

Cranial base superimposition for 3-dimensional evaluation of soft-tissue changes

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Introduction: The recent emphases on soft tissues as the limiting factor in treatment and on soft-tissue relationships in establishing the goals of treatment has made 3-dimensional (3D) analysis of soft tissues more important in diagnosis and treatment planning. It is equally important to be able to detect changes in the facial soft tissues produced by growth or treatment. This requires structures of reference for superimposition and a way to display the changes with quantitative information. **Methods:** In this study, we outlined a technique for quantifying facial soft-tissue changes viewed in cone-beam computed tomography data, using fully automated voxel-wise registrations of the cranial base surface. The assessment of soft-tissue changes is done by calculation of the Euclidean surface distances between the 3D models. Color maps are used for visual assessment of the location and the quantification of changes. **Results:** This methodology allows a detailed examination of soft-tissue changes with growth or treatment. **Conclusions:** Because of the lack of stable references with 3D photogrammetry, 3D photography, and laser scanning, soft-tissue changes cannot be accurately quantified by these methods. (*Am J Orthod Dentofacial Orthop* 2010;137:S120-9)

Soft tissues establish the limit to which the orthodontist can alter the dimensions of the dental arches and the position of the jaws from both esthetic and stability standpoints.¹⁻³ Assessment of soft-tissue changes produced by growth or treatment requires 3-dimensional (3D) analysis and superimposition because of the complexity of soft-tissue behavior and the inability to measure asymmetries in 2-dimensional (2D) images. Recently, technologies such as 3D photogrammetry⁴⁻⁸ and laser scanning⁹⁻¹² of the face have been used for 3D soft-tissue superimposition, but their major limitation has been the inability to standardize registration of the images over time. Current procedures to integrate 3D facial images had significant errors in head positioning,¹³ and potential errors in facial expression have not been assessed.¹⁴

The variability of soft-tissue surface appearance has important consequences for the choice of approaches for adequate registration of longitudinal images. A stable reference for superimposition of images is required for a standardized record of the relationship between the facial soft tissues and the underlying skeletal and dental structures. Currently, cone-beam computed tomography (CBCT) allows the use of stable reference structures.

No soft-tissue structures are stable enough to allow registration between pretreatment and posttreatment images, because the soft tissues change with growth, treatment, head posture, weight gain or loss, aging, and facial expression. In 2D cephalometrics, the cranial base often is used for superimpositions to show both hard-tissue and soft-tissue profile changes because it has minimal changes after neural growth is completed. Although 2D landmark location is hampered by overlapping structures, locating 3D landmarks on complex curving structures is significantly more difficult and prone to identification errors.^{14,15} Even though landmark-based geometric morphometric methods¹⁶ have been increasingly applied to the study of human form over the last 2 decades, the use of landmarks is not sufficient because they cannot describe biologic forms and patterns.^{15,17,18} Craniofacial structural information is represented by surfaces, curves, and outlines. The sliding semilandmark method was proposed to analyze outlines extending the standard Procrustes superimposition procedure.¹⁹⁻²¹ In addition to translating, scaling, and rotating landmarks optimally, the semilandmark points are slid along the outline curve until they match as well as possible the

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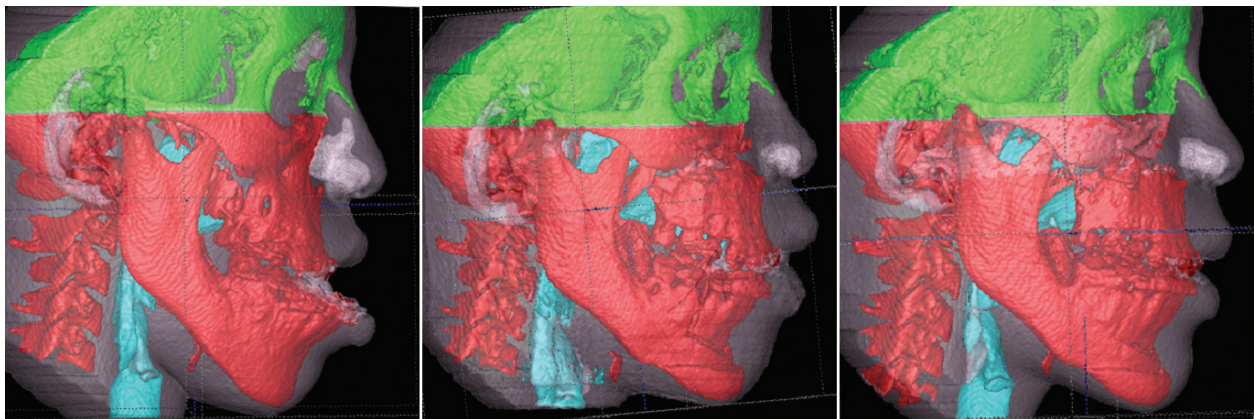


Fig 1. Construction of 3D models of a patient treated with 2-jaw surgery with visualization of color labeling of anatomic structures. **A**, Pretreatment models; **B**, 1-week postsurgery. **C**, 6-week follow-up.

positions of corresponding points along an outline in a reference configuration.²² However, semilandmarks do not include information from the whole curves and surfaces. A workable interpretive system of the biology of craniofacial growth demands the assessment of the complex cause-and-effect interactions among bones growing simultaneously, but with different timing.²³

Fortunately, 3D registration can be based on stable surfaces instead of landmarks. The purposes of this study were to determine whether 3D imaging technology can quantify soft-tissue changes, describe a method for cranial superimposition of CBCT data to accurately evaluate soft-tissue treatment outcomes, and put problems in combining other 3D imaging modalities with CBCT in perspective. We demonstrated the application of a fully automated voxel-wise rigid registration at the cranial base to evaluate 3D soft-tissue changes. Establishing this technology has been the focus of several previous studies,^{15,24-27} and our progress to date is described here.

MATERIAL AND METHODS

The steps in the process of 3D image acquisition and analysis for evaluation of facial change are the following.

Images are acquired with CBCT equipment specialized for maxillofacial imaging with a relatively low dose of radiation and a convenient way to follow changes in facial morphology in 3 dimensions for both growing and nongrowing subjects. For studies of facial changes, the CBCT scans should be acquired with a large field of view so that the entire facial anatomy can be viewed. For the subjects of our study, either the iCat (16 × 22-cm field of view; Imaging Sciences, Hatfield, Pa) or the NewTom 3G (12-in field of view; AFP Imaging, Elmsford, NY) scanner was used. The images were

reformatted²⁴ to yield a voxel size of 0.5 mm and then cropped to facilitate image analysis. Experimental protocols were approved by the institutional review board and the radiation safety committee of the University of North Carolina.

The serial CBCT images to evaluate changes over time were analyzed in a sequence of 4 steps: (1) model construction, (2) image registration, (3) transparency overlay, and (4) quantitative measurement.

Surface 3D models were constructed by using open-source software (ITK-SNAP, National Library of Medicine and National Institutes of Health, Bethesda, Md; available for free).²² A surface model of the cranial base was created for the registration in our approach (Fig 1). Construction of surface models requires the generation of an intermediate surface representation (triangular mesh) of the craniofacial structures that is different from the methods used in currently available commercial softwares that create a 3D projected view directly from the volume data (volume rendering). The surface-based method facilitates establishing boundaries between anatomic structures and assigning the proper color label and transparency values to obtain separate displays of the mandible, the maxilla, and the cranial base.

The IMAGINE software (National Institutes of Health, Bethesda, Md; available for free) was modified at the University of North Carolina and then used to mask facial structures displaced with growth or treatment, and to perform a fully automated, voxel-wise, rigid registration at the cranial base.²⁵ The registration of the cranial base uses maximization of mutual information to avoid observer-dependent techniques based on overlap of anatomic landmarks. After the software masks the maxillary and mandibular structures, it compares the gray level intensity of each voxel in the cranial base to register the 2 CBCT

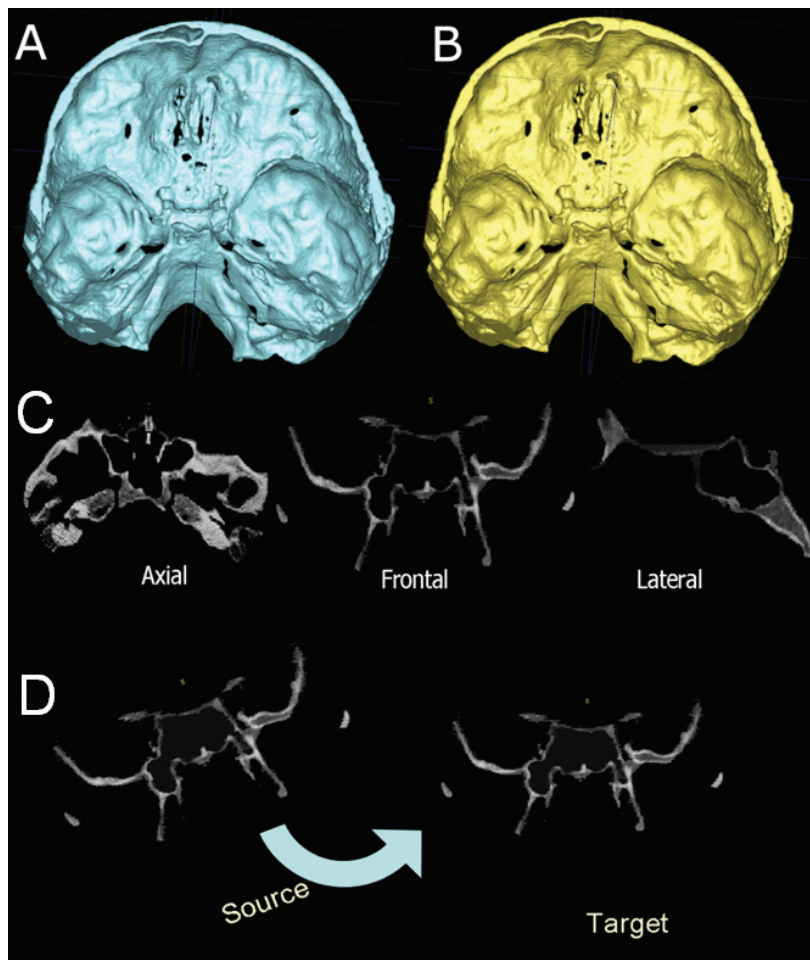


Fig 2. Anatomic structures used for superimpositions of 3D models of nongrowing subjects. **A**, Pre-treatment cranial base models; **B**, post-treatment cranial base models; **C**, the model in *B* was used to mask all anatomic structures that changed with treatment and generate a gray-level intensity image containing only the cranial fossa for calculation of registration parameters; **D**, fully automated calculation of rotational and translational parameters between the images.

images.²⁴ These rotation and translation parameters are also applied to register the 3D models. After registration, we can assess the overlay of the 3D models.

For subjects whose cranial base growth is complete, registration is done with the gray level CBCT data sets at the whole surface of the cranial base (Figs 2 and 3). The larger the surface used, the more robust the registration. For this reason, for adults, the whole cranial base surface is used for registration. For growing patients, the registration requires 2 steps. First, an initial head alignment is done by using the whole cranial base, with a finer registration at the stable structure on the anterior cranial base.²⁴

For growing subjects, there is still growth in the sphenoccipital synchondrosis, the lateral wall of the skull, and the frontal lobes and sinuses. For this

reason, the registration of the before-and-after treatment CBCT images of growing subjects requires 2 steps.²⁶ First, the head is aligned by using the whole cranial base, and then a finer registration with optimal alignment gray level CBCT data sets is performed with subvoxel accuracy at the stable structures on the anterior cranial base (IMAGINE software, Fig 3).^{15,27} This registration uses a smaller surface area that includes anterior cranial base structures that have completed growth by age 7: anterior wall of the sella, anterior clinoid processes, planum sphenoidale, lesser wings of the sphenoid, superior aspect of the ethmoid and cribriform plates, cortical ridges on the medial and superior surfaces of the orbital roofs, and inner cortical layer of the frontal bones (Fig 4).²⁸

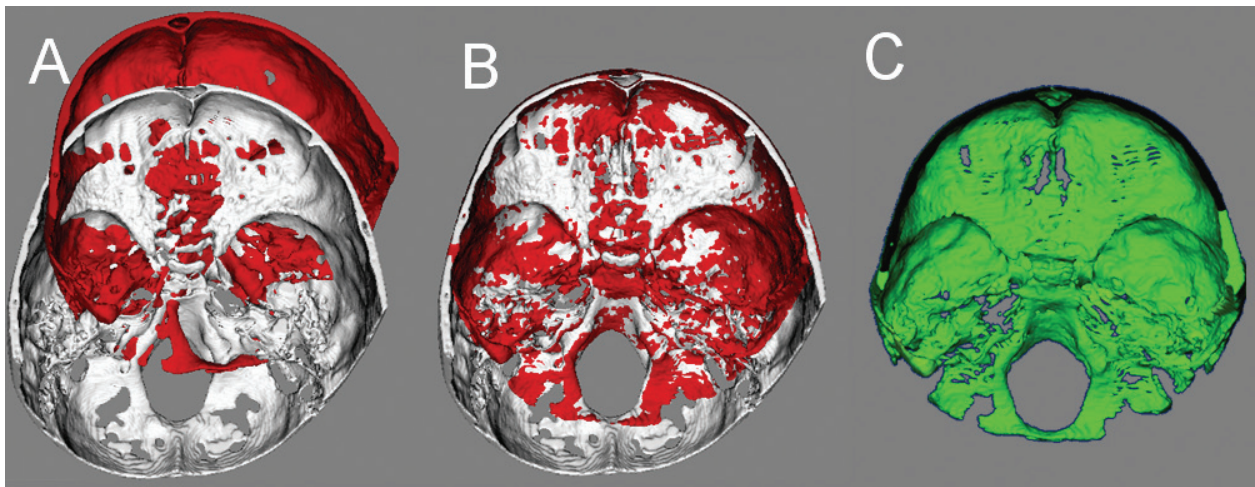


Fig 3. Cranial base matching: **A**, pretreatment cranial base model (*white*) and posttreatment cranial base model (*red*); **B**, pretreatment and posttreatment matching of the cranial base as a result of the voxel-based registration shown in Figure 2; **C**, color map of the surface distance between the registered pretreatment and posttreatment models shown at 0-mm surface distances (*green*).

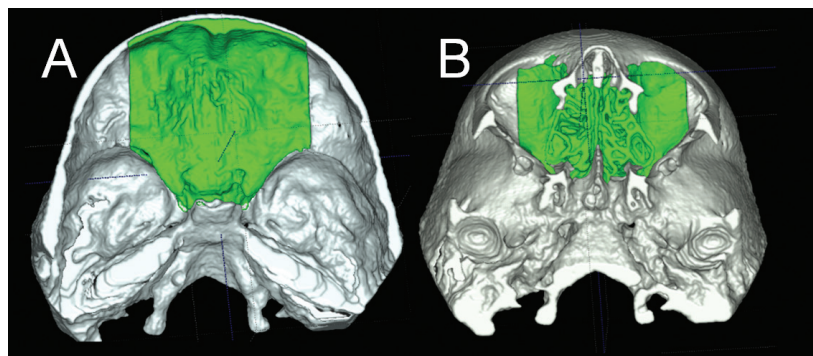


Fig 4. Anatomic structures used for superimpositions of 3D models of growing subjects. The anterior cranial fossa region of the cranial base 3D surface models after treatment was used for registration. **A**, Superior view; **B**, inferior view.

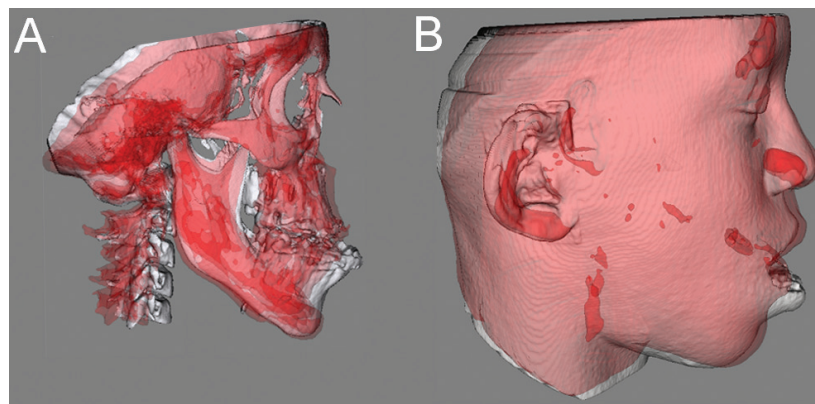


Fig 5. Transparency overlays of the patient in Figure 2. Superimposition of presurgery (*white*) and 6 weeks after 2-jaw surgery (*red*) models of nongrowing patient at the cranial base: **A**, hard-tissue changes; **B**, soft-tissue changes.

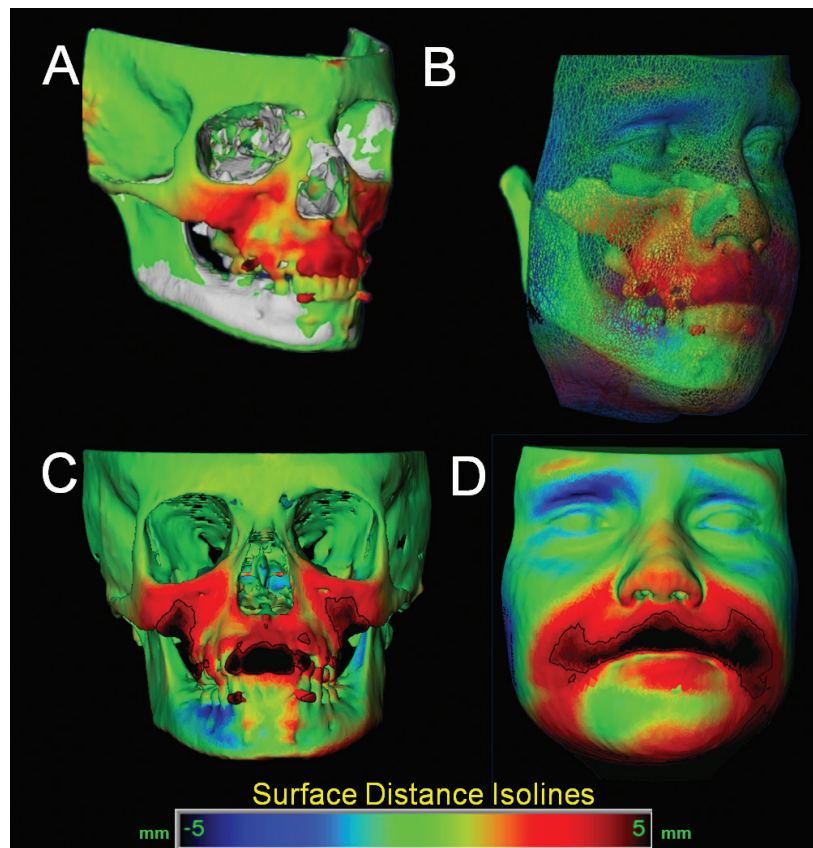


Fig 6. Quantification of soft-tissue changes: **A**, superimposed pretreatment (white) and posttreatment 3D models of the surface distance changes in a color map of the hard-tissue changes; **B**, color map for comparison of hard- and soft-tissue regional changes; **C**, isoline contours adjusted to quantify the changes in the zygomatic process of the maxilla; **D**, isoline contours adjusted to quantify the changes in the upper lip region.

Validation studies of the registrations of growing²⁶ and nongrowing²⁴ subjects have shown that maximum registrations errors are smaller than the image spatial resolution of 0.5 mm.

The next step in the analysis involves overlaying the 3D model surfaces that are registered in the same coordinate system. This is done with another tool, CMF software (Maurice Müller Institute, Bern, Switzerland).²⁹ This tool allows different degrees of transparencies to assess visually the boundaries of the soft-tissue structures between superimposed models from 2 time points. This clearly identifies the location and direction of dental, bone, and soft-tissue displacements, and allows correlation of hard- and soft-tissue changes (Fig 5).

The CMF software is then used to measure overall facial changes²⁹ and display color maps generated from closest-point distances between the surfaces as proposed by Gerig et al.³⁰ The CMF tool calculates thousands of color-coded surface distances in millimeters between before

and after treatment 3D models by using surface triangles at 2 times, so that the difference between the 2 surfaces at any location can be quantified. Isolines (contour line tool) are used to delineate and quantify surface changes for specific regions of interest, such as the nose, cheeks, upper and lower lips, and chin (Fig 6). Soft-tissue changes are described as displacements relative to the cranial base.

The quantitative changes are visualized by using color maps, which can be used to indicate inward (blue) or outward (red) displacement between overlaid structures, registered at the cranial base. An absence of changes is indicated by the green color code. For example, in mandibular advancement surgery, forward chin and lower lip displacement would be shown in a red color code; in mandibular setback surgery, lower lip and chin surfaces would be shown in the blue color code (Figs 7 and 8). This method for showing quantitative changes at many locations has been validated and used since 2005.²⁴

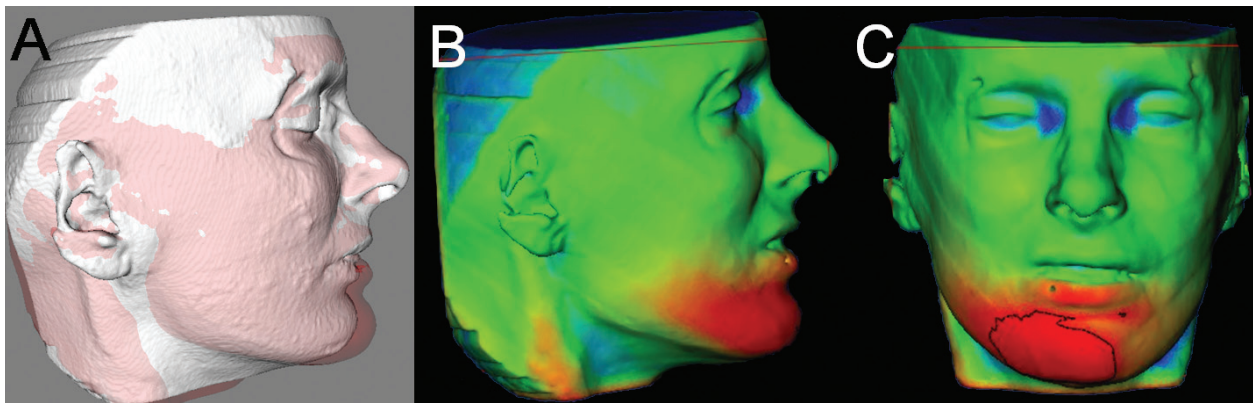


Fig 7. Soft-tissue changes 1 year after mandibular advancement surgery: **A**, transparency overlays superimposed before surgery (*white*) and 1 year after surgery (*red*); **B** and **C**, surface distance color maps of soft-tissue changes in the chin area.

DISCUSSION

Image registration is a core technology for many imaging tasks. Research efforts over the past 20 years in dentistry, medicine, and anthropology have been directed to developing 3D registration tools for quantitative assessment of facial soft and hard tissues. According to the transformation applied to the images, registration procedures can be classified into 2 main groups: rigid and nonrigid. The transformation involved in a rigid registration procedure includes translation and rotation; that of a nonrigid registration includes translation, rotation, scale, and affine properties. Rigid registration can be based on landmarks,^{15,16,31} semilandmarks,^{19-22,32-34} curves,^{35,36} planes,³⁷ surfaces,³⁸ or voxels (mutual information).^{39,40} Nonrigid registration can be based on landmarks,⁴¹ elastic models,^{42,43} fluid models,⁴⁴ splines,²⁷ and finite element models.^{45,46} The 2 obstacles to widespread clinical use of nonrigid (elastic and deformable) registration are computational cost and quantification difficulties as the 3D models are deformed. Nonrigid registration would be required to create a composite of several jaw shapes to guide the construction of template or standard, normal 3D surface models. To evaluate longitudinal changes, rigid registration is acceptable, and we used voxel-based registration on the cranial base of the before-and-after treatment CBCT images.

Although CBCT images are lower in contrast than computed tomography (CT) images, the soft and hard tissues are well visualized. Diagnostic benefit and dose detriment tradeoffs are important considerations in choosing radiographic procedures. Concern has recently been raised about the increasing numbers of CT examinations in the United States and the increased cancer risks, especially in children, from these examinations.⁴⁷ Dental CBCT can be recommended as a dose-sparing

technique compared with alternative standard medical CT scans for common oral and maxillofacial radiographic imaging tasks.⁴⁸ Until we have clear evidence for a threshold dose below which our patients are not at risk, we must assume that radiography involves a small, but real, risk to our patients. CBCT volumes also allow reconstruction of 2D panoramic, lateral, anteroposterior, and axial x-rays, eliminating the need for additional radiographic acquisitions.

Although CBCT images show the soft-tissue surfaces accurately and therefore are excellent for displaying changes from growth, aging, or treatment, 3D photographs provide additional information about color and surface texture, as well as higher resolution of soft-tissue surfaces.⁴⁹ Because of the low radiation dose, the soft tissues visualized in CBCT can have a somewhat roughened texture. Currently available software programs have tools for superimposition of 3D photographs on landmarks or surface-based regions in the soft tissues, but these soft-tissue structures are not stable enough to serve as superimposition references. The result is an unknown amount of distortion. Even though the patient “wow” factor with morphed 3D photos might be advantageous from a marketing perspective, no data validate the accuracy of the changes that are displayed to quantify them over time. It seems a desirable goal to combine CBCT and 3D photography.

There are problems in registering 3D soft-tissue photographs to CBCT soft tissues (Fig 9). For 3D photographs and CBCT images obtained at close but separate times, Maal et al⁴⁹ reported that the registration errors between 3D photographs and CBCT images were relatively large at the lateral neck and mouth, and around the eyes, with 90% to 95% of the error in the

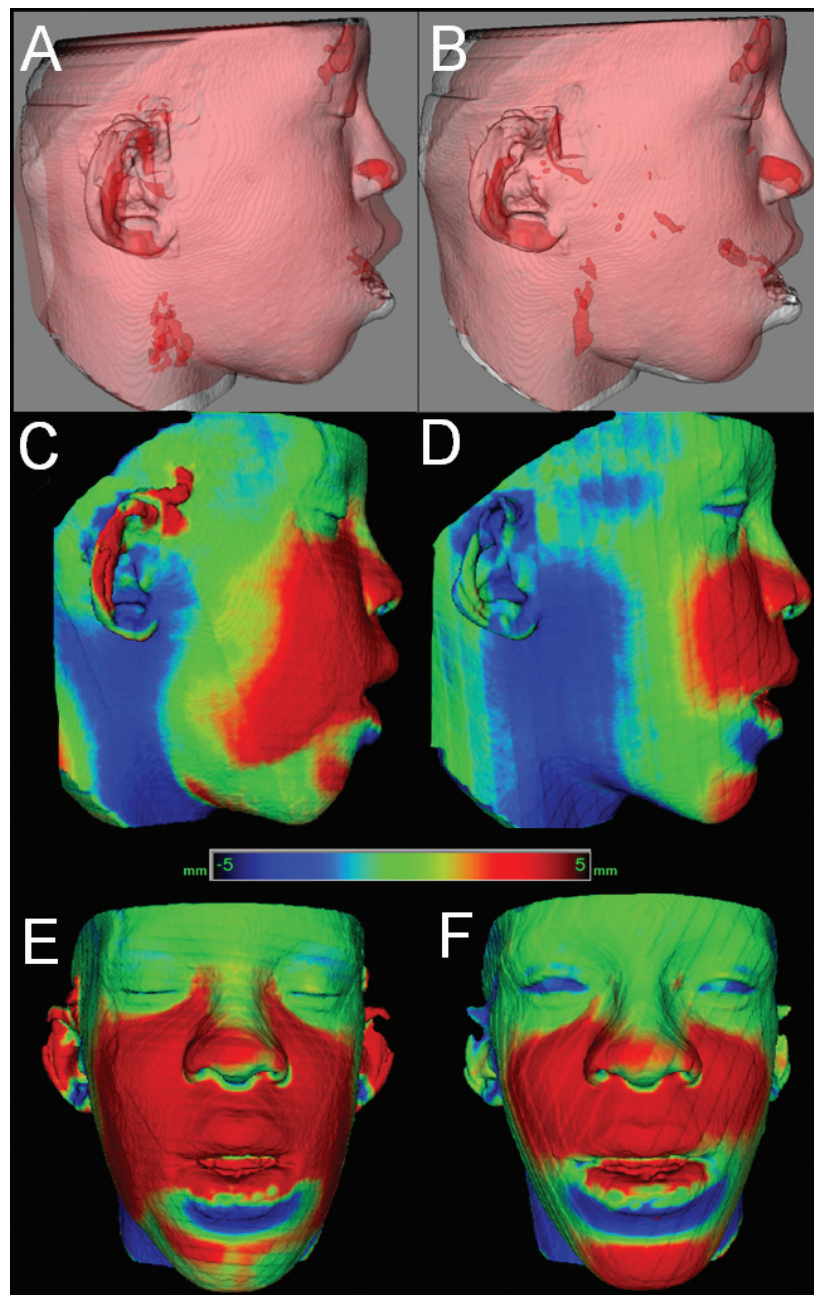


Fig 8. Differences in the assessment of soft-tissue changes 1 week and 6 weeks after maxillary advancement and mandibular subapical osteotomy: **A** and **B**, transparency overlays. **A**, Superimposition of presurgery (*white*) and 1-week postsurgery (*red*) images. **B**, Superimposition of presurgery (*white*) and 6 weeks postsurgery (*red*) images. **C-F**, Surface distance color maps of **A** and **B** superimpositions. **C** and **D**, Lateral views; **E** and **F**, frontal views. Note the 1-week postsurgery swelling and that *blue* surface distances at the neck are artifacts caused by differences in cervical positioning between the 1-week and 6-weeks 3D imaging acquisitions.

± 1.9 -mm range. Even after exclusion of artifact regions from the matching process, 90% to 95% of the error was within ± 1.5 mm. An important step toward overcoming

these problems would be simultaneous acquisition of CBCT and 3D photographs, but that is not possible now and might not be in the future. Problems that need to be

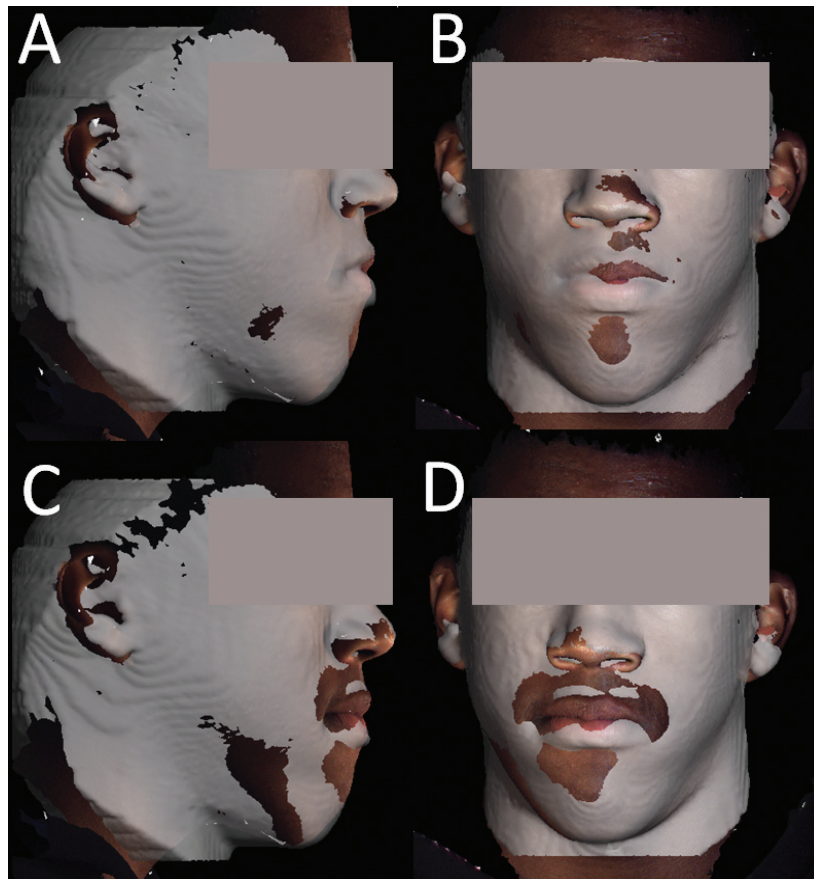


Fig 9. Differences in registration of the 3D photography to 2 CBCT images taken on the same day. **A** and **B**, First CBCT acquisition registered to 3D photograph taken the same day. **C** and **D**, Second CBCT acquisition taken the same day. Note that, even though the photograph and the CBCT surface model appear to be registered at the forehead, the contours of the lower lip, chin, and neck on the CBCT image do not match the contours of the 3D photograph because of subtle differences in facial expression and head posture.

overcome with 3D photograph superimposition include (1) inadequate use of fiducials, (2) head position in acquisition, (3) soft-tissue capture errors, and (4) current use of nonrigid registration deformation of soft-tissue contours to allow matching of 3D photographs to CBCT soft tissues.

Until CBCT and 3D photographs can be acquired simultaneously, the use of fiducials for both CBCT and 3D photograph acquisition can decrease errors because of the choice of surface regions or landmarks, but fiducials cannot control for soft-tissue distortions caused by head positioning, different facial expressions, and artifacts during image acquisition.¹³ For example, if the patient's head is turned upward during either the CBCT or the photograph acquisition, the neck and perioral soft tissues are stretched, and this cannot be corrected by registration on the fiducials.

For CBCT acquisition, patients' heads are usually held in a fixed position with a strap on the forehead, a chin support, or both, or they are lying down, depending on the scanner. To minimize deformation of soft tissues around the mouth, the chin support should be avoided. Because a strap on the forehead causes errors in the forehead region from small soft-tissue deformations, this should also be avoided if possible. There is currently no standardization of head position during CBCT and 3D photograph acquisition.¹³ Differences in head position between the CBCT and 3D photograph acquisitions result in registration errors, which are greatest in the neck region, but, as Maal et al⁴⁹ noted, relatively large elsewhere in the face.

Registration errors also result from errors in the capture of soft-tissue surfaces in both CBCT and stereophotogrammetry imaging. With CBCT, the soft-tissue surface can appear roughened because of the low radiation

dose. With stereophotogrammetry, it is impossible to capture the eye region correctly, because the light pattern used to reconstruct a 3D photograph interferes with light reflection in the lenses of the eyes.⁴⁹

In a rigid registration algorithm, only translational and rotational movements are allowed as the data sets are fused. To register the textured surface of a 3D photograph to the untextured surface of a CBCT image, rigid registration of the surfaces frequently is not sufficient. This can be due to the rougher surface of the CBCT image, different facial expressions during the 2 acquisitions at separate times, or acquisition artifacts.

A possible solution is the use of nonrigid registration algorithms, which allow deformational movements of the surface as well. Unfortunately, these algorithms deform the images and contribute to errors rather than remove them. At present, they should be avoided.

Registration tools using "best fit" between 3D renderings, landmarks, or surfaces that have changed with time do not allow quantification of local changes, and this can lead to misleading interpretations of changes (Fig 7). The superimposition methods we studied not only allow visualization, but also provide precise localization of the soft-tissue growth and adaptation to skeletal changes.

Although it seems reasonable that a combination of data from 3D photographs and CBCT would be better than either method alone, the added value of 3D photographs still needs to be assessed in carefully controlled studies. The superimposition methodology presented here allows quantification of soft-tissue surface changes from any 3D data set, but its application to other imaging modalities such as laser scanners and 3D cameras requires registration to the CBCT data sets. This would require either simultaneous acquisition of the photograph and the CBCT images or standardization of head position with calibration of the CBCT and 3D camera acquisition parameters. Because of recent technological advances in imaging, there is now the promise that many if not most criteria for an ideal standardized record of the relationship between the soft-tissue facial mask and the underlying skeletal and dental structures can be met. The potential in the future for melding 3D facial photography with CBCT could provide a record that is 3D, easily obtained, able to capture facial and dental display, is measurable, and can be used as a longitudinal record. From a clinical diagnostic standpoint, the record will depict all soft- and hard-tissue structures with 6 degrees of freedom.

We are applying the methodology presented here to research in progress. Currently, superimposition of 3D surface models is still too time-consuming and computing-intensive to apply these methods routinely. Our

current focus is on developing a simplified analysis so that these methods can soon be used clinically. This approach to 3D image-analysis methods has been streamlined and continuously updated with new methods for quantification, with collaboration from the Maurice Müller Institute, and the University of North Carolina medical image analysis group, neuroimaging laboratory, and the statistical modeling group in the Biomedical Research Imaging Center.

REFERENCES

1. Tessier P. Subperiosteal face-lift. *Ann Chir Plast Esthet* 1989;34:193-7.
2. Ackerman JL, Proffit WR. Soft tissue limitations in orthodontics: treatment planning guidelines. *Angle Orthod* 1997;67:327-36.
3. Ackerman JL, Proffit WR, Sarver DM, Ackerman MB, Kean MR. Pitch, roll, and yaw: describing the spatial orientation of dentofacial traits. *Am J Orthod Dentofacial Orthop* 2007;131:305-10.
4. Aldridge K, Boyadjiev SA, Capone GT, DeLeon VB, Richtsmeier JT. Precision and error of three-dimensional phenotypic measures acquired from 3dMD photogrammetric images. *Am J Med Genet A* 2005;138A:247-53.
5. Ayoub AF, Xiao Y, Khambay B, Siebert JP, Hadley D. Towards building a photo-realistic virtual human face for craniomaxillofacial diagnosis and treatment planning. *Int J Oral Maxillofac Surg* 2007;36:423-8.
6. Goos MI, Alberink IB, Ruifrok AC. 2D/3D image (facial) comparison using camera matching. *Forensic Sci Int* 2006;10;163:10-7.
7. Sawyer AR, See M, Nduka C. 3D Stereophotogrammetry quantitative lip analysis. *Aesthetic Plast Surg* 2009;33:497-504.
8. Weinberg SM, Naidoo S, Govier DP, Martin RA, Kane AA, Marazita ML. Anthropometric precision and accuracy of digital three-dimensional photogrammetry: comparing the Genex and 3dMD imaging systems with one another and with direct anthropometry. *J Craniofac Surg* 2006;17:477-83.
9. Nishii Y, Nojima K, Takane Y, Ishiki Y. Integration of the maxillofacial three-dimensional CT image and the three-dimensional dental surface image. *J Jpn Orthod Soc* 1998;57:189-94.
10. Terai H, Shimahara M, Sakinaka Y, Tajima S. Accuracy of integration of dental casts in three-dimensional models. *J Oral Maxillofac Surg* 1999;57:662-5.
11. Kau CH, Cronin AJ, Richmond S. A three-dimensional evaluation of postoperative swelling following orthognathic surgery at 6 months. *Plast Reconstr Surg* 2007;119:2192-9.
12. Kau CH, Richmond S, Savio C, Mallorie C. Measuring adult facial morphology in three dimensions. *Angle Orthod* 2006;76:773-8.
13. Hajeer MY, Millett DT, Ayoub AF, Siebert JP. Applications of 3D imaging in orthodontics: part II. *J Orthod* 2004;31:155-62.
14. Curry S, Baumrind S, Carlson S, Beers A, Boyd R. Integrated three-dimensional craniofacial mapping at the Craniofacial Research Instrumentation Laboratory/ University of the Pacific. *Semin Orthod* 2001;7:258-65.
15. Cevidanes LH, Franco AA, Gerig G, Proffit WR, Slice DE, Enlow DH, et al. Assessment of mandibular growth and response to orthopedic treatment with 3-dimensional magnetic resonance images. *Am J Orthod Dentofacial Orthop* 2005;128:16-26.
16. Rohlf FJ, Marcus LE. A revolution in morphometrics. *TREE* 1993;8:129-32.

17. Oxnard CE. One biologist's view of morphometrics. *Ann Rev Ecol Syst* 1978;9:219-41.
18. Moyers RE, Bookstein FL. The inappropriateness of conventional cephalometrics. *Am J Orthod* 1979;75:599-617.
19. Green WDK. The thin-plate spline and images with curving features. In: Mardia KV, Gill CA, Dryden IL, editors. *Image fusion and shape variability*. Leeds, United Kingdom: University of Leeds Press; 1966. p. 79-87.
20. Bookstein FL. Applying landmark methods to biological outline data. In: Mardia KV, Gill CA, Dryden IL, editors. *Image fusion and shape variability*. Leeds, United Kingdom: University of Leeds Press; 1966. p. 59-70.
21. Bookstein FL. Landmark methods for forms without landmarks: localizing group differences in outline shape. *Med Image Anal* 1997;1:225-43.
22. Adams DC, Rohlf FJ, Slice DE. Geometric morphometrics: ten years of progress following the 'revolution'. *Ital J Zool* 2004;71:5-16.
23. Enlow D. Discussion. *Am J Orthod Dentofacial Orthop* 2000;117:147. In: Takada K, Sorihashi Y, Stephens CD, Itoh S. An inference modeling of human visual judgment of sagittal jaw-base relationships based on cephalometry: Part I. 2000;117:140-7.
24. Cevidanes LH, Bailey LJ, Tucker GR Jr, Styner MA, Mol A, Phillips CL, et al. Superimposition of 3D cone-beam CT models of orthognathic surgery patients. *Dentomaxillofac Radiol* 2005;34:369-75.
25. Yushkevich PA, Piven J, Hazlett HC, Smith RG, Ho S, Gee JC, et al. User guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *Neuroimage* 2006;31:1116-28.
26. Cevidanes LHS, Heymann G, Cornelis MA, DeClerck HJ, Tulloch JF. Superimposition of 3-dimensional cone-beam computed tomography models of growing patients. *Am J Orthod Dentofacial Orthop* 2009;136:94-9.
27. Rueckert D, Sonoda LI, Hayes C, Hill DLG, Leach MO, Hawkes DJ. Nonrigid registration using free-form deformations: application to breast MR images. *IEEE Trans Med Imaging* 1999;18:712-21.
28. Melsen B. The cranial base. The postnatal development of the cranial base studied histologically on human autopsy material. *Acta Odontol Scand* 1974;32(Suppl 62):86-101.
29. Chapuis J, Schramm A, Pappas I, Hallermann W, Schwenzer-Zimmerer K, Langlotz F, et al. A new system for computer-aided preoperative planning and intraoperative navigation during corrective jaw surgery. *IEEE Trans Inf Technol Biomed* 2007;11:274-87.
30. Gerig G, Jomier M, Chakos M. Valmet: a new validation tool for assessing and improving 3D object segmentation. In: Niessen W, Viergever M, editors. *MICCAI 2001: Proceedings of the International Society and Conference Series on Medical Image Computing and Computer-Assisted Intervention*; 14-17 Oct 2001. Utrecht, Netherlands. Berlin: Springer; 2001. p. 516 -28.
31. Rohr K. Landmark-based image analysis: using geometric and intensity models. *Computational imaging and vision series*. Volume 21. Dordrecht, Boston, London: Kluwer Academic Publishers; 2001.
32. Andresen R, Bookstein FL, Conradsen K, Ersboll BK, Marsh JL, Kreiborg S. Surface-bounded growth modeling applied to human mandibles. *IEEE Trans Med Imaging* 2000;19:1053-63.
33. Gunz P, Mitteroecker P, Bookstein FL. Semilandmarks in three dimensions. In: Slice DL, editor. *Modern morphometrics in physical anthropology*. New York: Kluwer Academic/Plenum Publishers; 2005.
34. Perez SI, Bernal V, Gonzales PN. Differences between sliding semi-landmark methods in geometric morphometrics, with an application to human craniofacial and dental variation. *J Anat* 2006;208:769-84.
35. Subsol G, Thirion JP, Ayache N. A scheme for automatically building three-dimensional morphometric anatomical atlases: application to a skull atlas. *Med Image Anal* 1998;2:37-60.
36. Subsol G, Roberts N, Doran M, Thirion JP, Whitehouse GH. Automatic analysis of cerebral atrophy. *Magn Reson Imaging* 1997;15:917-27.
37. Baumrind S, Moffitt FH, Curry S. The geometry of three-dimensional measurement from paired coplanar x-ray images. *Am J Orthod* 1983;84:313-22.
38. Thompson PM, MacDonald D, Mega MS, Holmes CJ, Evans AC, Toga AW. Detection and mapping of abnormal brain structure with a probabilistic atlas of cortical surfaces. *J Comput Assist Tomogr* 1997;21:567-81.
39. Maes F, Collignon A, Vandermeulen D, Marchal G, Suetens P. Multimodality image registration by maximization of mutual information. *IEEE Trans Med Imaging* 1997;16:187-98.
40. Swennen GR, Mollemans W, De Clercq C, Abeloos J, Lamoral P, Lippens F, et al. A cone-beam computed tomography triple scan procedure to obtain a three-dimensional augmented virtual skull model appropriate for orthognathic surgery planning. *J Craniofac Surg* 2009;20:297-307.
41. Crum WR, Hartkens T, Hill DL. Non-rigid image registration: theory and practice. *Br J Radiol* 2004;77(Special number 2):S140-53.
42. Rohr K, Stiehl HS, Sprengel R, Beil W, Buzug TM, Weese J, et al. Point-based elastic registration of medical image data using approximating thin-plate splines. In: Hohne K, Kikinis R, editors. *Proceedings of the 4th International Conference on Visualization in Biomedical Computing*, 22-25 Sep, 1996. Hamburg, Germany. Lecture Notes in Computer Science. Volume 1131. Berlin: Springer-Verlag; 1996. p 297-306.
43. Bajcsy R, Kovacic S. Multiresolution elastic matching. *Comp Vis Graph Image Proc* 1989;46:1-21.
44. Christensen GE, Rabbitt RD, Miller MI. Deformable templates using large deformation kinematics. *IEEE Trans Image Processing* 1996;5:1435-47.
45. Hajnal JV, Hill DLG, Hawkes DJ, editors. *Medical image restoration*. Boca Raton, Fla: CRC Press; 2001.
46. Shenton ME, Gerig G, McCarley RW, Szekely G, Kikinis R. Amygdala-hippocampal shape differences in schizophrenia: the application of 3D shape models to volumetric MR data. *Psychiatry Res* 2002;115:15-35.
47. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. *N Eng J Med* 2007;357:2277-8.
48. Ludlow J, Ivanovic M. Comparative dosimetry of dental CBCT devices and 64-slice CT for oral and maxillofacial radiology. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008;106:106-14.
49. Maal TJ, Plooi JM, Rangel FA, Mollemans W, Schutyser FA, Bergé SJ. The accuracy of matching three-dimensional photographs with skin surfaces derived from cone-beam computed tomography. *Int J Oral Maxillofac Surg* 2008;37:641-6.