

# Automated Global Positioning Layout (*GPL*) for accuracy assessment in CAD-CAM mandibular reconstruction – Method validation

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1 **Automated Global Positioning Layout (*GPL*) for accuracy assessment in**  
2 **CAD-CAM Mandibular Reconstruction - Method validation**

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34 **Keywords:** Mandibular reconstruction, Computer-Aided Design; Computer-  
35 Aided Manufacturing; Prosthesis; Accuracy Assessment, Validation

36 **Abstract:**

37 The lack of a standardized methodology complicates accuracy assessment in  
38 computer-assisted mandibular reconstruction. Existing landmark-based  
39 methods are susceptible to operator variability, while surface-based  
40 comparisons can mask local deviations.

41 This study validates a novel, automated protocol, the Global Positioning Layout  
42 (GPL), to quantify the 3D discrepancy between the virtual surgical plan and the  
43 postoperative outcome, by comparing its performance and reliability against  
44 Methods A and B. A retrospective cohort of 17 patients was analysed, with three  
45 operators performing all measurements on two occasions.

46 The GPL method demonstrated complete reproducibility, with no inter- or intra-  
47 operator variability, providing a detailed, spatially-oriented assessment of

48 deviations. In contrast, the landmark-based method showed poor  
49 reproducibility and systematic bias and was often inapplicable due to the  
50 absence of landmarks after resection. The surface-based method, while  
51 objective for its mean error metric, was operator-dependent for initial  
52 alignment and its non-directional output masked significant localized  
53 deviations.

54 This study validates GPL as a robust and fully reproducible tool that overcomes  
55 the critical limitations of established techniques. The GPL method provides a  
56 strong foundation for a standardized protocol, essential for the reliable  
57 comparison of surgical outcomes, refinement of surgical techniques, and  
58 improvement of long-term patient outcomes.

## 59 **INTRODUCTION**

60 The use of computer-aided design and manufacturing (CAD/CAM) has become  
61 integral to head and neck surgery, allowing for the creation of patient-specific  
62 solutions to restore facial aesthetics and function. By providing detailed 3D  
63 visualizations, virtual surgical planning (VSP) has significantly improved the  
64 precision of both surgical planning and execution. When combined with  
65 computer-assisted surgery (CAS), these technologies improve surgical accuracy  
66 and provide the consistent, objective data necessary for the robust evaluation  
67 of clinical outcomes [1,2].

68 Recent systematic reviews and efforts to create evaluation guidelines have  
69 underscored a lack of methodological standardization in accuracy assessment  
70 [3]. A variety of approaches have been reported in the literature, many of which  
71 have been developed for and partly validated in the context of reconstructions  
72 using microvascular free bone flaps. These methods generally rely on linear or

73 angular measurements derived from specific anatomical landmarks, but this  
74 approach often depends on manual point selection, introducing potential intra-  
75 and inter-operator variability [4-14]. Alternatively, three-dimensional (3D)  
76 surface comparison techniques provide a more global assessment of  
77 congruence, though their interpretation can be challenging and they may lack  
78 specific 3D spatial orientation information [9,15,16]. Another approach  
79 provides a comprehensive assessment by superimposing 3D models to generate  
80 a roto-translational matrix that numerically describes the spatial deviation,  
81 although a common limitation of this method is the lack of a standardized  
82 reference system [17].

83 To address these limitations, the Global Positioning Layout (GPL) method was  
84 developed to standardize the quantification of three-dimensional spatial  
85 discrepancies between planned reconstructions and postoperative outcomes,  
86 eliminating operator dependency[18]. The present study aims to validate the  
87 GPL method by comparing its performance against two established protocols  
88 from the literature that utilize manual, linear measurements [8] and global,  
89 three-dimensional surface analysis [16].

## 90 **MATERIALS AND METHODS**

### 91 **Patient population**

92 A consecutive series of patients who underwent mandibular reconstruction with  
93 custom-made prosthetic devices (REPLICA) at the Maxillofacial Surgery Unit,  
94 University Hospital of Padova, Italy[19] was retrospectively collected for  
95 validation. Of the 18 patients operated between March 2012 and June 2017, one  
96 who died from postoperative complications was excluded. The final series

97 comprised 17 patients (9 females, 8 males) with a median age of 67 years (IQR  
98 65-73). The study was conducted in accordance with the Declaration of  
99 Helsinki, and the protocol was approved by the Ethical Committee of the  
100 University Hospital of Padova (protocol number 24435/AOP1814 April 2019);  
101 all patients gave their written informed consent. Detailed patient  
102 characteristics, including demographics, primary diagnoses and defect  
103 classification[20] are summarized in Table 1.

104 *(Table 1 here)*

### 105 **Preparation and virtual workflow for accuracy assessment**

106 Each patient underwent preoperative volumetric or thin-slice computed  
107 tomography (CT) scanning, with the acquired data stored in DICOM format.  
108 Using Mimics software (Materialise, NV, Leuven, Belgium), the segmentation  
109 process was performed to isolate regions of interest, and Virtual Surgical  
110 Planning (VSP) was conducted using Geomagic Freeform software (3D Systems,  
111 Inc., South Carolina, USA), to establish the surgical plan and generate the  
112 preoperative 3D models. To evaluate the accuracy of the surgical outcome  
113 against the virtual plan, operated patients underwent a thin-slice CT scan one  
114 month postoperatively, according to a standard follow-up protocol. The  
115 postoperative DICOM data were then segmented to generate the corresponding  
116 postoperative model. A detailed description of the methodology used to  
117 generate the specific virtual models has been recently described [18].

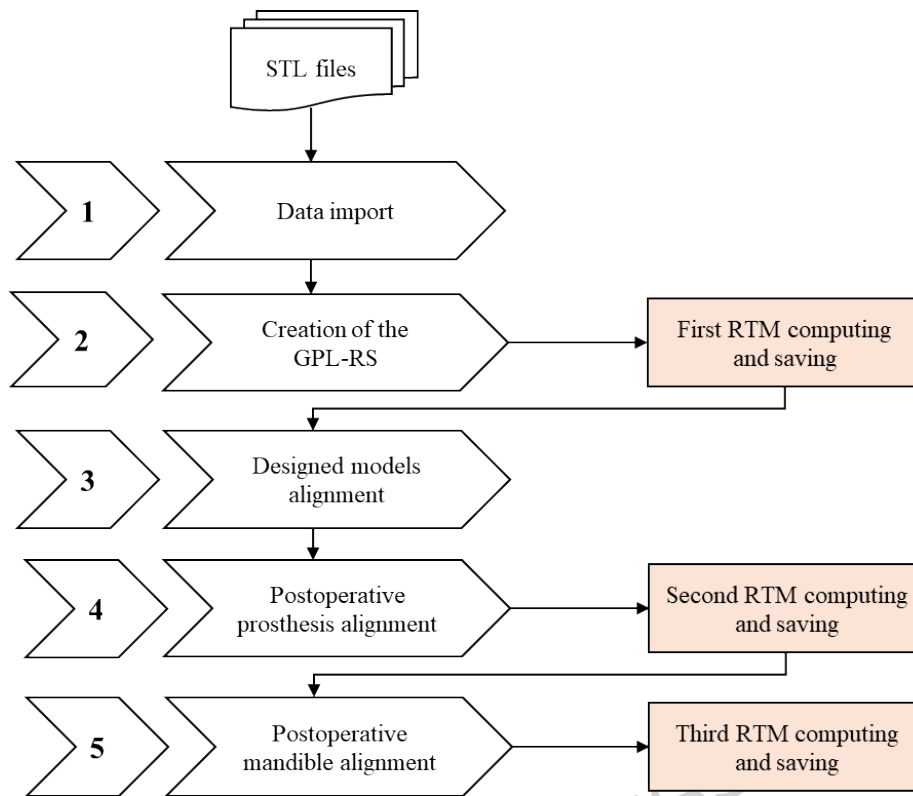
### 118 **Accuracy assessment methodologies**

119 To validate the Global Positioning Layout [18] method, its performance was  
120 compared against two established methodologies selected from the literature  
121 to represent different underlying principles:

122 Method A[8], a manual, landmark-based protocol using linear distance  
123 measurements, and Method B[16], a semi-automated, surface-based technique  
124 that assesses global model congruence via the Hausdorff distance. Each  
125 protocol is detailed in the following subsections. <sup>1816</sup>

## 126 **Global Positioning Layout**

127 Following the methodology previously described by our group [18], the GPL  
128 approach quantifies reconstruction accuracy via roto-translational matrices  
129 (RTMs) representing the 3D spatial deviations between planned and  
130 postoperative outcomes. A key feature is the establishment of a unique  
131 coordinate reference system (GPL-RS) based on the 'reference mandible'  
132 geometry, providing a stable and objective framework for comparison. The  
133 definition of the GPL-RS establishes an initial RTM which is used to align the  
134 planned mandible and the designed prosthesis within this reference system.  
135 Subsequently, the postoperative prosthesis (floating model) is registered to the  
136 designed prosthesis (fixed model) using an Iterative Closest Point (ICP)  
137 algorithm. This second RTM, obtained from prosthesis registration, is then  
138 applied to the postoperative mandible component, ensuring that both the  
139 designed and postoperative models are located within the GPL-RS. The third  
140 and final RTM, derived from aligning the postoperative mandible to the planned  
141 mandible, quantifies accuracy in terms of rotational and translational  
142 reconstruction errors. The methodological workflow is summarized in Fig. 1.

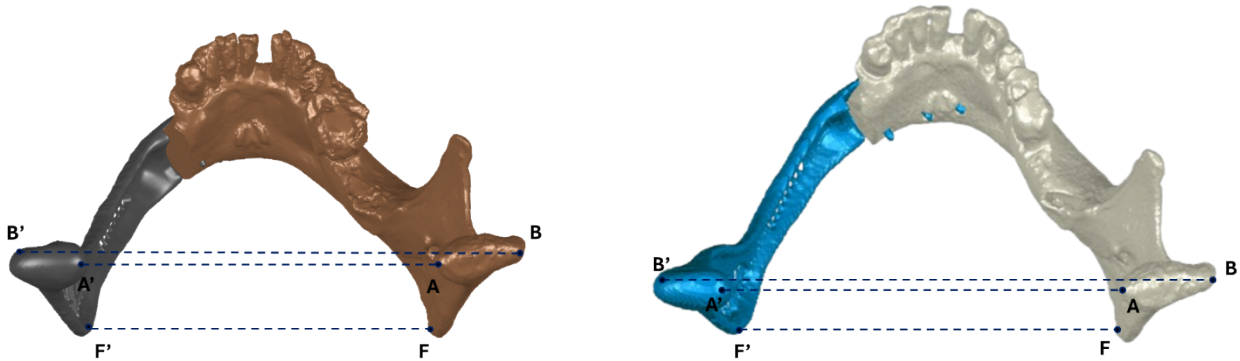


143

144 **Method A**

145 Initially described by Wilde et al.[8], this method defines mandibular  
 146 reconstruction accuracy by measuring the postoperative transverse deviation  
 147 of the mandibular rami from their preoperative position. Six corresponding  
 148 landmark pairs are identified on both the virtual surgical planning (VSP) and  
 149 postoperative models, where anatomically feasible: A-A' (*innermost point of*  
 150 *right mandibular condyle to innermost point of left mandibular condyle*), B-B'  
 151 (*outermost point of right mandibular condyle to outermost point of left*  
 152 *mandibular condyle*), C-C' (*lowest point of right mandibular notch to lowest*  
 153 *point of left mandibular notch*), D-D' (*tip of right lingula of the mandible to tip*  
 154 *of left lingula of the mandible*), E-E' (*tip of right coronoid process to tip of left*  
 155 *coronoid process*), and F-F' (*most caudal point of right mandibular angle to*  
 156 *most caudal point of left mandibular angle*). In our 17-case cohort, A-A', B-B',  
 157 and F-F' were consistently measurable in all patients (Fig. 2), whereas C-C' and

158 E-E' could be reliably identified in only two subjects due to specific anatomical  
 159 feature.



160

161 For each identified landmark pair, the distance between corresponding points  
 162 was measured three times on both models using the *Measure function* in  
 163 Geomagic Wrap® (Oqton, 3D Systems, Inc., South Carolina, USA). The mean of  
 164 these three measurements was calculated to determine the average VSP and  
 165 postoperative distances for each pair. Accuracy was then determined using the  
 166 Equation 1:

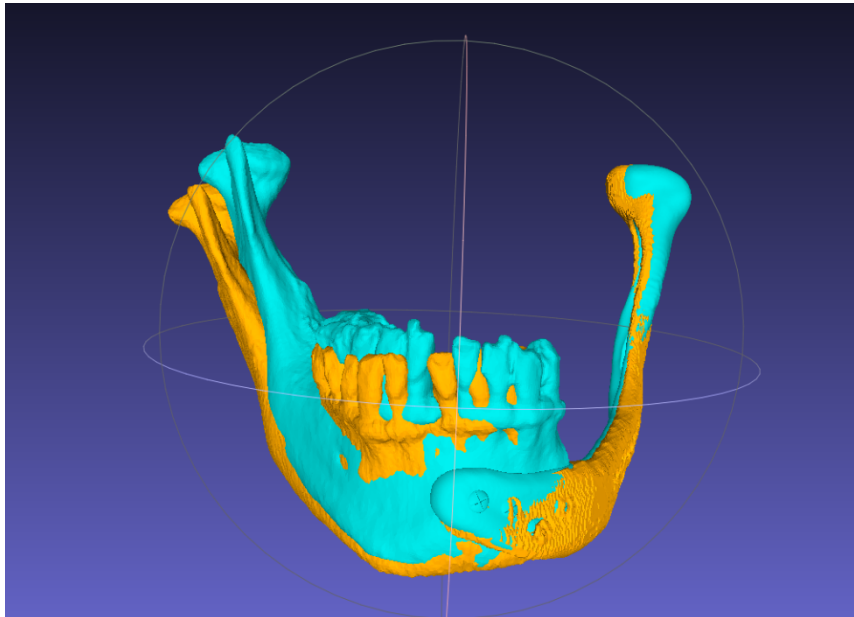
$$\text{Accuracy} = (\text{mean postoperative distance}) - (\text{mean VSP distance}) \quad (1)$$

## 167 **Method B**

168 This evaluation method described by Tarsitano et al.[21] leverages the three-  
 169 dimensional analysis.

170 Initially, the virtual surgical planning (VSP) and postoperative models are  
 171 imported into the open-source software MeshLab (Visual Computing Lab, ISTI-  
 172 CNR, Pisa, Italy). A semi-automated alignment is then performed (Fig. 3): the  
 173 operator manually selects at least four corresponding points on both models to  
 174 obtain an initial registration, which the software automatically refines to  
 175 complete the surface superimposition. Once aligned, the Hausdorff distance

176 function is used to calculate the final accuracy metrics - minimum, maximum,  
177 and mean Hausdorff distances ( $\pm$  RMS) - for each patient.



178

### 179 **Statistical analysis**

180 To evaluate the accuracy and reliability of all three assessment methods (GPL,  
181 Method A, and Method B), each protocol was performed by three independent  
182 operators (O1, O2, O3) on two separate occasions. A Linear Mixed-Effects  
183 Model (LMEM) was subsequently employed for the statistical analysis. This  
184 approach was chosen for its ability to properly handle repeated measurements  
185 clustered within patients, thus accounting for the correlation between  
186 observations. The model was specified to evaluate the impact of the operator,  
187 the measurement occasion, and their interaction as fixed effects on the outcome  
188 variable. To account for subject-specific variability, a random intercept was  
189 included for each patient. From the fitted model, estimated marginal means and  
190 95% confidence intervals were calculated, and pairwise comparisons were  
191 performed to quantify both intra- and inter-operator variability.

## 192 **RESULTS**

### 193 **Global Positioning Layout (GPL) analysis**

194 The accuracy results obtained with the GPL method are presented in Table 2.  
195 Regarding the rotational components, the mean deviations around the X and Y  
196 axes were 0.711 and -0.804 degrees, respectively, with 95% confidence  
197 intervals that spanned both positive and negative values. The largest rotational  
198 error was found around the Z axis, with a mean of -1.021 degrees. The  
199 confidence interval for this component contained exclusively negative values (-  
200 1.903 to -0.139), indicating a consistent rotational deviation in this direction  
201 across the patient cohort. For the translational components, the mean errors  
202 were all small in magnitude: 0.354 mm (X axis), -0.378 mm (Y axis), and -0.396  
203 mm (Z axis). The confidence intervals for all three translational components  
204 also spanned both positive and negative values, reflecting variability in the  
205 direction of the error across the patient sample. The detailed raw data for each  
206 individual measurement are reported in Supplementary Table S1, while a  
207 graphical summary of the statistical analysis for each roto-translational  
208 component is provided in Supplementary Figure S1.

209 *(Table 2 here)*

210 Reproducibility of the GPL method was also tested by three independent  
211 operators on two separate occasions. Due to its fully automated functionality,  
212 the GPL method produced identical results regardless of operator or  
213 measurement occasion.

### 214 **Method A: Landmark-Based analysis**

215 The results for the accuracy and reliability assessment of Method A are  
216 presented in Tables 3, 4, and 5. The analysis focused on the A-A', B-B', and F-F'

217 landmark pairs, as these were consistently measurable across all 17 patients.  
218 While data for the C-C' and E-E' landmark pairs were also collected, they have  
219 been excluded as they could only be reliably identified in two patients.  
220 Additionally, the distance between the two mandibular lingulae (D-D' landmark)  
221 could not be evaluated in any patient.

222 A detailed analysis of the reconstruction error (delta) revealed that the highest  
223 degree of accuracy was achieved at the F-F' landmark, where the mean  
224 reconstruction error consistently ranged between 1.0 mm and 2.1 mm across  
225 all operators and occasions. Conversely, the lowest degree of accuracy was  
226 identified at the A-A' landmark where the mean reconstruction error was  
227 consistently the largest, typically exceeding 2.5 mm and reaching up to 2.8 mm.

228 *(Table 3 here)*

229 The analysis of intra-operator reliability, summarized in Table 4, revealed that  
230 measurement consistency varied considerably depending on the landmark pair.  
231 The highest consistency was observed for the B-B' landmark, where the mean  
232 differences between sessions were small (ranging from -0.247 mm to 0.397 mm)  
233 and the confidence intervals were the narrowest. In contrast, the F-F' landmark  
234 and the A-A' landmark showed lower precision. For these pairs, the mean  
235 differences were larger, reaching up to 0.637 mm, and the confidence intervals  
236 were substantially wider, in some cases spanning a range of over 1.7 mm (e.g.,  
237 -0.227 to 1.500 mm for A-A')

238 *(Table 4 here)*

239 The inter-operator reliability analysis, summarized in Table 5, revealed  
240 evidence of operator-dependent variability. The most notable finding was for  
241 the B-B' landmark pair during the second measurement occasion. Here, the

242 comparison between Operator 1 and Operator 3 yielded a mean difference of -  
243 0.307 mm, with a 95% confidence interval ranging from -0.555 to -0.059 mm.  
244 The exclusively negative range of this interval confirms a systematic  
245 disagreement between the two operators. For the other landmark comparisons,  
246 while numerical differences were present, their 95% confidence intervals were  
247 wide and spanned both positive and negative values, indicating a lack of  
248 precision and consensus among the operators for those measurements.

249 *(Table 5 here)*

250 The detailed raw data for each measurement are reported in Supplementary  
251 Table S2, while a graphical summary of the statistical analysis for each  
252 landmark is provided in Supplementary Figures S2 (A, B, C).

### 253 **Method B: Surface-based analysis**

254 The results for the accuracy and reliability assessment of Method B are  
255 presented in Tables 6, 7, and 8. The analysis focused on the mean (Hmean) and  
256 maximum (Hmax) Hausdorff distances; the minimum Hausdorff distance was  
257 excluded as it was consistently 0 mm, and the Root Mean Square (RMS) data  
258 were not analysed independently as the RMS value is a measure of variance  
259 directly associated with the mean.

260 The accuracy results for Method B (Table 6) provided two distinct metrics: the  
261 mean (Hmean) and maximum (Hmax) Hausdorff distance. A notable difference  
262 in magnitude was observed between these two values. The mean Hausdorff  
263 distance (Hmean) indicated a low global deviation, with values consistently  
264 around 0.8 mm across all operators and occasions. In contrast, the maximum

265 Hausdorff distance (Hmax) was substantially higher, with values around 10 mm,  
266 indicating the presence of larger, localized points of deviation.

267 *(Table 6 here)*

268 The analysis of intra-operator reliability (Table 7) for Method B demonstrated  
269 excellent consistency, particularly for the mean Hausdorff distance (Hmean).  
270 The mean differences between measurement occasions for Hmean were  
271 negligible for all operators, with values as low as -0.002 mm. The narrow  
272 confidence intervals all included zero, confirming an absence of systematic bias  
273 and very high reproducibility for this metric. The maximum Hausdorff distance  
274 (Hmax) showed slightly more variability, although it was not statistically  
275 significant.

276 *(Table 7 here)*

277 The analysis of inter-operator reliability (Table 8) showed that the maximum  
278 Hausdorff distance (Hmax) had larger numerical differences between  
279 operators, particularly during the second occasion, indicating less agreement  
280 for this specific metric. In stark contrast, the reliability for the mean Hausdorff  
281 distance (Hmean) was high. In the first measurement occasion, the agreement  
282 was nearly perfect, with mean differences between operators consistently  
283 below 0.02 mm and confidence intervals as narrow as 0.057 mm in range.  
284 During the second measurement occasion, the inter-operator variability for the  
285 Hmean metric increased slightly. The mean differences between operators rose  
286 to a maximum of 0.060 mm, and the associated confidence intervals widened,  
287 indicating a minor decrease in measurement precision. Despite this, the overall

288 agreement for the Hmean metric was maintained, confirming a substantial  
289 degree of precision and objectivity.

290 *(Table 8 here)*

291 The detailed raw data for each measurement are reported in Supplementary  
292 Table S3, while a graphical summary of the statistical analysis for each  
293 landmark is provided in Supplementary Figures S3(A, B).

## 294 **DISCUSSION**

295 Ensuring surgical accuracy is critical in computer-assisted mandibular  
296 reconstruction to achieve optimal functional and aesthetic outcomes.  
297 Quantitative assessment comparing postoperative results with the virtual  
298 surgical plan (VSP) is required for quality control and technique refinement.  
299 However, the field still lacks a standardized, universally accepted evaluation  
300 methodology. Variability in assessment techniques, measurement parameters,  
301 and workflows makes it difficult to compare accuracy results across studies and  
302 institutions, highlighting the need for robust and objective evaluation protocols  
303 [3].

304 Within this context of methodological heterogeneity, the present study  
305 validated a novel automated method - the Global Positioning Layout (GPL) and  
306 compared its performance with two representative techniques from the  
307 literature: a manual, landmark-based analysis (Method A) and a semi-  
308 automated, surface-based comparison (Method B).

309 The primary criterion for selecting reference protocols was their potential for  
310 broad applicability across all patients undergoing mandibular reconstruction,

311 regardless of surgical technique. Methods requiring linear, angular, or  
312 volumetric measurements of individual bone segments were excluded, as they  
313 are applicable only to reconstructions with microvascular osseous free flaps  
314 [13,14,22-24]. Approaches using extra-mandibular reference frames on the  
315 midface were also excluded to avoid non-eliminable sources of imprecision,  
316 such as intrinsic mandibular mobility, surgically induced soft-tissue changes,  
317 and the lack of a clear and unequivocal definition of patients occlusion during  
318 CT acquisition [25].

319 The GPL method proved high objectivity, as its automated protocol yielded  
320 identical results across different operators and sessions, eliminating inter- and  
321 intra-operator variability. The analysis showed high translational accuracy,  
322 with mean errors below 0.5 mm on all three axes. Regarding the rotational  
323 components, minimal deviations were quantified around the X- and Y-axes,  
324 while a consistent rotational deviation was identified around the Z-axis across  
325 the patient cohort. This systematic deviation likely stems from a combination of  
326 procedural and biomechanical factors, potentially involving the intrinsic  
327 tolerances of the cutting guides, the biomechanical seating of the prosthesis  
328 upon fixation, and the influence of the surrounding soft tissues. The ability to  
329 quantify deviations through their distinct translational and rotational  
330 components within a standardized reference system is a major advantage of the  
331 GPL method, as it enables a complete spatial assessment of the final construct's  
332 position and orientation.

333 Although a standardized correlation between technical accuracy metrics and  
334 long-term functional outcomes has not yet been fully established [3,13], the  
335 precision achieved by the GPL method compares favourably with currently

336 accepted benchmarks. While linear deviations below 2.0 mm and angular  
337 deviations below 3.0°-4.0° are generally regarded as clinically negligible [6,9-  
338 11], the sub-millimetric translational accuracy ( $< 0.5$  mm) and the minimal  
339 rotational error ( $\sim 1.0^\circ$ ) obtained in this study fall well within these ranges,  
340 suggesting a precision that exceeds current clinical requirements.

341 Method A showed significant reproducibility limitations compared with GPL.  
342 Intra-operator analysis of Method A revealed low precision, evidenced by the  
343 wide 95% confidence intervals for repeated measurements which, in some  
344 cases, spanned over 1.7 mm. Overall, this indicates that even a single operator  
345 struggles to replicate measurements with high precision. Inter-operator  
346 analysis further confirmed operator-dependent variability, For the B-B'  
347 landmark, the comparison between two operators yielded a mean difference of  
348 -0.307 mm with a 95% confidence interval that did not include zero [-0.555 to -  
349 0.059], confirming a systematic bias. In contrast, the automated workflow of  
350 the GPL method eliminates these sources of imprecision and bias,  
351 demonstrating superior reproducibility. Moreover, Method A could not be  
352 applied to all patients due to absent anatomical landmarks after extensive  
353 resections, whereas GPL was applicable in all 17 cases. In addition, Method A's  
354 definition of accuracy - based on transverse distances only - excludes angular  
355 informations, potentially classifying a reconstruction as accurate despite  
356 clinically significant inclinations or malocclusions.

357 In contrast, the Roto-Translational Matrix (RTM) used in GPL avoids this  
358 limitation by providing a complete three-dimensional description of positional  
359 discrepancies.

360 Method B's reliability analysis showed a marked difference between its two  
361 primary metrics. The mean Hausdorff distance (Hmean) was generally

362 reproducible, with minimal inter-operator differences ( $<0.06$  mm). However,  
363 precision was lower for one operator, as reflected by a wider confidence interval  
364 ( $-0.132$  to  $0.043$  mm). In contrast, the maximum Hausdorff distance ( $H_{max}$ )  
365 showed greater variability, with wider confidence intervals in both intra- and  
366 inter-operator comparisons.

367 While  $H_{mean}$  demonstrated high reproducibility, Method B is not fully  
368 automated and it requires manual selection of at least four corresponding points  
369 to initiate surface alignment. The GPL method, in contrast, automates the entire  
370 process, eliminating manual input during critical steps. A more significant  
371 limitation of Method B is that the Hausdorff distance is a non-directional,  
372 absolute measure, providing no information about error orientation or location.  
373 Although  $H_{mean}$  indicated a small average global error ( $\sim 0.8$  mm),  $H_{max}$   
374 revealed localized errors up to  $\sim 10$  mm, highlighting the risk of  
375 underestimating clinically relevant deviations when relying solely on mean  
376 values. In contrast, the Roto-Translational Matrix (RTM), with its separate  
377 spatial components, provides a more comprehensive and clinically interpretable  
378 description of discrepancies between 3D models.

379 The reproducibility and applicability issues seen in Methods A and B reflect the  
380 broader methodological diversity in the literature (Supplementary Table 4).  
381 Current accuracy assessment approaches can be grouped into four main  
382 categories. The most common are manual, landmark-based methods, (e.g.,  
383 Method A), which are intuitive but prone to operator variability [6,8,10-13,26].  
384 The second are semi-automated, surface-based comparisons (e.g., Method B),  
385 which are semi-automatic but provide only non-directional, global error values  
386 that may mask clinically relevant local deviations [15,16].

387 The remaining two categories, though technologically advanced, were excluded  
388 from our comparative analysis for specific methodological reasons. The third  
389 category, represented by a single roto-translational method, could not be  
390 directly compared due to insufficient methodological detail for reliable  
391 replication. The fourth category includes geometric feature-based approaches  
392 [14,23], which evaluate the internal assembly accuracy of free flap segments  
393 rather than the overall position and orientation of the reconstructed mandibular  
394 arch. In contrast, this focus on internal assembly differs from the primary aim  
395 of the GPL, which assesses the final three-dimensional position and orientation  
396 of the entire reconstructed arch; thus, direct comparison would be  
397 methodologically inconsistent.

398 However, the present study is subject to certain limitations. First, the analysis  
399 is based on a retrospective cohort, which inherently introduces potential bias;  
400 to mitigate this, a consecutive series of patients meeting strict inclusion criteria  
401 was selected to ensure sample homogeneity. Second, the sample size was  
402 limited to 17 patients. Although this cohort covered representative mandibular  
403 defect types, future multi-center trials are necessary to confirm these findings  
404 across a broader range of clinical scenarios.

405 Future work should extend the validation of the GPL method to larger,  
406 prospective, and multicenter cohorts, incorporating diverse CAD-CAM  
407 reconstruction techniques and free-flap designs. Despite the comprehensive  
408 numerical description provided by RTM components, clinical interpretation  
409 remains challenging. Translating matrix-derived deviations into clinically  
410 intuitive visual outputs will be necessary to help surgeons identify procedural  
411 errors, implement corrective strategies, and prevent recurrence. Enhancing the

412 clinical interpretability of GPL outputs is therefore a key priority for future  
413 development.

414 Additionally, correlating GPL-derived accuracy metrics with long-term  
415 reconstructive outcomes will be essential to define clinically relevant thresholds  
416 for acceptable error margins. Establishing such correlations may guide surgical  
417 planning, improve patient-specific device design, and support the creation of  
418 evidence-based guidelines for quality control in computer-assisted mandibular  
419 reconstruction.

420 In conclusion, this study validates the Global Positioning Layout (GPL) method  
421 as a robust and fully reproducible tool for assessing the accuracy of computer-  
422 assisted mandibular reconstruction.

423 By eliminating inter- and intra-operator variability, overcoming the limitations  
424 of missing anatomical landmarks, and providing a comprehensive three-  
425 dimensional analysis of both translational and rotational discrepancies, the GPL  
426 method demonstrates a clear methodological advantage over established  
427 approaches. This ensures the data reliability which is a critical prerequisite for  
428 correctly correlating surgical precision with functional outcomes.

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**521 Author contributions**

522 Conception, V.E., T.L., Bet.G., M.R., B.A. Methodology, V.E., Bed.G., M.R., B.A.  
523 Acquisition of data: M.G., T.L.,F.P., S.G., Bet.G. Analysis of data: V.E., Bed.G.,  
524 M.R, B.A. Writing and original draft preparation: V.E., B.A.,M.R. Revision and  
525 critical editing: T.L., Bet.G., M.G.,F.P., S.G, Bed.G., M.R. All authors have read  
526 and approved the submitted version of the manuscript. All Authors have agreed  
527 both to be personally accountable for the author's own contributions and to  
528 ensure that questions related to the accuracy or integrity of any part of the  
529 work, even ones in which the author was not personally involved, are  
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531 literature.

**532 Data Availability**

533 All the data supporting our findings are presented in the paper.

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**536 Competing interests**

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541 **Institutional review board statement**

542 The study was conducted in accordance with the Declaration of Helsinki, and  
 543 the protocol was approved by the Ethical Committee of the University Hospital  
 544 of Padova (protocol number 24435/AOP1814 April 2019); all patients gave their  
 545 written informed consent."

546 **Figure legends**

547 **Fig. 1:** Schematic flowchart of the Global Positioning Layout (GPL) workflow.

548 **Fig. 2:** Selected landmarks for a type H defect in the planned model (left) and  
 549 the postoperative model (right).

550 **Fig. 3:** Superimposition of the two 3D virtual models using the Align function  
 551 of the MeshLab software. VSP model (light blue) and postoperative model  
 552 (orange).

553 **Tables**

554 ***Table 1.** Demographics, clinical characteristics, and mandibular defect*  
 555 *classification of the study cohort.*

<b>Patient characteristics</b>	<b>N=17</b>
<i>Sex:</i>	
Woman	9
Man	8
<i>Age (years):</i>	67 (65;73)
<i>Race:</i>	
Caucasian	17
<i>Operational diagnosis:</i>	
Ameloblastoma	2
Medication-related osteonecrosis of the jaw	7
Osteoradionecrosis	2
Squamous cell carcinoma of the oral cavity	2
Mandibular reconstruction plate failure	3
Chronic osteomyelitis	1
<i>Underlying disease:</i>	
Metastatic breast cancer	5

Personal history of orofaringeal cancer (SCC)	1
Multiple myeloma	2
None	4
Ossifying fibroma	1
Metastatic prostate cancer	1
Squamous cell carcinoma of the oral cavity	2
Radiodermatitis (II grade)	1
<i>Mandibular defect (Boyd et al, 1993 [20]):</i>	
LCL left	1
L right	1
L left	1
HCL right	2
HCL left	1
HC left	1
H right	3
H left	7

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*Table 2. Results obtained with the GPL method.*

<b>RTM components</b>	
Rot-X	0.711 (-0.619, 2.041)
Rot-Y	-0.804 (-1.981, 0.374)
Rot-Z	-1.021 (-1.903, -0.139)
Trans-X	0.354 (-0.274, 0.982)
Trans-Y	-0.378 (-1.002, 0.245)
Trans-Z	-0.396 (-1.150, 0.358)

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*The table shows the mean values and 95% confidence intervals. Rotations are expressed in degrees and translations in millimeters.*

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**Table 3.** Results for the accuracy measurements obtained through Method A by analysing the different landmarks (A-A', B-B', F-F').

<b>Occasion</b>		<b>O1</b>	<b>O2</b>	<b>O3</b>
A-A'	1	2.581 (1.625, 3.537)	2.172 (1.296, 3.049)	2.503 (1.578, 3.428)
	2	2.667 (1.349, 3.986)	2.809 (1.673, 3.945)	2.620 (1.799, 3.441)
B-B'	1	2.075	1.724	2.176

		(1.041, 3.108)	(0.885, 2.564)	(1.264, 3.088)
	2	1.827 (0.863, 2.792)	2.121 (1.182, 3.061)	2.134 (1.185, 3.083)
F-F'	1	1.063 (0.475, 1.651)	1.568 (1.039, 2.097)	1.636 (0.919, 2.353)
	2	1.653 (0.942, 2.364)	2.077 (1.437, 2.716)	1.824 (1.339, 2.308)

562 *Mean values and 95% confidence intervals are reported for each operator on*  
563 *the two analysis occasions (1, 2). All measurements are express in millimeters.*

564 **Table 4.** *Intra-operator variability in the accuracy measurements obtained*  
565 *with Method A, analysing the different landmarks (A-A', B-B', F-F').*

	O1	O2	O3
A-A'	0.086 (-0.563, 0.736)	0.637 (-0.227, 1.500)	0.117 (-0.549, 0.783)
B-B'	-0.247 (-0.540, 0.045)	0.397 (-0.177, 0.971)	-0.042 (-0.360, 0.276)
F-F'	0.590 (-0.106, 1.286)	0.509 (-0.282, 1.299)	0.188 (-0.695, 1.071)

566 *Mean values and 95% confidence intervals are reported for each operator. All*  
567 *measurements are express in millimeters.*

568 **Table 5.** *Inter-operator variability in the accuracy measurements obtained*  
569 *with Method A*

	Occasion	O1 vs O2	O1 vs O3	O2 vs O3
A-A'	1	-0.505 (-1.420, 0.410)	-0.573 (-1.208, 0.063)	-0.068 (-1.125, 0.989)
	2	-0.424 (-1.540, 0.693)	-0.171 (-0.897, 0.556)	0.253 (-0.619, 1.125)
B-B'	1	0.350 (-0.306, 1.007)	-0.102 (-0.631, 0.428)	-0.452 (-1.123, 0.219)
	2	-0.294 (-0.782, 0.194)	-0.307 (-0.555, -0.059)	-0.013 (-0.495, 0.469)
F-F'	1	0.408 (-0.498, 1.315)	0.078 (-0.772, 0.927)	-0.331 (-1.640, 0.978)
	2	-0.142 (-1.099, 0.816)	0.047 (-1.023, 1.116)	0.189 (-0.479, 0.856)

570 *Mean values and 95% confidence intervals are reported for the two occasions*  
 571 *(1, 2). All measurements are expressed in millimeters.*

572 **Table 6.** *Results for the analysis obtained with Method B, describing the*  
 573 *maximum and mean Hausdorff distance.*

Occasion		O1	O2	O3
Hmax	1	10.124 (7.348, 12.900)	10.160 (7.430, 12.890)	10.123 (7.398, 12.849)
	2	9.931 (7.191, 12.671)	10.186 (7.403, 12.968)	9.433 (6.836, 12.031)
Hmean	1	0.824 (0.630, 1.018)	0.810 (0.607, 1.013)	0.807 (0.615, 0.998)
	2	0.823 (0.624, 1.021)	0.783 (0.602, 0.964)	0.763 (0.585, 0.940)

574 *Mean values and 95% confidence intervals are reported for each operator on*  
 575 *the two analysis occasions (1, 2). All measurements are expressed in*  
 576 *millimeters.*

577 **Table 7.** *Intra-operator variability in the analyses obtained through Method B,*  
 578 *describing the maximum (Maximum) and mean (Mean) Hausdorff distance.*

	O1	O2	O3
Hmax	-0.193 (-0.415, 0.029)	0.025 (-0.158, 0.209)	-0.690 (-1.928, 0.549)
Hmean	-0.002 (-0.034, 0.031)	-0.027 (-0.084, 0.030)	-0.044 (-0.132, 0.043)

579 *Mean values and 95% confidence intervals are reported for each operator. All*  
 580 *measurements are expressed in millimeters.*

581 **Table 8.** *Inter-operator variability in the analyses obtained with Method B,*  
 582 *describing the maximum (Maximum) and mean (Mean) Hausdorff distance.*

Occasion		O1 vs O2	O1 vs O3	O2 vs O3
Hmax	1	-0.036 (-0.431, 0.359)	0.001 (-0.295, 0.298)	0.037 (-0.293, 0.367)
	2	-0.254 (-0.710, 0.201)	0.498 (-1.015, 2.011)	0.752 (-1.069, 2.574)
Hmean	1	0.015 (-0.034, 0.063)	0.017 (-0.030, 0.065)	0.003 (-0.026, 0.031)
	2	0.040 (-0.038, 0.119)	0.060 (-0.042, 0.162)	0.020 (-0.118, 0.159)

583 *Mean values and 95% confidence intervals are reported. All measurements*  
584 *are expressed in millimeters.*

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