TECHNICAL REPORT

Volumetric difference evaluation of registered three-dimensional pre-operative and post-operative CT dental data

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Objective: The purpose of this study is to propose a complete methodology for automatically registering three-dimensional (3D) pre-operative and post-operative CT scan dental volumes as well as to provide a toolset for quantifying and evaluating their volumetric differences.

Methods: The proposed methodology was applied to cone beam CT (CBCT) data from 20 patients in order to assess the volume of augmented bone in the alveolar region. In each case, the pre-operative and post-operative data were registered using a 3D affine-based scheme. The performance of the 3D registration algorithm was evaluated by measuring the average distance between the edges of the registered sets. The differences between the registered sets were assessed through 3D subtraction radiography. The volume of the differences was finally evaluated by defining regions of interest in each slice of the subtracted 3D data and by combining all respective slices to model the desired volume of interest. The effectiveness of the algorithm was verified by applying it to several reference standard-shaped objects with known volumes.

Results: Satisfactory alignment was achieved as a low average offset of 1.483 ± 1.558 mm was recorded between the edges of the registered sets. Moreover, the estimated volumes closely matched the volumes of the reference objects used for verification, as the recorded volume differences were less than 0.4 mm^3 in all cases.

Conclusion: The proposed method allows for automatic registration of 3D CBCT data sets and the volumetric assessment of their differences in particular areas of interest. The proposed approach provides accurate volumetric measurements in three dimensions, requiring minimal user interaction.

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Introduction

In many medical fields (thoracic oncology, maxillofacial surgery, periodontology etc.) assessing the volumetric differences between two modalities with anatomical information (CT, MRI) acquired at various time intervals is often required.¹ By quantitatively evaluating those differences, experts are able to identify volumetric changes in image features that are solely related to the progression

or regression of a particular disease or to a pathomorphological condition and thus evaluate the effectiveness of a certain therapy or surgical procedure.^{2,3}

The simplest and most effective way to estimate the differences between two dental data sets, acquired at different time periods, is through digital subtraction radiography.^{1–4} Studies have shown that the success of subtraction radiography depends on the level of standardization of the projection geometry.⁵ However, the standardization of the projection geometry during acquisition is only the first step towards successful subtraction radiography. Since the reproducibility of

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imaging geometry cannot be guaranteed, spatial registration is often required before subtraction.^{6,7} In the literature, a wide range of registration techniques have been proposed for aligning two-dimensional (2D) medical images of various modalities.^{8,9} Although those techniques are accurate and effective when applied to 2D images, the projection geometry involved when dealing with three-dimensional (3D) image sets requires a different approach. Several crucial features, such as the location of the mandibular canal, the maxillary sinuses, the nasal cavity and the angle of the alveolar crest, cannot be fully represented in two dimensions and hence cannot be considered in the registration process.¹⁰ Furthermore, it is of great importance for clinicians to evaluate 3D volumetric changes following reconstructive procedures (*e.g.* integration of regenerated or augmented tissues) and also to observe the long-term stability and behaviour of surgically reconstructed hard tissues.^{11,12}

For this reason, numerous methods have been proposed to register 3D data sets.¹³ In general, most 3D registration techniques follow the principles of traditional 2D registration and operate on 3D reconstructed models acquired from a series of 2D misaligned images.^{14,15} A transformation model is estimated to align a specified data set (floating set) to a reference data set through the minimization of a multivariate function, the Measure of Match (MoM).¹ 3D registration methods may be classified into two broad categories: feature-based and intensity-based. Feature-based methods rely on the identification and alignment of distinctive features between the subject sets, such as landmark points, ridges or surfaces.^{16–18} Features may be detected manually (where user intervention is required) or through specialized automatic detection algorithms. All contour-based and point-based techniques fall into this category. Feature-based methods usually provide a significant speed advantage over intensity-based approaches but their effectiveness is directly proportional to the performance of the feature detection algorithm; therefore, spurious features may negatively affect the registration process. However, intensity-based registration methods operate directly on the voxel intensities of the subject 3D data sets.^{19,20} The particular methods are usually much slower than most feature-based approaches but they are usually more accurate as they lack the need for feature detection.

Once the subject 3D volumetric data have been successfully aligned, their differences may be estimated by applying standard digital subtraction radiography techniques.^{1–4} Commonly, experts perform linear measurements on the reference and floating 3D volumes in order to assess their differences in selected areas of interest, using specialized proprietary software packages [*e.g.* maxillofacial cone beam CT (CBCT)—iCAT Vision;²¹ Imaging Sciences International, Hatfield, PA]. The reason for this is that it is not always possible to manually estimate the volume of the differences owing to their geometrical shape or their position. Linear

measurements, however, may only provide a rough estimate of the volumetric changes between the subject 3D data sets in the region of interest (ROI). In many cases this is perfectly acceptable. There may be other cases, nevertheless, where increased accuracy is required or when differences are not easily perceivable by the human observer. In such cases, software-aided volumetric evaluation is necessary.^{22,23}

This paper presents a complete methodology for registering 3D pre-operative and post-operative CT data sets for assessing their volumetric differences, corresponding to bone augmentation in the alveolar region for the particular sets. Therefore, the purpose of this study is twofold; firstly, to describe the methods and techniques used to automatically align the 3D data and secondly, to define a suitable volumetric assessment scheme in order to quantify and evaluate the difference between the pre-operative and the aligned post-operative data sets. 20 sets, each consisting of 2 volumes (for the pre-operative and post-operative data), were used in this study. The two volumes in each set were aligned using a 3D registration technique. The aligned post-operative volume was then compared with the pre-operative volume. The comparison was performed in terms of digital subtraction radiography in order to reveal the differences between the two subtracted volumes. The difference in selected ROIs was considered for assessing the diversity of the pre-operative and post-operative data in the particular regions. In most cases, the proposed registration method was able to successfully align the 3D volumes, hence improving the volumetric assessment results.

Materials and methods

The proposed volume assessment scheme comprises two distinct phases: the registration of the subject 3D data and the evaluation of their volumetric differences over a selected ROI. The complete methodology is illustrated in Figure 1. This section describes the methods used to register the pre-operative and post-operative data in each set, as well as the techniques used for the volumetric assessment of the differences between the registered sets.

Data acquisition

20 patients requiring implant therapy and presenting alveolar defects were treated in a 2-stage surgical approach. The first stage involved an augmentation procedure, using a partial thickness flap design. If possible, implants (Branemark/Replace; Nobel Biocare, Göteborg, Sweden) were simultaneously placed. The edentulous ridge was augmented vertically and horizontally with non-resorbable bovine mineral (Bio-Oss; Geistlich, Wolhusen, Switzerland) and locally retrieved autogenous bone chips. After grafting, a non-resorbable titanium membrane (FRIOS® Bone Shield; Dentsply Friadent, Mannheim, Germany) or a resorbable

Figure 1 Schematic block diagram of the complete proposed scheme for assessing the volumetric differences between two volumes

membrane (Resolut Adapt LT; Gore, Flagstaff, AZ) was trimmed and adapted over the grafted area. The membrane was fixed by titanium pins (FRIOS® Membrane Tacks; Dentsply Friadent). Re-entry was performed 9–12 months post operatively. Clinically, the vertically and horizontally enlarged alveolar ridge displayed a similar clinical appearance to the neighbouring bone. Previously exposed implant surfaces were covered by newly formed hard tissue. Fixation screws and cover screws were removed to allow access for abutment connection. Finally, healing abutments were inserted. 20 data sets were produced from the applied surgical protocol for alveolar ridge augmentation described above, one for each patient. The surgical procedures were performed and the resulting sets were provided by PW at the Department of Periodontology, Semmelweis University, Budapest, Hungary.

The data sets featured in this study were acquired following approval granted by the Semmelweis University Regional and Institutional Committee of

Science and Research Ethics (reference number: 77/2011). Each set consists of two volumes of CBCT images for the pre-operative and post-operative representation of each patient. The combined CT slices in each case comprise a full 3D representation of the patients, focusing on alveolar changes, before and 9–12 months after surgery. All CBCT scans were obtained by the Classic i-CAT® (Imaging Sciences International) X-ray source equipment. The data sets were obtained during complex augmentative and implant-related prosthodontic treatment of the patients. Taking into account that the dosage of an i-CAT scan is not significantly higher compared with a smaller volume CBCT, the i-CAT system was preferred since in all of the cases there were additional surgical sites and endodontic treatments to be evaluated.

All data sets were acquired using a common set of parameters for the i-CAT scanner: high frequency, constant potential, fixed anode 120 kVp, 3–8 mA (pulse mode). The image detector was an amorphous silicon flat panel with a size of 20 × 25 cm. Image acquisition was performed in a seated position by a single 360° rotation with a standard 40 s scanning time.

All available data sets were formatted in the digital imaging and communications in medicine (DICOM) standard as a series of 16-bit greyscale images (corresponding to individual CT slices). The size of all images was 400 × 400 pixels, with a 0.4 × 0.4 mm pixel size. The interslice distance was kept constant for all sets at 0.4 mm. The number of slices (images) in each set was 322–327, depending on the patient. In order to simplify the processing of the data, all DICOM sets were converted to 8-bit greyscale RAW data sets using the open-source XMedCon utility.²⁴

3D registration methodology

The proposed volumetric assessment technique is based on the direct comparison of the pre-operative and post-operative 3D volumes. The comparison is performed in terms of the difference between the two volumes on a slice-by-slice basis. This process, however, requires that the two compared sets are properly aligned. Since this study is concerned with volumetric data, a suitable 3D registration scheme has to be employed in order to align the volumes in question. In our case, the post-operative volume is registered to the pre-operative volume. Hence, the pre-operative volume is considered as the reference data set and the post-operative volume is considered as the floating set throughout the study.

The volumetric data sets of this study may be represented as a series of planar images, each of which signifies a volume slice. As with any registration method, the proposed technique has three major components:

1. A transformation function to accordingly transform the point coordinates of the floating volume.
2. An MoM (or objective function) to calculate the error between the reference volume and the estimated transformed volume.

3. An optimization method that will use the MoM in order to estimate optimal parameters for the transformation model. The optimal parameters should accomplish the best possible alignment of the floating volume to the reference volume.

The affine model: The transformation function preferred in the proposed 3D registration scheme is an affine transformation capable of transforming points in the 3D space. The 3D affine model used in this study is shown in Equation 1:

$$\begin{pmatrix} x' \\ y' \\ z' \end{pmatrix} = \begin{pmatrix} a_1 & a_2 & a_3 \\ b_1 & b_2 & b_3 \\ c_1 & c_2 & c_3 \end{pmatrix} \begin{pmatrix} x \\ y \\ z \end{pmatrix} + \begin{pmatrix} dx \\ dy \\ dz \end{pmatrix} \quad (1)$$

where the 12 independent parameters of the affine model are (a_i, b_i, c_i) for $i = 1, 2, 3$ and dx , dy and dz . Therefore, points from the floating volume with initial coordinates (x, y, z) can be transformed to their new coordinates (x', y', z') by considering the following equalities:

$$\begin{aligned} x' &= a_1x + a_2y + a_3z + dx \\ y' &= b_1x + b_2y + b_3z + dy \\ z' &= c_1x + c_2y + c_3z + dz \end{aligned} \quad (2)$$

By applying the transformation function described in Equation 2 in every point of the floating 3D volume, the entire volume can be spatially transformed according to the rotation, scaling and translation defined by the 12 parameters of the transformation model. Since all parameters are real numbers, the calculated transformed coordinates are also real numbers. For this reason, the proposed scheme employs the trilinear interpolation technique, where eight neighbouring points are considered in order to estimate the intensity of each transformed point.²⁵

The absolute difference objective function: In general, image registration is a recursive trial and error process. In every iteration, a newly transformed estimate is evaluated against the reference image or data set. The evaluation is performed by means of an objective function or MoM. Most image registration schemes employ well established objective functions such as the correlation coefficient, mutual information, the distance map and so on.^{26,27} Those functions are very efficient for 2D registration but involve a relatively large number of arithmetic calculations that render them impractical for large volumes of data. Unfortunately, the size of the data sets used in our study (of more than 320 CT slices each) only allows rather simple objective functions to be employed.

Therefore, the objective function preferred in this study is the average absolute difference between the reference and the aligned volume on a point-by-point basis. Mathematically this may be expressed as shown in Equation 3:

$$\bar{D} = \frac{1}{N \times W \times H} \sum_{z=0}^{N-1} \sum_{y=0}^{H-1} \sum_{x=0}^{W-1} |V_R(x', y', z') - V_F(x, y, z)| \quad (3)$$

where $V_R(x', y', z')$ is the intensity (grey level) of point (x', y', z') from the reference volume and $V_F(x, y, z)$ is the intensity of point (x, y, z) from the floating volume. In effect, Equation 3 calculates the average absolute difference between the reference and the transformed floating volume over all slices (N), with width (W) and height (H) points. It follows that the lower the average absolute difference measurement, the better the reference and the transformed floating volumes match.

The simplex optimization method: The transformation function and the MoM described in the previous sections need to be properly combined in order to achieve the alignment of the two subject volumes. Therefore, in each iteration of the registration scheme, the transformation function has to be supplied with a new set of parameters that should ideally minimize the objective function. In most registration schemes, this is usually achieved through an optimization method. The optimization process estimates new transformation parameters in an attempt to bring the two volumes spatially closer after each iteration. In our case, this is achieved by the minimization of the average absolute difference MoM described in Equation 3.

The proposed 3D registration scheme uses the downhill simplex method for optimizing the transformation parameters.²⁸ The particular method is a repetitive procedure that makes its own way downhill through an M -dimensional topography until it encounters at least a local minimum (or maximum). The downhill simplex method has to be initialized with $M + 1$ positions, defining an initial simplex. If one of these positions is an initial starting point, then the other M positions could be expressed as $P_i = P_0 + e_i$, where the e_i values are M unit vectors. The algorithm then takes a series of steps by replacing the positions where the objective function is maximized (worst solution) with a new position. The new position is determined by extrapolating the behaviour of the objective function measured at each position that is arranged as a simplex. Two termination criteria were defined in our case: the simplex was moved less than a predefined tolerance in a particular iteration (negligible improvement has been achieved) or the maximum number of iterations has been reached.

Registration evaluation: The effectiveness of the alignment process can be evaluated by estimating the average edge distance between the pre-operative volume

and the aligned post-operative volume. The algorithm employed in our case comprises the following steps:

- extraction of the edges of all slices from the reference set (pre-operative) using a canny edge detector²⁹
- extraction of the edges of all slices from the aligned floating set (post-operative) using the same method
- calculation of the mean edge distance (MED) criterion to estimate the shortest distance between each edge-point of the reference and aligned floating volumes on a slice-by-slice basis.

The MED criterion between the reference volume (V_R) and the aligned floating volume (V_{TR}) is calculated as follows:

$$\text{MED} = \frac{1}{N} \sum_{z=1}^N \left(\frac{1}{E_z} \sum_{i=1}^{E_z} DM_z(\tilde{x}_i, \tilde{y}_i) \right) \quad (4)$$

where E_z is the number of edge points in slice z of the aligned floating volume, $(\tilde{x}_i, \tilde{y}_i)$ are the coordinates of an edge 2D point from slice z of the aligned floating volume and DM_z is the distance map of slice z from the aligned floating volume.³⁰ In effect, Equation 4 describes a two-step process:

1. calculation of an average distance from the distance map of each slice pair
2. calculation of an average distance over all slices.

The MED value is measured in points (pixels) but if the metric pixel dimensions of the acquired data sets are known beforehand, the measurements can be converted to any metric unit (millimetres, centimetres etc). The evaluative results are presented in the following sections.

Volumetric assessment

The registration scheme described previously was employed to allow for an effective volumetric evaluation of CT scan volumes after surgery. This is to be achieved by directly comparing the aligned pre-operative and post-operative data and assessing their differences. For this purpose, a volumetric assessment scheme was devised, based on digital subtraction radiography.

The basic idea of the proposed volumetric assessment method is that the volume difference between the pre-operative and post-operative data sets in a particular area of interest should be revealed after digitally subtracting aligned versions of the two sets. Hence, there should be no need to obtain volume measurements from both data sets, as the volume difference could be calculated by just examining the subtraction result. The proposed algorithm comprises the following processes in a sequential manner:

- digital subtraction of the pre-operative and the aligned post-operative volumes on a slice-by-slice basis
- definition of ROIs in each slice of the subtraction resultant volume (difference volume)
- volumetric measurements by combining the defined ROIs.

Digital subtraction: Provided that the two subject data sets are properly aligned, digital subtraction between those two sets should highlight their differences. More specifically, in case of 3D data, those differences can be modelled as objects in 3D space. This is ideally suited to our case where we need to assess the changes in 3D post-operative data compared with pre-operative data for the same patient.

Typical digital subtraction radiography is usually performed by obtaining the absolute difference between the compared images or data sets. In our case, this principle is extended to three dimensions, with the third dimension being the slice depth. Therefore, a new volume (V_{diff}) is composed, which corresponds to the absolute difference between the pre-operative and the post-operative volumes on a slice-by-slice basis. This may be expressed mathematically as shown in Equation 5 for volumes of N slices with width (W) and height (H):

$$\begin{aligned} V_{diff}(x, y, z) &= |V_R(x, y, z) - V_{TR}(x, y, z)| \\ &\quad x = 0, \dots, W - 1 \\ \forall(x, y, z) \quad &\quad y = 0, \dots, H - 1 \\ &\quad z = 0, \dots, N - 1 \end{aligned} \quad (5)$$

Practically, the intensity of each point of V_{diff} in the 3D space is the absolute difference between the intensity of the respective point of the pre-operative volume (V_R) and the aligned post-operative volume (V_{TR}). Provided that the two compared volumes were successfully aligned, V_{diff} should be a low intensity (dark) volume distinguishing the differences between the two subject volumes. In this study, those differences correspond to newly formed hard tissues that result from the surgical procedure described previously.

Definition of regions of interest: Once the difference volume has been extracted, the area of interest can be defined. The particular area is the section of the 3D volume which contains the changes that need to be assessed. As mentioned, all data sets used in this study are composed of a series of 2D images corresponding to the volume slices. Therefore, by defining a ROI in each slice, the volume of interest (VOI) can be composed after combining all successive regions. ROI definition can be described as a problem of image segmentation. As a result, any typical 2D segmentation method could be employed, as long as it is applied to all volume slices.

For the purposes of this study, a scheme based on the region growing segmentation method was preferred.³¹ The proposed scheme comprises the following sequential steps, which are applied on the subtraction product (difference volume) of the pre-operative and post-operative volumes:

- manual definition of a wide search area for all slices
- process the first slice:
 - the centre of the search area is considered as the initial seed point for the region growing algorithm
 - apply region growing using the initial seed point, limited to the search area:
 - compare the seed point to its neighbouring points
 - the region is grown from the seed point by adding its similar neighbouring points, increasing the size of the region. The similarity is determined according to a predefined tolerance threshold
 - the newly added points are considered as the new seeds and their neighbours are examined. The examined points are added to the region if they exhibit similarity
 - the process is iterated until:
 - no new points have been added (there are no seeds)
 - all points of the search area have been added
- repeat for all slices.

The proposed algorithm is a semi-automatic process that only requires the definition of a search area. However, there may be some slices where the region growing algorithm fails to detect a region. This may be contributed to either an invalid initial seed point or an unsuitable threshold. In such cases, manual adjustments are necessary.

An additional segmentation technique was used in this study as an alternative to region growing. This technique relies on the extraction of threshold-based intensity zones in each slice of the subject volume. The alternative segmentation technique, which is also applied on the subtraction product of the pre-operative and post-operative volumes, can be summarized thus:

- Manual definition of a wide rectangular search area or multiple polygonal search areas in each slice
- Definition of a fixed number of intensity threshold zones (by defining the upper and lower boundaries of each zone)
- Process the first slice:
 - Classify the points of the search area(s) to one of the predefined intensity zones, according to their intensity

- Manually select one or more zones as the slice's ROI
- Repeat for all slices.

The procedure described above requires more user intervention than the relatively automated region growing technique illustrated previously, but in general achieves more accurate segmentation than region growing.

Volumetric measurements: The final stage of the volumetric assessment algorithm is to obtain metric measurements of the VOI. By knowing the point metric dimensions (resolution) and the interslice distance of the data sets, the VOI can be expressed in metric units, using Equation 6:

$$v_{metric} = \sum_{z=1}^N \sum_{i=1}^{R_z} (X_{res} Y_{res} Z_{res}) \quad (6)$$

In Equation 6, the measurement is obtained over all N slices of the subtraction product volume. The quantities X_{res} , Y_{res} and Z_{res} correspond to the x -resolution, y -resolution and interslice distance, respectively, which are all equal to 0.4 for all sets in this study. In other words, Equation 6 defines the sum of all R_z ROI points with volume $X_{res} \times Y_{res} \times Z_{res}$ in each slice z and for all N slices.

Volumetric measurements verification: The obtained volumetric measurements were verified by estimating the volumes of five standard-shaped objects with known dimensions. The objects were measured manually and their real volumes were calculated mathematically. The proposed volume estimation algorithm was then applied to the same objects and the two obtained measurements were compared.

The first reference object used for the purposes of this study is a dental implant. The particular implant could be approximated as a half-cone shaped object with height $h = 8.5$ mm, top surface diameter $D_{top} = 3.57$ mm and bottom surface diameter $D_{bot} = 2.761$ mm. According to the mathematical properties of the half-cone, its volume can be calculated using Equation 7:

$$V_{half-cone} = \frac{\pi h}{12} (D_{bot}^2 + D_{bot} D_{top} + D_{top}^2) \quad (7)$$

The rest of the reference objects were four cylindrical implants of various sizes. The volume of a cylinder with diameter D and height h can be mathematically calculated using Equation 8:

$$V_{cylinder} = \frac{\pi h D^2}{4} \quad (8)$$

a

b

c

d

e

f

Figure 2 Fused pre-operative and post-operative volumes before and after the registration for visualizing the effects of the registration process on three-dimensional reconstructed versions of (a) Set I prior to registration, (b) Set I after registration, (c) Set II prior to registration, (d) Set II after registration, (e) Set III prior to registration and (f) Set III after registration

Results

This section presents the results obtained by applying the proposed method to all data sets featured in this study. More specifically, two aspects of the algorithm are examined: registration (alignment) and volume estimation.

Registration evaluation

The effectiveness of the proposed registration scheme was evaluated both qualitatively and quantitatively. The results are presented in the following sections.

Qualitative evaluation: Qualitative evaluation was performed by means of visual assessment. In order to achieve this, the pre-operative, post-operative and the aligned post-operative sets were reconstructed using a third party 3D volume viewer tool (ImageJ's volume viewer; see wayne@codon.nih.gov).³² The pre-operative and post-operative volumes were then fused together prior to and after the registration process in order to visually demonstrate the effects of the registration. Figure 2 shows those reconstructed volumes for three sets (Sets I, II and III). In Figure 2 the pre-operative volume is depicted, with the superimposed post-operative volume visible as shaded regions. As can be seen in Figure 2, there is notable improvement in all cases (Figure 2b,d,f) as a satisfactory alignment between the pre-operative and post-operative volumes has been achieved for the three cases examined (Sets I–III). On the other hand, in unregistered sets (Figure 2a,c,e), the floating volume exhibits quite a large spatial deviation compared with the reference volume, especially for Sets II and III (Figure 2c,e, respectively).

Quantitative evaluation: The proposed 3D registration scheme was also quantitatively assessed using the MED between two volumes. In our case, Equation 4 was employed to obtain MED measurements between the pre-operative and post-operative volumes before and after the registration process. The MED values before and after the registration may be considered as a quantitative assessment for the improvement achieved using the proposed 3D registration scheme as far as the alignment of the two volumes is concerned. MED measurements were obtained for all 20 patients prior to and after the application of the registration algorithm. For convenience, the measurements obtained from Equation 4 were converted to millimetres and the results for all sets are illustrated in Table 1.

As can be seen in Table 1, the improvement achieved depends directly on the characteristics of each set. In general, small MED values correspond to a close spatial match between the two volumes and hence better alignment. In 18 out of 20 cases, the proposed

registration scheme accomplished MED values of less than 2 mm. Moreover, in nine cases MED values of less than 1 mm were recorded. Those values correspond to nearly ideal alignment between the pre-operative and post-operative volumes in the ROIs. The relatively high measurements obtained, particularly for Sets IX and X in Table 1, are attributed to various metal artefacts on the particular sets that introduce unevenly distributed reflections. Those reflections are taken into account by the edge detector algorithm, causing the average edge distance value to slightly increase. Nevertheless, the affected sets are still usable, as discussed later, when performing the volumetric measurements.

Volumetric evaluation

As with the registration evaluation, volumetric evaluation was also performed by means of visual inspection and quantitative measurements. The results obtained for all sets are illustrated in the next sections.

Qualitative evaluation: The ROIs were extracted in each set from the difference volumes, using the proposed methodology. Visual assessment was performed in each slice of the difference volume in order to verify the validity of the extracted ROI. Some examples are shown in Figure 3a–c, where the defined ROI on selected difference volume slices from Sets I–III (circled areas) are depicted. By combining the detected ROI from all slices, we can obtain a VOI for each set. In Figure 3d–f, the detected VOIs are designated for Sets I–III (circled areas). The VOIs are illustrated on 3D reconstructed versions of the fusion

Table 1 Calculated mean edge distances (MED) in millimetres for all sets (assuming 0.4×0.4 mm pixel size)

Set	Before registration	After registration
I	4.090	0.988
II	5.072	0.758
III	12.996	1.143
IV	3.582	1.274
V	13.203	1.011
VI	5.739	1.982
VII	7.295	0.883
VIII	15.958	1.607
IX	34.452	5.787
X	15.881	5.824
XI	3.756	0.242
XII	11.754	1.614
XIII	11.710	1.665
XIV	13.323	0.102
XV	23.298	0.447
XVI	18.459	0.878
XVII	18.000	0.265
XVIII	14.910	1.037
XIX	7.508	1.182
XX	10.699	0.951
Mean $\pm$ SD	12.584 $\pm$ 7.535	1.483 $\pm$ 1.558

SD, standard deviation.

Figure 3 Regions of interest (ROIs) and volumes of interest (VOIs) for all sets. ROI for (a) Set I, (b) Set II and (c) Set III. VOI on three-dimensional reconstructed versions of (d) Set I, (e) Set II and (f) Set III

Table 2 Volumetric measurements for all 20 sets

Set	Volume (mm^3)
I	1076
II	914
III	1962
IV	1040
V	431
VI	431
VII	245
VIII	467
IX	512
X	330
XI	964
XII	1154
XIII	1512
XIV	383
XV	216
XVI	636
XVII	628
XVIII	480
XIX	407
XX	785

between the pre-operative set and the difference volume.

Quantitative evaluation: Quantitative measurements were obtained for each VOI using Equation 6. The volume of each VOI was expressed in the metric unit system as cubic millimetres. The results concerning the VOIs, as illustrated in Figure 3d–f for Sets I–III, respectively, are presented in Table 2 for all 20 sets featured in this study.

As mentioned, the volumetric measurements were verified by comparing the real volume of five reference objects to the measurements obtained after the application of the proposed scheme. Using Equation 7 and Equation 8 and substituting for the values measured for our reference objects, their real volumes were calculated. The volume estimation method described in Equation 6 was then applied to all reference objects, yielding their estimated volumes in metric units. The real and estimated measurements for each reference object are illustrated in Table 3. As can be seen in Table 3, the two measurements closely match in all

Table 3 Volumetric measurements for five reference objects in order to verify the volume estimation algorithm

Implant (shape)	Dimensions (mm)	Set	Real volume (mm^3)	Estimated volume (mm^3)
Implant 1 (half-cone)	$h = 8.5$	V	71.289	71.360
	$D_{top} = 3.75$			
	$D_{bot} = 2.761$			
Implant 2 (cylindrical)	$h = 10$	IX	110.491	110.528
	$D = 3.75$	X		110.464
		XVII		110.656
		XVIII		110.848
Implant 3 (cylindrical)	$h = 11.5$	IX	144.571	144.576
Implant 4 (cylindrical)	$h = 8.5$	IX	106.857	106.944
	$D = 4$			
Implant 5 (cylindrical)	$h = 8.5$	XVIII	93.917	93.888
	$D = 3.75$			

cases as their recorded differences are less than 0.4 mm^3 . An example of the first half-cone shaped reference object is shown in Figure 4a (circled area) in the 3D representation of Set V. Figure 4b illustrates a magnified section of Figure 4a, focusing on the area of interest.

Discussion

It is of great importance for clinicians to obtain linear measurements describing the utmost extent of the augmented hard tissues in vertical and horizontal dimensions. These linear measurements provide information on the success and limitations of a certain surgical technique. Although the particular linear measurements are quite accurate, they can only provide an estimate of the augmented bone's volume. In the vast majority of cases, it is impossible to calculate the particular volume owing to the non-standard geometrical shape of the VOI. In addition, the traditional approach requires two sets of measurements to be obtained (from the pre-operative and post-operative data) and several samples per measurement, which is a somewhat tedious and time-consuming process. Moreover, it is of great importance for clinicians to provide 3D volumetric measurements of newly formed hard tissues without taking estimated multiple linear measurements on two different, non-aligned data sets. The proposed methodology allows for evaluating the success of staged and simultaneous hard tissue augmentation procedures, as well as providing a novel approach for comparing the efficacy of different surgical approaches. Thus, a standardized methodology can be established to compare the volumetric results of different augmentative techniques. The proposed scheme obtains a single, reproducible volumetric measurement from the difference of the aligned pre-operative and post-operative volumes with minimum user interaction. By applying the proposed scheme for volumetric evaluation along with linear measurements, it may even be possible to compare the efficiency of different surgical techniques resulting in hard tissue changes.

The proposed scheme depends on digital subtraction radiography to expose the differences between the two subject 3D data sets. As with any other digital subtraction radiography method, successful alignment between the two sets is a strong requirement. In fact, the effectiveness of the entire scheme is directly proportional to the 3D registration quality. As mentioned previously, the registration scheme employed in this study utilizes the affine model as its transformation function, the absolute difference as its objective function and the downhill simplex technique as its optimization method.

In general, transformation models can be grouped into two broad categories: rigid and non-rigid. Non-rigid models are usually defined by elastic transformations that are able to freely distort the transformed object. On the other hand, rigid methods provide a

Figure 4 The half-cone shaped reference object (implant) used for verifying the proposed volume estimation scheme, illustrated in a three-dimensional reconstructed version of Set V. (a) Entire volume, original size and (b) magnified section of the implant

somewhat more controlled transformation model that distorts the transformed object relative to a finite number of planes. Hence, in the case of 3D data, the object can be transformed relative to the vertical and horizontal planes. Since the 20 3D data sets used in this study did not contain any major elastic deformations, a rigid model was incorporated in the proposed 3D registration scheme. In fact, the most generalized rigid model, the affine transformation, was preferred to account for a wide range of cases.

As mentioned, the sheer size of the data sets featured in this study requires a rather simple and fast objective function in order to align the 3D volumes within a reasonable time period. Typically, traditional 2D registration schemes employ rather complex MoM metrics, such as the correlation coefficient, the gradient correlation, the mutual information, the distance map and so on. Although those metrics provide increased accuracy they are only practical for evaluating single images or small image sequences. Several of those metrics were tested as an objective function in the proposed scheme, using some of the 3D data sets featured in this study. The registration quality was satisfactory in all cases but the increased time required to align the sets rendered the scheme impractical. For instance, it took around 5 h to register a 3D data set of 325 slices using the correlation coefficient and about 7 h for the same set using the mutual information as a MoM. On the other hand, the employed absolute difference scheme, described in Equation 3, required about 2 h for the same set. The execution time for the rest of the data was directly proportional to the size of the 3D data sets. In general, all featured sets comprised 322–327 slices, so the execution time slightly deviated around 2 h. All tests were performed on the same reference system [AMD Mobile Sempron processor

(Sunnyvale, CA) at 1.6 GHz, 2 GB of RAM, Microsoft Windows XP operating system (Redmond, WA)].

Execution time restrictions also imposed the use of the downhill simplex method alone as an optimization method for the proposed 3D registration algorithm. In most 2D registration cases, the simplex method is usually combined with other optimization methods (such as Powell's) for increased accuracy. However, such an approach would be impractical for the 3D sets of more than 320 slices featured in this study. The performance of the registration algorithm could be improved if down-sampled versions of the sets were used instead. In such a case, alignment would be much faster. However, this would also have a negative impact on the accuracy of the overall scheme, as volumetric measurements would have to be obtained on down-sampled, lower resolution volumes.

The ROIs were defined on the difference volumes using either of the two proposed semi-automatic segmentation methods: region growing or threshold-based intensity zones. Several trials were performed using both techniques on the same data sets and the extracted ROIs were examined by experts. It was concluded that the threshold-based intensity zones provided experts with a more controllable ROI definition method and hence were considered more accurate than region growing. As a result, this particular approach was preferred in the majority of the sets featured in this study.

All of the above remarks suggest that the proposed combinational registration and volume difference evaluation scheme is quite flexible. The modular design of the scheme itself provides several possibilities for improvements, optimizations and customizations according to the examined data. It follows that the algorithm used for the purposes of this study was specifically

tailored for the large 3D dental data sets of CT scans featured in the study.

Conclusion

This paper presented a method for automatically aligning 3D CBCT dental data sets. The proposed method was incorporated into a complete scheme for quantifying and evaluating volumetric differences between two data sets. Tests performed on a total of 20 sets showed that the proposed method successfully aligned the pre-operative and post-operative volumes in each set. This

allowed for effectively assessing the volumetric differences between the pre-operative and aligned post-operative volumes using the proposed evaluation technique, which is based on digital subtraction radiography. The presented novel radiographical approach introduces a qualitative and comparative method for evaluating hard tissue changes following certain interventions (e.g. bone augmentation procedures, endodontic treatment). The proposed scheme also allows for the follow-up of the progression or regression of certain pathological conditions in the maxillofacial region (e.g. chronic periapical inflammatory processes, hard tissue infiltrating tumours).

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