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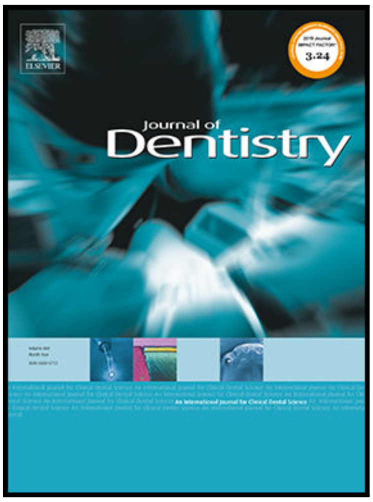

Evaluation of the accuracy (trueness, precision) and processing time of different 3-dimensional CAD software programs and algorithms for virtual cast alignment

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Evaluation of the accuracy (trueness, precision) and processing time of different 3-dimensional CAD software programs and algorithms for virtual cast alignment.

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Accuracy; best fit; alignment methods; superimposition tehcniques; virtual casts.

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Evaluation of the accuracy (trueness, precision) and processing time of different 3-dimensional CAD software programs and algorithms for virtual cast alignment

ABSTRACT

Objectives. This in vitro study aimed to evaluate the impact of different alignment algorithms and CAD software programs on alignment accuracy (trueness and precision) and processing time.

Methods. A mandibular typodont was digitized using a laboratory scanner (L2i) to obtain a reference STL (STLr) file. It was then scanned with an intraoral scanner (Primescan) and digitally duplicated ten times (n=10). Each scan was aligned with the STLr using 42 combinations of 3D CAD software and alignment algorithms. The tested software programs included Blender for Dental, BlueSkyPlan, Dental CAD App (Exocad), Medit Design, NemoSmile, and Meshmixer. Alignment accuracy (trueness and precision) and processing time were recorded using Python software (v3.8). Statistical analysis was performed with a two-way ANOVA test ($\alpha = .01$) to identify overall differences, followed by a post hoc Tukey Honestly Significant Difference test ($\alpha = .05$) to establish rankings.

Results. Significant differences in alignment accuracy were observed based on the software and algorithm used, affecting both trueness ($p<.01$) and precision ($p<.01$). Processing time also varied significantly ($p<.01$). Post hoc analysis identified the optimal algorithm for each software, revealing variations in trueness, precision, and processing time among the optimal versions. Medit Design achieved the best overall performance by combining high accuracy with the fastest processing time, while Meshmixer exhibited the lowest accuracy due to its lack of advanced algorithms.

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Conclusions. The choice of CAD software and alignment algorithm significantly influences alignment accuracy and efficiency. Best-fit and section-based provided the best results, offering valuable insights into the optimization of digital workflows in prosthodontics.

CLINICAL SIGNIFICANCE

Alignment protocols must be tailored to the specific CAD software program used, as no universal protocol was effective across all tested software. Optimizing alignment protocols reduces errors, enhances prosthodontic outcomes, and improves the reliability and efficiency of clinical and laboratory workflows, ultimately ensuring better patient care and treatment success.

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1. INTRODUCTION

Prosthetic dental treatments have incorporated advanced 3-dimensional (3D) technologies, including facial scanners, intraoral scanners (IOSs), and cone beam computed tomography (CBCT), to obtain digital data from patients. These technologies facilitate the integration of patient data, enhancing the creation of virtual patients [1-7]. For this reason, computer-aided design (CAD) software programs are crucial when executing the superimposition procedures required [8-13]. The primary objective of alignment procedures is to achieve the highest degree of concordance, producing a close match to the reference mesh. Accurate alignment is a crucial step in digital dentistry, enabling the seamless integration of digital patient data into CAD software for the design and planning of dental treatment devices. This process is essential, as it significantly influences the clinical outcomes, highlighting its critical role in contemporary prosthetic dentistry. Misalignments in patient data can result in issues such as improper contact points, inadequate crown margin fit, occlusal discrepancies, or poor integration with the patient's face, all of which can compromise the effectiveness and functionality of the treatment [11-12].

The primary best-fit (BF) methods for aligning 3D files can be classified as BF, section-based best-fit (SBF), landmark-based best-fit (LBF), or a combination of these (LBF + BF, LBF + SBF, SBF + BF) [10-12]. The BF uses an iterative closest point (ICP) algorithm to align the entire datasets of 2-point clouds by iteratively minimizing the distance between corresponding points [13-15]. Every iteration includes 3 main steps known as correspondence, transformation calculation, and update transformation. The SBF is a computational method of aligning 2 data sets which need to be equal in both meshes [16-17] by constraining the alignment process to areas or regions designated manually by the

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operator. The LBF algorithm also involves the alignment of 2 datasets by the human selection of identifiable common points between each data set [13-15].

Most available dental CAD software programs offer multiple alignment algorithms [16-23]. Each implements a different number and type of these algorithms, and, unfortunately, manufacturers do not provide clear guidelines or recommendations on which of these algorithms should be used. Moreover, studies on the effect of each of these different algorithms and/or CAD software programs on alignment accuracy are scarce in the dental literature.

The aim of the present in vitro study was to measure the alignment accuracy (trueness, precision) and processing time of different algorithms and 3D CAD software programs. The null hypothesis was that no significant differences would be found in alignment accuracy nor in processing time.

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2. MATERIAL AND METHODS

2.0 Overview

A mandibular typodont was digitized with a laboratory scanner to obtain a reference standard tessellation language file (STL_r) scanned with an IOS (Primescan; Dentsply-Sirona; Bensheim, Germany). The scan was manually aligned to the STL_r using six CAD 3D software programs with all their implemented algorithms (42 combinations). The process was repeated 10 times for each scan, resulting in 420 superpositions. Individual processing times were recorded. Once aligned, alignment accuracy (trueness and precision) was measured. A two-way ANOVA test ($\alpha = .01$) was performed to identify overall differences, followed by a post hoc Tukey Honestly Significant Difference test ($\alpha = .05$) to establish the performance of each alignment algorithm.

2.1 Data acquisition

A mandibular typodont (Hard gingiva jaw model MIS2010-L-HD-M-32; Nissin) was selected. Three metal markers (Suremark SL-10; Suremark) were fixed onto the mandibular typodont using cyanoacrylate resin (Scotch Super Glue; 3M ESPE, Seefeld, Germany) to aid in reliable landmark selection for future superimposition procedures. The markers were attached to the occlusal surfaces of the first left molar, first right premolar, and second right molar teeth. The typodont was then digitized by using a desktop laboratory scanner (L2i; Imetric, Courgenay, Switzerland) without scan powder to obtain the reference standard tessellation language (STL_R) file (Fig.1A). The laboratory scanner had been previously calibrated according to the manufacturer's recommendations. The manufacturer of this scanner specifies a trueness of <5 μm and a precision <10 μm.

The mandibular typodont was mounted on a dental simulator mannequin (NISSIN Type 2; Nissin, Kyoto, Japan). To reproduce the clinical environment, the interincisal opening was standardized to 50 mm. The typodont was digitized by a restorative dentist with extensive experience (a co-author of this study *initials omitted for review*) using a previously calibrated IOS scanner (Primescan; Dentsply Sirona, Bensheim, Germany) and scanning software program (Primescan; Dentsply Sirona, Bensheim, Germany) in a windowless room and with an ambient lighting condition of 1000 lux determined with a meter (LX1330B Light Meter; Dr. Meter Digital Illuminance, Union City, USA) (Fig.1B) [2-3]. The scanning protocol was performed once as follows: digital scans were started occlusally on the mandibular left second molar. The tip of the scanner was tilted 60 degrees in an oral direction and moved orally along the dental arch up to the mandibular right second molar. Then, the scanner was guided occlusally from the mandibular right second molar across the entire dental arch back to the mandibular left second molar. Finally, the scanner was tilted 60 degrees in a buccal direction to complete the scans and moved buccally along

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the entire dental arch. The resulting STL scanned file was duplicated 10 times as STL_1, STL_2, $_{...}$, STL_{10}.

2.2. Digital scan alignment

Six different 3D CAD software programs were tested: B4D (Blender v.3.6.5; B4D, Queensland, Australia), BSP (BlueSkyPlan v.4.13; BlueSkyBio, Illinois, USA), DCA (DentalCAD v.3.2; Exocad, Darmstadt, Germany), MD (Medit Design v.2.1.4; Medit, Seoul, South Korea), NMS (NemoSmile v.24.0.0.3; Nemotec, Madrid, Spain), and MSH (Meshmixer v.3.5.474; Autodesk, California, USA).

Each of these software programs incorporated different algorithms, which were classified into 12 groups (Table 1). The number of implemented algorithms ranged from 3 to 11 (no single software was capable of performing all 12 algorithms). A total of 42 different software program and alignment algorithm combinations were available and tested (Table 2).

Each available 3D CAD software program and alignment algorithm combination was tested by the same operator, an expert clinician (and co-author of this study *initials omitted for review*) with 8 years of experience in 3D CAD software programs. Nonetheless, to incorporate intra-operator reliability, the process was repeated 10 times for each software program and algorithm combination, resulting in a total of 420 alignments. Each time, the STL_R file and digital scan were imported into the tested CAD software program (Fig.2AD), the STL_R file was marked as the reference mesh, and the digital scan was aligned using the tested algorithm, with the resulting aligned STL files being stored.

2.3. Processing time

All 10 repetitions of each software/algorithm combination were performed consecutively using the same computer. The alignment procedures were performed on a system equipped with an MSI Intel Core i7–10870H CPU operating at 2.20 GHz, 32 GB of RAM, an NVIDIA GeForce RTX 3080 GPU, and running the Windows 11 Pro operating

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system. The time required to apply each algorithm was computed by using the creation time stamp in the metadata of each resulting STL file and reporting the mean elapsed time among all 9 pairs when using that software program and algorithm (Fig. 3AC).

2.4 Alignment accuracy

Proprietary python software code (Python v3.8; Python, Delaware, USA) was used to measure alignment accuracy (trueness and precision) between each of the resulting aligned STL files (N=420) and the reference mesh STL_R.

The STL file format represented data as a connected triangular mesh (M) composed of a number (NV) of 3D vertices $V = \{v_1 \ldots v_{NV}\} \in \mathbb{R}^3$ and a number (NF) of Faces $F = \{f_1 \ldots f_{NF}\}$, where each face is a triangle composed by 3 distinct vertices $f_i = \{(a, b, c) \in [1, NV] \wedge a \neq b \neq c\}$. Vertices appear on more than one face, forming a connected mesh. No unreferenced vertices or duplicate or empty faces were present. To compute alignment accuracy, triangular meshes $M(V, F)$ were first converted into a list of (NF) 3D points $P = \{p_1 \ldots p_{NF}\} \in \mathbb{R}^3$, each defined as the centroid position of each Face triangle $p_i = \left[v_{ai} + v_{bi} + v_{ci} \big/ 3 \right]$.

Given the list of points from the aligned STL mesh (P^{scan}) and reference's STL_R (P^{ref}), Euclidean distance in three dimensions was computed between each pair of closest points: $Dist(p_{id}^{scan}, p_{id}^{ref}) = \sum_{d=1}^{3} \sqrt{\left(p_{id}^{scan} - p_{id}^{ref}\right)^2} \Big/ 3$. Note: since the scanned STL presented imperfect outlier boundaries which were not present in the reference STL_R, these points were manually selected and removed beforehand (Fig. 1C).

Alignment accuracy was evaluated in accordance with ISO 5725-1 [24,25] and previous studies [2-4] using metrics of trueness and precision. Trueness was determined by

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calculating the mean difference between distances in the STLr and the control groups, while precision was quantified as the standard deviation for each alignment technique.

2.4. Statistical analysis

The number of repetitions necessary for each group was estimated via power sampling to have a confidence interval of CI=95% and a width for the interval of one. N=10 was established in accordance with prior studies [2-4]. Once all metrics (trueness, precision and processing times) had been obtained, individual results were reported, as well as the averages of different groups. Then, significance tests were performed to compare the software and algorithms as independent factors. To establish whether any interactions occurred between the two and/or whether significant differences existed in each factor group, trueness, precision, and processing time were tested separately using a nonparametric type II two-way ART ANOVA (Aligned Rank Transform ANOVA). The nonparametric version of ANOVA was selected, since data were found to be nonhomoscedastic (Levene test, $p<.01$) and nonnormal (Kolmogorov–Smirnov test, $p<.01$). Since not all software programs can perform all algorithms and the number each one is capable of performing varied greatly, we used different factorial balanced designs to test for the effect of each factor and the interactions between the two in different scenarios.

Finally, we conducted post hoc testing using the Turkey Honestly Significant Difference (HSD) to analyze the statistical results of algorithms from each software and to establish the performance of each software. All statistical analysis calculations were performed using proprietary python software code (Python v3.8; Python, Delaware, USA).

3. RESULTS

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The alignment accuracy and processing time of each of the 42 combinations of CAD software program and alignment algorithm is shown in Table 2. Mean trueness ranged from 67 to 162 μm, while mean precision ranged from 51 to 83 μm. Mean processing time ranged from 33 to 561 seconds. Figure 4 shows a 2D visualization of the results from Table 2.

The average result for each of the algorithm groups (selecting only the software capable of performing that algorithm) is shown in Table 3. Mean trueness ranged from 70.51 to 106.68 μm, while mean precision ranged from 54.57 to 68.04 μm. Mean processing time ranged from 68 to 348 seconds. The algorithms that obtained the best results were those that incorporated best-fit (BF), followed by section-based (SBF), and finally, landmark-based (LBF).

To test the significance of the results of the different algorithms, a two-way ART ANOVA was performed on three different sets:

1) the four software programs (B4D, BSP, DCA, NMS) capable of performing landmark-based algorithms (LBF-$3_{xyz,}$ LBF-$6_{xyz,}$, LBF-3_{o}, LBF-6_{o});

2) the four software programs (B4D, MD, MSH, NMS) capable of performing section-based algorithms (SBF-3 and SBF-All);

3) the three software programs (B4D, DCA, NMS) capable of performing best-fit algorithms (LBF-$3_{xyz,}$+ BF, LBF-$6_{xyz,}$+ BF, LBF-$3_{o,}$+ BF, LBF-$6_{o,}$+ BF).

In all cases, the software and algorithms had no interaction effect on each other in either trueness, precision, or time ($p>.05$). After removing that term, the algorithm used always showed a significant effect on trueness, precision, and time ($p<.01$) in all three scenarios. Finally, the software was also found to have a significant effect on trueness and precision in the last two scenarios (SBF and BF algorithms, $p<.01$).

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The Turkey Honestly Significant Difference (HSD) post hoc test was then conducted. First, the optimal algorithm for each software was established. The optimal algorithm was defined as the fastest one (HSD processing time p<.05) among those with similar accuracy (trueness p>.05 and precision p>.05) compared with the overall best (lowest trueness and precision). Then, each optimal software/algorithm combination was ranked from best to worst, grouping together those not showing significant differences between them in some of the three metrics (trueness, precision or processing time) (Table 4).

MD using BF algorithm fared as the overall best combination, being faster than any other while reaching similar accuracy (trueness p>.05 and precision p>.05) compared with the optimal versions of three other software programs (B4D, DCA, MSH). NMS reached similar Trueness (p>.05) but worse Precision (p<.05) and was slower (p<.05). Finally, MSH fared as the worst overall, reaching worse trueness (p<.05), precision (p<.05), and processing time (p<.05) because it did not implement either SBF or BF algorithms.

4. DISCUSSION

This study evaluated the accuracy, in terms of trueness and precision, of twelve different alignment algorithms and six software programs for virtual cast alignment. While previous authors have assessed the impact of various alignment algorithms, they did not test the same dataset among six dental and nondental CAD software programs with 12 alignment algorithms or measure the processing time required for each alignment [22].

Based on the results obtained in this study, the BF algorithms tested showed significant differences in both alignment error values (mean trueness and precision) and mean processing time; hence, the null hypothesis that no significant differences would be found in the alignment accuracy and the processing time among the reference and digital casts using the different alignment strategies tested was rejected. The SBF algorithms obtained lower

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discrepancies in trueness compared with the LBF algorithm methodologies. However, the processing time needed to perform the SBF algorithms was higher if compared with that of the LBF algorithms. SBF and LBF protocols need a human operator to select common landmark points or areas between the two 3D meshes. However, the errors introduced by manual procedures could be minimized by using a second-pass BF algorithm, thereby obtaining the highest alignment accuracy regarding trueness and precision.

Digital prosthetic treatments, including computer-aided dental implant planning, diagnostic waxing procedures, prosthetically driven devices, CAD designs, and three-dimensional virtual patient representations, require the highest alignment accuracy to facilitate the development of multidisciplinary diagnostics, treatment plans, and training simulations before clinical procedures. The present in vitro study revealed discrepancies of up to 95 µm in trueness and 31 µm in precision among the alignment algorithms tested in the selected CAD software programs, demonstrating that the algorithm selected affected the final outcome. While most dental CAD software programs allow users to select the alignment algorithm, there is a notable lack of scientific evidence guiding these choices, an oversight given the critical role alignment accuracy plays in treatment success. As far as we know, an established clinical threshold for virtual casts alignment in digital dentistry has not been published. Therefore, minimizing alignment errors is crucial to ensure a reliable digital workflow. Previous authors have reported accuracies in virtual cast alignments with trueness ranging from 150 µm to 200 µm and precision ranging from 1 µm to 37 µm, leading to an overall virtual cast alignment accuracy ranging from 149 µm to 237 µm [22]. Furthermore, studies that evaluated the impact of different alignment protocols on the superimposition accuracy of complete arch meshes are sparse. Moreover, disparities in research methodologies and differences among the data sets used in each study make comparisons challenging. Becker et al [19] studied the alignment error discrepancies using LBF

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procedures by selecting 10 anatomic points and evaluated improvements when ICP methodologies were used in an open-source software program (Meshlab). The authors stated that LBF could produce alignment discrepancies higher than 0.5 mm and that ICP algorithms could successfully reduce initial alignment discrepancies when they were below 0.5 mm. The authors concluded that ICP algorithms could improve LBF procedures, consistent with the present study. Revilla-León et al [22] assessed the following alignment algorithms: entire data set BF, 3 or 6 occlusal LBF, and 3 teeth SBF, concluding that LBF algorithms produced the highest alignment discrepancies compared with the entire BF and SBF. However, their results showed that both BF and SBF obtained the highest trueness and precision. Also, they reported statistically significant differences among 3 occlusal points LBF and 6 occlusal points LBF, while the results of the present study showed no significant differences in trueness (p=.056) or processing time (p=.907). However, statistically significant differences were found in precision (p=.004) when LBF-3o and LBF-6o were compared. Moreover, no statistically significant differences were found in trueness (p=.296), precision (p=.134), and processing time (p=.077) when LBF-3_{xyz} and LBF-6_{xyz} alignment algorithms were compared.

Regarding SBF algorithms, all CAD software programs implementing the SBF algorithms performed similarly in selecting SBF-3 or SBF-6, except the NMS software program (NemoSmile), which performed better implementing an SBF-All algorithm (69.92 ± 57.35 µm) when compared with SBF-6 (71.57 ± 57.84 µm) and SBF-3 (84.64 ± 69.03 µm). The results reported by Revilla-León et al [22] were partially consistent with the results of the present study, since BF algorithms were demonstrated to be the alignment procedure of choice with the fewest RMS errors. The discrepancies could be explained as differences in the reference extraoral scanners used to obtain the reference STL file, the IOS used for digitization, or the differences in the software programs and protocols tested in both studies. Dede et al [23] compared a metrology-grade software program (Geomagic Control X) with a

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nonmetrology-grade freeware program (Medit Design) to measure RMS deviations in complete arch implant-supported frameworks. They concluded that no significant differences were present between the software programs when overall RMS values were considered. None of these studies measured the time needed to perform each alignment procedure.

The authors are unaware of previous studies on the alignment accuracy of 6 different dental and nondental CAD software programs used in clinical and laboratory practice, testing 12 different alignment procedures, and measuring the processing time needed to perform each alignment procedure. Regarding alignment accuracy, the ideal software program can be defined as one that achieves the highest alignment accuracy in the shortest time [13]. Most previous studies have focused solely on accuracy values, without considering the time required for alignment, which is crucial in daily clinical and laboratory routines. Independently of the CAD software program used, the algorithm affected trueness, precision, and time ($p<.01$). The results of the present investigation show that the best alignment algorithm was BF followed by the LBF in conjunction with a second-pass BF for performing cast alignment procedures. Finally, the CAD software program used had an impact on trueness and precision when section-based (SBF) and second-pass best-fit (BF) algorithms were used. Table 4 shows a comparison between the best and fastest alignment algorithms for each software program tested. Faster alternative alignment algorithms were defined as those reaching similar alignment accuracy according to Turkey Honestly Significant Difference testing ($\alpha=0.05$) and requiring significantly less processing time. In absolute terms of accuracy, the best CAD software program was B4D, which obtained an accuracy of 66.73 ± 54.24 µm but required 438 seconds to perform the alignment using a SBF-6 alignment protocol. However, the faster alternative algorithm for the same software obtained an accuracy of 67.04 ± 54.59 µm and required 124 seconds. This means a reduction of 3.5× of the time needed to perform the alignment, with no impact on the global accuracy alignment

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obtained. Moreover, considering the fastest software program, the MD software program obtained its best alignment accuracy of 70.44 ± 56.46 µm in 40 seconds using the LBF-3o algorithm. However, the faster alternative algorithm obtained a mean trueness of 70.79 µm and mean precision of 56.31 µm, requiring 33 seconds with only a best-fit algorithm. The mean time spent on each software program and procedure combination showed considerable differences, with multipliers of 17× between the fastest and slowest combination (33 seconds versus 561 seconds) (Table 2). Regarding the results of the present investigation, the differences in trueness between the best and the fastest software was similar (3.71 µm in trueness and 2.22 µm in precision), while the differences in the time required to perform the same alignment differed by 398 seconds.

The findings of this investigation suggest valuable guidance for clinicians and laboratory technicians in selecting the most appropriate alignment algorithm and protocol based on the CAD software used. An additional consideration is software licensing and pricing, as shown in Table 5. Some of the CAD software tested in this study are free, such as Meshmixer and Medit Design, while others use a free or premium model (BlueSkyPlan) or require a paid annual license (Exocad and Nemotec) or a modular one-time purchase, (Blender for Dental). This distinction may impact the accessibility and selection of software by users. However, the findings of this study indicate no direct relationship between software cost and virtual cast alignment accuracy. Notably, Medit Design and Blender for Dental offered the best value for money, combining affordability with high alignment accuracy.

It must be taken into account that when alignments are made in CAD software, there are different methods of visual representation of the alignment performed. Medit, Exocad and Blender software provide a visual scale with a color map. In Medit, a green alignment means a discrepancy of 0 microns, blue -0.2, and yellow 0.5 mm (Fig.3A), while in evoked and Blender software, a blue color means a discrepancy between 0 a 0.01 µm, a green color

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means a discrepancy between 0.04 and 0.05 µm, and a red color means a discrepancy up to 0.1 µm (Fig.3B). However, Nemotec software does not provide visual information through a color map. Instead, this software offers the alignment error performed by RMS value, which is less intuitive for the user to understand the error obtained in the alignment. The more this value tends to zero, the better the alignment obtained. However, two software programs tested in this study, Meshmixer and BlueSkyPlan, do not provide any type of information, visual or numerical, about the alignment obtained.

The digital files used in this study were composed of a typodont digitized using two different noncontact optical scanners: a laboratory scanner (L2; Imetric 4D Imaging) and an IOS (Primescan; Dentsply Sirona). The intraoral scanner (IOS) used in this study demonstrated a reported accuracy in a previous investigation, achieving a trueness of 69.5 µm and a precision of 97.5 µm [3]. Also, the scanning protocol performed followed the manufacturer’s recommendations and was additionally supported by findings from Piedra-Cascón et al [3]. The combination of a laboratory scanner and the selected IOS was used to simulate a clinical situation.

Limitations of this study included the in vitro design and the evaluation of only a single intraoral scanner (IOS). Additionally, the laboratory scanner used had a specified trueness of <5 µm and a precision of <10 µm, which could have influenced the results. Potential scanning inaccuracies may also have arisen because of the metal markers attached to the occlusal surfaces of the typodont. Differences in the results regarding alignment procedure selection, accuracy, and processing time needed should be expected when aligning STL files with higher differences between the meshes, such as edentulous areas resulting in fewer common references for alignment. Further in vivo and in vitro studies are needed to evaluate alignment accuracy depending on the clinical situation.

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5. CONCLUSIONS

Based on the findings of this in vitro study, the following conclusions were drawn:

1. The top performer alignment algorithm in terms of accuracy and processing time was the BF algorithm implemented by Medit Design software.

2. The worst performer alignment algorithm in terms of accuracy and processing time was the LBF-6o algorithm implemented by BlueSkyPlan software.

3. Section-based BF procedures significantly improved trueness compared with landmark-based BF methodologies but significantly increased the time required.

4. Incorporating second-pass best-fit algorithms into alignment procedures improved trueness and precision while not significantly impacting the required time.

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TABLES

Table 1. Description of anatomic landmarks for each alignment algorithm group.

ALIGNMENT PROCEDURE	**LANDMARKS AND SURFACES**
BF	Entire dataset
LBF-3_o	3 markers attached to the occlusal surfaces.
LBF-6_o	3 occlusal markers + distobuccal of second left molar cusp, left canine cusp, and mesiobuccal cusp of first left molar
LBF-3_{xyz}	Occlusal marker on left first molar, gingival zenith of right first central incisor, and mesiolingual cusp of right first molar
LBF-6_{xyz}	3 markers + distobuccal cusp of left second molar, gingival zenith of right first central, and mesiolingual cusp of right first molar
SBF-3	First left molar, first right premolar, and second right molar teeth
SBF-6	First left molar, first right premolar, second right molar, second left premolar, left lateral incisor, and right lateral incisor
SBF-All	All teeth
LBF-3_o + BF	First alignment: 3 markers attached to occlusal surfaces.

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	Second alignment: best-fit of pre-aligned entire data
LBF-3$_{xyz}$ + BF	First alignment: Occlusal marker on left first molar, gingival zenith of right first central incisor, and mesiolingual cusp of right first molar
	Second alignment: best-fit of pre-aligned entire data
LBF-6$_{o}$ + BF	First alignment: 3 markers + distobuccal of second left molar cusp, left canine cusp, and mesiobuccal cusp of first left molar
	Second alignment: best-fit of pre-aligned entire data
LBF-6$_{xyz}$ + BF	First alignment: 3 markers + distobuccal cusp of left second molar, gingival zenith of right first central incisor, and mesiolingual cusp of right first molar
	Second alignment: best-fit of pre-aligned entire data

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Table 2. Alignment errors for each alignment procedure performed on each 3D CAD software program tested.

Num	**CAD Software**	**Alignment algorithm**	**Trueness (µm)**	**Precision (µm)**	**Processing time (seconds)**
1	B4D	LBF-3o	110.70	70.79	196.0
2	B4D	LBF-3o + BF	67.35	55.52	230.0
3	B4D	LBF-3xyz	96.78	68.31	184.0
4	B4D	LBF-3xyz + BF	70.62	58.49	212.0
5	B4D	SBF-3	68.67	54.75	336.0
6	B4D	LBF-6o	99.78	65.90	98.0
7	B4D	LBF-6o + BF	67.04	54.59	124.0
8	B4D	LBF-6xyz	86.56	60.04	222.0
9	B4D	LBF-6xyz + BF	70.05	58.98	270.0
10	B4D	SBF-6	66.73	54.24	438.0
11	B4D	SBF-All	66.94	54.69	561.0
12	BSP	LBF-3o	161.80	83.04	66.0
13	BSP	LBF-3xyz	148.18	77.53	72.0
14	BSP	LBF-6o	128.92	62.10	66.0
15	BSP	LBF-6xyz	129.14	63.67	86.0
16	DCA	LBF-3o	105.60	69.72	160.0

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17	DCA	LBF-3o + BF	70.09	57.07	167.0
18	DCA	LBF-3xyz	90.17	62.27	168.0
19	DCA	LBF-3xyz + BF	70.08	57.05	176.0
20	DCA	LBF-6o	79.00	59.34	184.0
21	DCA	LBF-6o + BF	70.09	57.05	203.0
22	DCA	LBF-6xyz	84.33	60.79	208.0
23	DCA	LBF-6xyz + BF	70.09	57.05	222.0
24	MD	SBF-All	71.09	56.59	130.0
25	MD	LBF-3o	70.44	56.46	40.0
26	MD	LBF-3xyz	70.53	56.53	55.0
27	MD	SBF-3	71.66	57.14	106.0
28	MD	BF	70.79	56.31	33.0
29	MSH	SBF-3	74.64	57.05	194.0
30	MSH	SBF-6	76.94	54.09	236.0
31	MSH	SBF-All	74.67	51.66	262.0
32	NMS	LBF-3o	84.88	60.20	68.0
33	NMS	LBF-3o + BF	76.62	66.55	88.0
34	NMS	LBF-3xyz	90.28	60.15	74.0

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35	NMS	LBF-3xyz + BF	75.67	65.03	78.0
36	NMS	SBF-3	84.64	69.03	216.0
37	NMS	LBF-6o	92.73	62.95	80.0
38	NMS	LBF-6o + BF	76.75	66.76	102.0
39	NMS	LBF-6xyz	94.97	63.02	94.0
40	NMS	LBF-6xyz + BF	76.83	66.74	108.0
41	NMS	SBF-6	71.57	57.84	318.0
42	NMS	SBF-All	69.92	57.35	348.0

Software

B4D (Blender; Blender for Dental, Queensland, Australia).

BSP (BlueSkyPlan; BlueSkyBio, Illinois, USA).

DCA (Dental CAD App; Exocad, Darmstadt, Germany).

MD (Medit Design; Medit, Seoul, South Korea).

NMS (NemoSmile; Nemotec, Madrid, Spain).

MSH (Meshmixer; Autodesk, California, USA).

Algorithms

LBF: Landmark Based Fit algorithm (see Table 1 for more details)

SBF: Section Based Fit algorithm (see Table 1 for more details)

BF: Best Fit algorithm (see Table 1 for more details)

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Table 3. Average alignment error for each alignment procedure group tested and the association of each alignment algorithm with its corresponding CAD software.

Alignment algorithm	CAD Software	Trueness (µm)	Precision (µm)	Processing time (seconds)
LBF-3o	B4D, BSP, DCA, MD, NMS	106.68	68.04	68.0
LBF-3o + BF	B4D, DCA, NMS	71.36	59.71	167.0
LBF-3xyz	B4D, BSP, DCA, MD, NMS	99.19	64.96	74.0
LBF-3xyz + BF	B4D, DCA, NMS	72.12	60.19	176.0
LBF-6o	B4D, BSP, DCA, NMS	100.11	62.57	89.0
LBF-6o + BF	B4D, DCA, NMS	71.29	59.47	124.0
LBF-6xyz	B4D, BSP, DCA, NMS	98.75	61.88	151.0
LBF-6xyz + BF	B4D, DCA, NMS	72.32	60.92	222.0
SBF-3	B4D, MD, MSH, NMS	74.90	59.49	205.0
SBF-6	B4D, MSH, NMS	71.75	55.39	318.0
SBF-All	B4D, MD, MSH, NMS	70.51	54.57	348.0

Software

B4D (Blender; Blender for Dental, Queensland, Australia)

BSP (BlueSkyPlan; BlueSkyBio, Illinois, USA)

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DCA (Dental CAD App; Exocad, Darmstadt, Germany)

MD (Medit Design; Medit, Seoul, South Korea)

NMS (NemoSmile; Nemotec, Madrid, Spain)

MSH (Meshmixer; Autodesk, California, USA)

Algorithms

LBF: Landmark Based Fit algorithm (see Table 1 for more details)

SBF: Section Based Fit algorithm (see Table 1 for more details)

BF: Best Fit algorithm (see Table 1 for more details)

Table 4. Software and alignment algorithms performance, trueness, precision and processing time based on Turkey Honestly Significant Difference statistical test.

Performance	**CAD Software**	**Alignment Algorithm**	**Trueness (µm)**	**Precision (µm)**	**Processing time (seconds)**
Best Overall	MD	BF	70.79	56.31	33.0
Comparable accuracy but slower (p<0.05)	B4D	LBF-6o + BF	67.04	54.59	124.0
	DCA	LBF-3xyz + BF	70.08	57.05	176.0
	MSH	SBF-All	74.67	51.66	262.0
Comparable trueness but worse precision and slower (p < 0.05)	NMS	LBF-3xyz + BF	75.67	65.03	78.0
Worse trueness and precision and slower (p< 0.05)	BSP	LBF-6o	128.92	62.10	66.0

<u>Software</u>

B4D (Blender; Blender for Dental, Queensland, Australia)

BSP (BlueSkyPlan; BlueSkyBio, Illinois, USA)

DCA (Dental CAD; Exocad, Darmstadt, Germany)

MD (Medit Design; Medit, Seoul, South Korea)

NMS (NemoSmile; Nemotec, Madrid, Spain)

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MSH (Meshmixer; Autodesk, California, USA)

Algorithms

LBF: Landmark Based Fit algorithm (see Table 1 for more details)

SBF: Section Based Fit algorithm (see Table 1 for more details)

BF: Best Fit algorithm (see Table 1 for more details)

Table 5. Licensing for each CAD software program.

Software	Licensing
Medit Design	Free
Blender for Dental	One-time purchase
DentalCAD	Annual License
Nemosmile	Annual License
Meshmixer	Free
BlueSkyPlan	Freemium (Pay-per-use)

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FIGURES

Figure 1A-C. A, Reference STL with 3 metal markers on occlusal surfaces. B, Test group STL. C, Test group boundary imperfections manually removal.

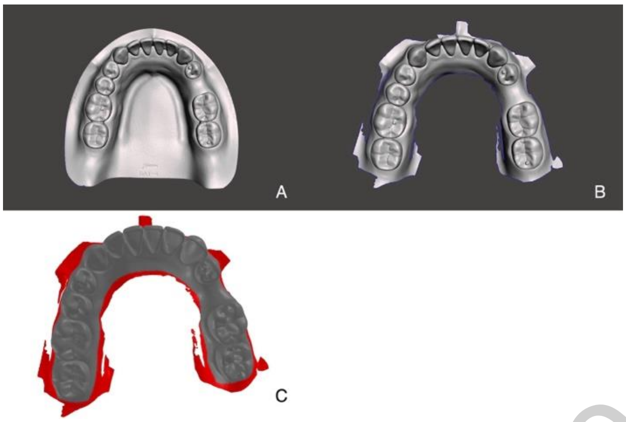

Figure 2 A-D. Illustrative representations of different alignment algorithms performed in different CAD software programs. A) LBF-3$_{xyz}$ Medit Design; Medit Link, B) SBF-3 NemoScan; Nemotec, C) SBF-6 Meshmixer; Autodesk, D) LBF-6$_o$ NemoScan; Nemotec.

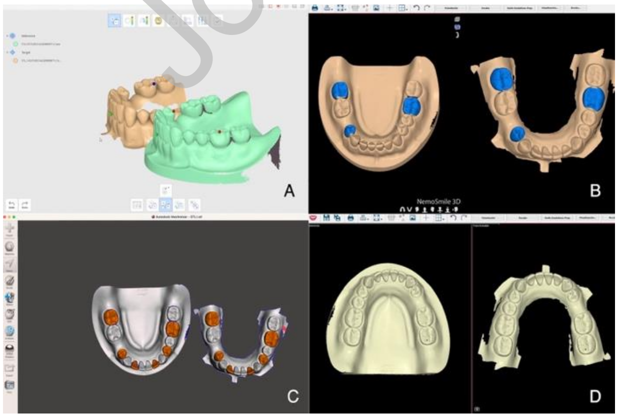

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Figure 3A-D. Colored deviation maps between reference STL $_{\text{file}}$ and intraoral digital scan. A, SBF-All Medit Design; Medit. B, LBF-3_{xyz} DentalCAD App; Exocad GmbH. C, LBF-3_o + BF B4D; Blender Foundation. D, LBF-3_o NemoSmile 3D; Nemotec.

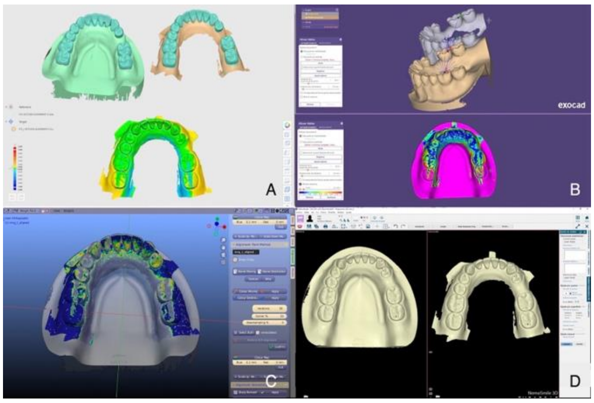
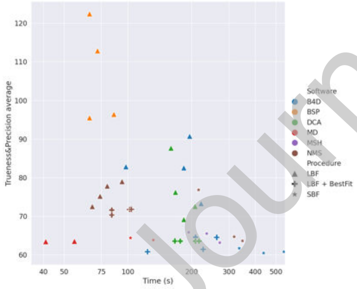


Figure 4. Average alignment accuracy versus time required for each software program and alignment combination. X-axis: Time required (seconds). Y-axis: alignment accuracy **(µm)**.



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Dear Prof. Dr. Lynch,

Please find described the contributions of each author to the present manuscript.

- Wenceslao Piedra-Cascón*: Conceptualization, protocol development, in vitro documentation, and manuscript writing.
- Xavier Paolo Burgos-Artizzu: Protocol development, contributed to manuscript writing and measurements.
- Óscar González Martín: Contributed to manuscript writing and proof reading.
- Carlos Oteo-Morilla*: Conceptualization, protocol development, in vitro documentation, and manuscript writing.
- Jose Manuel Pose-Rodriguez: Contributed to statistical analysis.

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- Mercedes Gallas-Torreira: Conceptualization, protocol development, and manuscript writing.

All authors discussed the evolution and commented on the manuscript at all stages.

Thank you very much for your time. Looking forward to hearing from you soon.

Kind Regards,

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* The first, second and fourth authors shared significant roles in carrying out the present study, indicating an equal contribution. A, B and D conceived and designed the experiments, carried out the experiments and analyzed the data.

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Conflict of Interest

The authors did not have any conflict interest, financial or personal, in any of the materials described in this study.