Digital Comparative Method for Analysis of Body Remodeling and Neoformation: Case Report

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Abstract: Replace lost teeth in the anterior area of the maxilla is complex and challenging, therefore in these cases, it's essential that reverse planning lead the case. For implants can be correctly positioned, the surgeon should use grafts and bone substitutes to stabilize, maintain, and restore bone architecture. The cone-beam computed tomography (CBCT) allows a high-quality, three-dimensional view of craniofacial bone structures, and is widely used for assessing bone availability and planning for implant surgery. CBCT is also used to evaluate surgical results as it allows the visualization of the grafted area without the interposition of structures and the study of multiple areas in a single exam. The superimposed technique is one of the methods used to evaluate surgical results, consisting of superimposed the images obtained through CBCT and the intra-oral scanning, allowing a precise quantitative and qualitative analysis of tissues. The present case shows the importance of using CBCT to confirm the diagnostic hypothesis. The patient had a fracture in the abutments of the fixed partial denture (FPD) in the 11 to 21 area. Thus, the planned treatment was the extraction of the 11 and 22 roots and bone regeneration of area 22 for later installation of dental implants. The graft was performed using the modified socket seal proposed by Misch. After six months of regeneration, a new CBCT was performed and the results were measured by the superimposing technique. In a second surgery, four dental implants were installed, in a position determined by reverse planning. After four months, the temporary crowns were installed for gingival conditioning. The case was concluded with ceramic crowns, offering functionality and aesthetics to the patient. The main objective is to describe a technique of comparative digital analysis between dimensional changes of the different phases of bone structures and soft tissue.

Keywords: Cone-Beam Computed Tomography, Bone Regeneration, Bone Density, Bone, Three-Dimensional Imaging, Surface models, Soft tissues

1. Introduction

Replacing lost teeth in the anterior area of the maxilla is complex and challenging for the dental surgeon, as it deals with high expectations and great aesthetic demands (1).

In such cases, treatment must be guided by planning by diagnostic waxing, to determine the desired positioning of osseointegrated implants for prosthetic restorations at the end of treatment. Reverse planning, and provide greater security to the dentist, is also associated with higher satisfaction scores of the patient with treatment (2) (3).

The ideal positioning of implants depends on the bone availability of the area, to minimize the loss of bone volume, which occurs after tooth extraction. Bone grafts and substitutes have been used to stabilize, maintain, and recover the desired bone architecture (4) (5). Guided bone regeneration (GBR) is a procedure that offers structural support, minimizing bone resorption, and thus favoring the positioning of the implant (5). In 1999, Misch proposed the alveolus sealing surgical technique, which provides connective tissue, periosteum, and trabecular bone in a single surgical maneuver, which shows a series of advantages, as the connective tissue graft allows the surrounding tissues to migrate and form epithelium with color and texture similar to that of the grafted area, in addition to the autogenous bone showing more predictable results and the transfer with the intact periosteum layer facilitating revascularization (6).

For assessing bone availability and planning surgeries for bone augmentation, the use of periapical radiographs is not recommended, as it is impossible to measure the available bone thickness (7)- (9). Conical beam computed tomography (CBCT) was developed in 1998 and revolutionized dentistry, as it allows a three-dimensional and high-quality visualization of craniofacial bone structures, taking less time to acquire, emitting less radiation, and having a lower cost when compared to computed tomography. for medical use (7). Therefore, CBCT is widely used to assess bone availability and plan implant surgery (10).

CBCT is also widely used for the evaluation of surgical results because the software analysis allows the visualization of the grafted area without the interposition of structures, as well as the planning of the implant installation. Also, visualization in transversal, coronal and sagittal sections is possible, allowing linear and volumetric measurements of multiple areas in a single exam (11) - (14).

The image overlay technique is one of the methods used to evaluate surgical results (15). It consists of superimposing both the images obtained by CBCT and those obtained by scanning (STL), which allows assessment of soft and hard tissues, as well as the results obtained by surgical techniques (16).

This case had as main objective to describe a technique of comparative digital analysis between the dimensional changes of the several phases of the bone structures and soft tissue, where a surgical technique of bone preservation after extraction was used, described by Misch et al. 1999.

2. Case Report

2.1 Clinical Case

A female patient, 49, smoker, leucoderma, sought dental care, the main complaint of instability partial fixed prosthesis (PFP) of the area of 11 to 22, without the presence of the same in the mouth (Figure 1).



Figure 1: 11 fractures coronal and apical periodontitis and tooth 22 fractures root vestibular part medium.

In history, the patient had good health in general, without any problem of the order systemic. After clinical examination and Tomographic, I will get it was found on the tooth 11 fractures coronal and apical periodontitis (Figure 1a) and tooth 22 fractures root vestibular part medium (Figure 1b), which was designed extractions thereof, with regenerate the O bone will the area of 22, to avoid dehiscence due to partial loss of buccal bone plate, which is not shown in element 11, for future rehabilitation through implants. As the surgical procedures would be performed in two stages, tooth 12 was kept, if necessary, in the second stage, it would be extracted.



Legenda **Figure 2A:** Panoramic radiographic image; 2B: initial tomographic image of element 22 with vestibular radicular fracture of the middle third indicated by the red arrow

To make it possible level evaluates the dimensional changes of the soft tissues per í different anodes, and molding was planned scanning of models. A protocol was adopted for molding and making plaster models, always performed by the same professional. Moldings were performed with Hydrogum 5 alginate (Zhermack ® / Italy) following all the manufacturer's recommendations. To obtain tomographic references, a rigid individualization guide made of EVA (Ethylene Copolymer and 100% Vinyl Acetate), 3 mm thick, was made. The guide was positioned 3 mm from the alveolar mucosa, where markings at 3 points were made and filled with gutta-percha (Dentsply Sirona / Germany) on the cervical third, the middle third, and the apical third, the guide being used in all CT scans (figure 3) (17).



Figure 3A- model, **3B** - tomographic guide with points marked in gutta-percha (blue arrows), **3C** - tomographic image with guide in marked position (blue arrows)

The patient was medicated 48 hours before the surgical procedure with amoxicillin 500 mg (GSK ® / England), every 8 hours and with 4 mg dexamethasone (Aché®Laboratórios Farmacêuticos / São Paulo-SP) prescribed 1 hour before the procedure. Postoperatively prescribed two di doses will holiday 600 mg ibuprofen/arginine (Zambon ® / Italy) and prevention of infections was prescribed three is doses are di will holiday 500 mg of amoxicillin (GSK ® / England) for 5 days, and antiseptic mouthwash with a base digluconate, chlorhexidine 0.12% (Periogard / Colgate Periogard ®/ USA), and guidance about postoperative care and hygiene recommendations.

Previous oral asepsis was performed with 2 % aqueous chlorhexidine digluconate. (Riohex ®/ Rioquimica). Anesthesia was induced by infiltration technique mepivacaine in 2% with epinephrine 1: 100,000 (New DFL ® / Rio de Janeiro, RJ). The intra-alveolar incision was performed using l â 15C mine (Swann-Morton / England) in teeth 11 and 22 had a detached light gingival tissue so that it was not damaged to preserve the vascularization of the bone wall utilizing Perio Steo.

The extraction was with the use of a straight periotome (Maximus / MG) to maintain a better structure to existing bone. The alveolus was cured with a Lucas curette and the integrity of the bone walls was verified with a millimeter-gauged probe. In the alveolus of tooth 11, the bone walls were intact; and tooth 22 showed a bone loss in the buccal wall, which was attributed to the existing root fracture in the tooth.

After the extraction was performed with debridement of epithelial tissue diamond drill 3168 (KG Sorensen / da) in the corresponding socket to the tooth 22, to increase the supply blood e neo graft and preventing apical migration of epithelial tissue. After preparation, the ileum was measured to select the trephine drill used to collect the graft (figure 4).



Figure 4: Incision, extraction and preparation of the recipient site

The area of the left maxillary tuberosity under an esthesia was performed using an infiltrative technique with 2% mepivacaine and epinephrine 1: 100,000 (Nova DFL $\ensuremath{\mathbb{B}}$ / Rio de Janeiro-RJ). The bone and connective tissue graft were obtained using the alveolar sealing technique proposed by Misch.

A 10 mm diameter drill bit was used with a speed of 400 rpm against a 20: 1 contra-angle (kavo-Kerr / Germany), with profuse irrigation. In the introduction of this drill, small lateral movements were performed to provide a space between it and the bone of the cavity, sufficient to generate a fracture and detach the graft, lodging it within the trephine, respecting a predetermined bone height of 5 mm on tomography and avoiding bucco-sinusal communication (figure 5)).



Figure 5: Obtaining the graft and positioning in the recipient area

The will area donor mononylon was sutured with 5.0 (Ethicon (USA)) with a single suture.

The graft was inserted into the socket of tooth 22 and compressed until the soft tissues were at the same level, obtaining a good coaptation of the edges of the gingival tissue of the graft and the socket. The graft was stabilized and sutured with 5.0 mononylon thread (Ethicon @ / USA) with simple stitches.In the area of tooth 11, the clot was maintained inside the alveolus and was sutured with 5.0 mononylon thread (Ethicon @ / USA) with compressive suture (figure 6).



Figure 6: Positioning and suturing of the graft

The patient returned for postoperative follow-up after 12 days, when the sutures were removed and an impression was made (figure 7).



Figure 7: Postoperative control after 12 days

For 6 months, the patient used a partial denture removable acrylic, suitably relieved to not graft pressure on will areas surgery necessary time to occur bone and tissue regeneration.

After this period, a new tomographic examination was performed where it was found that tooth 12 was compromised, so it was decided to extract and install four implants to replace teeth 12, 11, 21, and 22, eliminating the need for pontic and facilitating the cleaning of the prosthesis. Using diagnostic waxing, the placement of implants and soft tissues was planned, and a surgical guide was created to guide them to the most ideal position possible The patient was medicated one hour before the surgical procedure with 2g of amoxicillin (GSK® / England), 4 mg of dexamethasone (Aché®Laboratórios Farmacêuticos / São Paulo-SP), and in the postoperative period, two daily doses of 600 mg ibuprofen arginine (Zambon® / Italy), rinse with 0.12% antiseptic digluconate chlorhexidine (Periogard Colgate® PerioGard® / USA) 4 times a day.

Anesthesia was performed using the infiltrative technique with articaine 4% with epinephrine 1: 100,000% (Nova DFL [®] / Rio de Janeiro-RJ), supra-crestal incision performed with a 15C blade (Swann-Morton / England) in the area of teeth 12-22, and sulcular incision around the adjacent teeth. A full-thickness flap was used, the tooth was extracted 12 e of use with periotome to preserve the maximum the bone

Volume 10 Issue 2, February 2021

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structure present. The sequence of punching for subsequent implants was performed following the manufacturer's guidelines use with drill lance O A 2.0 plus and helical drill Alvim ® 3.5 plus (Neodent-Straumann ® / LATAM) and installation of four implants Alvim ®CM (Straumann - Neodent® / LATAM).

In area 12, a 3.5x13 mm implant was installed with a torque of 45 N / cm2 with an immediate scar of 2.5x3.3 mm; in will area of the implant 11 has been installed 3.5x11.5mm with torque 60 N / cm2 with the immediate healing abutment of 1.5x3.3mm; in will area of 21 was installed 3.5x9 mm with torque 60 N / cm2 with the immediate healing abutment of 2.5x3.3mm, and at will area of the implant 22 has been installed 3.5x11.5mm with torque 45 N / cm2 with the immediate healing abutment of 1.5x3.3mm, and at will area of the implant 22 has been installed 3.5x11.5mm with torque 45 N / cm2 with the immediate healing abutment of 1.5x3.3mm, all implants Alvim @CM (Straumann-Neodent@ / LATAM). We opted for the installation of immediate healers, to prevent bone growth on the cover screws, which facilitates the reopening surgery. The will area mononylon was sutured with 5.0 (Ethicon @ / USA) suture contains e naked scalloped (Figure 8).



Figure 8: Extraction of tooth 12, installation of four implants and suture (6 months)

After 4 months, surgery was performed to reopen the implants, using an infiltrative anesthesia technique with 2% mepivacaine with epinephrine 1: 100,000 (Nova DFL® / Rio de Janeiro-RJ), supra-crestal incision with a 15C blade (Swann Morton / England), where the immediate healers were removed and exchanged for new ones, with sufficient height to remain exposed.

In the area of tooth 12, a 3.5x3.3mm scar was installed; the healing abutment tooth 11 of 3.5x4.5mm in 21 cicatrizer of 4.5x4.5mm and at will tooth area 22 cicatrizer of 3.5x3.3mm (Neodent-Straumann @ / LATAM). The entire area was sutured with 5.0 mononylon thread (Ethicon @ / USA) with simple sutures (figure 9).



Figure 9: Reopening and installation of the healing abutments (10 months)

The provisional prosthesis was again relieved so that the installed components would not compromise its stability. For postoperative pain control, two daily doses of 600 mg ibuprofen arginine (Zambon® / Italy) were prescribed for 3 days, and rinse with 0.12% chlorhexidine digluconate antiseptic (Periogard Colgate® PerioGard® / USA), 4 times a day.

After one month, CM universal sleeves (Straumann-Neodent \circledast / LATAM) were installed. In areas 12 and 22, 3.5x6mm sleeves were installed, and in areas 11 and 21, 4.5x6mm sleeves. The torque of the prosthetic components was 32 N/ cm2, performed according to the manufacturer's recommendation. The provisional prostheses were made and installed (figure 10).



Figure 10: Installation of provisional prostheses (11 months)

After the installation of provisional prostheses, contact with the patient was lost, who returned to the clinic after 3 years. It was the replacement of these prostheses indicated for four crowns metalloceramicindividual upside (Figure 11) and new CT scan request together with the plaster models.



Figure 11: Finalized case (after 3 years)

After this period in which the patient was absent from the clinic, the implants show no signs or symptoms of inflammation and no mobility. Tomographically, there are no signs of bone loss, and the patient is satisfied with the functional and aesthetic result obtained.

2.2 Method of verification by joining

All CT scans were performed on the same high-resolution conical beam CT scanner (PreXion Elite; PreXion Co. Tokyo, Japan), adjusted with a 56mm x 56mm field of view (FOV), 0.099 mm voxel size and acquisition of 33.5 seconds (with 90KV and 4MA), to monitor dimensional changes, using a lip retractor during image acquisition, thus avoiding overlapping gingival and lip structures, following the protocol adopted by CHAPPUIS et. al. 2015 (18), however with different configurations of the tomography, as they used FOV of 4 to 4 cm, with voxel size of 0.08 mm, while in this case report FOV of 56mm x 56mm and voxel of 0.099

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mm was used, obtaining an image with a much higher resolution than the mentioned study.

DICOM sets The data (Digital Imaging and Communications in Medicine) were segmented by digital imaging software and a subsequent surface mesh model was generated by ImplantViewer® software, (Anne Solutions, São Paulo, Brazil). The surface mesh models were then superimposed and automatically aligned, using anatomical landmarks defined by the software itself (19). The distances between the surface meshes were presented as color-coded figures to identify areas prone to dimensional changes in soft tissues and calculated as total tissue loss (20).

Digitized soft tissue images were obtained by the flatbed scanner (3d open technologies scanner, Italia) in STL format by scanning plaster models, following a standard molding and making protocol for these models, using Hydrogum 5 alginate material (Zhermack® / Italy) and cast in type IV plaster (Durone, Dentsply®USA), by the same operator (21).

During the import of the files with the ImplantViewer (Anne Solutions®), a chronology was adopted, first the DICON file of the initial tomography, then the other CT scans, however in STL, followed by the other STL files, acquired by scanning the models (figure 12).

Exam type	Accomplished Period	Elapsed Time	Denomination Adopted	Adopted colors
Initial Computed Tomography	pre surgical	pre surgical	ствс 1	
Molding and scanning the model	pre surgical	pre surgical		A State
Molding and scanning the model	graft post	after 12 days	scan 2	10 40
Computed Tomography	pre implants	after 6 months	ствс 2	1. 10
Molding and scanning the model	pre implants	after 6 months		and and
Computed Tomography	after 3 years	after 3 years	ствс 3	
Molding and scanning the model	after 3 years	after 3 years		all man

Figure 12: Descriptive table of the types of exams and elapsed time and their name.

An ImplantViewer program tool (Anne Solutions®) called "foster " was used to merge the images, uniting them by superimposing the three-dimensional meshes of all objects, resulting in a single file, enabling the comparison and measurement of changes, both in bone and soft tissues, among all the seven files inserted, in the sagittal and axial sections of the program (figure 13).



Figure 13: Paraxial tomographic initial image of element 12 and the overlapping images represented by lines of different colors

The effectiveness of this combination occurs by choosing common and invariable reference points with the same characteristics between all files, DICON and STL, so the program can understand that one image is linked to another. For this junction to be considered effective, the maximum difference margin must be less than 0.14 mm, therefore, differences below this value are considered acceptable (22). For the measurements to be reproducible, a local coordinate system was defined in the center of the tomographic guide's demarcations, positioned so that the X-axis was in the center of the reference points of the tomographic guide (figure 14a) and the Z-axis perpendicular to it (figure 14b), allowing the measurement of thickness by measuring parallel to the X plane (figure 14c) and in height parallel to the Z plane (Figure 14d)



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Figure 14 (a): x axis located in the center of the coronal reference point of the tomographic guide; Figure 14 (b): Z axis perpendicular to X;

Figure 14 (c): Measurement of soft tissue changes with a plane parallel to the x-axis;

Figure 14 (d): Height measurement using x-axis perpendicular to the most coronal point of the images and parallel to Z

3. Results

Dimensional bone changes in the left upper incisor demonstrated at the coronal level a horizontal bone increase of 1.44 mm between tomography 2 (after 6 months) and 1.06mm on tomography 3 (3 years), compared to tomography 1 (initial) which was taken as the basis for all measures. At a medium level, a decrease of 1.04 mm and 0.83 mm is observed, at the apical level an increase of 0.62 mm and 0.23 mm, tomography 2 and 3, respectively. Regarding the vertical bone change, there was an increase of 3.15 mm in tomography 2 and 1.16 mm in tomography 3, represented in graph 1 (figure 15).



Figure 15: Graph 1: Dimensional changes of bone tissues in tooth 22

Although there was bone loss at the middle alveolar level and a slight gain at the apical level, we have a considerable gain in height and thickness in the coronal third,

The change dimensional soft tissue in the upper left incisor is described in the graphic will get 2 (Figure 16).

Result of soft tissue measurements at the midpoint





At the midpoint, it initially appears that bone gain occurred shortly after the graft, but post-operative edema should be taken into account, which would justify the increase in volume. A gradual bone loss is noted in all periods, even after implant placement.

The height of the soft tissues at the level of the vestibular bone crest was not taken into account due to the digital models 3 and 4, having healing and provisional, respectively, occurring in the adopted method, the impossibility of distinguishing between soft tissue and components on the implants.

4. Discussion

Alveolar bone resorption begins immediately after tooth removal, promoting both bone and gingival sequelae (23).

The presence of bone defects in teeth with root fractures is a common finding, and the most prevalent defect is dehiscence, present in about 90% of cases (24).

Therefore, the main focus in the treatment of extraction cavities in the aesthetic zone aims to avoid the retraction of tissues after extraction and the preservation of the volume of these to the greatest extent possible, to improve the conditions of the tissues, for late implant placement, it makes it appropriate to graft the extraction cavity with soft tissues (25).

Thus, defects of four walls, which normally do not have the buccal bone wall, require the use of some type of barrier membrane (26), among the materials available for bone grafting, the gold standard is considered the autogenous bone, which has osteogenic, osteoconductive and osteoinductive properties (27) (28).

However, primary closure and absence of pressure on soft tissues is necessary, in addition to avoiding graft micromovements that can result in graft failure, so the use of autogenous grafts in these situations is more advantageous, as they have structural resistance and can be adequately stabilized, preventing the micro-movement of the grafted material (29), since the use of particulate grafts, need separate epithelium and conjunctive coverage, increasing the failure rate and in the case of guided tissue regenerations (GTR) the dehiscence rates with resorbable membranes and non-resorbable are significantly high (20)

An option for coverage is free gingival grafts, where the blood supply depends on the gingival wall of the cavity and the underlying clot, providing a very high failure rate (30). In coronal displacement flap surgery, the flap produces primary soft tissue closure, but displaces the mucogingival junction with the result of aesthetic losses in this sensitive area; consequently, coronal displacement flaps should no longer be used to close extraction areas in the aesthetic region (20). One of the key factors for transplant survival is the rapid insertion of the soft tissue transplant into a nutritious environment, that is, the greater the time of insertion of the graft into the donor area, the lower its survival rate (25), which would justify the removal of a single block using a trephine, as it provides rapid removal and a pre-defined shape and size, similar to the alveolus of the extracted tooth, which considerably decreases the surgical time, composite graft enables better blood nutrition of the soft tissue, as it improves the adaptation of the soft tissue graft to the marginal gingiva of the extraction cavity, as it is the only area with an active blood supply. By obtaining a graft slightly larger than the opening of the extraction socket, it is possible to obtain a " pressure adjustment " of the soft tissue, proposed by Landsberg & Bichacho in 1994 (31), who recommended that" its shape was slightly longer than the outline of the extraction socket hole ". This helps establish a contact r will pale and e intimate between the graft and the recipient site (25). The alveolar sealing technique avoids contamination and physical interference, and the graft acts as a barrier preventing the proliferation of undesirable cells (31). The technique modified by Misch (6) proposes to seal the alveolus with a graft composed of connective tissue, periosteum and bone. The advantage of using a conjunctive graft to keratinized is the production, after healing, of a keratinized tissue equal to that of the adjacent regions, with

the same color and texture. Also, the graft with autogenous bone has more predictable bone formation (6) (27).

From an anatomical point of view, two different regions can be defined for harvesting soft tissue grafts: the palate region and the tuberosity, with the tuberosity showing significantly greater thickness of the soft tissues compared to the hard palate, allowing the harvest from deeper grafts (20) an additional advantage of harvesting the tuberosity seems to be the healing process. A very limited postoperative pain experience for the patient, generally compared to the premolar region, allows for a more pleasant healing process for the patient (25)

Different techniques that describe soft tissue variation have been developed, such as intraoral techniques (5), photographic techniques (32), optical projection (33), plaster measurements (4), (34), (35) and measurements using 3D digital models (36).

One of the methods for evaluating surgical gains is the use of the same reference points in adjacent structures in the pre and postoperative measurement, however, this technique may not be very accurate [(9), (27), (28)]. The evaluation of surgical gains by superimposing tomographic images and scanning before and after the surgical procedure has shown greater efficiency in analyzes and measurements, as well as showing the interaction of soft and hard tissues more precisely (16), (37), (38)]. A great advantage of the image overlay technique is that it is always possible to check any structure, compared to other images, regardless of the time of image acquisition. The use of the technique of obtaining digital models by molding with alginate, plaster model, and scanner table not be the gold standard (polyether molding and scanner table) still provides more reliable results than the scanners intraoral (21).

The joining of images and the detection of reference points were performed automatically, due to the ease and mainly the greater precision, when compared to that performed by an operator manually (19) and according to the study by Liang et al., in 2010 (22), so that this junction is considered effective, the maximum difference margin must be less than 0.14 mm, and the program automatically signals, through the color changes of the structures, if they are not within this parameter, decreasing the index of errors.

Thus, in this case, bone loss at the middle alveolar level and a slight gain at the apical level are observed, however, we have a considerable gain in height and thickness in the coronal third, a region in which the result can be directly influenced by the graft, taking into account considering the difference of the results of the study that ABDELHAMID et. al in 2016, which showed a more significant loss in the area of the alveolar bone crest, when the graft was not used (23).

5. Final Considerations

The graft technique described by Misch seems to be a good option for cases of reconstruction of the buccal bone wall, of the anterior teeth, as it achieves initial stability of the bone graft, unlike particulate grafts, besides protecting this graft through the keratinized tissue the covers. However, the graft

Volume 10 Issue 2, February 2021 <u>www.ijsr.net</u> Licensed Under Creative Commons Attribution CC BY had a tendency of bone resorption observed throughout the follow-up period, although the literature presents this technique for preservation, they are based on case reports and, therefore, there was no research, mainly longitudinal, with analysis of dimensional changes and morphological corroborating for this technique or even challenging it.

How this case was carried out, in the joining of 7 images at different times, became innovative and unprecedented, making it necessary to research with large samples, to determine the accuracy of this study model, however, researches are using 3 superimposed images, with great accuracy, signaling positive results in the use of this technique for gauging or any comparative factor between the structures.

Another necessary factor is the development of software that can work with several images simultaneously quickly because currently, we have many problems in execution, occurring bugs, such as crashes and even shutdown of the processors, causing an extremely long time, becoming almost unfeasible, even if extremely powerful computers are used, as current programs were not designed to perform this function with multiple images.

6. Conclusion

The use of the joined digital models proved to be effective for this case, therefore, the methodology used for measurements showed reproducibility making it interesting for this type of analysis.

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Volume 10 Issue 2, February 2021

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Volume 10 Issue 2, February 2021