Craniofacial anomalies and three-dimensional imaging modalities with reference to the Egyptian experience

Mennat Mehrez[a], Tarek ElBadry[a], Amany Nemat[b], Mona El Batran[c], Nadia Soliman[c], Eman AboulEzz[c]

[a]Department of Oro-Dental Genetics, Human Genetics and Genome Research Division Departments of [b]Oral Surgery [c]Basic Dental Science, Dental Research Division, National Research Center, Cairo, Egypt

Correspondence to Mennat Mehrez, BSc, MSc, DDS, Associate Professor of Oro-dental genetics, Oro-Dental Genetics Department, Human Genetics and Genome Research Division National Research centre, Cairo, Egypt
Tel: +20 1094614657
e-mail: mehrezmi@outlook.com

Received 03 June 2021
Revised 05 August 2021
Accepted 05 August 2021
Published 09 October 2021

Middle East Journal of Medical Genetics
2021,10:8–12

Craniofacial anomalies are defined as the abnormalities in this anatomical area. It could be due to genetic causes or environmental ones. Broadly, they can be clefts, craniosynostoses, craniofacial microsomia, midline defects, eye, ear, jaw, dental, and vascular malformations.
Due to the complexity of the head and neck anatomy, they are best visualized using three-dimensional (3D) imaging technologies. This impacts the diagnosis of disorders and can even change it at some instances.
Treatment planning using 3D imaging modalities as well as interventions, particularly with the advent of computer-aided design/computer-aided manufacturing and 3D printing technologies, have considerably impacted the outcome of maxillofacial surgeries or orthodontic rehabilitation. It is safe to say that they left nothing to the imagination during surgeries, provided you have the indicated technique for the case.
Finally, the Egyptian experience was found to be full of novel techniques utilizing these modalities, particularly in diagnosis, treatment, and follow-up, yet the number of studies was scanty and the fact that craniofacial anomalies are rare makes it mandatory to go for multicenter studies. This review recommends that these studies start by 3D morphometric measurements of the Egyptian head using 3D technologies in all governorates.

Keywords:
Anomalies, Craniofacial, 3D imaging, syndromes

Middle East J Med Genet 10:8–12

2090-8571

Introduction

Craniofacial anomalies (CFAs) are a wide and versatile group of abnormalities that occur in this anatomical area, as defined by the WHO in their report on the registry and database of CFAs. They added that they can be classified according to pathogenesis to include malformations, deformations, disruptions, and dysplasias, or according to etiology, which could be genetic or environmental or both. Furthermore, they can be clinically categorized into isolated CFAs, syndromic or sequences (Mossey and Castilla, 2003).

The craniofacial system is naturally a complex structure. This complexity would be better depicted using three-dimensional (3D) imaging. This will consequently impact the visualization of CFAs if present and ensuing treatment planning. The diagnostic process in some instances can start as early as the embryonic stage using ultrasonography or MRI in CFAs. Postnatally, there are multiple techniques, which include those that utilize ionizing radiation and those that use nonionizing ones (Lewyllie *et al.*, 2018).

The impact of 3D imaging is not restrictive to diagnosis, in fact, it has revolutionized treatment planning and intervention, with computer-aided design/computer-aided manufacturing (CAD/CAM) and 3D printing technologies applied in plastic and reconstructive surgeries of CFAs. Added to that, follow-ups and reevaluations after treatment are currently more quantified quality wise due to these techniques (Lopez *et al.*, 2018; Oh, 2018).

This review will focus on the most common CFAs with special regard to congenital and syndromic CFAs. CFAs due to environmental causes such as teratogens, tumors, or traumas will be excluded. The review will also demonstrate the different 3D imaging modalities available to date and will highlight those that are commonly used with CFA in both diagnosis and treatment procedures postnatally. The Egyptian experience in that field will be hinted upon as well.

Three-dimensional imaging modalities

Necessity, which is the main reason for all creations, fuels the light-speed evolution and development in the field of medical imagery. The necessity being the need to exactly replicate body tissues in images to help assess, diagnose, and plan treatments to the extent of doing mock-up surgeries, implants, and dental splints' designs using advanced softwares that utilize information from 3D imaging modalities (Chen *et al.*, 2016). Generally, imaging modalities are classified into those that utilize ionizing radiation and those that use nonionizing ones (Karatas and Toy, 2014; Guberina *et al.*, 2016) (Table 1).

Applications in craniofacial anomalies

The following is an account on the impact of 3D imaging on both diagnosis and treatment planning in congenital and syndromic CFAs. Modalities used are multislice computed tomography (CT), cone-beam computed tomography (CBCT), MRI, 3D laser scanners, and stereophotogrammetry. It was noted that 3D imagery is mainly used when surgery is contemplated and even though it poses immense benefits, it is not used as much in diagnosis. This could be due to costs, availability, and scan time.

Cleft lip and/or palate

Cleft lip and/or cleft palate type and extent is best viewed using 3D imaging modalities. In their systematic review, Kuijpers *et al.* (2014) concluded that all aforementioned modalities are used to document the cases of cleft lip and palate in terms of bone and soft-tissue involvement and that digital models were generated from these images in the majority of cases. On the other hand, Awarun *et al.* (2019) assert that the most used modality in CFAs is CT scanning, particularly when bony changes are to be checked, laser scanners and stereophotogrammetry follows. 3D models using CT scans and 3D printers proved to be a helpful tool for planning surgeries and as an educating tool for the patients and their families (Chou *et al.*, 2018).

In unilateral clefts, CBCT was used to identify the amount of bone needed for the grafting and it was correlated with the novel GAND classification (gap, arch, nasal, and dental quantification), the study stated that the GAND classification cannot be used to identify the volume of graft material needed, instead the use of CBCT was more accurate (Barbosa *et al.*, 2016).

Table 1 Types of three-dimensional imaging modalities (Karatas and Toy, 2014; Guberina *et al.*, 2016)

Ionizing radiation techniques	Nonionizing radiation techniques
CT scanners and TACT	MRI and micro-MRI
Cone beam CT	3D ultrasonography
Micro-CT and nano-CT	3D laser scanners
3D rotational angiography	Stereophotogrammetry

3D, three-dimensional; CT, computed tomography.

After preclinical planning comes the intervention that usually involves a multidisciplinary approach. Reconstruction of clefted alveolar bone might involve 3D printing of scaffolds to be seeded with biostimulatory cells that helps in bone and soft-tissue regeneration (Ahn *et al.*, 2018). In addition, clefts may be associated with hypodontia, which might necessitate implant placement. Mock-up surgeries are performed using associating softwares (Wermker *et al.*, 2014). After the intervention, treatment outcome is also evaluated using 3D imaging techniques, particularly CBCT (Patel *et al.*, 2018).

Facial clefts

Other facial clefts, which are comparably rare, are usually identified according to the classification presented by Tessier (1976). They are classified from 0 to 30 according to their relation to the eye.

It is recommended that a full craniofacial scan be done in case of these clefts as it might change the diagnosis of the case. For instance, Tessier 30, which is the median clefting of the mandible, is usually hinted upon by a pseudo-lower labial cleft or a full cleft, which was not the case of a child of 27 months, who suffered from an open anterior fontanelle and metopic suture and was referred for cranial reconstruction, and upon performing full 3D CT reconstructs for the patient, the symphysial clefting was discovered. It is worth noting that follow-up on the rate of growth after the surgeries was evaluated by 3D morphometry (Mahajan *et al.*, 2018).

Craniosynostoses

Advanced imaging techniques impacted diagnosis, treatment planning, as well as the intervention in these cases. Quantification of the outcome of the treatments is now bettered owing to the adjunct softwares available alongside these techniques. Perhaps, craniosynostoses are among the most radically impacted anomalies. Treatment of craniosynostoses involves craniectomy, the 3D images are used to create a 3D model that is used to simulate cut areas for the new head and a mock-up of how the final outcome will look like. A 3D-printed cap for the patient is used to secure in the cut cranial bones as puzzle pieces (Laure *et al.*, 2019).

Craniofacial microsomia

Craniofacial microsomia are a group of disorders that include first and second mandibular arch anomalies. They include hemifacial microsomia, Goldenhar syndrome, Treacher–Collins syndrome and Nager syndrome (Brandstetter and Patel, 2016). According to Day *et al.* (2018), computer-assisted surgeries bettered the outcome of the reconstructive surgeries in these cases.

Holoprosencephaly

These cases are usually diagnosed off the two-dimensional CT and MRI by neurologists, yet according to Richieri-Costa *et al.* (2019), what was thought to be a simple case of holoprosencephaly associated with orofacial clefting was suggested to be a possible new syndrome due to nasal findings on the 3D CT scans. This augments their importance in diagnosis.

Micrognathia

Pierre–Robin sequence (PRS) is considered one of the common causes of micrognathia, it can be isolated or part of a syndrome. According to Saal (2016), 50% of PRS are syndromic. Using 3D morphometry, it was found that the length of the body of the mandible in PRS patients is considerably shorter than in normal controls, while patients with Treacher–Collins syndrome showed abnormally short ramus of the mandible. According to Tucunduva *et al.* (2016), using CBCT, it was found that the region between the two mental foramina in both disorders had no significant difference. The treatment of choice is usually surgical where mandibular distractions are done, and this is where 3D imaging intervention has been applauded. The 3D models and virtual planning allows for symmetrical cutting of bone and screw placement, which positively affects the outcome considerably (Day *et al.*, 2018).

Maxillofacial anomalies

A new era had begun in dentistry with the advent of CBCT, it marked computer-assisted surgeries, orthodontic treatment, as well as follow-ups and outcome evaluations. Before that, CT has been utilized, but the availability of CBCT and the ease of the scan when compared with CT made it the modality of choice in everyday dentistry. Yet, the accuracy of CBCT in comparison with multislice CT has been compromised in the fabrication of surgical guides using CAD/CAM when it was found that CBCT had a margin of error (Widmann *et al.*, 2016).

In follow-ups, CBCT was comparable to micro-CT in the assessment of bone around the implants in maxillary defects (Kulah *et al.*, 2019). On the other hand, it was inconclusive in bony temporomandibular joint affection (Shahidi *et al.*, 2018). As per the visualization and treatment of maxillofacial and dental anomalies, CBCT proved efficient, especially when coupled with 3D printing (Celikoglu *et al.*, 2015; Lopez *et al.*, 2018). A new method of 3D rendering might eliminate the need of 3D models in some cases, which is cinematic reconstruction into realistic photo-like images from CT and CBCT two-dimensional images (Rowe *et al.*, 2018).

Temporomandibular joint anomalies, on the other hand, are best viewed with MRI to better visualize the disc and the ligaments of the joint. Additionally, CBCT has been used to assess the bony defects of temporomandibular joint. A new method that aims to marry both views involves superimposition of sagittal views of MRI and CBCT lateral cephalometric images. It aimed to visualize the soft and hard tissue together (Al-Saleh *et al.*, 2016).

As per applications in syndromes that are rather few with regard to diagnosis, CBCT was used to evaluate the maxillary sinus and maxilla in patients with cleidocranial dysostosis and was found to be hypoplastic when compared with normal controls (Kulczyk *et al.*, 2018).

As for dental anomalies in syndromes, CBCT was used to evaluate large roots in a case of oculo–facio–cario–dental syndrome (Kato *et al.*, 2018).

Vascular malformations

According to Venkatraman *et al.* (2014), 3D-reformatted images help diagnose, classify, and view the associated bone anomalies and subsequently aid in the surgical interventions.

The Egyptian experience

Advanced imaging modalities have been used in Egypt for over 40 years and 3D imaging modalities followed that after their mass production abroad. It has been used in diagnosis, treatment, and follow-up, as well as research purposes. This section will include a few examples of the recent usage of 3D imaging modalities in CFAs in Egypt.

First, in clefts, they have been used in the evaluation of patients with clefts and formulation of a treatment plan involving regenerative techniques. For instance, 3D CBCT images were done preoperatively and postoperatively to assess the efficiency of the novel method described, which involved seeding of a collagen sponge with stem cells derived from the bone marrow, nanohydroxyapatite, and platelet-rich fibrin, which proved efficient (Al-Ahmady *et al.*, 2018).

Moreover, a recent study, in the Faculty of Dental Medicine at Al-Azhar University, the girls' branch, in collaboration with the National Research Centre in Cairo, utilized 3D-printed scaffolds as opposed to iliac crest grafting in alveolar clefts and it showed promising results (Farouk *et al.*, 2020).

Second, in the diagnosis of disorders, multislice CT was used in the diagnosis and classification of a severe case of cherubism, while cone beam CT was contemplated to scan this case, the field-of-view FOV limitation hindered that, and it was finally captured with CT, which showed the lesion to extend to the base of the skull (Fig. 1) (Temtamy *et al.*, 2012).

Third, postoperative evaluations: the use of MRI though comparably lesser than CT owing to cost differences and the limitations posed by the patients, it has been used in several Egyptian studies, among them one that correlated palatal muscles after cleft-palate repair and speech defects. The study showed that MRI is the technique of choice to compare both. The study showed that there were anatomical abnormalities and were to cause these speech defects (Ali *et al.*, 2018).

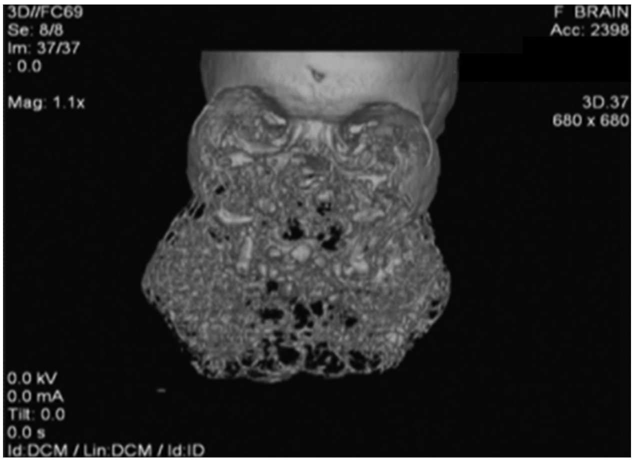
CBCT was also utilized by Abdel-Kader *et al.* (2019), in the assessment, treatment, planning and follow-up of alveolar-ridge augmentation and implant placement in a case of regional odontodysplasia.

It is worth noting that most studies included fewer number of participants than observed in worldwide studies, as well as the number of studies themselves, this could be due to the high cost of these scans and their lack of availability in certain areas of Egypt, in addition to the rarity of CFAs.

Conclusion

The evolution of 3D imaging modalities in both medical imaging and research is driven by the need for advanced technologies that will allow the replication of human tissues by the millimeter to ensure proper visualization, assessment, diagnosis, treatment planning, accurate intervention, and follow-ups. CFAs, particularly congenital and syndromic anomalies, being in a complex system like that of the head, and the need for quick and accurate intervention, make 3D technologies the convenient resort in these cases.

Figure 1



Three-dimensional reconstructs of multislice CT for a stage-4 patient with cherubism (Temtamy *et al.*, 2012). CT, computed tomography.

According to the literature, CT is the most used technology that could be due to the fact that MRI is more costly and poses difficulties for a portion of patients that cannot be neglected.

Application wise, surgical outcomes are better since the utilization of these techniques in addition to the use of CAD/CAM and 3D printing technologies to do 3D models of the anomaly and do custom-made implants or designs for patients. Doing measurements using 3D morphometry is more accurate as well. Yet, it was noted that 3D imagery is mainly used when surgery is contemplated and even though it poses immense benefits, it is not used as much in diagnosis.

There are still tremendous and continuous efforts to have the best depictions for an anomaly. Trials like the advent of the cinematic approach or doing image subtractions using different modalities like superimposing MRI and CBCT images to get the best of the two worlds are still ongoing.

Finally, the Egyptian experience was found to be rich with novel ideas in the utilization of these modalities as in the use of CBCT to plan surgeries and follow-ups or the usage of 3D printers to make custom-made scaffolds for alveolar clefts.

Recommendations

3D imaging is rather costly, which might affect the output of research in Egypt. The rarity of CFAs makes that even more difficult, that is why it is recommended that there will be multicenter studies of CFAs using 3D techniques.

In order to achieve comparative studies as those used in the comparison between the size of the mandible in Treacher–Collins and PRS, it is recommended to do an Egyptian 3D morphometric study in all governorates, to have norms for future comparisons. It is worth noting that this study would benefit researchers in many fields, such as orthodontists, surgeons, anthropologists, as well as geneticists.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

Abdel-Kader MA, Abdelazeem AF, Ahmed NE, Khalil YM, Mostafa MI (2019). Oral rehabilitation of a case with regional odontodysplasia using a regenerative approach—a case report and a review of literature. *Spec Care Dent* **39**:330–339.

Ahn G, Lee JS, Yun WS, Shim JH, Lee UL (2018). Cleft alveolus reconstruction using a three-dimensional printed bioresorbable scaffold with human bone marrow cells. *J Craniofac Surg* **29**:1880–1883.

Al-Ahmady HH, Abd Elazeem AF, Bellah Ahmed NE, Moataz Shawkat WM, Elmasry M, Abdelrahman MA, Abderazik MA (2018). Combining autologous bone marrow mononuclear cells seeded on collagen sponge with Nano Hydroxyapatite, and platelet-rich fibrin: Reporting a novel strategy for alveolar cleft bone regeneration. *J Cranio-Maxillofac Surg* **46**:1593–1600.

Ali AM, El Shamy MI, AbdElmonem AA, Hamza FA, El Banoby TM (2018). Role of MRI in detection of repaired cleft palate muscles and correlation to speech. Egypt J Hosp Med **73**:7604–7609.

Al-Saleh MA, Alsufyani NA, Saltaji H, Jaremko JL, Major PW (2016). MRI and CBCT image registration of temporomandibular joint: a systematic review. *J Otolaryngol Head Neck Surg* **45**:30.

Awarun B, Blok J, Pauwels R, Jacobs R (2019). Three-dimensional imaging methods to quantify soft and hard tissues change after cleft-related treatment during growth in patients with cleft lip and/or cleft palate: a systematic review. *Dentomaxillofac Radiol* **48**:20180084.

Barbosa GL, Emodi O, Pretti H, van Aalst JA, de Almeida SM, Tyndall DA, Pimenta LA (2016). GAND classification and volumetric assessment of unilateral cleft lip and palate malformations using cone beam computed tomography. *Int J Oral Maxillofac Surg* **45**:1333–1340.

Brandstetter KA, Patel KG (2016). Craniofacial microsomia. *Fac Plastic Surg Clin North Am* **24**:495–515.

Celikoglu M, Buyuk SK, Sekerci AE, Cantekin K, Candirli C (2015). Maxillary dental anomalies in patients with cleft lip and palate: a cone beam computed tomography study. *J Clin Pediatr Dent* **39**:183–186.

Chen X, Li X, Xu L, Sun Y, Politis C, Egger J (2016). Development of a computer-aided design software for dental splint in orthognathic surgery. *Sci Rep* **6**:1–10.

Chou PY, Hallac RR, Shih E, Trieu J, Penumatcha A, Das P, *et al.* (2018). 3D-printed models of cleft lip and palate for surgical training and patient education. *Cleft Palate-Craniofac J* **55**:323–327.

Day KM, Gabrick KS, Sargent LA (2018). Applications of computer technology in complex craniofacial reconstruction. *Plastic Reconstr Surg* **6**:3.

Farouk A, Al-Ahmady H, Abdul Rahman M (2020). Evaluation of 3D computer-assited patient's specific scaffold seeded with autogenous stem cells and plate; et-rich fibrin in alveolar cleft repair [DDS thesis]. Cairo, Egypt: Azhar University-Girl's branch.

Guberina N, Lechel U, Forsting M, Mönninghoff C, Dietrich U, Ringelstein A (2016). Dose comparison of classical 2-plane DSA and 3D rotational angiography for the assessment of intracranial aneurysms. *Neuroradiology* **58**:673–678.

Karatas OH, Toy E (2014). Three-dimensional imaging techniques: a literature review. *Eur J Dent* **8**:132–140.

Kato J, Kushima K, Kushima F (2018). New radiological findings and radiculomegaly in oculofaciocardiodental syndrome with a novel BCOR mutation: a case report. *Medicine (United States)* **97**:49.

Kuijpers MA, Chiu YT, Nada RM, Carels CE, Fudalej PS (2014). Three-dimensional imaging methods for quantitative analysis of facial soft tissues and skeletal morphology in patients with orofacial clefts: a systematic review. *PLoS ONE* **9**:0093442.

Kulah K, Gulsahi A, Kamburoğlu K, Geneci F, Ocak M, Celik HH, *et al.* (2019). Evaluation of maxillary trabecular microstructure as an indicator of implant stability by using 2 cone beam computed tomography systems and micro-computed tomography. *Oral Surg Oral Med Oral Pathol Oral Radiol* **127**:247–256.

Kulczyk T, Przystańska A, Rewekant A, Turska-Malińska R, Czajka-Jakubowska A (2018). Maxillary sinuses and midface in patients with cleidocranial dysostosis. *Ann Anat* **215**:78–82.

Laure B, Louisy A, Joly A, Travers N, Listrat A, Pare A (2019). Virtual 3D planning of osteotomies for craniosynostoses and complex craniofacial malformations. *Neurochirurgie* **65**:269–278.

Lewyllie A, De Llano-Pérula MC, Verdonck A, Willems G (2018). Three-dimensional imaging of soft and hard facial tissues in patients with craniofacial syndromes: a systematic review of methodological quality. *Dentomaxillofac Radiol* **47**:20170154.

Lopez CD, Witek L, Torroni A, Flores RL, Demissie DB, Young S, *et al.* (2018). The role of 3D printing in treating craniomaxillofacial congenital anomalies. *Birth Defects Res* **110**:1055–1064.

Mahajan S, Patel PK, Duan Y, Warshawsky N (2018). The median mandibular symphysis tessier 30 cleft: 3D imaging analysis and review of the literature. *Cleft Palate-Craniofac J* **55**:778–786.

Mossey P, Castilla E (2003). *Global registry and database on craniofacial anomalies report of a WHO Registry Meeting on Craniofacial Anomalies Human Genetics Programme Management of Noncommunicable Diseases World Health Organization Geneva*, Switzerland: WHO Library Cataloguing-in-Publ.

Oh J (2018). Recent advances in the reconstruction of cranio-maxillofacial defects using computer-aided design/computer-aided manufacturing. *Maxillofac Plast Reconstr Surg* **40**:1.

Patel DS, Jacobson R, Duan Y, Zhao L, Morris D, Cohen MN (2018). Cleft skeletal asymmetry: asymmetry index, classification and application. *Cleft Palate-Craniofac J* **55**:348–355.

Richieri-Costa A, Zechi-Ceide RM, Candido-Souza RM, Monteiro RA, Tonello C, de Freitas ML, *et al.* (2019). Holoprosencephaly, orofacial cleft, and frontonaso-orbital encephaloceles: genetic evaluation of a possible new syndrome. *Am J Med Genet* **179**:2170–2177.

Rowe SP, Zinreich SJ, Fishman EK (2018). 3D cinematic rendering of the calvarium, maxillofacial structures, and skull base: preliminary observations. *Br J Radiol* **91**:20170826.

Saal HM (2016). Genetic evaluation for craniofacial conditions. *Fac Plast Surg Clin North Am* **24**:405–425.

Shahidi S, Salehi P, Abedi P, Dehbozorgi M, Hamedani S, Berahman N (2018). Comparison of the bony changes of TMJ in patients with and without TMD complaints using CBCT. *J Dent (Shiraz, Iran)* **19**:142–149.

Temtamy SA, El Azeem AF, El Badry TH, Mehrez MA, El Kassaby M (2012). Cherubism. *Middle East J Med Genet* **1**:53–56.

Tessier *P* (1976). Anatomical classification of facial, cranio-facial and latero-facial clefts. *J Maxillofac Surg* **4**(C):69–92.

Tucunduva RM, Imada TSN, Lopes IA, Rubira-Bullen IR, De Carvalho IM (2016). Evaluation of interforaminal mandible region of individuals with Pierre Robin Sequence and treacher collins syndrome through the cone-beam computed tomography. *J Craniofac Surg* **27**:219–221.

Venkatraman B, Paul S, Varun B (2014). Imaging spectrum of hemangioma and vascular malformations of the head and neck in children and adolescents. *J Clin Imaging Sci* **4**:1.

Wermker K, Jung S, Joos U, Kleinheinz J (2014). Dental implants in cleft lip, alveolus, and palate patients: a systematic review. *Int J Oral Maxillofac Implants* **29**:384–390.

Widmann G, Fischer B, Berggren J, Dennhardt A, Schullian P, Reto B, Puelacher W (2016). Cone beam computed tomography vs multislice computed tomography in computer-aided design/computer-assisted manufacture guided implant surgery based on three-dimensional optical scanning and stereolithographic guides: does image modality matter? *Int J Oral Maxillofac Implants* **31**:527–533.