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Original Article

Computer-guided implant placement associated with computer-aided bone regeneration in the treatment of atrophied partially edentulous alveolar ridges: A proof-of-concept study

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Abstract *Background/purpose:* The existing literature lacks information regarding the use of digital workflows during pre-surgical planning of implant rehabilitations in resorbed edentulous ridges. Thus, the aim was to evaluate the effectiveness of computer-guided implant placement and simultaneous computer-aided guided bone regeneration (GBR) in the treatment of atrophic posterior alveolar ridges.
Materials and methods: Partially edentulous patients requiring GBR simultaneously to implant insertion were enrolled. Implant positions and the augmented missing bone were planned with specific software. A stereolithographic model of the grafted jaw was produced to transfer the virtual bone augmentation to the surgical field. A tooth-supported stent was used to guide implant insertion according to the virtual project. Visual analogue scales (VASs) were used to self-register postoperative pain, swelling, bleeding, and perception of the operation. Post-operative cone-beam computed tomography scan was superimposed to the virtual project to evaluate the accuracy of implant positions.
Results: Overall, 10 implants were placed in 5 patients. Healing proceeded uneventfully in all except one patient that showed a dehiscence of the lingual flap as early surgical complication. Nevertheless, complete filling of the bone defects was observed clinically and radiographically

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in all patients. Pain scored exceptionally high with respect to the other variables. Deviations of 0.73 ± 0.21 mm, 0.59 ± 0.28 mm, and $3.05^{\circ} \pm 1.22^{\circ}$ were found at implant head, apex, and long-axis respectively. Distal implants showed higher angular deviations compared to mesial implants ($p = 0.008$).
Conclusion: Computer-guided approach provided encouraging results in terms of efficacy and accuracy. Conversely, patient-centered outcomes were below the expectations.

Introduction

The correct three-dimensional (3D) implant position represents a crucial factor to obtain predictable and reliable long-term clinical results. To minimize implant malposition, advances in 3D digital implantology have made it possible to introduce computer-guided implant surgery.[1] Surgical and prosthetic phases can be virtually simulated by importing 3D data into implant planning software. Ideal implant positions are therefore planned before surgery according to bone quality and quantity, location of anatomical structures such as nerves, vessels, sinuses, prosthetic demands, and aesthetic evaluations.[2,3] Computer-guided implant placement techniques may be advantageous compared to conventional protocols when it comes to patients with limited amount of bone. Theoretically, bone augmentation procedures may be avoided or reduced by optimizing implant positioning in accessible bone.[4,5] On the other hand, the current evidence still lacks information concerning the use of computer-guided implant protocols to rehabilitate resorbed edentulous ridges. The use of an image-guided system in severely resorbed posterior maxillae has been proposed as a viable option to place implants in limited amount of bone.[6] Unfortunately, according to the latest systematic reviews,[7–9] only the aforementioned study answered the question whether computer-guided surgery can be used as an alternative to bone augmentation. Obviously, not all residual ridges allow achieving a compromise with respect to the position of the implant. This is particularly true in case of severe horizontal and vertical bone defects where the position of the implant is further limited by anatomical structures.

The fact that bone tissue is becoming part of the treatment plan is extensively corroborated by the concept of prosthetically-guided bone regeneration[10] as a direct evolution of the restoration-driven implant placement. In order to insert implants in the correct prosthetically-guided position, optimal conditions of the recipient bone in terms of quality and quantity are mandatory in the first instance. In this context, guided bone regeneration (GBR) has shown successful outcomes in the augmentation of alveolar bone width and height.[11]

The rationale of the present study was to merge together prosthetic-guided bone regeneration and implant placement within the same surgical phase with a full digital workflow, so as to exploit the advantages of both procedures simultaneously. This aspect constitutes an innovation since the combination of virtually-aided GBR and computer-guided implantology is, to the best of our knowledge, extremely under-explored so far. The aim was to evaluate the effectiveness of virtually-aided GBR and simultaneous computer-guided implant placement applied in critical clinical situations presenting an inadequate amount of bone, from clinical, radiological, and patient-centered outcomes.

Materials and methods

Study design

The present study was designed as a prospective monocentric single-cohort proof-of-concept study. All patients received thorough explanations and signed a written informed consent form before being enrolled. All procedures were conducted according to the principles outlined by the World Medical Association Declaration of Helsinki as revised in 2013.[12] The study protocol was approved by the Hospital Institutional Review Board (reference number #RC-2016-420-2).

Study population

Patients were recruited as a consecutive sample from 2016 to 2018 after consultation with clinical and radiological examinations including orthopantomograph and cone-beam computed tomography (CBCT) scan.

The following inclusion criteria were adopted: 1) partial edentulism with $\leq$3 missing teeth in the premolar and/or molar sectors; 2) loss/extraction of teeth occurred $\geq$2 months before the surgical procedure; 3) presence of an inadequate amount of bone in horizontal and vertical dimensions, which impedes an implant placement without recurring to simultaneous GBR procedures; 4) presence of $\geq$3 natural teeth with no metal restorations to avoid metal-induced radiographic artifacts; 5) mouth opening $\geq$40 mm; 6) full-mouth plaque and bleeding scores $\leq$25%; 7) no smoking habits; 8) no local and systemic conditions and no medications that may interfere with oral surgery procedures.

Virtual planning

Impressions of the edentulous jaw were taken with an irreversible hydrocolloid material. After the designated time interval, the impressions were poured with high-

precision type IV dental die stone (Fuji Rock®; GC Europe, Leuven, Belgium). Digital imaging and communications in medicine (DICOM) data were subsequently acquired from CBCT scan and imported into dedicated virtual planning software (3Diagnosys®, 3DIEMME®; Como, Italy). At the same time, the definitive diagnostic stone study cast related to the partially edentulous jaw was scanned with an optical scan. The STL (STereo Lithography interface format) data obtained from the optical scan were imported in the same virtual planning software and were superimposed with the DICOM data using an appropriate mathematical algorithm. The virtual wax-up of the artificial crowns of the teeth to be replaced was realized by designing the desired size and shape of the crowns that best fit the edentulous space according to the modern prosthetic needs. It was then possible to virtually plan the ideal position of the implants according to the virtual wax-up. Sandblasted and acid-etched surfaced titanium implants (Guide System CONELOG® Screw-line Implant, Promote® plus; Camlog Biotechnologies, Basel, Switzerland) were used to replace the missing teeth.

The anatomy of the residual bone was finally evaluated (Fig. 1A). The software allowed the clinician to virtually augment and contour the resorbed ridge in order to obtain at least 1 mm of regenerated bone circumferentially around each implant with a physiologic profile (Fig. 1B). Finally, the project was sent for 3D printing with rapid prototyping techniques. This resulted in: 1) stereolithographic real-size model of the partially edentulous jaw with the bone defect, the implant site osteotomies, and the virtually augmented bone (Fig. 1C); 2) tooth-supported stereolithographic surgical guide.

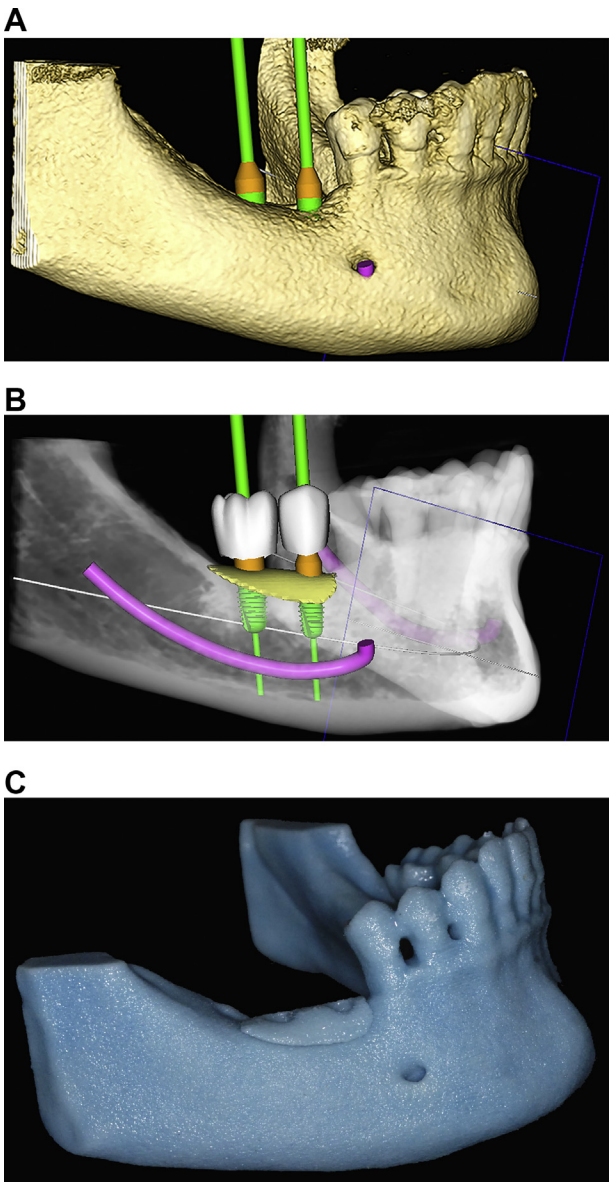

Figure 1 **A -** Virtual planning with implants in the ideal position in atrophic posterior mandible. **B -** Virtual bone augmentation (yellow) according to the implant position, the residual bone anatomy, and the virtual prosthetic wax-up. **C -** Stereolithographic model reproducing the virtual project.

Surgical procedures

The surgery was performed on an outpatient basis under local anesthesia (Fig. 2A). The stereolithographic models were used pre-operatively to trim and contour a non-resorbable dense-expanded polytetrafluoroethylene (d-PTFE) membrane (NeoGen™; Neoss®, Milan, Italy) so that its shape closely matched the anatomy and profile of the virtually augmented bone transferred in the stereolithographic models (Fig. 2B and C).

In brief, a mid-crestal horizontal incision extended with intrasulcular incisions at least one tooth mesially and distally, associated with vertical releasing incisions were made to mobilize a full-thickness flap. The bone crest was then exposed and debrided with a sterile curette and irrigated with saline solution to remove any remnants of fibrous tissue if present, and to prevent connective tissue encapsulation in the implant bed. The surgical guide was carefully leaned against the remaining teeth with the aid of guiding grooves carved in the template. Once the optimal adaptation and stability of the surgical guide has been checked for proper seating, it was possible to place the implants with a fully guided computer-aided approach according to the manufacturer's instructions (Fig. 2D). Corresponding cover screws were applied to the implants and the surgical template was removed (Fig. 2E). Subsequently, GBR could be performed according to the virtual project. Cortical perforations of the recipient bed were performed to favor the nourishment and revascularization of the graft. The latter consisted of autogenous bone chips harvested nearby the surgical site mixed with deproteinized bovine bone mineral (DBBM) particles (Bio-Oss®; Geistlich Pharma AG, Wolhusen, Switzerland) in a 70:30 ratio respectively and wetted with physiological saline solution. The d-PTFE membrane previously shaped was adjusted to cover the graft maintaining a minimum distance from the periodontium of the neighboring teeth of 1.5 mm (Fig. 2F). Endosseous screws (Maxil®, inner square ø 1.5 mm, lengths 3—5 mm; Omnia® S.p.A., Fidenza, Italy) were used to fix and stabilize the membrane over the graft to the recipient bone at buccal and lingual/palatal aspects (Fig. 2G). Finally, periosteal horizontal releasing incisions were

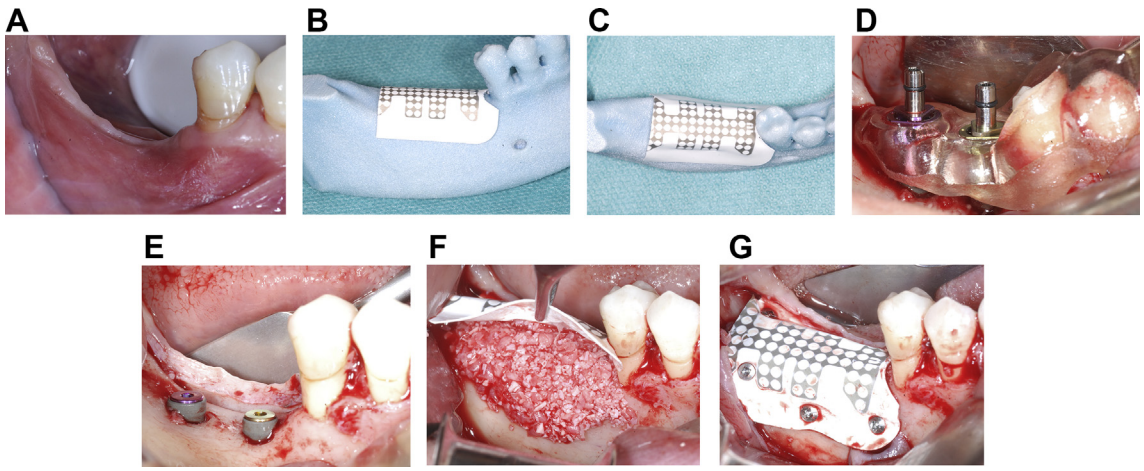

Figure 2 **A -** Preoperative intraoral view of the partially edentulous resorbed mandibular ridge. **B, C -** Pre-operative views of the d-PTFE membrane trimmed and contoured with the aid of the stereolithographic model to recreate the physiological profile of the edentulous atrophic ridge after bone augmentation procedure. **D -** Computer-guided implant insertion. **E -** Implants positioned in the correct prosthetically-guided position. **F -** Autogenous chips and DBBM particles grafted to three-dimensionally augment the atrophic ridge. **G -** Non-resorbable d-PTFE membranes fixed in the proper position by means of osteosynthesis screws.

performed to mobilize the buccal flap and obtain a passive closure. Horizontal mattresses and single stitches were performed with non-resorbable monofilament e-PTFE suture. Suture was removed after 3 post-operative weeks. Patients were instructed to follow antibiotic and anti-inflammatory therapy.

Re-entry surgery

The re-entry surgery to remove the d-PTFE membrane was performed after 8 months from the bone augmentation and implant placement surgery. Prior surgery, a CBCT scan was acquired to evaluate the healing and the amount of augmented bone. Briefly, under local anesthesia, a muco-periosteal flap was raised to expose the d-PTFE membrane. Once the fibrous tissue was curetted from the underlying bone, it was possible to identify and remove the osteosynthesis screws used to stabilize the d-PTFE membrane. At this point, the d-PTFE membrane was carefully detached from the surgical site and removed gently. Following copious irrigation with physiological saline solution, the overlying soft tissues were repositioned with non-resorbable single stitches. The prosthetic phases were commenced thereafter.

Primary outcome

The primary outcome was to evaluate the effectiveness of the surgical procedure considering both clinical and patient-centered outcomes. The following clinical-centered outcomes were evaluated: 1) occurrence of intra-operative complications; 2) occurrence of post-operative complications assessed at each recall scheduled every week during the first month and monthly thereafter up to the re-entry surgery; 3) quality of the augmented bone, assessed radiographically by means of CBCT scans and clinically at the re-entry surgery; 4) surgical time, measured as the time elapsed between the incision and the end of suture completion.

The following post-operative patient-centered outcomes were evaluated: 1) pain; 2) swelling; 3) bleeding; 4) perception of the operation. The analysis of the patient-centered outcomes was accomplished through a questionnaire given to each patient about the postoperative course from 5 to 6 h postoperatively (before intake of the prescribed analgesics) and until the seventh postoperative day. A 100-mm visual analogue scale (VAS) with extreme end points ("no" and "extreme") was used for each variable to record the intensity of postoperative pain, the severity of swelling and bleeding from the wound on the day of surgery, and at 1, 2, 3, and 7 days after surgery. Furthermore, on the day of the surgery, the patients scored their satisfaction with their perception of the operation ("not" and "very unpleasant"). By means of a ruler, the VAS scores were measured and rounded off to the nearest millimeter.

Secondary outcome

The secondary outcome aimed to analyze the accuracy of computer-guided implant placement. The locations and axes of planned and placed implants were compared by merging together the post-operative CBCT scan with the virtual project, aligning selected anatomic landmarks. For each planned and placed implant, two points were identified: the neck (center of the most coronal portion of the implants) and the apex (center of the implant apex). The distance between the centers of the simulated and real implants (mm) and the angle (°) that occurred between the long axes of the simulated and real implants were calculated as lateral and angular deviations respectively.

Statistical analysis

The statistical analyses were done using IBM SPSS Statistics software version 24.0 (IBM Corp., Armonk, NY, USA). Data were expressed as means $\pm$ standard deviation (SD), and 95% confidence interval (CI) where appropriate. The Shapiro—Wilk test was used to assess the normality of data

distribution. Because distribution of data in some datasets did not meet the requirements for normality and homogeneity of variance assumptions ($p < 0.05$), non-parametric quantitative data were analyzed using non-parametric tests. More in detail, the Wilcoxon signed-rank test was used to analyze the VAS scores of pain, swelling, and bleeding between the different study periods; the Spearman's rank correlation coefficient was used to investigate possible correlations between the perception of the operation and pain, swelling, and bleeding VAS scores. The Mann—Whitney U test was used in the accuracy analysis to investigate possible differences in terms of implant site (mandible versus maxilla) and implant position (mesial implant versus distal implant).

Results

Overall, 6 patients were initially screened for eligibility. One patient opted for a removable partial denture and was therefore not included in the study. Ultimately, 2 males and 3 females subjects were considered eligible and were consecutively enrolled and treated. The mean age was 52.2 ± 6.41 years. Each patient received a total of two implants. All patients completed the study, and no implants failed up to the delivery of the final restoration.

Primary outcome

Considering the clinical-centered outcomes, no intra- and post-operative complications related to the experimental procedure were observed. In one patient, the lingual flap was slightly traumatized during the surgical procedure by the Prichard periosteal elevator used to protect the lingual tissues. This resulted in a partial iatrogenic laceration of the coronal portion of the lingual flap of approximately 7 mm in a mesio-distal direction (Fig. 3A). The flaps were sutured according to the described procedure so that the laceration was included within the entry and exit points of the horizontal mattress in order to minimize flap tension and promote wound healing. Nevertheless, in that point complete healing was not achieved. Indeed, a dehiscence of roughly 2 mm in ongoing epithelialization phase persisted at the mesial aspect of the lingual flap during the healing period. This complication was managed with 0.12% chlorhexidine mouthwashes and topical application of 1% chlorhexidine gel twice a day until re-entry surgery and recalls every 2 weeks for clinical inspection and plaque removal. In correspondence of the partial laceration, healing resulted in scar tissue with a lack of keratinized tissue at the occlusal aspect. Nevertheless, a fine vascular architecture could be identified in the apical portion of the lingual flap directed toward the overlying keratinized tissue (Fig. 3B). In view of the position of the dehiscence, close to muscular attachments with consequent continuous traction of the lingual flap and partial exposure of the d-PTFE membrane, it was decided to anticipate the re-entry surgery at 5 months to reduce the risk of infection. Despite membrane exposure, a satisfactory amount of newly formed bone-like tissue was observed (Fig. 3C).

In the rest of the patients, the healing proceeded uneventfully (Fig. 4A). Macroscopically at the re-entry surgery, the d-PTFE membrane appeared to be surrounded by a dense connective tissue without any clinical signs of infection. The d-PTFE membrane appeared to adhere firmly to the newly formed hard tissue. After removal, a whitish inflammation-free periosteal-like tissue was present underneath. The space under the d-PTFE membrane was completely filled by hard tissue with macroscopic features of newly formed bone. Particles of bone substitute not encapsulated in fibrous tissues and integrated within the surrounding hard tissue were hardly distinguishable in some areas. The graft appeared vascularized and well incorporated into the native bone. From a clinical aspect, no residual bone defects were observed and a significant horizontal and vertical bone gain was found circumferentially around the implants in all patients (Fig. 4B and C).

This result was supported by the radiological findings, showing augmented radiopaque hard tissue integrated with the recipient bone. No signs of unusual resorption, infection, and soft tissue ingrowth within the graft were detectable. Dental implants appeared completely surrounded by the remodeled graft, and no radiographic pathological signs of radiolucent regions or peri-implant bone resorption were observed. At the same time, it was

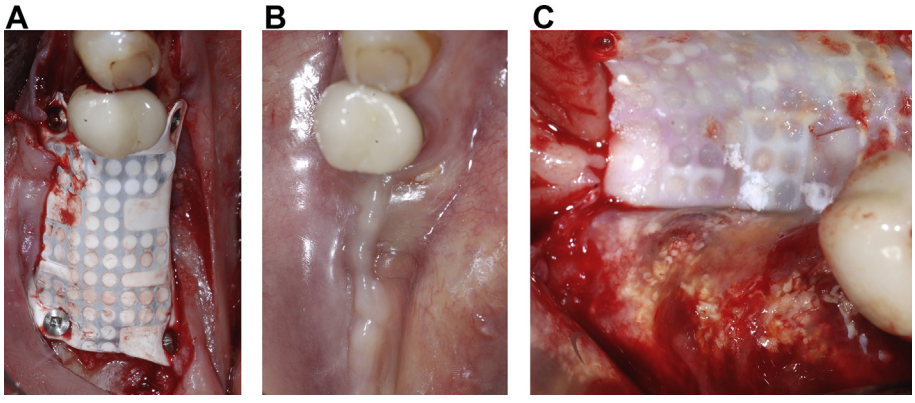

Figure 3 **A -** Iatrogenic partial laceration of the lingual flap occurred during the surgical procedure. **B -** Occlusal view of the surgical site after 5 months. **C -** Re-entry surgery after 5 months showing ongoing bone remodeling with granules of bone substitute still encapsulated in immature bone matrix.

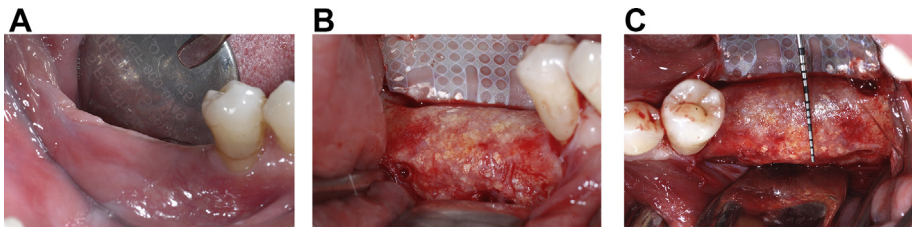

Figure 4 **A -** Clinical intraoral view of the healed site after 8 months. **B, C -** Intraoral view of the augmented bone from lateral and occlusal aspects after a healing period of 8 months.

possible to identify the d-PTFE membrane closely adapted and stabilized to the underlying bone.

The mean duration of the surgery was 92 min from first incision to the end of the suture.

With respect to patient-centered outcomes, the trends of mean VAS scores with respect to pain, swelling, and bleeding during the different study periods were illustrated in Fig. 5 and summarized in Table 1. The mean VAS score for the patients' perception of the operation was 36 ± 8.63. A correlation was not found between the perception of the operation and pain (Spearman's $\rho = -0.2$; $p = 0.74$), swelling (Spearman's $\rho = 0.5$; $p = 0.39$), and bleeding (Spearman's $\rho = 0.3$; $p = 0.62$).

Secondary outcome

Overall, a total of 10 implants underwent statistical evaluation of the accuracy level by matching the preoperative planning with the actual position of the fixtures obtained during the surgical procedure.

Considering the linear deviations at the implant neck and apex, values of 0.73 ± 0.21 mm (95% CI: 0.58—0.89 mm) and 0.59 ± 0.28 mm (95% CI: 0.38—0.79 mm) were respectively observed. The angular deviation of the long axis between the planned and actual positions of the implants was $3.05° \pm 1.22°$ (95% CI: 2.18°—3.92°).

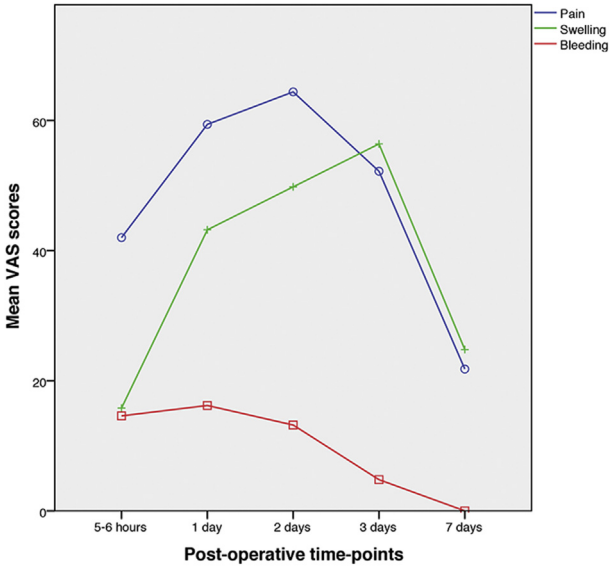

Figure 5 Trends of VAS scores during consecutive study periods for pain, swelling, and bleeding.

The results of the comparisons related to implant site and position were illustrated in Table 2.

Discussion

The purpose of the present study was to evaluate the effectiveness of a newly developed computer-guided protocol combining GBR and implant surgery. No intra- and post-operative complications strictly related to the study protocol were encountered. One patient exhibited a dehiscence of the lingual flap due to a lack of visibility. The conventional free-hand approach allows better visualization of the surgical site, since the template has a reduced size and is removed after the first pilot drill. On the other hand, in the present study the surgical template has been used during all the drilling sequence up to the implant insertion, in accordance with a fully-guided approach. Furthermore, the size of the surgical stent was bulkier with respect to a conventional free-hand template. In view of the aforesaid, once the periosteal elevator was introduced between the lingual flap and the jawbone and the stent secured in the proper position, it was extremely difficult to maintain and verify the position of the instrument during the entire procedure. Therefore, it may be presumed that in the case exhibiting flap dehiscence, the periosteal elevator has been inadvertently displaced against the soft tissues instead of the bone, causing a partial laceration of the lingual flap. The partial laceration became evident only after removal of the surgical template after implant insertion. The fact that bone regeneration was not apparently affected by flap dehiscence is consistent with other studies reporting on d-PTFE membrane exposures. In particular, Ghensi et al. reported a case of d-PTFE membrane exposure 14 days after GBR. Similarly to the present study, evidence of an epithelial seal at the site involved, with no detachment on probing or suppuration was observed. The re-entry surgery took place 4 months after the GBR surgery, and the defect appeared almost completely filled.[13] These findings are in agreement with other studies showing that intentionally exposed d-PTFE membranes for socket preservation procedures[14] as well as GBR procedures[15] did not exhibit significantly compromised regeneration outcomes.

Inappropriate trimming of non-resorbable barrier has been reported as another potential factor attributed to membrane exposure.[16] In order to overcome such drawback, in the present study a stereolithographic real-size model realized with the augmented bone according to the virtual project, has been used before the surgical

Table 1 Self-registered mean VAS scores for pain, swelling, and bleeding during the different study periods. Data are expressed as mean ± standard deviation.

	VAS scores per study period					
Variable	5–6 h	1 day	2 days	3 days	7 days	Significance
Pain	42 ± 6.20*	59.4 ± 5.94	64.4 ± 5.17*'**	52.2 ± 2.86	21.8 ± 3.11**	*p = 0.042 (5–6 h versus 2 days); **p = 0.033 (2 days versus 7 days)
Swelling	15.8 ± 4.14*	43.2 ± 6.34	49.8 ± 7.01	56.4 ± 8.14*'**	24.8 ± 4.81**	*p = 0.024 (5–6 h versus 3 days); **p = 0.037 (3 days versus 7 days)
Bleeding	14.6 ± 3	16.2 ± 2.58	13.2 ± 2.16*	4.8 ± 0.83*	0	*p = 0.035 (2 days versus 3 days)

*,** = Statistically significant difference.

Table 2 Comparison of the accuracy level according to implant site and position in terms of linear and angular deviations. Data are expressed as mean ± standard deviation.

Deviation	Site				Position			
	Mandible	Maxilla	Difference	P-value	Mesial	Distal	Difference	P-value
Coronal (mm)	0.67 ± 0.14	0.84 ± 0.27	−0.16 ± 0.3	0.476	0.66 ± 0.21	0.81 ± 0.2	−0.15 ± 0.29	0.222
Apical (mm)	0.49 ± 0.32	0.73 ± 0.16	−0.24 ± 0.35	0.1	0.55 ± 0.19	0.62 ± 0.38	−0.06 ± 0.42	0.889
Angular (°)	2.97 ± 1.28	3.17 ± 1.29	−0.19 ± 1.81	0.543	2.10 ± 1.01	4 ± 0.24	−1.9 ± 1.03	0.008*

* = Statistically significant difference.

procedure. In the traditional approach, the membrane is usually placed several times in the surgical site to verify the correct size, shape, and adaptation. Furthermore, the trimming phase is normally performed before the augmentation procedure. Therefore, the clinician has to contour the membrane on the basis of an empirical evaluation of the future volume of bone that will be grafted in the surgical site. This may lead to possible inconsistencies between the size and shape of the membrane and the underlying graft. Conversely in the present study, the membrane has been trimmed and adapted directly on the model replicating the augmented bone. Hence, the risk of incongruity between the graft and the contour and dimension of the d-PTFE membrane has been reduced. At the same time, the minimum distance between the d-PTFE membrane and the periodontium of the neighboring teeth of 1.5 mm in order to prevent possible infiltrations through the gingival sulcus has been easily respected. This aspect has been managed by contouring the membrane with hourglass-shape directly on the model with excellent visualization of both buccal and oral aspects. This represented another advantage compared to the standard procedure, where the correct distance between the barrier and the periodontium could be masked by the blood or the surfaces of adjacent teeth.

In the present study, the use of a stereolithographic real-size surgical model had an impact on another study variable, which was the duration of the surgical procedure. The fact that the d-PTFE membrane has been shaped extra-orally before the beginning of the surgical procedure resulted in a global reduction of the operative time. The mean surgical duration was approximately 1 h and half. Since no other studies could be found in literature that assessed the operative time in case of computer-guided implant placement and virtually-aided GBR, it is difficult to make comparisons. Obviously, the advantages introduced with the virtual planning such as determination of implant locations, drill-depth control, and pre-contouring of the d-PTFE membrane contributed to reduce the operation time in the present study.

Notwithstanding the reduced surgical time, other variables seem to have influenced the patient-centered outcomes evaluated in the present study. As a matter of fact, in the present study pain showed the highest scores compared to the other variables. Pain can be considered to be multifactorial and may thus be influenced by the patient's expectations regarding the forthcoming surgical procedure. Thus, high values of pain perception might be explained by false expectations in view of a procedure believed by the patient to be less painful with respect to a standard surgery. In the present study, patients reported mean VAS score for pain >64, consistent with severe pain. This threshold value might be explained by the fact that two implants per patient were inserted into more extensive horizontal and vertical defects that required the use of non-resorbable membrane to stabilize the graft. Thus, it might be inferred that extensive harvest of autogenous bone, extended flap design and horizontal periosteal releasing incisions to mobilize and passivate the flaps, could have caused a more intense pain. Interestingly, in the present study swelling scored lower. This indicates that aspects other than merely the surgical procedure may be involved in the process of pain intensity perception. As a matter of fact, pain was perceived more compared to swelling, which can be regarded as an indicator of how invasive the performed surgery was and thereby the succeeding trauma to the soft tissue. As already mentioned, large flap had to be passivated and mobilized in order to gain soft tissue closure. Periosteal incisions have significant impact in post-operative swelling, which could explain high VAS scores recorded up to the third post-operative day. One may further expect that postoperative bleeding would be

an issue of concern following extensive periosteal incisions. This was, however, not the case because the mean VAS regarding oozing from the wound, which peaked on 1 day postoperative, was rather low and declined rapidly. Topical infiltrations of dexamethasone sodium phosphate, and application of cold packs for 48 h post-operatively may have helped to avoid postsurgical bleeding and reduce post-operative swelling. The perception of the operation was moderate. It is noteworthy that no correlation could be found between perception of the operation and the study variables. Thus, it might be speculated that subjective emotional component rather than the outcome of the surgical procedure itself led to a moderate perception of the operation, particularly with respect to exceptionally higher scores for pain. There was a general feeling that patients had a worst attitude to pain because they were told they would have undergone shorter and less invasive surgical procedure. However, the surgery still remained invasive and longer compared to their expectations and hopes. In view of the aforesaid, the patients obviously cannot be promised they will have no pain by using the computer-guided approach, especially if implants are to be placed near a vital structure. Moreover, telling to the patient that they will experience less pain, and that their pain will be shorter in duration could be hazardous and misleading in consideration of the present surgical approach.

The secondary outcome of the present study aimed to evaluate the accuracy of the experimental procedure according to three parameters: deviation at the entry point; deviation at the apex; and deviation of the long axis. These parameters are currently used as references to calculate the overall deviation reflecting the clinical accuracy.[17] Mean coronal, apical, and angular deviations were 0.73 ± 0.21 mm; 0.59 ± 0.28 mm; and $3.05^{\circ} \pm 1.22^{\circ}$ respectively.

Up to now, it remains unclear how much inaccuracy can be accepted. Unreported t-test showed that the coronal, apical, and angular deviations were statistically different from zero. This might underline a certain level of inaccuracy from a mathematical point of view. The question whether this level of accuracy is clinically acceptable has been answered by several paper, at least with respect to linear deviations. The literature seems to indicate that one has to accept an inaccuracy of $\pm$ 1.5 mm,[9,18,19] which is clearly less than that observed in the present study.

Similarly to the present study, Younes et al. evaluated the accuracy of tooth-supported fully guided surgery in the posterior sectors of partially edentulous patients.[20] The authors compared the accuracy with tooth-supported pilot-drill guided implant placement and free-handed surgery. Fully-guided surgery was the most accurate, followed by the pilot-drill guided implant insertion, which achieved higher accuracy when compared to free-handed surgery, specifically in the horizontal plane. For such reason, the authors claimed that the use of a pilot drill guide might not be obsolete, particularly in those cases where a fully guided surgery is not feasible (e.g. a thin alveolar crest). This assumption has been undermined by the present study, in which a fully guided implant insertion has been successfully accomplished in resorbed and atrophic alveolar ridges. Interestingly, although screw-retained restorations were planned for all implants, the authors reported cement-retained restorations in 19.2% and 4.2% of implants placed with a free-hand or pilot-drill guided approach respectively. This emphasizes the fact that inaccuracy is a risk factor not only for biological, but also for prosthetic complications as previously mentioned herein.

One of the crucial factors for precision is the stability of the template position during implant placement. In the present study, tooth-supported surgical guides stabilized by the residual dentition were used. In the literature, it is recommended to have at least two or more teeth without mobility to improve template stability and thus accuracy.[21] In the present study none of the patients exhibited tooth mobility, a fact that might have had an impact on the correct seating of the surgical guide.

Other factors inherent to the surgical protocol itself might have had a remarkable role in the degree of accuracy obtained with the present study. Among these, the use of single-guide system that, differently from multiple-guides, allowed placing the implant without changing the template for each drill diameter throughout the surgery, thus reducing the likelihood of deviations from the planned position. In addition, the use of disposable drills may have improved the accuracy of the system, thereby enhancing the cutting potential and consequently preventing possible deviations originating from excessive wear. Moreover, drills had a physical and not a visual stop, with better control of the preparation depth. The accuracy of implant position was further increased by using a fully-guided approach, which assisted the clinician in every step of the surgery, starting from the first drill up to the implant insertion without switching the guiding sleeves in the said stent. The advances in digital technology allowed a virtual superimposition of the diagnostic stone study cast with the CBCT scan by a matching process on the corresponding structures. Thus, both the osseous and prosthetic structures were visible in one single 3D application. This made it possible to consider surgical and prosthetic aspects in the virtual environment without recurring to a radiological template. The elimination of a radiological template reduced the number of steps required to complete the virtual planning. A reduced number of steps might be interpreted in light of the fact that deviations may reflect the sum of all errors occurring from imaging to the transformation of data into a guide, to the improper positioning of the latter during surgery. Thus, all errors, although seldom occurring, can be cumulative. For this reason, reducing the number of steps needed to plan the surgical and prosthetic phase could have played a substantial role in increasing the accuracy of the workflow.

The present proof-of-concept study has some limitations that need to be addressed. First of all, the sample size represented an issue of no little significance. Unfortunately, after an extensive review of the literature, no studies were available using computer-aided GBR and implant placement to rehabilitate partially edentulous patients. Actually, no studies were found applying computer-guided implant placement in clinical situation presenting an inadequate amount of bone that needed to be augmented simultaneously with implant insertion. Therefore, the calculation of the sample size could not be performed properly. This was probably due to the nature of the present study, namely a proof of principle study. As a

consequence of the small sample size enrolled in the present study, this may have hidden some differences between groups.

Another limitation is related to the convenience sample used in the present study rather than large randomly selected population sample, which bears the risk of selection bias. Even the operator experience might be considered a cofounding factor. Indeed, guided implant surgery is technically demanding and not free from specific procedure-related complications. Surgical skills and experience of the clinician using this surgical technique go above and beyond those necessary for providing regular implant surgery.[22] All of these concerns recognize the absence of external validity and demand that the reported results should be interpreted with caution.

Within the limitations of the present study, computer-guided implant placement with computer-aided guided bone regeneration may be considered a viable tool in case of atrophic partially edentulous ridges to correctly place implants in a prosthetically guided position in association with prosthetically-driven GBR. In consideration of patient-centered outcomes, some concerns still persist with respect to the perception of the operation reported by the patients. Although the procedure has been developed to minimize the post-operative patient morbidity, this advantage could not be validated in the present study. Lastly, the application of computer-guided implant placement in demanding anatomical situations characterized by less than ideal availability of residual bone resulted in acceptable degrees of accuracy. Further short-, medium-, and long-term studies are required to evaluate the outcomes of this protocol in terms of early and late survival, success, and complication rates of both implants and prostheses.

Declaration of Competing Interest

The authors claim to have no financial interest, either directly or indirectly, in the products or information listed in the paper.

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