Costochondral graft in growing patients with hemifacial microsomia case series: Long term results compared with non treated patients

Running Title: CCG in HFM type III - Long term

M. C. Meazzini, V.M.A. Battista, R. Brusati, F. Mazzoleni, F. Biglioli L. Autelitano.

M.C. Meazzini DMD, MMSC, is Adjunct Professor and Orthodontic Consultant, Regional Center for Cleft Lip and Palate, Scientific Coordinator of the Smile House-CLP Center Department of Maxillo-Facial Surgery, San Paolo Hospital, University of Milan, Milan, Italy. Orthodontic consultant at San Gerardo University Hospital, Università Milano Bicocca, Monza, Italy.

V.M.A. Battista: M.D., Surgical Consultant, Regional Center for Cleft Lip and Palate, Smile House-CLP Center Department of Maxillo-Facial Surgery, San Paolo Hospital, Italy.

R. Brusati: MD, Full Professor, Maxillo Facial Surgery, Regional Center for Cleft Lip and Palate, Smile House-CLP Center, San Paolo University Hospital, Università degli Studi di Milano, via di Rudinì 8, Milan, Italy.

F. Biglioli: MD, is Full Professor, Head of the Maxillo-Facial Surgery Department, San Paolo University Hospital, Università degli Studi di Milano, via di Rudinì 8, Milan, Italy

F. Mazzoleni: MD Adjunct professor and Surgical Consultant San Gerardo University Hospital, Università Milano Bicocca, Monza, Italy

L. Autelitano: MD, is Adjunct Professor, Regional Center for Cleft Lip and Palate, Clinical Coordinator of the Smile House-CLP Center Department of Maxillo-Facial Surgery, San Paolo Hospital, Università degli Studi di Milano, Milan, Italy

Corresponding author: V.M.A. Battista, via De Predis 2, 20155, Milano, Italy. Phone number: +39 3495308344, e-mail vma.battista@gmail.com

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/OCR.12398

DR VALERIA MARINELLA AUGUSTA BATTISTA (Orcid ID : 0000-0002-8777-9138)

Article type : Original Article

INTRODUCTION

Costochondral graft (CCG) has been traditionally used in growing patients with severe mandibular hypoplasia, both congenital, such as hemifacial microsomia (HFM), and acquired , after resection in temporo-mandibular joint (TMJ) ankylosis or tumor resection.The rationale for the use of a CCG is that the cartilaginous portion of the rib graft is considered to have growth potential[1] and adaptive capabilities.Some authors have shown that the growth of a CCG in unpredictable[2] and not linear[3-7].Attention has been mostly pointed on the action of intrinsic factors of the cartilaginous portion of the CCG, leading to growth. In particular, Peltomaki suggested that rib growth depends mainly on the action of intrinsic factors acting on the germinative area of the cartilaginous portion[8]. This area is only 4-5 mm away from the osteocartilaginous junction of the rib, and it is alleged to ensure growth of the rib[9]. Kaban and Perrot[2], stated that graft overgrowth may depend on the excessive thickness of the cartilage cuff of the graft. Most authors seem to be more concerned by a potential overgrowth rather than a deficient growth of the graft.In the literature on CCG, little attention has been given to the action of extrinsic factors, such as the etiology of the mandibular hypoplasia and subsequently the quality of the neuromuscular environment. A review of the literature on CCG has shown that growth of the reconstructed mandibular ramus with costochondral grafts in patients with TMJ ankylosis mostly equals the growth of the unaffected side, while an overgrowth is present in 20 to 50% of patients[2]. On the contrary, the sporadic literature on CCG explicitly regarding HFM patients, suggests that there is a short term phenotype recurrence, given the congenital nature of the asymmetry[10]. it is possible, therefore, that the underlying pathology (the extrinsic factors), might play an important role in CCG growth, and that, therefore, prognosis of CCG in HFM might be different from CCG in other types of mandibular hypoplasia. The objective of this study was, therefore, to analyze the long term growth in a homogeneous sample of children affected by

Type III HFM subjected to CCG at an early age and compare it with a sample of Type III HFM patients who were never subjected to surgical treatment.

MATERIAL AND METHOD

Patient sample selection (CCG patients)

In our Center, between 1995 and 2006, 70 procedures of ramus condyle reconstruction by CCG were performed.

To obtain a homogeneous sample in terms of type of pathology, severity and age at surgery, inclusion criteria were:

I. Growing patients affected by HFM type III11.
II. Costochondral graft for mandibular reconstruction performed during early
III. growth (6-8 years) by the same surgeon.
IV. Successful CCG, considered as the presence, at the time of the first observation, of a healthy and stable graft which allowed free movement and function of the mandible, as established by clinical and radiological examination.
V. A minimum of 8 years of follow up: no patients younger than 15 years of age at the longest follow up, were included in the sample
VI. No intermediate surgeries (ie lipofilling) performed during the follow up time.
VII. No associated macrostomia.
VIII. No associated facial palsy.

Of the 70 CCG procedures, 13 were performed on very young patients affected by HFM type III deformity, according to Pruzansky. Of these patients 10 had complete pre-surgical and post-surgical records and follow up records longer than 8 years.

Control Group (CG): Non operated sample selection

A control sample was retrospectively collected. Ten patients were never offered or did not accept treatment during growth.

Selection criteria were:

I. HFM type III with records during early growth (6-8 y.o.).
II. Never subjected to surgical treatment.

III. Records at 15-17 years, prior to any surgical procedures

IV. No associated macrostomia.

V. No associated facial palsy.

Surgical approach in CCG

The patients were all treated by the same senior author according to our protocol: the approach to the articular area was achieved through a preauricular curved incision, sometimes extended to the temporal region. A second retromandibular or submandibular approach was used to allow access to the distal stump of the mandibular body. A temporal muscle myofascial flap was rotated to reconstruct the joint. Through a submammary skin incision the convex surface of the 7th-8th rib was exposed. As stated by several authors[12], care must be taken to preserve the perichondrium and periosteum at the bone-cartilage junction in order to prevent detaching of the cartilage from the bony segment. The osteocartilaginous segment harvested is molded to obtain an anatomic adaptation to the recipient site.The thickness of the cartilaginous portion left attached to the bony rib ranged between 4 and 6 mm. The length of the bony portion reflected the distance between the mandibular stump and the deformed glenoid cavity. Intermaxillary rigid fixation was positioned and then the CCG is secured to the ramus with wire, bicortical bone screws or plates. Intermaxillary fixation was kept in place for a period of 2-4 weeks depending on the type of graft stabilization (4 weeks for wire stabilization, 2 weeks for screws and plates). The intermaxillary fixation was followed by functional rehabilitation for 6 months. Before discharge, all patients had a panoramic X Ray taken. The average radiographic and photographic long term follow-up was 8.6 years.

Method

Skeletal evaluation

Occlusal plane inclination was calculated in both samples (CCG Fig 1 and CG Fig 3) as the angle between the Infraorbital (IO) line, the line passing through the lowest points of the orbits, and the Occlusal Plane (OCCL) through to the lowest molar cusps. It was calculated in the CCG group on the pre-operative, the immediate post-operative panoramic X Ray and after an average follow up of 8 years. In the CS group the Occlusal Plane was assessed on the Panoramic X Ray at an average age of 7 years and after an average follow up of 8 years. The growth of the reconstructed ramus was calculated in the CCG sample analyzing the panoramic X Rays in the immediate postoperative control and at the longest follow up. The mandibular height was calculated on the non affected side as the distance between the most superior point of the condylar head (Co) and the point of intersection between the line

tangent to the mandibular body and the line tangent to the mandibular ramus (Go)13,14. On the affected side, height was calculated as the distance between the most superior point of the condylar head and a landmark considered stable through the years, as close as possible to the junction between the mandible and the costochondral graft (Go) (in many instances a screw or a hole of the plate). All of the points mentioned are depicted in Fig 1. Vertical accuracy of panoramic X Ray is well accepted[15,16].Therefore, as a parameter for investigation, we adopted the ratio between the affected and the non affected side.Landmark identification was performed by the same trained operator at two different time points to ensure reliability.

Evaluation of soft tissue morphology: Photometric Study

To assess facial symmetry a photometric evaluation on the frontal view was carried out by the same trained operator. In the CCG patients the preoperative, the postoperative photograph and the photograph after a mean of 8,6 years (from 7,3 to 10 years) were compared in order to assess changes in facial symmetry. In the CG a photometric evaluation in the frontal view at 7 years ad after a mean long term follow up of 8 years were compared.The facial deviation was expressed as the angle between the facial midline (FM), the line passing through Nasion (N) and the central chin point (CP), and the inter pupillary line (IP). Another index chosen for the evaluation of facial symmetry and facial growth was the ratio between the hemi facial contour. This was measured by first drawing a line passing through the corners of the lips, with lips at rest: the Cheilon Cheilon Line (Ch-Ch). This line intersected the facial contour on either side of the face. The distance from the FM to the facial contour of the cheeks intersecting Ch-Ch was measured, and their ratio was calculated to assess the symmetry of face: Hemifacial Ratio (HR). The angle between the Alar Base Plane (ABP), the line passing through left and right alar base, and the FM and the angle FM^Ch-Ch were also measured (all points and measurements are described in Fig 2 for CCG group and Fig 4 for CG group). Landmark identification and measurements were performed twice by the same trained operator at 4 months interval, which is suitable to assess test-retest reliability. A Cronbach α Intraclass Correlation Coefficient (ICC) was used to assess intra-examiner reliability. Statistical analysis was carried out with Stata 10 software (StataCorp. 2007. Stata Statistical Software: Release 10. College Station, TX: StataCorp LP).

RESULTS

The intraclass Correlation Coefficient used to assess consistency of the single rater was 0.91, thus providing an indication of good intrarater reliability.

Skeletal Evaluation in the CCG group

The IO-OCCL angle remained stable in 2 patients, decreased in 4 patients and increase in 4 patients, the mean angle in the immediate postoperative period was 2,6° and at 8 years, it was still on average 2.6°, although with a standard deviation of 2°. Mandibular ratio in the immediate postoperative period was on average 0.95 and after a mean follow up of 8 years it was 0.87, with an average reduction of 8%.(Table 1).

Skeletal Evaluation in CG

The mean IO-OCCL angle was 0,8°(SD: 0.4) in the first Panoramic X Ray and increased slightly during the years: 1.4° after 8 years of follow up.(Table 1).

Photometric Study in CCG

HR increased in all patients post operatively (average: 26%), but in the long term an almost total relapse of the original proportion was seen (19%).There was a recurrence of the original facial deviation expressed as the MF^IP angle: it increased on average of 3.4° at T1 and decreased of 3° at Tlt (Table 1).

Photometric Study in CG

HR increased of 5% in the long term and MF^IP increased on average of 0.4°. Therefore, facial asymmetry was stable during the years (Table 1).

DISCUSSION

To our knowledge, this is the first study in the literature to report long term skeletal and soft tissue results in a sample of HFM type III treated with CCG at an early age. Peculiar interest to the study is given by the comparison with a non treated sample. Bertin et al[17]. reported results in 10 Type III HFM patients. All needed multiple osteotomies at the completion of growth, mainly a Le Fort 1 to correct occlusal canting. Results in terms of architectural changes and stability were reported together with Type II A and B, therefore no specific assessment could be made on type III patients. Recurrence of mandibular asymmetry was noted. As no control sample was used, the paper was unable to demonstrate whether CCG reduced the subsequent burden of surgical care[17].The main limit of the present study is the relatively small number of cases. Notably, though, the same problem is present in most of the other studies in the literature [2,7,18–20].The second obvious limit of the study is the fact that it is retrospective and not prospectively randomized. On the other hand, the main advantage of this study is the homogeneity of the sample in terms of age, severity of the pathology, as well as the length of follow up.The problem in most of the literature on CCG is, notably, the wide heterogeneity in the population analyzed and their method for evaluation of results. Many well known studies show procedural bias that limit their value: lack of quantitative

data[2], lack of distinction between underlying pathology of patients requiring mandibular reconstruction mixing ankylosis, the three types of HFM[21-23], and Goldenhar syndrome. Wide disparity in age and follow up time[13, 24, 25] lack of indication of technical modifications through the years[23]. Recently, Bin Zhang et al. reported a follow up of 4 children operated at an average age of 3.8 affected by type III, but also type IIb, with a follow up ranging from 23 to 64 months (final follow up at 4.5 to 9 yeas). No control sample was reported. All new ramuses grew, but no quantitative assessment on facial symmetry was carried out. In terms of method, in the literature there is no consensus regarding the best way of measuring growth of costochondral grafts or assessing their success. Ko et al [20] used linear measurements on lateral cephalometric analysis. Padwa et al [13] evaluated growth measuring the inclination of planes on Postero-Anterior cephalometric X Rays. Ross measured the inclination of the midline on Postero-Anterior cephalometric X Rays and Basion-Nasion^Pogonion angle in Lateral cephalometry [23]. In this study mandibular ratio[7,14,26] calculated on Panoramic X Rays, was used for two reasons: Panoramic X Ray is considered reliable for vertical measurements[16] and the ratio obviates the error caused by measuring Panoramic X Rays with different magnification.Of course, new technologies such as CBCT and 3D software are now more commonly used and would have allowed a more accurate evaluation of growth in the vertical and the lateral planes. Unfortunately, given the length of follow up, in our sample only the panoramic X Rays were available in the initial records of most of the patients, to be compared with the long term records. Furthermore, in this study only patients reconstructed between 6 and 8 years of age were selected. Including older children in the study would have introduced a severe bias[14]. In the CCG sample no overgrowth was observed. One of the hypotheses that could explain the lack of overgrowth of the reconstructed ramus, might not only be related to the thickness of the cartilage cuff, but especially to the fact that patients with HFM have missing or hypoplastic masticatory muscles and, therefore, a different functional matrix compared to acquired mandibular asymmetry. Interestingly, 8 years post grafting the proportion between grafted side and non affected side is only mildly reduced from 95% to 87%, with a relapse of 8% of the proportion after lengthening. This amount of relapse is much less than what is seen after distraction osteogenesis (DO) in Type I and Type II Pruzansky[26,27]. Therefore, in contrast with the long term results after DO, where the recurrence of the skeletal asymmetry is complete, the actual loss of vertical dimension of the graft is much slower and there is never a complete relapse. Nevertheless, even though the skeletal length of the graft is not completely lost, the presence of the residual CCG does not seem to improve either the dental or the facial symmetry in the long term, compared to non treated patients. Furthermore, once adulthood is reached, most residual CCGs are not useful for further surgery and are not functional (Fig 5). The occlusal plane in type III Pruzansky, as shown in the literature[16], is very variable; in

seven CCG and in all non treated patients it was essentially flat, while only in three of the CCG patients it was canted of 4°-5°, which is considered a moderate canting[10]. In the long term the occlusal plane again varied, but, in those CCG patients who had an initial canting, it was not improved in the long term. In the non treated patients an occlusal plane worsening of an average of 0.6° was measured, which it is not a clinically significant value. Hemifacial Ratio (HR) on the affected side in CCG relapsed almost completely in the long term follow up, thus showing a tendency in HFM patients to re-express their congenital facial proportion, as seen after distraction osteogenesis (DO) in Type I and Type II[26,27]. The average recurrence of asymmetry, measured as HR, was 19% in 8 years.In the non treated patients, interestingly, from infancy to adulthood, the HR improved 5% with no treatment, although, again, standard deviation was high (Tab 1). Clinically, therefore, there seems to be very little difference in the long term, in terms of facial contour of the affected side, compared to the non affected side, whether a CCG has been placed or not. Both in CG and in CCG patients growth and symmetry were highly unpredictable, as supported by the high Standard Deviations in all data.

CONCLUSIONS

In patients with type III HFM, restoring the height of the ramus with CCG leads to an immediate correction of facial asymmetry. In the long term there is a partial return towards asymmetry of the bony ratio and a complete return of the asymmetry of the facial appearance and contour in most of the patients.

	T0				T1		T lt			
	Mean +- SD		RANGE		Mean +- SD	RANGE	Mean +- SD		RANGE	
	CCG	NS	CCG	NS			CCG	NS	CCG	NS
AGE	6.8 +- 0.7	7 +- 0.7	6 - 8	6-8	7.2 +- 0.8	7 - 9	16 +- 1	16.4 +- 0.9	15 - 17	15 - 17
IO-OCCL angle (°)	-	0.8 +- 0.4	-	0-1	2.6° +-2.7°	1°-6°	2,6+- 2	1.4 +- 0.1	1-3	1-3
Man-dibu-lar Ratio	-	-	-	-	0.95 +- 0.2	0.8-1,3	0.87 +- 0.1		0.68 - 1.07	-
MF^IP (°)	83.8 +- 4,8	83.8+-4.3	77 - 90	78 - 89	87.2 +- 1.8	85 - 89	85.6 +- 4.7	84.2+ -4.4	85 - 90	79 - 89
ABP^ MF	85.4 +- 3.1	86.4 +- 2	82 - 90	84 - 89	88.4 +- 2.2	85 - 91	88. 2 +- 3.1	85.6 +-3.2	85 - 93	82 - 90
Ch-Ch^MF	86.8 +- 2.3	85.6 + - 2.9	83 - 89	82 - 89	88.4 +- 0.5	88 - 89	87 +- 4	88 +- 1.9	87 - 90	85 - 90
Hemifacial Ratio	0.72 +- 0.13	0,6+-0.12	0.5 - 0.8	0,44 - 0,73	0,98 +- 0.06	0.89 - 1.04	0,79 +- 0.05	0. 65 +- 0.08	0.73 - 0.88	0,57 - 0,77

Table 1 - Skeletal Evaluation and Photometric Study: Mean, Standard Deviation and Range of all of the parameters measured are listed for CCG group at the immediate pre-operative period (T0), 6 months after surgery (T1), and at the long term evaluation (Tlt). F
or CG are listed results at a mean age of 6.3 y.o (T0). and at 16 y.o. (Tlt).Parameters are listed are: IO^OCCL expressed in degrees (°), Mandibular Ratio (MR), MF^MP expressed in degrees (°), ABP^MF expressed in degrees, Ch-Ch^MF (°), Hemifacial Ratio (HR)

PROCESS 2018 Checklist			
Section	**Item**	**Checklist Description**	**Page Number**
Title	1	Both the words “case series” and the area of focus should appear in the title (e.g. disease, exposure/intervention or outcome)	1
Abstract	2a	Introduction - what is the unifying theme of the case series.	V
	2b	Methods - describe what was done, how and when was it done and by whom.	
	2c	Results - what was found.	
	2d	Conclusion - what have we learned and what does it mean	
Introduction	3	Background and relevance - Explain the scientific background and rationale for the case series (e.g. specify the unifying theme - common disease, exposure, intervention and outcome). The introduction should explain why this study needed.	1-2

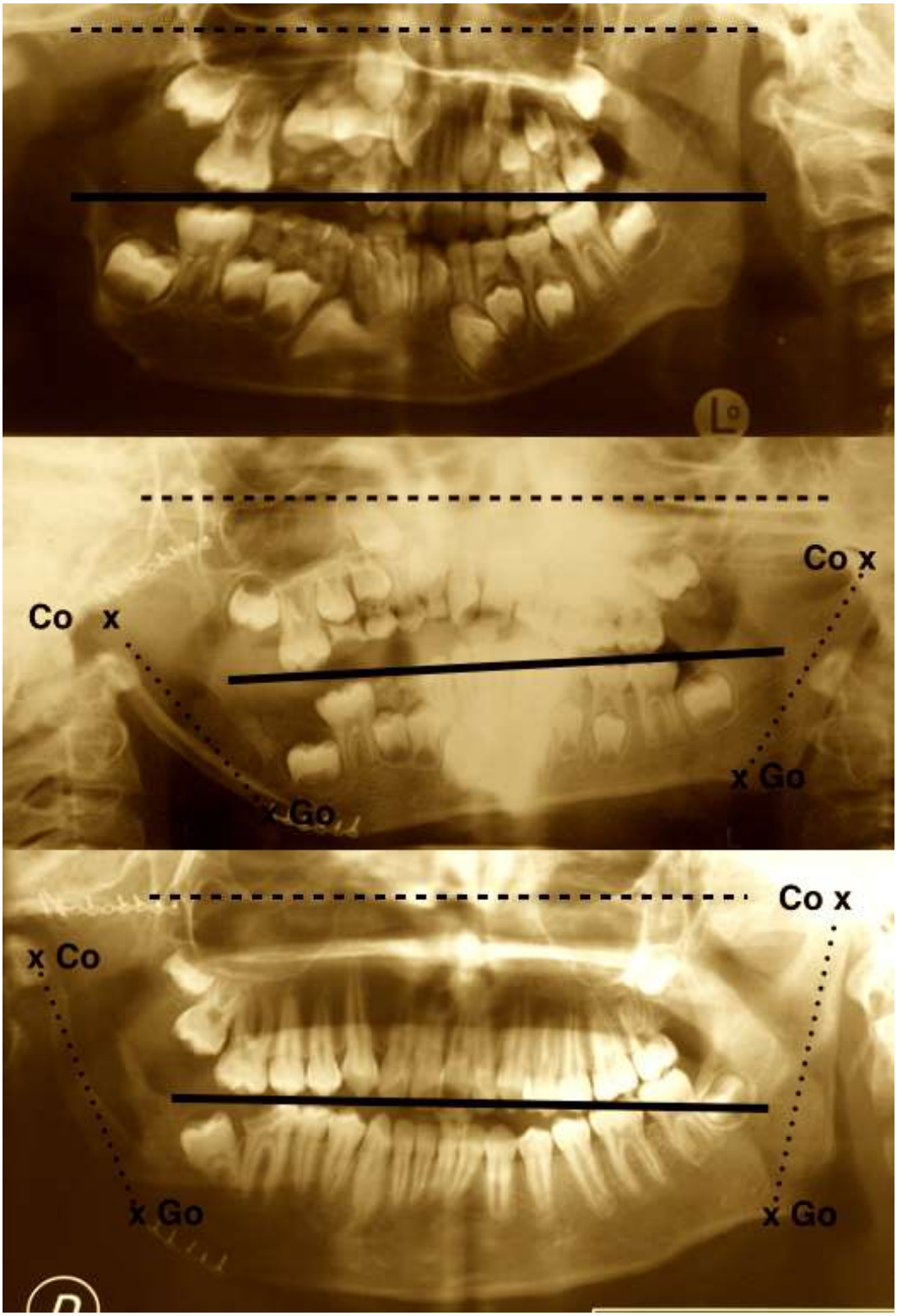
Methods	4a	Registration - state the research registry number in accordance with the declaration of Helsinki - "Every research study involving human subjects must be registered in a publicly accessible database" (this can be obtained from; ResearchRegistry.com or ClinicalTrials.gov or ISRCTN). If a protocol exists already, state where it can be accessed (must be publicly accessible).	2-4
	4b	Study design - state the study is a case series. In addition, it is necessary to state whether the case series is: 1) prospective or retrospective in design; 2) single or multi-centre; and 3) cases are consecutive or non-consecutive.	2-4- 5
	4c	Setting - describe the setting(s)and nature of the institution in which the patient was managed; academic, community or private practice setting? Location(s), and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2-4
	4d	Participants - describe the relevant characteristics of the participants (comorbidities, tumour staging, smoking status, etc). State any eligibility (inclusion/exclusion) criteria and the sources and methods of selection of participants. Describe length and methods of follow-up.	2-4-5

	4e	Pre-intervention considerations e.g. Patient optimisation: measures taken prior to surgery or other intervention e.g. treating hypothermia/hypovolaemia/hypotension in burns patients, ICU care for sepsis, dealing with anticoagulation/other medications and so on.	2-4
	4f	Types of intervention(s) deployed (pharmacological, surgical, physiotherapy, psychological, preventive) and reasoning behind treatment offered.	4
	4g	Intervention details – details on how the intervention was carried out. For surgery, for example, include information on anaesthesia, patient position, use of tourniquet and other relevant equipment, preparation used, sutures, devices, surgical stage (1 or 2 stage, etc). For pharmacological therapies, include formulation, dosage, strength, route and duration.	4
	4h	Who performed the procedures – the operator position and their experience experience (position on the learning curve for the technique if established, specialisation and prior relevant training). For example, 'A junior resident, three years into specialized training'. Degree of novelty for a surgical technique/device should be mentioned and a comment on learning curves should be made for new techniques/devices.	4

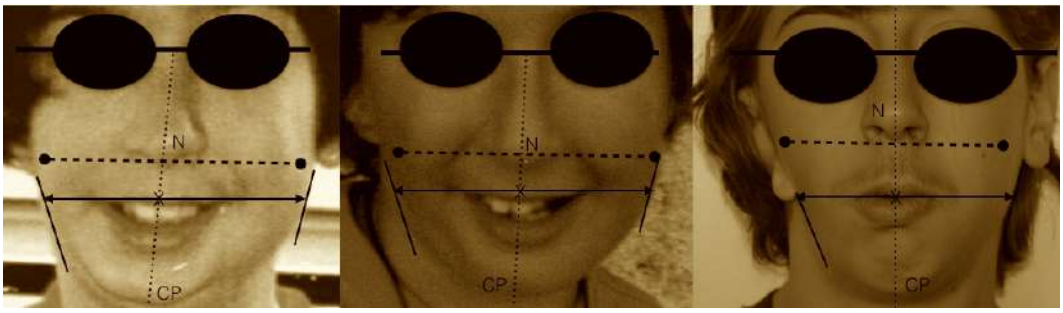
	4i	Quality control - what measures were taken to reduce inter or intra-operator variation, ensure quality, and maintain consistency between each case in the delivery of the intervention e.g. independent observers, lymph node counts, standard surgical technique.	3-4
	4j	Post-intervention considerations – following the main intervention: 1) when were the patients followed-up; 2) where; 3) what did follow-up entail (additional tests, scans, clinical examination) and what were the results of these; and 4) were there any post-operative instructions.	3-4
Results	5a	Participants - reports numbers involved and their characteristics (including, most importantly, their comorbidities and smoking status, as well as other demographic details). For all cancer patients it is necessary to include details on tumour staging (e.g. TNM)	6-7
	5b	Changes to reports – report any changes in the interventions during the course of the case series (what the change was, reasons for the change, what learning occurred, together with rationale and a diagram if appropriate).	/

	5c	Outcomes and follow-up - Clinician assessed and patient-reported outcomes (when appropriate, including, for example questionnaires or comments at outpatient visits) should be stated. Include details on the time periods at which assessed. Relevant photographs/radiological images should be provided e.g. 12 month follow-up. Describe loss to follow-up (express as a percentage) and any explanations for it.	6-7
	5d	Intervention adherence/compliance - where relevant how well patients adhered to and tolerated their treatment. For example, post-operative advice (heavy lifting for abdominal surgery) or tolerance of chemotherapy and pharmacological agents.	/
	5e	Adverse events – all complications and adverse or unanticipated events should be described in detail and ideally categorised in accordance with the Clavien-Dindo Classification. How they were prevented, diagnosed and managed. Blood loss, operative time, wound complications, re-exploration/revision surgery, 30-day post-op and long-term morbidity/mortality may need to be specified. If there were no complications or adverse outcomes this should also be included.	/
Discussion	6a	Summarise key results	7-8-9-10

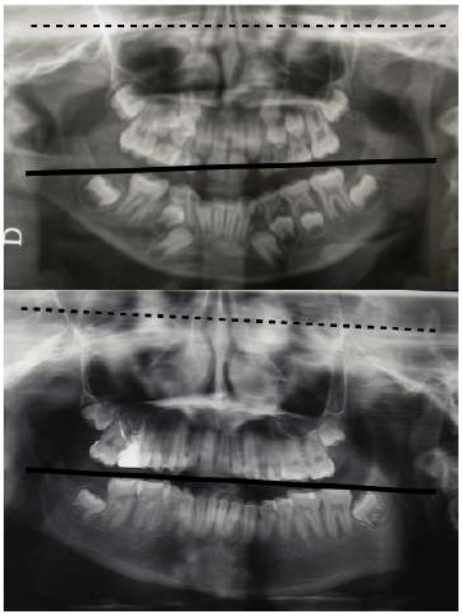
	6b	Placing results in context – describe all relevant literature, describe the prevailing gold standard should one exist, and describe how findings reported compare with established therapies. State the implications for clinical practice guidelines and any relevant hypotheses that have been generated as a result of this worth	7-8-9-10
	6c	Strengths and limitations of the study	7-8-9-10
	6d	Future – State the further research that can be done to build on the findings and methodology discussed. State the study design next best suited to address these areas.	7-8-9-10
	6e	Rational – ensure any conclusions made have strong rationale	7-8-9-10
Conclusions	7a	State the key conclusions from the study	10
	7b	State what needs to be done next, further research with what study design.	10
Additional Information	8a	State any conflicts of interest	V
	8b	State any sources of funding	V
	8c	State Ethics - state whether ethical approval was needed and if so, what the relevant judgement reference was?	V



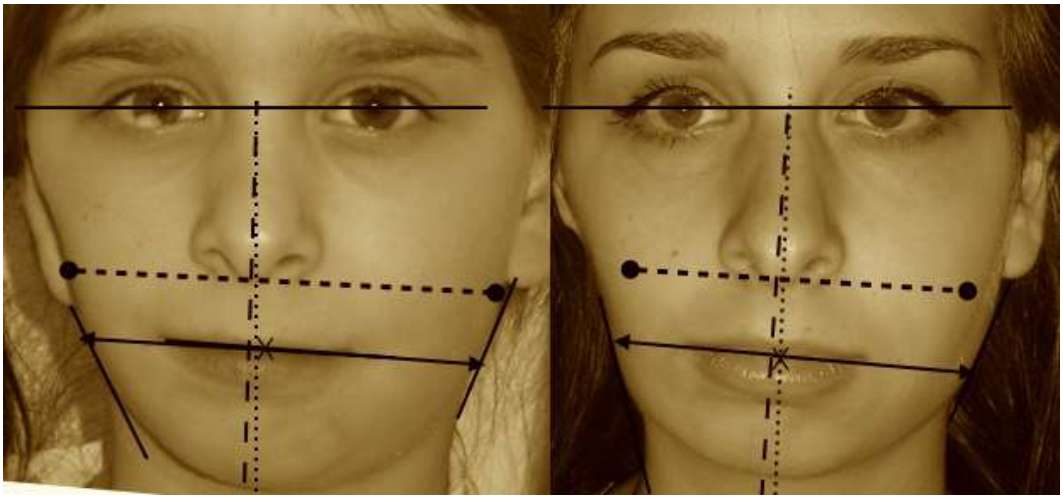
ocr_12398_f1.jpg



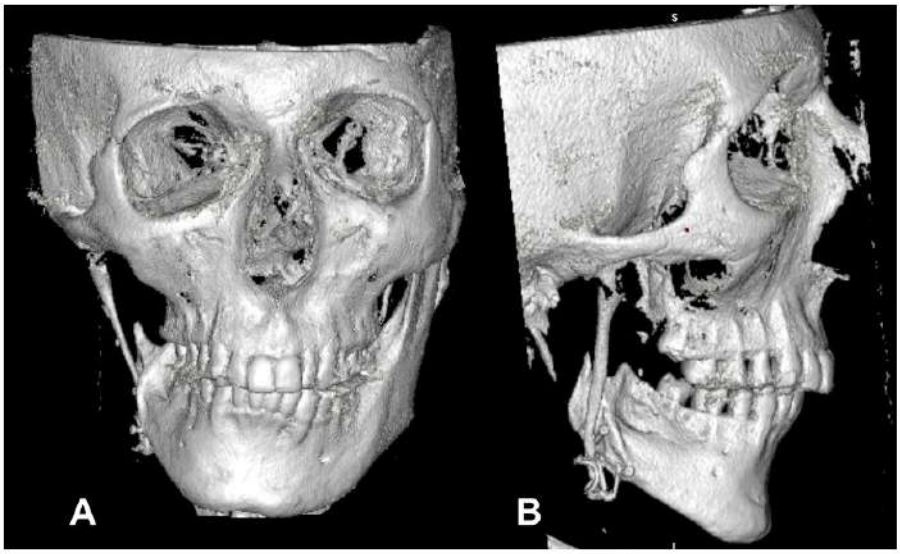
ocr_12398_f2.jpg



ocr_12398_f3.jpg



ocr_12398_f4.jpg



ocr_12398_f5.jpg