RESEARCH

Novel information theory based method for superimposition of lateral head radiographs and cone beam computed tomography images

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Objectives: The aim was to introduce a novel alignment criterion, focus mutual information (FMI), for the superimposition of lateral cephalometric radiographs and three dimensional (3D) cone beam computed images as well as the assessment of the alignment characteristics of the new method and comparison of the novel methodology with the region of interest (ROI) approach.

Methods: Implementation of a FMI criterion-based methodology that only requires the approximate indication of stable structures in one single image. The robustness of the method was first addressed in a phantom experiment comparing the new technique with a ROI approach. Two consecutive cephalometric radiographs were then obtained, one before and one after functional twin block application. These images were then superimposed using alignment by FMI where the following were focused on, in several ways: (1) cranial base and acoustic meatus, (2) palatal plane and (3) mandibular symphysis. The superimposed images were subtracted and coloured. The applicability to cone beam CT (CBCT) is illustrated by the alignment of CBCT images acquired before and after craniofacial surgery.

Results: The phantom experiment clearly shows superior alignment when compared to the ROI approach (Wilcoxon $n = 17$, $Z = -3.290$, and $P = 0.001$), and robustness with respect to the choice of parameters (one-sample t -test $n = 50$, $t = -12.355$, and $P = 0.000$). The treatment effects are revealed clearly in the subtraction image of well-aligned cephalometric radiographs. The colouring scheme of the subtraction image emphasises the areas of change and visualizes the remodelling of the soft tissue.

Conclusions: FMI allows for cephalometry without tracing, it avoids the error inherent to the use of landmarks and the interaction of the practitioner is kept to a minimum. The robustness to focal distribution variations limits the influence of possible examiner inaccuracy.

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Introduction

The superimposition of specific anatomical structures in lateral cephalometric radiographs plays an important role in the evaluation of orthodontic treatment progress, craniofacial growth and surgical outcomes. The basis for

this superimposition consists mostly, of cephalometric tracing and the indication of landmarks. Alignment based on tracing and landmarks is labour-intensive and its accuracy is influenced by statistical fluctuations in the identification of exact landmark location. Furthermore, the accuracy of superimposition depends on the examiner's experience.^{1,2} When detected automatically, the error in location remains dependent on the landmark to be detected.³ At present the validity of tracing methods and of methods to detect the locations of landmarks are

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still research questions.⁴ In a literature study, published in 2008, Leonardia *et al*⁵ came to the conclusion that the automatic landmark and tracing systems described are not sufficiently accurate to be used in clinical practice and the errors generated by these systems are greater than those expected with manual tracing.

In a wide variety of clinical applications the criteria of choice to align images are pixel- or voxel-based similarity measures, such as mutual information (MI).^{6,7} In cephalometry, the straightforward application of an MI-based superimposition on the whole of the reference and test image is deemed inappropriate. The origin of misalignment is in the nature of cephalometry and, among others, in the fact that traditional MI assigns an equal weight to all the pixels of the images. Elements of craniofacial bone structures exhibit differential growth and may move with respect to each other; however, the transformation for superimposing the images has to be limited to rotations and translations for measurements of angles, distances and proportions to be correct. A measure of alignment quality, taking into account all structures at once, will in general fail to superimpose the parts of the images in a way that is useful for orthodontic diagnosis. A current practice is to reduce the alignment criterion to a region of interest (ROI) that only includes a stable reference structure, and apply the resulting superimposition to the entire image.^{8,9}

The aim of this paper is to introduce a more subtle and robust approach by using focus mutual information (FMI). The criterion for quality of the alignment FMI emphasises the contribution of the alignment of structures that will serve as a reference for measurement and reduce the contribution of regions unimportant to the alignment or counteracting the desired superimposition. FMI registration is immediately applicable to two dimensional (2D), three dimensional (3D) and 3D–3D image registration in about the same way as MI registration is. In what follows, FMI image registration will be applied to lateral cephalometric images. The 2D nature of the images allows for a clear demonstration of the FMI methodology. In orthodontics the use of 2D images is still common practice. This study will show that the FMI approach outperforms the use of ROI. The method is applied to pre- and post-treatment 3D cone beam CT (CBCT) images.

Materials and methods

Focus mutual information

When picking a point in the overlap of two well aligned images of the same structure, the grey value of the reference image and the grey value of the test image will correspond. To test the alignment, a series of test points are chosen at random in the overlap of the superimposed images and the correspondence between the grey values of the reference and the test images are checked. An ordinary correlation coefficient would be a good candidate to measure this correspondence; how-

ever, images, although acquired in a standardized setting, may show artefacts and non-linear distortions of the grey-level scale that disturb correlation-type correspondence measures. These phenomena make such measures unreliable.

MI was originally designed as a measure of information shared between the transmitter and receiver at either end of a communication channel.¹⁰ The use of MI as a measure of alignment was proposed independently by Viola and Wells,⁶ and by Collignon *et al*.⁷ A more robust normalized variant of MI, denoted by Y , was introduced by Studholme *et al*.¹¹ MI and Y were introduced as a measure of correspondence of grey values, robust to variations in grey-value distributions. To model alignment in a communication context, the superimposition itself can be regarded as the communication channel. A test transmission is modelled as a series of points chosen at random in the overlap of the reference image and the floating image. The series of grey values of the reference image at the selected points is considered to be the transmitted signal and the series of grey values of the superimposed image is the received signal. The superimposition defining the “communication channel” is sought to optimize the transmission of a signal between the reference image and the superimposed image, or, more specifically, maximizing the MI between transmitted and received signal. Traditionally, the distribution used for choosing the points is the uniform distribution. FMI involves replacing the uniform distribution by a distribution (focus distribution) concentrated around those structures helpful to the desired alignment. In what follows, this study will clarify how such a focus distribution can be obtained. A wide variety of methodologies to define this focus distribution can be adopted. An elementary method is to roughly indicate the structure to be used as a basis for the alignment through a set of points (focus points). These points are used as centres of equal isotropic bell-shaped Gauss functions, acting as building blocks for the focus distribution. The standard deviation (SD) of these Gauss functions (focus SD) can be used to tune their width. Their sum attributes to each pixel a strictly positive value. To normalize these values to a probability they are divided by their sum. To create a sampling distribution more appropriate for the alignment of curvilinear structures, a slightly more sophisticated approach can be used. First the structure is indicated through a few points, a curve is then drawn through these points. The pixels on this curve are used as the centres of the Gauss functions mentioned above.

Experiments

A. Mandibular phantom experiments

A series of radiographs was made of a human mandible phantom. This phantom was fixed on a rotating stage between an X-ray source and a charge coupled device (CCD) captor (Figure 1). Images of the phantom were

Figure 1 Setup of the region of interest (ROI)-focus experiment illustrating the relative position of the mandibular phantom with respect to the X-ray source and the charge coupled device (CCD) captor

taken at angles ranging from -4° to 4° in steps of 0.5° , resulting in a set of 17 images. In a second series of 17 images, the lower left second premolar was displaced in a mesial direction with respect to the neighbouring teeth (Figures 2a and 2b). Radiographs were recorded using a dental CCD captor (Gendex Visualix Des Plaines, IL) and appropriate software (Vixwin 2000, Gendex, Des Plaines, IL). The images were stored as tagged image file format (TIFF) at a resolution of 640×488 pixels with 256 grey values. Registration was done with respect to the lower left second premolar.

In such a standardized environment, the quality of the alignment of the lower left second premolar can be assessed by the square root of the sum of squared grey-

value difference (SDDI) between the superimposed reference image and the transformed test image. For all aligned pairs, the SDDI is evaluated over the area of the lower left second premolar, as delineated in Figure 2c.

In the first experiment, the robustness of both ROI and FMI registration with respect to a size-of-domain parameter has been compared. The focus distribution has to be defined for one of the images, by definition this will be called the reference image. The image of the mandibular phantom in the initial position was used as the reference image. In the test image, the lower left second premolar was displaced mesially and the mandible was rotated over 0.5° . The slight rotation simulates a small misalignment error in the neighbouring teeth surrounding the lower left second premolar.

In the second experiment, the alignment of all image pairs has been compared with the corresponding rotation angles using both FMI and ROI with optimal size-of-domain parameters.

In the third experiment, the robustness of FMI alignment has been tested with respect to deviations in focus centres. The same reference and test images as the first experiment were used.

1. Robustness of FMI vs ROI

ROI registration: The smallest rectangle around the lower left second premolar consisting of 125×332 pixels was taken as the reference ROI (Figure 2d). Its width was shrunk and extended with respect to the centre in constant steps of 2 pixels, and its height was

Figure 2 (a) Reference phantom image. (b) Test phantom image with the lower second left premolar displaced in the mesial direction. (c) Area delineating the lower second left premolar. (d) Initial rectangular region containing the lower second left premolar. (e) Focus centres indicating the central (vertical) axis of the lower second left premolar. (f) Sum of squared grey-value differences (SDDI) as a function of ROI size (dashed) and focus standard deviation (solid), showing FMI outperforming the ROI based alignment for a similar domain parameter size

adapted proportionally. This resulted in a set of nested windows of increasing size with a width ranging from 3 to 201 pixels. For each of these cropping windows the optimal alignment, using Studholm Y as criterion, was computed. In Figure 2f, the dotted line shows the SDDI of the resulting alignments as a function of the width of the ROI. To speed up the search in each alignment experiment, a least squares initial guess was calculated from four reference points on the lower left second premolar in the reference image and the test image.

FMI registration: On the central (vertical) axis of the lower left second premolar in the reference image (Figure 2e), approximately eight equidistant focus points were chosen and FMI registrations were calculated with SD ranging from 1 to 101 pixels in steps of 2. In Figure 2f the solid line shows the SDDI of the resulting alignments as a function of the SD.

2. Overall performance of ROI vs FMI: For each of the 17 image pairs with corresponding rotation angles, the procedure of the first experiment was repeated to obtain ROI and FMI alignment, both with optimal size-of-domain parameters. The results (SDDI) were compared with a paired Wilcoxon test.

3. Robustness to deviations in focus point indication: The FMI registration of the first experiment with a focus SD of 43 pixels was repeated 50 times. At each repetition the focus centres were perturbed according to a normal distribution with variance-covariance matrix $\Sigma = 102 \text{ I}$. The results (SDDI) were compared with the optimal ROI result of the first experiment with a one-sample *t*-test.

B. Lateral cephalometric radiographs experiment

Two consecutive cephalometric radiographs were anonymously retrieved from patient files before and after functional twin block application. Images were obtained with a Cranex3 source (Soredex, Helsinki, Finland) at

71 kV, 0.6 s and 10 mA (see Figure 3). The treatment period between the radiographs was 7 months. At the start the patient was 10 years and 8 months of age. They had a skeletal Class II relationship, counter-clockwise growth, and a dental angle Class II division 1 with overbite of 10 mm and vertical overbite of 3 mm. A full Class II was observed at the first molar. A frontal lip interposition was present.

Images were stored at a resolution of approximately 1520×1920 pixels, with 256 grey values. Before registration, the images were resized to 1000×1264 pixels (ACDSee Version 8.0 Build 39. ACD Systems Ltd, Victoria, Canada).

Construction of the focus distribution: A reference image was taken before treatment. When dealing with 2D lateral cephalometric images, several longitudinal structures can be used as a basis for guiding the superimpositions. Each of these structures was indicated with four points (Figure 4a1, 4b1, and 4c1). The choice to indicate each of the structures with four points is somewhat arbitrary; for example, for the palatal plane two points would have sufficed, but at least four points were required to indicate the shape of the mandibular symphysis.

A smooth line was drawn through each of those sets of four points (the fitted curve was a cubic B-spline). A focus SD of 40 pixels was chosen to emphasise a region with a width of about 80 pixels along the smooth line (Figure 4a2, 4b2 and 4c2).

Alignment experiments: In the first experiment, the cranial base and the acoustic meatus were focused to visualize overall growth and treatment effects. Then the palate was focused to study maxillary growth, changes in dentition and orthodontic treatment. In the last experiment, the mandibular symphysis was chosen as the focus to assess mandibular growth, changes in dentition and orthodontic treatment. The alignments were based on stable structures as described by Björk and Skieller.¹² Figure 4a1 shows the reference image

Figure 3 Two consecutive cephalometric radiographs before and after functional twin block application, showing the mandibular changes from Class II in a dental Class III relation with temporary negative overjet and vertical open bite relation in the lateral region

Figure 4 a1 b1 c1, Reference image with indicated features: (a) on the cranial base; (b) on the palate, and (c) on the mandibular symphysis. a2 b2 c2, Focus distribution defined on the reference image only based on the indicated points in images a1, b1, and c1. a3 b3 c3, Subtraction image for the alignment on the cranial base, on the palate, and on the mandibular symphysis respectively. Darker regions indicate the situation before treatment with a twin block functional appliance. a4 b4 c4, Coloured subtraction image for the alignment on the cranial base, on the palate, and on the mandibular symphysis respectively. The pixels of the subtraction image are subdivided in three fractions by dividing the grey-value differences in three levels. The different fractions are represented using shades of red (more radiodensity in test image than in reference image), shades of green (comparable radiodensity in test and reference images), and shades of blue (less radiodensity in test image than in reference image)

with four points indicating the cranial base and four points indicating the external acoustic meatus. Figure 4a2 is a visualization of the resulting focus distribution. Four points indicating the palate (Figure 4b1), were translated into the focus distribution (Figure 4b2). The mandibular symphysis was focused (Figure 4c2) based on the four points (Figure 4c1). After alignment the images were subtracted (Figures 4a3, 4b3, and 4c3). The pixels of the subtraction image were subdivided into three grey-value bins of equal size. The pixels corresponding to the lowest bin (meaning more radiodensity in the test than the reference image) were represented using shades of blue. Pixels with a grey value in the middle bin (small or no difference between test and reference images) were represented using shades of green. Pixels with a grey

value in the higher bin (lower radiodensity compared to the reference image) were represented using shades of red (Figures 4a4, 4b4 and 4c4).

C. CBCT experiment

From the file of a patient, pre- and post-surgery CBCT images were obtained. There was a time interval of 7 days between the first and the second image acquisition (by a Galileos 3D Cone Beam Imaging System, Sirona Dental Systems GmbH, Bensheim, Germany). The patient had a skeletal II pattern for which a bilateral sagittal split osteotomy was performed.

Construction of the focus distribution: The sample distribution consisted of the combination of three smoothed spherical distributions. Two of these dis-

tributions were centred between the lower (mandibular) molar and the premolar at the level of the cervixes. The third one is centred between mandibular central incisors at the cervical level. It was accepted that the dentition did not change substantially based on the relatively small time difference between pre- and post-treatment images (7 days). The mandible itself was not focused since the treatment was designed to remodel the mandibula.

Results

A. Mandibular phantom experiments

1. *Robustness of FMI vs ROI*: Only one pair of images was used in this experiment, therefore, statistical analysis was not relevant. The best FMI focus SD is 43 pixels and the corresponding SDDI is 30% smaller than the SDDI of the registration at the best ROI size (Figure 2f).

2. *Overall performance of ROI vs FMI*: In 15 out of the 17 image pairs the minimum SDDI in FMI registration was smaller than the minimum for ROI registration. This result was statistically significant (Wilcoxon $n = 17$, $Z = -3.290$, and $P = 0.001$).

3. *Robustness to deviations in focus point indication*: The minimal SDDI was 0.063, the mean 0.068 and the SD 0.011. In 90% of the cases the SDDI alignment based on the perturbed focal centres was better than the minimal SDDI found for ROI alignment in the first experiment (SDDI = 0.0874). In 10% of the cases the alignment based on the perturbed focal centres was superior to the unperturbed case. Despite the perturbations the SDDI of the FMI registrations was significantly smaller than the minimal SDDI obtained with a ROI registration (one-sample t -test $n = 50$, $t = -12.355$, and $P = 0.000$).

B. Lateral cephalometric radiographs experiment

In Figure 4 the grey-value subtraction images provide a basis for the direct measurement of linear distances and movement. The coloured images in Figure 4 provide a qualitative impression of the changes and their effect on the soft tissue. Orthodontic and orthopaedic changes were clearly visible. The proclination of the lower incisors as a result of the twin-block therapy was observed. Dento-alveolar changes and mandibular growth changes were also revealed by the colour coding. Little or no treatment effect could be noticed in the upper jaw.

Pre- and post-orthodontic changes were observed indicating the orthodontic treatment effect. For all three superimpositions, the observations match with those from classic superimpositions traced manually, based on conventional cephalometric structures.

C. CBCT experiment

The subtraction of the 3D superimposed CBCT images clearly identified the location, magnitude and direction of the surgical displacement of the chin. The position of the chin plate is projected to follow the curve of the mandibular outline, proving a good fit of the osteosynthesis plate (Figure 5). The mandible clearly was displaced with respect to the skull base between the pre-operative image and the post-operative image. Aligning the mandibula by means of the calculated rigid transformation resulted in the misalignment of the cranial base.

Discussion and conclusions

The results of the first phantom experiment suggest that FMI registration showed a more robust behaviour with respect to changes in focus SD than the ROI approach does with respect to changes in ROI size. In the second phantom experiment, FMI alignment displayed a better overall performance than ROI alignment. The last phantom experiment demonstrated the robustness of FMI with respect to deviations in focal centres.

When FMI is applied to consecutive lateral cephalometric images the focused structures are well aligned for the superimposition of the cranial base as well as the regional superimpositions on the palatal plane and the mandibular symphysis. Although it is possible to assess the evolution of the mandibular and dental components, based on the alignment of the cranial base alone, a small orientation misalignment of the cranial base will result in possibly disproportionally large errors in the measurement of displacement and orientation in the maxillary and mandibular region.^{13,14} Efstratiadis *et al*¹⁴ found that cranial and maxillary superimpositions could lead to different conclusions with respect to growth and treatment contributions. The displacement of maxillary and mandibular basal bones with respect to each other, and the movement of the maxillary molars relative to the maxillary basal bone, is critical for the assessment of occlusal changes as well as the movement of the mandibular molars with respect to the mandibular basal bone. Efstratiadis *et al*¹⁴ recommend the incorporation of maxillary and mandibular superimposition in orthodontic procedures. The observations, for all three superimpositions considered, match with those from classic superimpositions, based on conventional cephalometric structures. Similar conclusions can be drawn when FMI is compared with a more classical method of superimposition for the evaluation of dental and skeletal changes. Correct regional alignment can be of great value to the practitioner as it allows for an immediate interpretation and reduction in measurement error.

Current cephalometric practice consists of tracing and identification of landmarks manually or aided by software tools. Tracing and indication of landmarks remains labour intensive, and the accuracy depends

Figure 5 (a) Sagittal slice 108 of the CBCT subtraction image, with clear illustration of the surgical movement performed in the chin region. (b) Horizontal slice 276 of the CBCT subtraction image: illustration with perforation of the lingual cortex. (c) Frontal slice 393 of the CBCT subtraction image: illustration of the result of the actual frontal chin surgery procedure

critically on the skills of the practitioner and on landmark features. Gliddon *et al*¹ investigated the accuracy of four methods for cephalometric superimposition. The methods showed significant differences and “the accuracy of superimposition is consistently associated with the examiner’s experience, no matter what methods the examiner uses”.¹ Another study by Santoro *et al*² pointed out that the effect of operator experience might be as important as the effect of the tracing method. Even when automatic detection of landmarks is introduced, the error on the location remains dependent on the landmark to be detected.³ In a comparison of traditional manual identification *vs* computer-aided digital indication, Chen *et al*¹⁵ found that the effect of the specific landmark and of the quality of the radiograph had a greater influence on the error than the indication method. Furthermore, each landmark has a specific error pattern.^{16,17} Since the error of linear measurements between landmarks is composed of both the alignment error and the error in indication of the landmarks involved in the measurement, the overall measurement will critically depend on the landmarks used in the alignments.¹

When FMI alignment is used, dependency of the alignment error on the practitioner is a less critical factor due to the robustness of FMI alignments to changes in choice of focal parameters, location and extent of the focus. The structure used to align the images requires only an approximate indication in one of the images. When the alignment error is reduced, the measurement accuracy of displacement of landmarks may increase drastically.

At present, it cannot be expected that automated detection of landmarks will replace the manual indication of landmarks for clinical purposes, due to a lack of accuracy.⁵ Even if landmarks are to be indicated manually, a significant gain in time can be achieved through reduction of the number of landmarks to be indicated. FMI limits the number of landmarks to be indicated to those involved in the measurement, and

enables immediate qualitative appreciation of the evolution through fusion images and the immediate measurement of displacements on the digital subtraction image.

FMI alignment was applied successfully to 3D CBCT images acquired before and after craniofacial surgery. The location, magnitude, and direction of displacements due to the surgical procedure are identified without 3D model superimposition, yet the displacement is clearly visible. A graphical user interface to apply FMI alignment to 3D CBCT images is under development by the authors.

One could consider the use of surface registration to align anatomical structures in consecutive CBCT images. In its elementary form, surface registration consists of mapping a selected part of the image corresponding to a structure and its 3D surface model. The transformation, minimizing a nearness measure between the selected part and the 3D surface model, is sought.¹⁸ When aligning two consecutive images with respect to a specific anatomical structure, the surface of this structure has to be reconstructed and a 3D surface model has to be created, based on the reference image. In the test image the pixels corresponding to the structure have to be selected through segmentation. Segmentation, as well as 3D model reconstruction, is computationally intensive, needs manual verification and possibly correction and/or recalculation. The FMI alignment criterion does not imply reconstruction of surfaces nor require segmentation, and leads to interpretable superimpositions. If it is imperative to visualize aligned surface reconstructions, this can be done by applying the transformation found through FMI on the surface reconstruction in the test image in analogy to what has been done by Cevidanes *et al*⁸ using ROI in combination with MI registration. Further research could determine whether it is possible to improve on a final alignment result of 3D CBCT images, based on anatomical landmarks through the use of FMI with foci around the detected landmarks. A reliable, but approximate, automatic feature detection algorithm

could be combined with FMI to produce a high quality automatic alignment of CBCT images.

The methodology was developed to obtain more discriminating information to benefit from CBCT images. However, radiation especially in children should be as low as reasonably achievable. Issues of radiation risk, particularly for children, as well as mechanisms for dose reduction are still under discussion.^{19,20}

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In conclusion, FMI is a promising criterion to align lateral cephalometric images semi-automatically. The method is less time-consuming than tracing and is easy to handle. The interaction of the practitioner is kept minimal, as structures are indicated roughly and in one image only. The robustness to variations in focal distribution can limit the influence of possible examiner inaccuracy.