Objectifying Micrognathia Using 3D Photogrammetric Analysis: a pilot-study.

Hanneke Basart, MD, PhD[1,2], Michael Suttie, MSc[3], Amel Ibrahim, MD[4], Patrizia Ferretti, PhD[4], Chantal M.A.M. van der Horst, MD, PhD[1], Raoul C. Hennekam, MD, PhD[2*], Peter Hammond, PhD[3*]

[1] Department of Plastic and Reconstructive Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

[2] Department of Pediatrics, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

[3] Big Data Institute and Nuffield Department of Obstetrics and Gynecology, University of Oxford, Oxford, United Kingdom

[4] UCL Great Ormond Street Hospital Institute of Child Health, University College London, London, United Kingdom

*These authors contributed equally to this study

Corresponding author: Dr RC Hennekam, Department of Pediatrics, Room H7-236, Academic Medical Center, Meibergdreef 9, 1105AZ Amsterdam, Netherlands. Phone +31 20 566 8844. Fax : +31205669683. Email r.c.hennekam@amc.uva.nl

ABSTRACT

Background: Micrognathia occurs isolated and as part of entities like Robin sequence (RS). An objective measurement of mandible size and growth is needed to determine the degree of micrognathia and enable a comparison of treatment outcomes. We undertook a pilot study to investigate the usability of 3D facial photogrammetry, a fast, non-invasive method, to estimate mandible size and growth in a small cohort of newborns and infants.

Methods: We estimated *exterior* mandibular volume using a tetrahedron defined by four facial landmarks. We selected 12 patients with RS with different etiologies and obtained photogrammetric images prospectively in three patients with RS in whom mandibular growth in the first year of life was determined. We used three tetrahedra defined by six landmarks on mandibular CT scans to estimate an *interior* mandibular volume, which we compared to the exterior mandibular volume in 10 patients.

Results: The exterior mandibular volume using 3D photography could be determined in all patients. Signature heat maps allowed visualization of facial dysmorphism in three dimensions; signature graphs demonstrated similarities of facial dysmorphism in patients with the same etiology and differences from those with other diagnoses and from controls. The correlation between interior (3D photogrammetry) and exterior mandibular volumes (CT imaging) was 0.8789.

Conclusion: 3D facial photogrammetry delineates the general facial characteristics in patients with different syndromes involving micrognathia, and can objectively estimate mandibular volume and growth, with excellent correlation with bony measurement. We conclude that 3D facial photogrammetry could be a clinically effective instrument for delineating and quantifying micrognathia.

Key Words:

Micrognathia

3D Photogrammetry

3D Facial scanning

Robin Sequence

Mandibular volume

CT imaging

INTRODUCTION

The combination of micrognathia and glossoptosis in a neonate is called (Pierre) Robin Sequence (RS). The co-existence of these signs typically causes upper airway obstructions, which result in respiratory and feeding problems of varying severity. A cleft palate is present in the majority of RS patients (1-2). In 66% of the patients, RS is part of a more extended syndrome or accompanied by other abnormalities (3-4).

Various protocols are available for the management of newborns with RS, each having its benefits and disadvantages (5). To compare management strategies and outcomes, objective criteria for the presence and degree of micrognathia are required. Several options are available to measure mandibular size after birth, of which lateral cephalometry, low-dose multi-slice or cone beam Computed Tomography (CT) scanning, and the Jaw Index are the most important ones. A protocol for (2D-)cephalometry was described by Pruzansky and Richmond in 1954 (6), in which lateral cephalographs of infants and adolescents are studied for mandibular size and the effect of craniofacial growth in patients with RS. However, this technique has the disadvantages of radiation exposure and difficulties in accurately positioning and immobilizing an infant for lateral skull radiography. CT scans can provide a clear three-dimensional image of the mandible and detailed measurements of its size, but normative CT data for various populations are lacking, and, as in cephalometry, the radiation exposure and need for positioning and immobilizing the infant prevent routine use. The Jaw Index is determined by measurement of the child with tape and caliper and subsequently calculation of the index of the distance between the alveolar processes of upper and lower jaw (overbite) compared to the distance between the left and right tragus over the subnasal point (upper arch) and the same distance over the pogonion point (lower arch) (7). In principle, these measurements are simple and could be used by a broad range of health professionals such as physicians, midwives, and nurses. Significant disadvantages are the relative inaccuracies of manual measurement, absence of adequate intra-observer and inter-observer validations, and absence of reference values for populations of various ethnic backgrounds.

3D facial photogrammetry is a fast, harmless and non-invasive way of imaging the complete face (8). It enables accurate, objective measurement of facial morphological characteristics and facilitates comparisons of individuals of all ages. A small number of homologous facial landmarks can be used to register a set of 3D facial surfaces and produce a dense surface model (DSM) of face shape variation of the densely corresponded surface points. In such a DSM, each constituent face surface can be resynthesized in terms of a weighted sum of derived principal components. Similarity between the face shape of two individuals or two groups is computed as the square root of the sum of squares of differences of the DSM weightings for the individuals or the group means. For an individual face, we refer to the set of normalized displacements of the corresponded vertices relative to the mean of a group as its face signature (9). This technique can be applied to the DSM representation of faces to delineate discriminating shape differences between controls and individuals with dysmorphic syndromes (10). Therefore, we hypothesized it would be an excellent tool to support diagnosis and screening in the heterogeneous group of entities that involve micrognathia.

Here, we present a pilot-study describing the use of 3D facial photogrammetry and dense surface modelling to measure facial characteristics in general in an objective manner in a small, selected group of RS patients of variable age and etiology. We propose a technique to estimate the size of the mandible in an objective manner. We describe an objective method to determine the size of the mandible using CT scanning images, and compare results of measurements using both 3D facial imaging and CT scanning in the same individuals. Thus, we have demonstrated how 3D photogrammetry can provide a practical technique to measure mandibular growth over time.

MATERIAL AND METHODS

Participants

The participants for the present study were chosen from a cohort of 61 RS patients followed in the Academic Medical Centre in Amsterdam. A detailed description of the cohort can be found elsewhere (3). RS patients with an existing outpatient appointment were contacted and invited to participate in the study. Facial 3D scanning is performed as part of standard care in patients with RS. For the present pilot study, we selected images of 4 patients with isolated RS, 4 patients with Stickler syndrome (the most common

Mendelian disorder involving RS), and 4 patients in whom the RS was part of a syndrome (Femoral Hypoplasia Unusual Facies Syndrome, Cornelia de Lange-like syndrome caused by a *RAD21* mutation, and Schillbach-Rott syndrome in 2 patients). The diagnoses in all study participants had been reliably confirmed in a separate study (3). For the prospective pilot study of mandibular growth, we selected the 3D facial photographs of one patient with isolated RS, one with Stickler syndrome and one with Treacher Collins syndrome in whom we obtained four images with an interval of approximately 3 months in the first year of life. As controls, we gathered images from unaffected relatives of individuals with chromosome anomalies or individuals with de novo autosomal dominant disorders, and from students and other volunteers gathered from meetings specifically set-up to gather control images. Controls originate from both the Netherlands and the UK. For CT scanning, the controls retrieved from a pre-existing control dataset that was part of a study of Treacher Collins syndrome (11).

3D facial scanning technique and analysis

Image capture was performed using a commercial photogrammetric camera (Canfield Imaging System, Inc., U.S.A.). Young children (<3years of age) sat on the lap of one of their parents or caretakers during the image capture, while older children and adults sat on a chair unaided. The picture is taken with the mouth in a neutral position. All images subsequently received a numerical code for privacy reasons before further analysis.

Analysis was performed as published before (8). One single person (PH) annotated all images manually with 22 3D-landmarks, previously validated for accuracy and reproducibility (12). For the annotation and building of DSMs, software developed in-house was used (13-14). The face signatures, i.e. face shape differences normalized against age, ethnicity and sex matched controls, of all participants in the pilot study were compared to one another with respect to similarity as described before (9).

We developed a measure to estimate mandibular size. We reasoned this measure should incorporate the size of the mandible in both the anterior-posterior and the cranial-caudal directions, as both are important in offering space to the tongue to allow unobstructed respiration. Using region bounding landmarks of otobasion inferior (ear), labium inferius (lip2), and gnathion (gn) (Figure 1a), both the volume and surface area of the mandible can be objectively estimated. The corresponding face surface area measurement will be influenced by subcutaneous tissue. The corresponding tetrahedron volume measurement is defined by points that are hardly influenced by subcutaneous tissue, and represents the bony structures of the mandible more closely. We used the volume of the tetrahedron demarcated by the lines linking the defining landmarks. If marked asymmetry is present in a patient's mandible, which occurs in entities that involve micrognathia such as oculo-auriculo-vertebral (Goldenhar) syndrome, one can also determine the size and growth on each side of the mandible separately. We have named this tetrahedral mandibular volume, realizing it is a correlate of the true mandibular volume only.

Mandibular intraoral volume estimated from the CT images

Six landmarks were placed manually by the same individual who landmarked the 3D photographs (PH) on each mandible surface. The wedge formed by these landmarks approximates the intraoral volume contained by the mandible (Figure 1b). Its volume is computed as the sum of three constituent tetrahedra. More information on these calculations can be found in a supplementary document.

RESULTS

Patient characteristics

The main characteristics of the 16 participating patients are provided in Table 1. Of four isolated patients, 4 Stickler patients and 4 patients with other syndromes, one 3D facial image was available for each patient, and in addition 4 images in the first year of life were obtained of 2 isolated patients, one with Stickler syndrome and one with Treacher Collins syndrome.

RS patients with different aetiology

The face signature is visualized as a colour heat map using red/green/blue to depict surface contraction/coincidence/expansion respectively relative to a matched mean in the normalized comparison. The extremes of the red-blue heat map scale are “less than –3” and “greater than +3” standard deviations respectively. As expected, the signature heat maps of the 4 patients with isolated RS show differences from one another, as the aetiology of isolated RS is markedly heterogeneous. In Figure 1c, a signature graph connects the most similar signature heat maps of 4 patients with isolated RS, 4 with Stickler syndrome, 4 with one of the other syndromes, and a small group of controls. It contains sub clusters that demonstrate the similarity of the facial dysmorphism of the 4 individuals with the same entity (Stickler syndrome) and differences for the isolated RS patients and those with other syndromes. In addition, the differences in facial dysmorphism between the patients with different syndromes are well delineated. In the facial signature graph, the RS patients are outliers at the periphery with the least dysmorphic controls placed more centrally. The spontaneous growth of the mandibular volume over time in three patients with RS is depicted in Figure 1d.

Facial growth in RS patients in the first year of life

Figure 2 shows the signature heat maps of isolated RS and Stickler syndrome patients from different ages. The severity of mandibular underdevelopment is different and does not seem age dependent in these patients. Also it demonstrates the changes over time in the heat maps of a single patient with isolated RS, Stickler syndrome and Treacher Collins syndrome. The gradual growth of the mandible over time is clearly visible in the isolated RS and the Stickler syndrome patient, while the underdevelopment of the malae is also well delineated. In the Treacher Collins patient, no large facial changes seem to appear in the heat map.

The mandibular volume growth of the isolated patient seems to be comparable to the control group. The mandibular volume of the Treacher Collins patients follows a similar growth rate as the controls, but remains very low and does not seem to show catch-up growth. In contrast, the Stickler patient possibly does show catch-up growth with a somewhat steeper ascending growth trajectory (Figure 1d).

Correlation between the mandible volume estimates based on the 3D facial photograph and CT image

The correlation between the mandibular volume derived from the 3D facial photograph (Face estimate) and derived from the bony tissue using CT imaging (Mandible estimate) performed each time in the same individual was 0.8789 (Figure 3).

DISCUSSION

The present pilot-study demonstrates the usability of 3D facial photogrammetry and analysis to objectify facial signs when using various entities that involve RS. Heat maps enable visualization of facial comparisons of the RS patients to controls in all three dimensions at a glance. Signature graphs enable visualization of the degree of similarity of facial dysmorphism of RS patients with differing pathogeneses. Signature graphs combining patients and controls delineate the relative degree and location of facial dysmorphism of different RS pathologies to each other and to controls. These different ways of depicting facial dysmorphism are useful both for research and for patient care.

Mandibular size can be easily and objectively estimated using tetrahedral mandibular volume as a sign. The absolute mandibular size can be compared to normal values and small changes over time can be objectively determined. The mandibular volume determined by 3D facial photogrammetry shows an excellent correlation with the mandibular volume determined by CT imaging. This correlation is determined in this pilot study for a small number of study participants, and needs confirmation in a larger population. Due to the radiation exposure ethically CT scanning of the face to obtain the mandibular bony volume will only be allowed if the scanning is indicated for patient care, and it will take time to obtain these.

The normal values we have used in the present pilot study were obtained from Caucasian controls from both the Netherlands and the UK. We realize that there are differences between our patients and individuals from the UK (15), but we lack sufficient controls to allow for normal values from each of these countries separately. At present it remains unknown, however, whether the mandibular volume differs significantly between the two populations, as the previous study did not address all facial characteristics (15). The number of controls is still relatively small (n=387) for taking both age and gender into account, and therefore the comparison with controls should be used with caution. We have initiated a study to obtain a sufficiently large number (n>1,000) of individuals from the Netherlands in infancy and childhood. In particular, 3D facial images of infants below 1 year of age are lacking, while these are needed to determine normal growth of the mandible over time at this age. Fortunately, the change in mandibular volume over time is not dependent on the availability of normal values and for our current aims 3D facial analysis is already usable. Recent developments in camera technology, for example based on smart phone and tablet, will support inexpensive and rapid capture of 3D facial images (16).

We conclude that 3D facial photogrammetry can be used to determine general facial characteristics and mandibular volume in an objective manner. Changes over time within a patient and comparisons between patients can be determined reliably. Comparisons with normal values will need image acquisition, especially in the first year of life. Three-D facial photogrammetry will be helpful in objectively diagnose the degree of micrognathia in patient care, predict the risk for respiratory issues, and allow for comparisons of outcomes of various management modalities. Eventually , this should yield an improved quality of care.

DECLARATIONS

Financial disclosure

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Competing interests

All authors declare that there is no conflict of interest and that there are no financial or personal relationships with other people or organizations that could inappropriately influence this work.

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Ethics approval

The Medical Ethics Committee of the Academic Medical Centre in Amsterdam had approved the study (W13_076# 13.17.0096).

Consent for to participate and publication

All participants and parents or caretakers gave informed consent for publication.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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CAPTIONS TO ILLUSTRATIONS

Figure 1. Facial 3D-landmarks. The Landmarks 4 (labium inferius), 2 (gnathion) and 1/3 (otobasion inferior) define the tetrahedron (1,2,3,4). The volume of the tetrahedron is calculated as (1/6)* det (a_x a_y a_z 1; b_x b_y b_z 1; c_x c_y c_z 1; d_x d_y d_z 1).

Figure 1b. CT-scan landmarks. Landmarks used to calculate mandible estimate: 1 (most inferior midline point to the spinae mentalis), 2/3 (inferior tip of pterygoid tuberosity), 4 (most superior point on symphysis lingually), and 5/6 (most prominent point of the head of the mandibular condyle). The mandibular volume is estimated as the sum of the volumes of tetrahedron (5,4,6,1) + tetrahedron (5,2,6,1) + tetrahedron (2,3,6,1).

Figure 1c. Facial Signature Graph of 16 Patients with Robin Sequence Compared to a Control Group (n=387). Please note that patients with the same entity group together, and RS patients are located outside the normal range. As number of controls for age and gender are small the present controls are shown only as illustration and no statistical analysis has been performed.

Figure 1d. Spontaneous Change over Time of Mandibular Volume of three RS patients (one isolated RS, one Stickler syndrome, one Treacher Collins syndrome).

Figure 2. Signature heat-maps of RS patients. A. Four different patients with isolated RS at different ages. B. Four different Stickler syndrome patients at different ages. C. One patient with isolated RS at different ages. D. One Stickler syndrome patients at different ages. E. One Treacher Collins syndrome patient at different ages.

Figure 3. Correlation between the Mandibular Volume determined by 3D Facial Photogrammetry and by CT imaging, each time performed in the same individual.