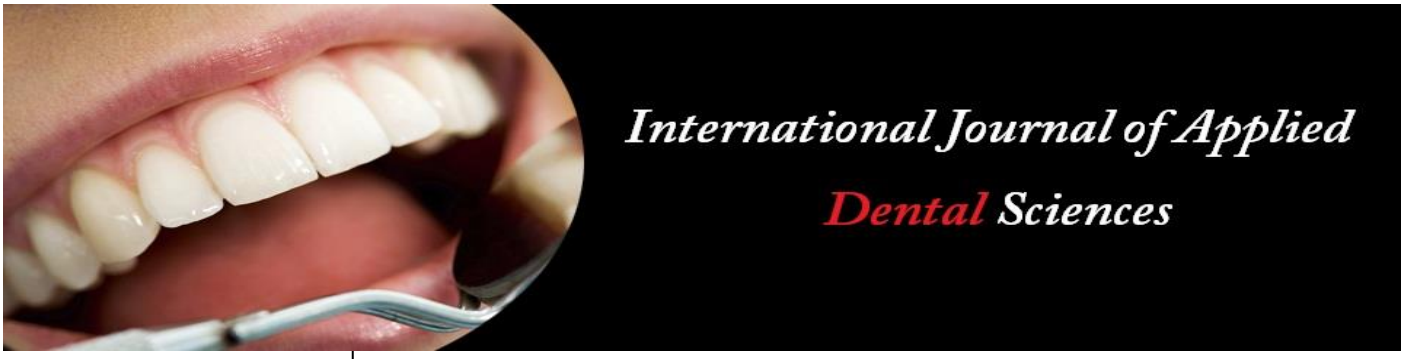

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Internal validation and standardization of methods for evaluating the safety and effectiveness of dental care products in research studies: Within dentistry

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Abstract
Background: Numerous methods are available for assessing effectiveness of oral/dental care products in clinical studies. However, a persistent debate surrounds the preference for specific methodologies over others. Intra- and inter-examiner variability are major concerns in both instrumental and visual examinations, as they can significantly influence the outcomes obtained.
Aim: This study standardised various techniques and methods used in dental clinical studies, to achieve bias-free, accurate, consistent and reliable outcomes.
Methods: This standardization and validation study was carried out by internal staff of NovoBliss Research, post receiving training from panel of dentists and periodontists on various aspects of dental evaluations. Study included method validation for measurement of oral malodour, teeth-shade and scoring for teeth shininess, along with intra- and inter-operator reliability for common assessments in dental clinical studies. Analysis was carried out using SPSS version 26.0.
Results: After receiving training, high intraoperator reliability and instrument accuracy was observed for Tanita HC-205 breath analyzer (90% similarity) for measuring malodour and for Vita Easyshade V (100% similarity) for determination of teeth shade. Shade determination through Vita Easyshade V and Vita Classical Shade Guide exhibited statistical similarity between their outcomes (p<0.0001). Good level of inter-operator agreement was observed for Tanita HC-205, Vita Easyshade V and Vita Classical Shade Guide with Fleiss' multirater kappa of 0.66, 0.73 and 0.72, respectively (all p<0.001). Very good inter-observer agreement was observed between scorers for extrinsic stain score, while good agreement was found for plaque index and gingival index with Fleiss' multirater kappa of 0.84, 0.71 and 0.73, respectively (all p<0.001).
Conclusion: Method validation conducted in present study can serve as a reliable model for future dental clinical studies on oral or dental care products, ensuring consistent, accurate, and reproducible results. It further highlights the importance of controlled testing methods, essential for the successful execution of efficacy studies on dental care products.

Keywords: Dental care products, dental clinical studies, method validation, standardization, inter-examiner reliability, intra-examiner reliability

Introduction
Over the past 20 to 30 years, there has been substantial global advancement in standards and methods for promoting and achieving good oral health [1]. Both oral care and dental aesthetics hold equal importance in influencing the physical and mental health of an individual. Improved dental appearance has a positive impact on individual's self-esteem, social life, confidence in their dento-facial appearance and overall quality of life as it includes more than just the absence of oral diseases and dysfunction. This aligns with the definition of quality of life provided by the World Health Organization (WHO) [2].
Increasing awareness on dental aesthetic has led to extensive research for development and advancement of various dental health boosting products that provide high patient satisfaction [3]. A significant change taking place this century is the introduction of digital technology into dental practice; "Digital Dentistry" is becoming more prevalent each year [4].

There are numerous instruments used in digital dentistry like Tanita breath analyzer for assessment of oral malodour or halitosis [5], Vita Easyshade V digital spectrophotometer for instrumental tooth shade assessment and Vita Classical Shade Guide for visual assessment of tooth shade [6]. Visual method of shade determination is the most popular and widely used method among dentists. Tooth shade is determined by comparing tooth colour with shade tabs and choosing the most appropriate colour which resembles the colour of the tooth [7]. The arrangement of Vita Classical Shade Guide tabs from lighter to darker is as follows: B1 A1 B2 D2 A2 C1 C2 D4 A3 D3 B3 A3.5 B4 C3 A4 C4 [8].

To this day, there remains an ongoing debate in the field of research regarding which method is more reliable for assessing tooth shade, with some vouching for visual shade determination [9]. and others for the instrumental evaluation [10, 11]. Method Validation and appropriate handling of instruments play a significant role in determining the true outcome of any research. Trained instrument experts and study staff are crucial in accurately collecting data to ensure reliable results [12].

The present study serves as an internal validation study aimed at bridging the gap in research by assessing the reliability of commonly used dental instruments. It also aimed to measure intra and inter-operator reliability (for instruments) and inter-observer reliability (for various dental parameters) to obtain reliable results and their subsequent positive outcomes.

Material and Methods

Ethical consideration

The study was conducted in according to the principles originating from the Declaration of Helsinki (Brazil, October 2013), Good Clinical Practices for clinical research in India, 2005, International Conference of Harmonization Guideline for Good Clinical Practice E6 (R2), Indian Dental Association Code of Ethics, New Drugs and Clinical Trials Rules, 2019 and with Indian Council of Medical Research's national ethical guidelines for biomedical and health research involving human participants, 2017.

Study Design and Population

The present study is a clinical validation study with main objectives being: the validation of dental instruments, including the HC-205 breath analyzer (Tanita, Tokyo, Japan) and Vita Easyshade V ® (VITA Zahnfabrik, Bad Sackingen, Germany); assessing inter-operator reliability for the instruments; comparison between spectrophotometer and visual method of tooth shade determination; visual scoring by dentist on teeth shininess; evaluating inter-observer reliability for the assessment of various dental parameters, such as extrinsic stain, organoleptic assessment of oral malodour, plaque index, gingival index, dental erosion, and teeth sensitivity, between dentists, periodontists, and dentist-trained evaluators.

Inclusion criteria comprised of subjects with either sex aged between 18 and 55 years (both age inclusive). Both healthy adult males and non-pregnant/non-lactating females were enrolled. Subjects were in good health, as indicated by recent medical history. Individuals who consumed pan/gutka, did smoking, or have an extrinsic stain intensity score greater than 1 in the extrinsic stain index were also included. Additionally, subjects with a score above 0 on Tanita breath analyzer and a score above 1 in plaque index and gingival index were included. Enrolled subjects had no history of restorations done in anterosuperior teeth. Furthermore, subjects did not have dental pain.

Exclusion criteria encompassed subjects undergoing treatment for gingivitis, periodontitis, or caries. Additionally, subjects with fixed orthodontic appliances on the facial surfaces of the maxillary arch were not eligible for participation. Those with dental crowns, veneers, or composite restorations on gradable maxillary anterior teeth (canine to canine) or mandibular anterior teeth were also excluded. Subjects presenting with any oral pathologies or gross neglect of home care requiring prompt treatment, including periodontal disease, as evidenced by purulent exudate, exposed root surfaces (generalized recession), tooth mobility, and/or other signs indicating that the integrity of the data collected for that subject might be compromised were not included. Furthermore, subjects with pre-existing oral or medical conditions to pose increased health risks from study participation were excluded. Meaningful malocclusion impacting ease of viewing or scoring by trained study staff/dentist/periodontist resulted in exclusion. Those with known allergies to oral hygiene products, plaque disclosing solution or any other orally used product were ineligible for the participation.

Study procedures

Training by Dentists and Periodontists

Before initiating the overall study conduct, all the qualified study staff of NovoBliss Research Private Limited, Ahmedabad, India, received a well-documented theoretical training from the dentists and periodontists on different dental perspectives including the detailed anatomy and physiology of oral cavity with primary focus on teeth. The session focused on training of evaluators on various aspects of teeth including scoring of extrinsic stains using Lobene stain index [13] and scoring of gingiva using gingival index by Loe and Silness [14]. Training on dental plaque diagnosis using disclosing agent was also provided. These dyes work by changing the colour of dental plaque so that it contrasts with the white tooth surface. The training further focused on dental plaque scoring using modified Quigley Hein index [15]. Various other aspects of training included training on oral examination for dental erosion and teeth sensitivity. Post receiving training from the dentist and periodontist, the trained study staff were then referred to as dentist-trained evaluators. Furthermore, evaluators also received training in determining tooth shade using the Vita Classical Shade Guide by both dentists and periodontists, under standardized lighting conditions to mitigate the influence of external factors.

Instrument Validation and Intra-operator Variability

Prior to operating the instrument, all the dentist-trained evaluators received training from the instrument experts and the readings were taken as per the instrument manual to obtain precise readings. Instrumental validation for Tanita HC-205 breath analyzer and Vita Easyshade V was done in order to check the accuracy of the instrument upon repetitive readings from single site in order to provide accurate and reliable results for clinical studies.

For Vita Easyshade V, 10 repetitive readings were taken from single tooth (on the middle third of the vestibular surface of the maxillary lateral incisors) by a trained instrument operator. Instrument calibration along with proper positioning of participant and instrument was ensured. The readings were taken in a supine position to stabilize head in order to achieve accurate measurement (Figure 1). Similarly, for Tanita breath analyzer, 10 repetitive readings were taken from oral cavity of the same subject. The instrument was placed inside a closed container with its tip positioned near the subject's mouths. This is done to avoid external disturbance from environmental

air which may give false readings (Figure 2). The output for Tanita breath analyzer was provided in form of scores ranging from 0 (no odour) to 5 (extremely strong odour). 10 repetitive readings from single also enables assessment of intraoperator reliability. It refers to an individual operator's consistency of measurement. This consistency can be improved through training, monitoring, and continuous education.

Inter-Operator Reliability

Tanita Breathe Analyzer (HC-205)

Single readings from 30 subjects each were taken by 5 trained instrument operators. The readings derived from all the operators were compared with each other to check for the similarity between them.

Vita Easyshade V

Readings from the same tooth of 30 subjects were obtained by 5 trained instrument operators. The obtained readings were then analysed using appropriate statistical method to check for the similarity between the readings obtained from these instrument operators.

Vita Classical Shade Guide

For visual determination of tooth shade, same single tooth of 30 subjects were matched with the dental tabs of Vita Classical Shade Guide under the standardised lighting condition to avoid external influence on shade determination. The obtained shades were then checked for their similarity between trained instrument operators.

Similarity between outcomes of Vita Easyshade V **and Vita Classical Shade Guide**

Shade determination of single tooth was done for 30 subjects digitally using Vita Easyshade V, followed by the visual assessment of the same tooth using Vita Classical Shade Guide. Post assessment, the shades obtained from both spectrophotometer and visual method were compared to check for similarity of outcomes between the instruments.

Inter-Observer Reliability

To derive this, two dentists, two periodontists, one physician and five dentist-trained evaluators examined 30 same subjects. Evaluations included scoring of plaque index, gingival index, extrinsic stain index, teeth sensitivity and dental erosion. For determination of plaque and gingival index, examination of six teeth also known as Ramfjord teeth was done for each subject. These teeth include maxillary right first molar (tooth 16), maxillary left central incisor (tooth 11), maxillary left first bicuspid (tooth 24), mandibular left first molar (tooth 36), mandibular right central incisor (tooth 41) and mandibular right first bicuspid (tooth 44) [16]. The individual subject's index score was determined by dividing the total of each score by the number of teeth examined.

Moreover, the evaluation of malodour utilizing an organoleptic scale was done by two dentists and two periodontists. This assessment was conducted by employing Rosenberg Scale ranging from 0 to 5 points, where 0: absence of odour, 1: barely noticeable odour, but not recognised as malodour, 2: slight malodour, 3: moderate malodour, 4: strong malodour, and 5: severe malodour [17].

Statistics

The statistical analysis was done using SPSS software (Version: 26.0). Pearson's chi square test was applied to compare the outcomes between Vita Easyshade V and Vita Classical Shade Guide. Inter-operator and inter-observer reliability were measured using Fleiss Multirater Kappa. $p<0.05$ was considered significant for all tests.

Results

Instrument Validation and Intra-operator Variability

Upon repetitive readings from the same site, Tanita HC-205 breath analyzer exhibited 90% similarity (9 out of 10) between the readings indicating the high accuracy of the device in measuring halitosis. This also indicates a strong level of intraoperator reliability for this instrument (Table 1). Similarly, measurement of teeth shade using Vita Easyshade V under similar lighting conditions and following manufacturer's recommended positioning of participant and the instrument, 100% accuracy was observed upon repetitive measurements. This also confirms a strong level of intraoperator reliability for this instrument (Table 2).

Table 1: Repetitive Reading from Tanita Breath Analyser

HC-205 Breath Analyzer	
Count of Repetitive Reading	**Obtained Score**
1	3
2	3
3	3
4	3
5	3
6	3
7	3
8	3
9	3
10	4

Table 2: Repetitive Readings from Vita Easyshade V

Vita Easyshade V	
Count of Repetitive Reading	**Obtained Shade**
1	A3
2	A3
3	A3
4	A3
5	A3
6	A3
7	A3
8	A3
9	A3
10	A3

Inter-Operator Reliability

The analysis of inter-operator agreement for Tanita HC-205 breath analyzer yielded good level of agreement between the trained instrument operators, as measured by Fleiss Multirater Kappa of 0.66 ($p<0.001$) (Table 3). The determination of teeth shade using Vita Easyshade V also demonstrated good level of agreement among the instrument operators, as evidenced by a Fleiss Multirater Kappa value of 0.73 ($p<0.001$) (Table 4). This highlights the importance of thorough training in instrumental operation, which can lead to precise and productive research outcomes free from bias. To avoid bias, the scoring of Vita Classical Shade Guide and Vita Easyshade V was done on different participant group. Shade determination using Vita Classical Shade Guide also showed good level of agreement between all the trained evaluators. Fleiss Multirater Kappa was at 0.72 ($p<0.001$) (Table 5).

The determination of teeth shade using both Vita Easyshade V and Vita Classical Shade Guide was done by an internal staff who is both a trained instrument operator and a dentist-trained evaluator. The results yielded a statistical significance ($p<0.0001$) in shade selected using the two methods (Table 6). Thus, it can be interpreted that the both the methods are equally reliable for tooth shade determination.

Table 3: Inter-Operator agreement on Tanita HC-205 breath analyzer readings

Tanita HC-205 Breath Analyzer				
Operator 1	**Operator 2**	**Operator 3**	**Operator 4**	**Operator 5**
3	3	3	3	3
2	1	2	2	2
1	2	1	1	1
4	3	4	4	3
2	2	2	2	2
3	3	3	3	3
1	1	1	1	1
3	3	1	3	1
3	3	3	3	3
2	1	2	2	2
2	2	2	2	2
3	3	3	4	3
1	1	1	1	1
2	2	2	2	2
4	4	3	4	3
3	3	3	3	3
2	1	2	1	2
1	2	1	1	1
4	4	4	4	4
2	2	2	2	2
3	3	3	3	3
1	1	1	1	2
3	3	1	3	1
3	3	3	3	2
2	1	2	2	2
2	2	2	2	2
3	3	3	3	3
1	1	1	2	1
2	2	2	2	2
4	4	3	3	3
Fleiss Multirater Kappa: 0.66				

Table 4: Inter-Operator agreement on Vita Easyshade V readings

Vita Easyshade V				
Operator 1	**Operator 2**	**Operator 3**	**Operator 4**	**Operator 5**
D4	D4	D4	D4	D4
A3	A3	A3	A3	A3
C1	C1	C1	C1	C1
C2	C2	C2	C2	C2
A3.5	A3	A3	A3	A3
C2	C2	C2	C2	C2
A4	A3.5	A3.5	A3.5	A3.5
C2	C1	C2	C1	C1
C4	C4	C4	C4	C4
D3	D4	D3	D4	D4
C2	C2	C2	C2	C2
A3	C1	C1	C1	C1
A3	A3	A3	A3	A3
C4	C4	A4	C4	C4
C1	C1	C1	C1	C1
A3	C1	C1	C1	C1
A3	A3	A3	A3	A3
C4	C4	A4	C4	C4
C1	C1	C1	C1	C1
D4	D4	D4	D4	D4
A3	A3	A3	A3	A3
C1	C1	C1	C1	C1
C2	C2	C2	C2	C2
A3.5	A3	A3	A3	A3
C2	C2	C2	C2	C2
A4	A3.5	A3.5	A3.5	A3.5
C2	C1	C2	C1	C1
C4	C4	C4	C4	C4
D3	D4	D3	D4	D4
C2	C2	C2	C2	C2
Fleiss Multirater Kappa: 0.73				

Table 5: Inter-Operator agreement on Vita Classical Shade Guide readings

Vita Classical Shade Guide				
Operator 1	**Operator 2**	**Operator 3**	**Operator 4**	**Operator 5**
A3	C1	C1	C1	C1
A3	A4	A4	A4	A4
C4	C4	A4	C4	C4
C1	C1	C1	C1	C1
D4	D4	D4	D4	D4
A3	A3	A3	A3	A3
C1	C1	C1	C1	C1
C2	C2	C2	C2	C2
A3.5	A3.5	A3.5	A3.3	A3.5
C2	C2	C2	C2	C2
A4	A3.5	A3.5	A3.5	A3.5
C2	C1	C2	C1	C1
A4	C4	C4	C4	C4
D3	D3	D3	D3	D3
C2	C2	C2	C2	C2
A3	C1	C1	C1	C1
A3	A4	A4	A4	A4
C4	C4	A4	C4	C4
C1	C1	C1	C1	C1
D4	D4	D4	D4	D4
A3	A3	A3	A3	A3
C1	C1	C1	C1	C1
C2	C2	C2	C2	C2
A3.5	A3.5	A3.5	A3.3	A3.5
C2	C2	C2	C2	C2
A4	A3.5	A3.5	A3.5	A3.5
C2	C1	C2	C1	C1
A4	C4	C4	C4	C4
D3	D3	D3	D3	D3
C2	C2	C2	C2	C2
Fleiss Multirater Kappa: 0.72				

Table 6: Comparison between Teeth Shades determined using Vita Easyshade V and Vita Classical Shade Guide

Statistics		**Vita Classical Shade Guide**								**Total**	**p-value**
		A3	**A3.5**	**A4**	**C1**	**C2**	**C4**	**D3**	**D4**		
Vita Easyshade V	A3	4	2	0	0	0	0	0	0	6	*p<0.001
	A3.5	0	2	0	0	0	0	0	0	2	
	A4	0	0	2	0	0	0	0	0	2	
	C1	0	0	0	6	0	0	0	0	6	
	C2	0	0	0	0	8	0	0	0	8	
	C4	0	0	0	0	0	2	0	0	2	
	D3	0	0	0	0	0	0	2	0	2	
	D4	0	0	0	0	0	0	0	2	2	
Total		4	4	2	6	8	2	2	2	30	
*Statistical significance obtained using Pearson's Chi-square test											

Inter-Observer Reliability

After receiving training from both dentists and periodontists, oral examination was done for 30 subjects at same site to derive the agreement on scores/outcomes between the dentist-trained evaluators, a physician, dentists and periodontists. Extrinsic stain index scoring showed a very good level of agreement between the observers as supported by Fleiss Multirater Kappa: 0.84 (p<0.001) (Table 7). Scoring on plaque index (Table 8) and gingival index (Table 9) yielded good agreement (both p<0.001), respectively between physician, dentist-trained evaluators, dentists and periodontists. Based on oral examination, presence or absence of teeth sensitivity (Table 10) and dental erosion (Table 11) was assessed and the agreement was obtained between the evaluators. Teeth sensitivity and dental erosion showed very good (p<0.001) and good level of agreement (p<0.001), respectively between the observers.

Furthermore, the organoleptic assessment of malodour showed very good agreement among the two dentists and two periodontists with Fleiss Multirater Kappa at 0.90 (p<0.001) (Table 12).

Figure 3 shows the assessment of teeth shininess as determined based on visual scoring by dentist. The score was based on a 5-pointer Likert scale, i.e. 1: Very Dull, 2: Dull, 3: Slightly Shiny, 4: Moderately Shiny and 5: Very Shiny.

Table 7: Inter-Observer agreement on Extrinsic Stain Index scoring

Extrinsic Stain Index Scores									
Physician	**Dentist-1**	**Dentist-2**	**Periodontist-1**	**Periodontist-1**	**Dentist-trained Evaluator-1**	**Dentist-trained Evaluator-2**	**Dentist-trained Evaluator-3**	**Dentist-trained Evaluator-4**	**Dentist-trained Evaluator-5**
3	3	3	3	3	3	3	3	3	3
3	3	3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
3	3	3	3	3	3	3	3	3	3
3	3	3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	3	2	2	2	3	3	2	3	2
3	3	2	2	3	3	3	2	3	2
2	2	2	2	2	2	2	2	2	2
3	3	3	3	3	3	3	3	3	3
3	3	3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
3	3	3	3	3	3	3	3	3	3
3	3	3	3	3	3	3	3	3	3
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2	2	2
2	3	2	2	2	3	3	2	3	2
3	3	2	2	3	3	3	2	3	2
2	2	2	2	2	2	2	2	2	2
Fleiss Multirater Kappa: 0.84									

Table 8: Inter-Observer agreement on Plaque Index scoring

Plaque Index Scores									
Physician	**Dentist-1**	**Dentist-2**	**Periodontist-1**	**Periodontist-1**	**Dentist-trained Evaluator-1**	**Dentist-trained Evaluator-2**	**Dentist-trained Evaluator-3**	**Dentist-trained Evaluator-4**	**Dentist-trained Evaluator-5**
2.67	2.33	2.67	2.67	2.67	2.67	2.33	2.67	2.67	2.33
2.00	2.17	2.17	2.17	2.00	2.00	2.17	2.17	2.00	2.17
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
2.67	2.50	2.67	2.67	2.67	2.67	2.50	2.67	2.67	2.50
2.83	2.67	2.83	2.83	2.83	2.83	2.67	2.83	2.83	2.67
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
3.00	3.00	2.67	2.67	3.00	3.00	3.00	2.67	3.00	3.00
3.33	3.33	2.67	2.67	3.33	3.33	3.33	2.67	3.33	3.33
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17
2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50
2.50	2.33	2.33	2.33	2.50	2.50	2.33	2.33	2.50	2.33
2.83	2.83	2.83	2.83	2.83	2.83	2.83	2.83	2.83	2.83
2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17
2.00	2.33	2.17	2.17	2.00	2.00	2.33	2.17	2.00	2.33
2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67
2.33	2.50	2.00	2.00	2.33	2.33	2.50	2.00	2.33	2.50
2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17
3.00	2.83	2.83	2.83	3.00	3.00	2.83	2.83	3.00	2.83
2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
2.67	3.00	3.00	3.00	2.67	2.67	3.00	3.00	2.67	3.00
3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
3.17	3.17	3.17	3.17	3.17	3.17	3.17	3.17	3.17	3.17
2.00	2.67	2.00	2.00	2.00	2.00	2.67	2.00	2.00	2.67
2.50	2.33	2.50	2.50	2.50	2.50	2.33	2.50	2.50	2.33
2.33	2.67	2.67	2.67	2.33	2.33	2.67	2.67	2.33	2.67
Fleiss Multirater Kappa: 0.71									

Table 9: Inter-Observer agreement on Gingival Index scoring

Gingival Index Scores									
Physician	**Dentist-1**	**Dentist-2**	**Periodontist-1**	**Periodontist-1**	**Dentist-trained Evaluator-1**	**Dentist-trained Evaluator-2**	**Dentist-trained Evaluator-3**	**Dentist-trained Evaluator-4**	**Dentist-trained Evaluator-5**
2.67	2.33	2.67	2.67	2.67	2.33	2.67	2.33	2.67	2.67
2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
2.67	2.50	2.67	2.67	2.67	2.50	2.67	2.50	2.67	2.67
2.83	2.67	2.83	2.83	2.83	2.67	2.83	2.67	2.83	2.83
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
3.00	3.00	2.67	2.67	3.00	3.00	3.00	3.00	2.67	2.67
3.33	3.33	2.67	2.67	3.33	3.33	3.33	3.33	2.67	2.67
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
3.33	3.33	2.83	2.83	3.33	3.33	3.33	3.33	2.83	2.83
2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50
2.50	2.33	2.33	2.33	2.50	2.33	2.50	2.33	2.33	2.33
2.83	2.83	2.83	2.83	2.83	2.83	2.83	2.83	2.83	2.83
2.33	2.50	2.33	2.33	2.33	2.50	2.33	2.50	2.33	2.33
2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33	2.33
2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17
2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67
2.33	2.50	2.00	2.00	2.33	2.50	2.33	2.50	2.00	2.00
2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50	2.50
2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17	2.17
3.00	2.83	2.83	2.83	3.00	2.83	3.00	2.83	2.83	2.83
2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
2.67	3.00	3.00	3.00	2.67	3.00	2.67	3.00	3.00	3.00
2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67
3.17	3.17	3.17	3.17	3.17	3.17	3.17	3.17	3.17	3.17
2.00	2.67	2.00	2.00	2.00	2.67	2.00	2.67	2.00	2.00
2.50	2.33	2.50	2.50	2.50	2.33	2.50	2.33	2.50	2.50
2.33	2.67	2.67	2.67	2.33	2.67	2.33	2.67	2.67	2.67
Fleiss Multirater Kappa: 0.73									

Table 10: Inter-Observer agreement on Dental Examination for Teeth Sensitivity

Teeth Sensitivity									
Physician	**Dentist-1**	**Dentist-2**	**Periodontist-1**	**Periodontist-1**	**Dentist-trained Evaluator-1**	**Dentist-trained Evaluator-2**	**Dentist-trained Evaluator-3**	**Dentist-trained Evaluator-4**	**Dentist-trained Evaluator-5**
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Present	Absent	Present	Absent	Absent	Present	Present	Absent	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Present	Absent	Present	Absent	Absent	Absent	Present	Absent
Absent	Present	Absent	Present	Absent	Absent	Present	Present	Absent	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Fleiss Multirater Kappa: 0.90									

Table 11: Inter-Observer agreement on Dental Examination for Dental Erosion

Dental Erosion									
Physician	**Dentist-1**	**Dentist-2**	**Periodontist-1**	**Periodontist-1**	**Dentist-trained Evaluator-1**	**Dentist-trained Evaluator-2**	**Dentist-trained Evaluator-3**	**Dentist-trained Evaluator-4**	**Dentist-trained Evaluator-5**
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Present	Absent	Present	Absent	Absent	Present	Absent	Present	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Absent	Present	Absent	Present	Present	Absent	Present	Absent
Present	Present	Absent	Present	Absent	Present	Present	Absent	Present	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Absent	Present	Present	Present	Present	Absent	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Absent	Absent	Present	Absent	Present	Absent	Absent	Present	Absent	Present
Absent	Present	Absent	Present	Absent	Absent	Present	Absent	Present	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Absent	Present	Absent	Present	Absent	Absent	Present	Absent	Present	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Fleiss Multirater Kappa: 0.76									

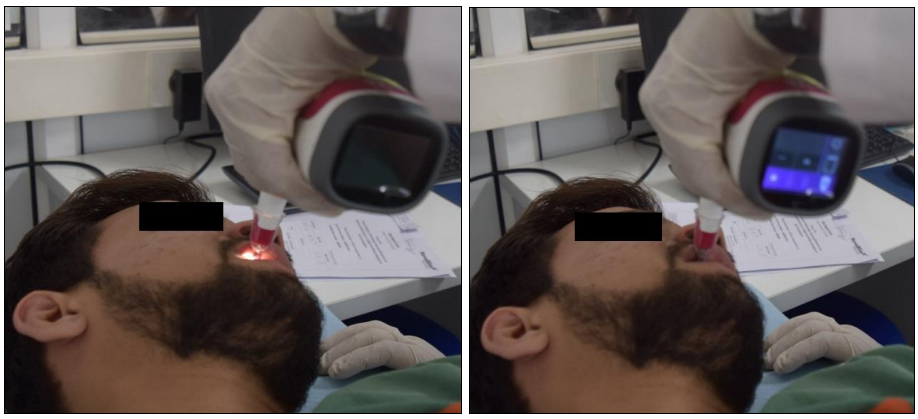

Fig 1: Teeth Shade Determination using Vita Easyshade V

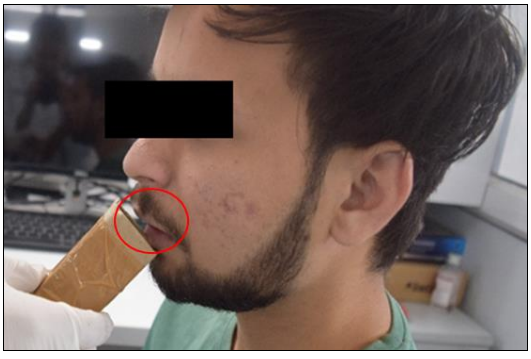

Fig 2: Malodour assessment using Tanita HC-205 Breath Analyzer

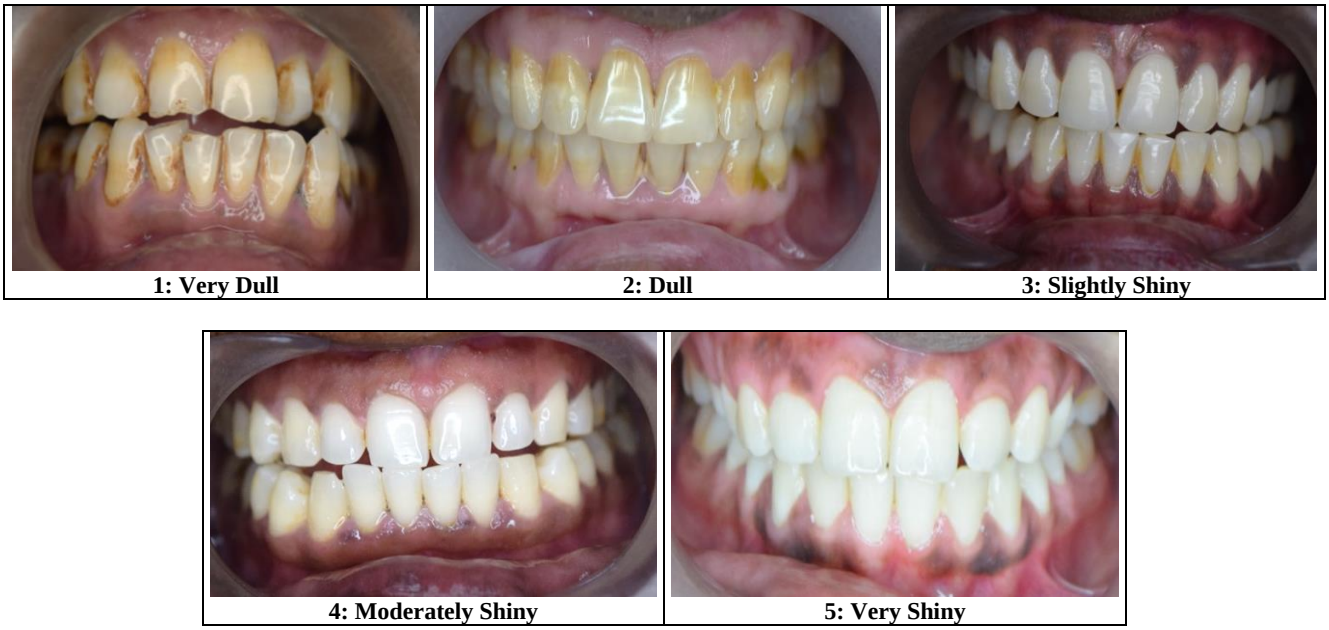

Fig 3: Visual Scoring by Dentist for Teeth Shininess

Table 12: Inter-Scorer agreement on Oral Malodour Evaluation using Organoleptic Scale

Organoleptic Assessment: Oral Malodour			
Dentist-1	**Dentist-2**	**Periodontist-1**	**Periodontist-2**
4	4	4	4
3	3	3	3
4	4	4	4
2	2	2	2
5	5	5	5
4	4	4	4
3	3	3	3
4	4	4	4
2	1	2	2
4	4	4	4
4	4	4	4
5	4	4	5
3	3	3	3
4	4	4	4
2	2	2	2
4	4	4	4
1	1	1	1
4	4	4	4
5	5	3	5
5	5	5	5
2	2	2	2
3	3	3	3
4	4	4	4
1	1	1	1
3	3	3	3
4	4	4	4
4	4	4	4
5	5	5	5
4	4	3	4
3	3	3	3
Fleiss Multirater Kappa: 0.90			

Discussion

The present study is an interval validation and standardization of dental assessments used to assess the efficacy of dental care products in dental *in-vivo* clinical research studies. The study assessed various dental assessment methods including both instrumental and visual examination.

Reliability and validity are the key indicators of the quality of the measuring instruments. Validity refers to the degree to which the interpretations of test results are justified, depending on the specific purpose for which the test is intended. In many healthcare applications, where enhancing outcomes through treatment is a key research objective, understanding the responsiveness of a measure to change becomes crucial. Inter- and intra-operator reliability is crucial for instrument operators as it ensures consistency and accuracy in data collection across different individuals performing the same task. It helps minimize variability and bias that may arise due to differences in operator technique or interpretation. By establishing consistent standards and protocols, inter- and intra-operator reliability promotes trustworthiness and validity of research findings. It also enhances the reproducibility of results, allowing for comparisons between different datasets. Ultimately, maintaining high inter- and intra-operator reliability ensures that the data obtained is dependable and can be confidently used to draw meaningful conclusions and make informed decisions [12].

This validation underlines the importance of receiving adequate training from qualified dental professionals and instrument experts before handling of the instruments in order to achieve precision in instrumental reading and scoring of various dental parameters. After receiving training from professionals, precision in instrument handling was observed for trained evaluators and instrument operators. Good level of agreement was seen among operators for both the digital instruments (both $p<0.001$). Similarly, good level of statistical agreement was also observed among dentist-trained evaluators, a physician, dentists and periodontists for dental examination including scoring for extrinsic stains, plaque and gingival index (all $p<0.001$). This highlights the importance of professional training.

Singh RK *et al.* [18] conducted a study in 2021, to compare tooth shades obtained using Vita Easyshade V and Vita Classical Shade Guide on 39 participants. The study revealed a statistical correlation ($p<0.001$) between results obtained using both the instruments. This study is in line with the present validation study which also demonstrated significant correlation ($p<0.0001$) between the two methods. Da Silva *et al.* [19] conducted a study to compare visual and instrumental shade determination methods. They found that colour

matching by using spectrophotometer can be more reliable method compared to visual method as it can also significantly reduce the unacceptable results. In contrast, the present validation study obtained significant association between the two method.

In a study conducted by Parameswaran V *et al*. [20] the spectrophotometric method exhibited a good level of inter-operator agreement, irrespective of the shade guide used. However, the agreement was fair in case of the visual method while using the VITAPAN 3D Master™ shade guide and was least for the visual method using VITAPAN Classical™ shade guide. The present study demonstrated good inter-operator agreement with for both Vita Easyshade V (spectrophotometric method) and Vita Classical Shade Guide (visual method).

Another study found a poor inter-operator agreement with Cohen's Kappa coefficient of 0.11 in shade selection by the 3 evaluators. As per the authors, the poor inter-operator agreement may be attributed to the disparity in training and experience of the operators before handling the instruments in the study [21].

Conclusion

The experience and training of study staff are powerful tools for achieving accuracy and yielding reliable results in evaluating dental parameters. The method validation conducted in the present study can serve as a model for future *in-vivo* dental clinical studies on oral care products in order to produce consistent, compatible, accurate, qualitative, and reproducible results. The favourable intra-operator, inter-operator, and inter-observer agreement observed in this validation highlights the effectiveness of controlled testing methods, essential for the successful execution of efficacy studies on dental care products.

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Conflict of Interest

All the authors declare no conflict of interest.

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