Review

Three-dimensional stereophotogrammetric analysis of nasolabial soft tissue effects of rapid maxillary expansion: a systematic review of clinical trials

Analisi tridimensionale degli effetti dell'espansione mascellare rapida sui tessuti molli nasolabiali mediante stereofotogrammetria: revisione sistematica degli studi clinici

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SUMMARY

The aim of this systematic review is to analyse the quality and clinical evidence in the literature analysing, through 3D stereophotogrammetry, the nasolabial soft tissue modifications that may occur after rapid maxillary expansion (RME). This systematic literature review was based on the PRISMA-P statement and was registered in the PROSPERO database with the following protocol ID: CRD42017079875. Pubmed, Cochrane, EBSCO, Scopus, Web of Science databases were searched with no restriction of year or publication status. Selection criteria were: randomised clinical trials, controlled clinical trials, cohort studies, cross-sectional studies, case-control studies on patients with unilateral/bilateral crossbite, transverse maxillary deficiency and crowding, treated with RME and monitored by 3D stereophotogrammetry. 652 articles were retrieved in the initial search. After the review process, 11 full-text articles met inclusion criteria. After the evaluation process, 4 publications were included for the present literature review. Due to the heterogeneous methodology meta-analysis was not possible; consequently, a systematic assessment of the studies and summary of the findings from the available evidence were used to answer the research question. The maximum widening of the alar cartilage is 1.41 ± 0.95 mm, whose clinical significance is open to question. The effect of RME on the mouth width remains controversial. In Altindis et al., the difference between pre-treatment and post-treatment mouth width (1.80 mm increment in the banded RME group) was statistically significant, while in Baysal 1.86 mm was considered a non-significant value. Inconsistencies and limitations in the study population and measurement protocols were detected between studies. These data underline the necessity for updated guidelines that allow to standardise, for this type of study, sample selection, measurement methods and collection of results.

KEY WORDS: Systematic review • Face • Nose • Photogrammetry • Soft tissue • Dentofacial orthopaedics • Growth

RIASSUNTO

In questa revisione sistematica, è stata analizzata la letteratura per analizzare i cambiamenti tridimensionali dell'area nasolabiale indotti dall'espansione rapida del mascellare (RME) misurati attraverso la stereofotogrammetria. La presente revisione è strutturata secondo lo schema PRISMA-P ed è stata registrata sul portale PROSPERO con il seguente ID: CRD42017079875. I database Pubmed, Cochrane, EBSCO, Scopus, Web of Sciences sono stati consultati senza nessuna restrizione di anno o di status della pubblicazione. 652 articoli sono risultati dalla ricerca iniziale. A seguito del processo di revisione, 11 articoli sono risultati conformi ai criteri di inclusione. Dopo la lettura in extenso dei lavori, 4 pubblicazioni sono state incluse nella seguente revisione. I criteri di selezione sono stati: studi clinici randomizzati e controllati, studi di coorte, studi caso-controllo su pazienti con crossbite uni/bilaterale o deficit trasversale del mascellare o affollamento dentale, pazienti che hanno eseguito espansione rapida del mascellare superiore e che sono stati monitorati mediante stereofotogrammetria. La metodologia eterogenea dei lavori ha reso una meta-analisi impossibile; di conseguenza, è stata eseguita un'accurata analisi degli studi ed una puntuale schematizzazione dei risultati ai fini di rispondere al quesito clinico. La massima distensione della cartilagine alare è stata di 1,41 ± 0,95 mm, la cui rilevanza clinica è questionabile. L'effetto dell'espansione mascellare sull'ampiezza della bocca rimane controverso. In Altindis et al., l'incremento di ampiezza del cavo orale post-trattamento (1,80 mm nel gruppo con RME su bande) è considerato statisticamente significativo, mentre in Baysal et al. il valore di 1,86 mm non risulta un cambiamento statisticamente significativo. Inconsistenze e limitazioni nella popolazione degli studi e nei protocolli di misurazione sono stati individuati all'interno degli articoli. I dati emersi dovrebbero essere confermati con un protocollo metodologicamente conforme, evitando bias di selezione e di misurazione.

PAROLE CHIAVE: *Revisione sistematica • Volto • Naso • Fotogrammetria • Tessuti molli • Ortopedia dento-facciale • Malocclusione • Crescita*

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Introduction

Rationale

Rapid maxillary expansion (RME) represents an orthopaedic and orthodontic procedure aimed at increasing maxillary transverse dimension in growing patients [1]. In orthodontic practice, the rapid maxillary expansion treatment approach is adopted to expand the maxillary arch and resolve skeletal/dentoalveolar cross-bites as well as arch perimeter deficiency in mild to moderate crowding case [2]. The rationale behind the approach is that heavy orthopaedic forces applied with a jackscrew can mechanically separate the maxillary segments at the level of the midpalatal suture [3].

Since the bone base and soft tissue envelope are closely related, this orthopaedic therapy may affect nasal shape and dimension [4-6].

Several techniques have been described to analyse nasolabial soft tissue changes following RME therapy: direct anthropometric measurements, photometric assessment, cephalograms and cone beam computed tomography (CBCT) scans [7-9].

Three-dimensional stereophotogrammetry involves the use of several digital cameras that simultaneously capture images of the same object from different viewpoints; software reconstruction algorithms integrate matching regions in both images to compute the coordinates of all the points that outline the surface frame of the 3-D object [10]. It is intuitive and demonstrated in the literature that 3-D stereophotogrammetry is a noninvasive gold-standard imaging modality for qualitative and quantitative soft tissue analysis of the orofacial region, because it offers better reproducibility and higher accuracy than two-dimensional representations of a three-dimensional object, such as standard 2-D cephalograms or photographs [11 12].

The clinical potential of 3-D photogrammetry lies in the development a realistic virtual model of the patient's head for documentation, treatment planning, prediction and long-term evaluation of treatment outcomes [13-15]. However, there is a paucity of knowledge documenting 3D facial changes induced by RME and an absence of reviews systematically investigating this topic.

Objectives

The aim of this systematic review was to investigate and summarise currently available data pertaining to the use of 3-D stereophotogrammetry for assessment of nasolabial soft tissue changes after rapid maxillary expansion.

The primary question of this review is: how does RME influence the nasolabial soft tissue development in growing patients?

The secondary question is: if present, can the aesthetic impact provided by RME appliances be considered clinically significant? How can the treatment effect be clinically interpreted? What guidelines can be drawn for future research?

The null hypothesis is that there are no statistically and clinically significant nasolabial soft tissue differences after RME. The alternative hypothesis is that the included studies report statistically and clinically significant differences between facial landmarks, measured before and after RME.

Materials and methods

Protocol and registration

The protocol for this systematic review was based on the PRISMA-P statement and was registered in the International Prospective Register of Systematic Review (www.crd.york.ac.uk/PROSPERO/) with the ID number: CRD42017079875.

Eligibility criteria

The full search strategy focused on four categories of terms, as suggested by the PICO approach (Population: face; malocclusion; Intervention: rapid maxillary expansion, Comparison: stereophotogrammetry, Outcomes: treatment effects). Only papers that met study admittance criteria reported were accepted (Table I). We choose not to include patients with reduced naso-respiratory function in the study population for the following reasons:

- patients with respiratory disorders often present morphological alterations, which make difficult to use them as a comparator [16];
- altered breathing pattern may have influence on craniofacial development; so, it can potentially bias the effects of rapid maxillary expansion [17 18].

Only papers published in English were considered. No limitation concerning publication year or publication status was included.

Information sources and literature search

On 11 July 2017, five electronic sources were systematically consulted: Pubmed, Scopus, Cochrane Central, Web of Science, EBSCO. The same search strategy was adapted for each mesh terms database (Supplementary material 1). In addition, http://clinicaltrials.gov, Google Scholar and grey literature searches were conducted. Manual search concerned references and citation list of the included studies. The publications of the authors listed in the accepted studies were checked as well.

Table I. Study selection criteria.

Study selection criteria by abstract	
Type of the study	Randomised clinical trials (RCTs), controlled clinical trials (CCTs), cohort studies, cross-sectional studies, case-control studies
Clinical research query	Studies on patients with unilateral or bilateral cross-bite, maxillary transverse deficiency, crowding Studies on patients who underwent rapid maxillary expansion in order to obtain a rapid increase in the upper arch available space. Follow-up three-dimensional images of the face have been acquired before and after treatment by means of stereo-photogrammetry
Control sample	Homogeneous patients not receiving RME treatment
Study selection criteria by full-text	
Inclusion criteria	**Exclusion criteria**
Type of study: randomised clinical trials (RCTs), controlled clinical trials (CCTs), cohort studies, cross-sectional studies, case-control studies	*Type of study*: case reports, case series with less than 10 patients, reviews, author editorials, technical papers, animal studies
Clinical research query: studies on patients with unilateral or bilateral cross-bite, maxillary transverse deficiency, crowding. Studies on patients who underwent rapid maxillary expansion in order to obtain a rapid increase in the upper arch available space. Follow-up: three-dimensional images of the face have been acquired at least before and after treatment by means of stereo-photogrammetry	*Clinical research query*: studies on patients with systemic disorders or impaired naso-respiratory function, studies about surgical-aided rapid maxillary expansion (SRME or SARME), studies regarding the use of photography or lateral cephalograms to evaluate soft tissue effects induced by RME
Control sample: must include homogeneous patients not receiving RME treatment	*Control sample*: must NOT include healthy patients not receiving RME treatment

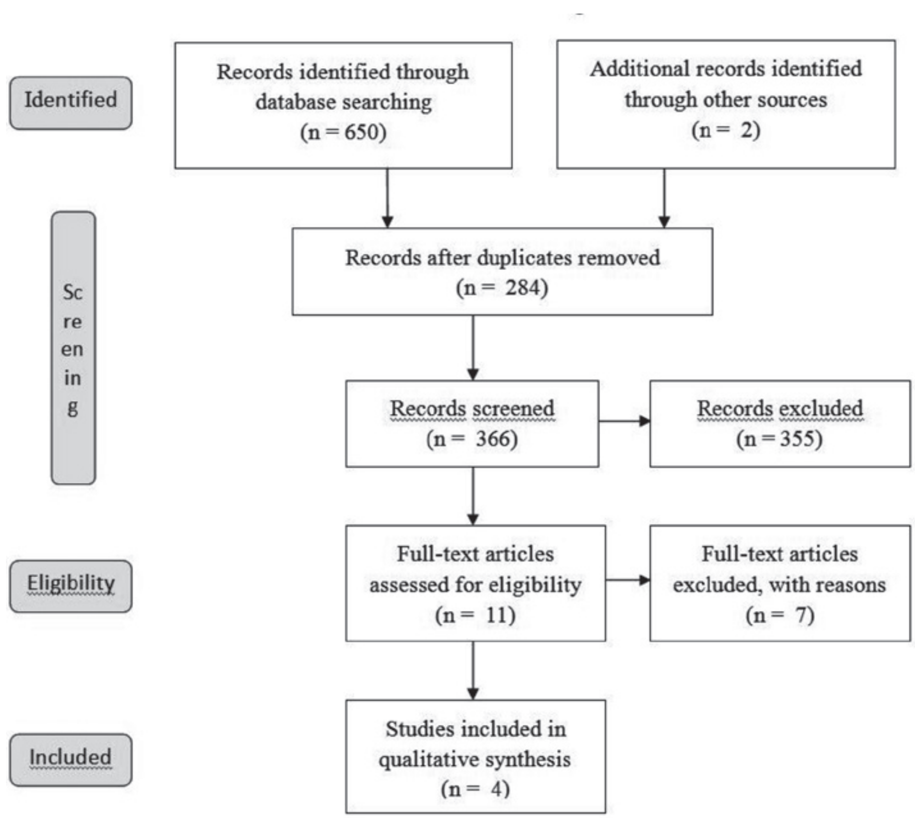

Fig. 1. PRISMA flow diagram for the identification and selection of studies.

Study selection and data collection
Eligibility of the articles was biphasically determined: two of the authors (ES and MDL) independently conducted the electronic search and performed a title and abstract (TIAB) screening to pre-select articles for full-text retrieval. Any disagreement was resolved in consensus with a third examiner (RP).
The articles selection process is described in the PRISMA Flow Diagram (Fig. 1).

Risk of bias in individual studies
The Cochrane Collaboration tool for assessing the risk of bias and Newcastle-Ottawa quality assessment scale were used by two Authors (ES and MDL) independently to rate the methodological quality of experimental and observational studies, respectively.
In order to uniformly rate the level of evidence of the included studies (confidence in effect estimates), the 3-point grading system, described by the Swedish Council on Technology Assessment in Health Care (SBU), was adopted [19 20].

Results

Study selection
Discarding 284 duplicates with Endnote®, a total of 652 titles were considered for possible inclusion. After a title and abstract (TIAB) screening to pre-select articles for full-text retrieval, 11 papers were identified.
Among the trials available, 4 articles were met inclusion criteria listed for the systematic review. The studies rejected after full-text evaluation were recorded in the excluded studies table (Supplementary material 2), together with the reasons for exclusion.

Study characteristics
In Table II, the evidence is quantitatively analysed and summarised; studies are classified according to the type of appliance used and the patient's age at the time of intervention.
Homogeneous landmarks were not adopted among the selected studies, and thus a meta-analysis could not be performed.

Result of individual studies
The included articles of Baysal et al. [21], Altındiş et al. [2], Altorkat et al. [22] report the use of the banded appliance in similar age groups, showing different results on the alar cartilage width effects (Table II): the study of Baysal [21] and Altındiş [2] found a statistically significant increase of the nasal width (1.16 mm and 1.42 in the banded RME group, respectively), while Altorkat et al. [22] reported a non-significant change of 0.4 mm. The difference between the increments is almost three times, but not clinically significant if a threshold value of 3 mm is established [23].
The effect of RME on the mouth width remains controversial. In Altındiş et al. [2], the difference between pre-treatment and post-treatment mouth width (1.80 mm increment in the banded RME group) was statistically significant, while in Baysal et al. [21] 1.86 mm was not considered to be a significant value (Table III).
Altındiş et al. [2] found that RME produces a more protrusive effect on the upper lip. Dindaroglu [23] found no significant changes on the labial area. Baysal [21] did not find any statistically significant changes for the lips, or for the intercantal and zygoma point distances.

Quality of evidence assessment
According to the SBU tool, the quality of the collected evidence was moderate (grade B) in three studies [2 21 23] and low (grade C) in one [22]. Thus, conclusions with a limited level of evidence could be drawn from the review process. The most important sources of bias were the absence of a growth status assessment, age of the treated sample, heterogeneity of follow-up protocols and lack of blinded standardised measurement procedures.

Discussion

Summary of evidence
In conclusion, nasal soft tissues after RME present small and variable immediate changes. Altorkat et al. [22] reported that there are significant changes in nasal transverse dimensions after RME, while Altindis et al. did not find any significant differences between different types of appliances.
In both studies, the absence of a control group makes it impossible to discriminate the nasolabial soft tissue modifications induced by RME with those occurring in a physiological growth pattern in an untreated population.
From a statistical point of view, the short-term effect of RME of morphology remains controversial. If present, the aesthetic impact provided by RME appliances may be considered as not clinically significant.

Limitations
The articles by both Altındiş et al. [2] and Altorkat et al. [22] did not consider gender differences in puberty timing, as other authors have done [24]; this seems to be in contrast with evidence supporting that the start and the advance of fusion of the midpalatal suture may be greatly influenced by gender [25].

Table II. Patient characteristics and quality of evidence of the included studies.

Trial	Setting	Sample size	Mean age (years)	Mean time between image acquisitions	Type of appliance	Skeletal development	Quality of the evidence (SBU grading system)[1]
Altındiş et al., 2016 [2]	RCT	42 (18 M, 24 F) **Banded RME: 6 M, 8 F Bonded RME: 7 M, 7 F Modified bonded RME: 5 M, 9 F	Banded RME: **12.7 ± 0.6 Bonded RME: 12.4 ± 0.8 Modified bonded RME: 15.5 ± 0.8	NA (at the end of the three months retention period)	**Banded RME, bonded RME, modified bonded RME	NA	B
Altorkat et al., 2016 [22]	Case-series	14 (7 M, 7 F)	12.6 ± 1.8	NA (at the end of the active phase)	Bonded RME	NA	C
Baysal et al., 2016 [21]	RCT	34 (18 M, 16 F) Exp: 9 M, 8 F Ctr: 9 M, 8 F	Exp: 13.4 ± 1.2 Ctr: 12.8 ± 1.3	6.1 months	Bonded RME	NA	B
Dindaroğlu et al., 2016 [23]	RCT	50 (26 M, 24 F) Exp: 14 M, 11 F Ctr: 12 M, 13 F	Exp: Male: 9.6 ± 0.9 Female: 10.1 ± 1.0 Ctr: Male: 9.2 ± 0.7 Female: 9.9 ± 0.9	15.6 days	Bonded RME	Not exceeding MP3 cap stage	B

[1] Articles were graded according to the SBU criteria as follow: 1) grade A (High level of evidence): randomised controlled trials (RCTs) or prospective study with a well-defined control group; presence of defined diagnosis and endpoints; well-described diagnostic reliability tests and reproducibility tests; blinding outcome assessment. 2) grade B (Moderate level of evidence): same criteria as grade A except for the blinding outcome assessment. 3) grade C (Low level of evidence): articles that do not meet the criteria of grade A and B.
SBU tool permitted to assess the level of the available evidence of the systematic review accordingly to the following classification: 1) strong: at least two studies of level A; 2) moderate: one study of level A and at least two studies of level B; 3) limited: at least two studies of level B; 4) scarce: fewer than two studies of level B.
*** Please note: in Altındiş et al. [2], only the banded type appliance RME group was included in this review. NA: Not Assessed*

Moreover, the authors did not classify the sample according to growth status: earlier beginning, peak, or end of the pubertal height growth spurt groups may present different soft-tissue nasolabial changes after RME [26]. Even if there is evidence supporting that growth increments of the soft tissue profile are at an unimportant level in such a short period [27], age is not a reliable indicator of the maturational stage of the midpalatal suture [25].

Clinical experience and bone biology studies highlight that the stage of sutural maturation might be related to

Table III. Definitions of soft tissue landmarks and comparison of mean differences between the included studies.

		Comparisons of treatment changes among the groups (mm)		
Abbreviation	Definition	Altındiş et al. [2]	Altorkat et al. [21]	Baysal et al. [22]
AlR-AlL	Distance between left and right alar: point located at left and right labial commissure	1.35 ± 1.08	1.6 (1.00 – 2.02)	1.42 ± 0.96
ChR-ChL	Distance between left and right chelion: most lateral point on left and right alar contour	1.80 ± 1.85	-	1.86 ± 1.35

** Please note: the study of Dindaroğlu et al. [23] does not report linear distances (AlR-AlL and ChR-ChL), but volumetric 3-D deviations. Therefore, Dindaroğlu's data are not included in this table.*

the success of orthopaedic expansion, emphasising that conventional RME treatment is indicated before the circumpubertal period [28]; in the studies of Altındiş et al. [2] and Altorkat et al. [21] the mean age is 12.7 and 12.6 years, in Baysal et al. [22] is 13.4 years, and thus it can be expected that patients would show more dentoalveolar than skeletal effects after RME treatment [29].

The longest follow-up evaluation in the included studies was six months [2]; additional studies are needed to gain a better understanding of the long-term effects of RME treatment on nasolabial soft tissues.

The inconsistency between nasal width values may be related to the fact that post-treatment 3-D stereophotogrammetry is scheduled at different time periods (Table IV).

No single study focused on inter-examiner reliability. This concept is crucial: none of the investigations mentioned the reference plane used to identify the soft tissue anthropometric landmarks. This bias should be masked if the examiner is still the same, but there could be significant differences in landmark positioning between different points of view.

All studies assessed intra-examiner reliability; however, inter-examiner reliability and blinding of the investigator who identified the facial landmarks are not reported. These methodological issues may cause bias in the results. In Dindaroğlu's analysis, the 3D deviation around the nasolabial area is automatically calculated by the software: this protocol reduces operator-related bias due to landmark identification error [23].

Statistically, the alar cartilage and mouth width of the included studies does not reach the clinically significant increment of 3 mm. However, in the study of Altorkat et al. [21], the "3 mm" cut-off parameter was made on the basis of a cephalometric study concerning skeletal modifications due to RME, even if it is not demonstrated that nasolabial soft tissue changes follow hard tissue modifications [30].

Conclusions

RME appliances produce slight clinically non-significant nasolabial soft tissue changes. RME is an effective therapeutic option for patients with maxillary transversal deficiency. Most of patients who seek orthodontic treatment are dissatisfied with their appearance. The treatment protocol that considers the impact of orthopaedic treatment on facial morphology represents an improved standard of care for patients [31]. This aspect of the treatment cannot be overstated. If the RME induced noticeable impairment, this strong discontent may continue throughout the patient's life. Advances in 3D-imaging techniques achieve high accuracy and reproducibility for capturing and superimposing facial images and measure changes in soft tissue position three dimensionally [32-34]. The novel use of stereophotogrammetry includes the quantification and assessment of immediate changes of the mid facial third following rapid maxillary expansion [35]. An increasing number of reviews is available in the current literature, so that high emphasis should be put on the methodological quality of the clinical trials. It is true that the strength of the evidence lies in the study design: in orthodontic practice, it is even more difficult than other disciplines to compare a multitude of variables.

Recommendations for further research

Updated guidelines for future research are outlined according to the PICOS approach:

Population: it should be staged according to the skeletal development status; even if Johnson et al. [24] showed that non-significant differences were noted between pre-pubertal and post-pubertal groups, they noted a significant increase in greater alar cartilage width between treated and untreated groups in a prepubertal male population from the beginning of the treatment to the 6-month follow-up.

Intervention: is it curious that we found only articles dealing with tooth-borne expanders; it could be interesting to compare soft-tissue changes bone-anchored (BAME) and traditional tooth-anchored rapid maxillary expanders (TAME). Lagravere at al. [36] pointed out that the difference in terms of skeletal expansion is almost null between TAME and BAME, and Nada et al. [37] stated that tooth-borne and bone-borne surgically assisted rapid maxillary expansion devices showed comparable results.

Comparison: we would strengthen the need for long-term follow-up studies; photometric studies show that differences between pre-pubertal and post-pubertal patients are significant in the short-term period, but may change during growth [38]. The sample should include homogeneous untreated patients and non-healthy individuals to investigate the differential growth pattern of nasolabial soft tissues.

Outcome: bias avoidance is fundamental for the development of a randomised controlled clinical trial. It is fundamental to standardise the anatomic landmark positioning because the methodology of the point selection results to be a critical step of the morphometric analysis. The anatomical structures are visually identified by the examiner; therefore, accuracy and reproducibility of the measurements reflects the precision of the point determination; experience and blinding of the investigators play a key role in the analysis of facial morphology [39].

Table IV. Risk of bias assessment.

Study	Rating scale		
Baysal 2016 [21]	**Cochrane's collaboration tool for assessing the risk of bias**		
Items	**Low risk**	**High risk**	**Unclear risk of bias**
Randomisation	x		
Allocation	x		
Blinding participant and personnel		x	
Blinding outcome assessor		x	
Missing outcome data	x		
Selective reporting	x		
Other bias		x (skeletal maturation; age of 13 years; 6-month follow-up)	
Dindaroğlu 2016 [23]	**Cochrane's collaboration tool for assessing the risk of bias**		
Items	**Low risk**	**High risk**	**Unclear risk of bias**
Randomisation	x		
Allocation			x
Blinding participant and personnel		x	
Blinding outcome assessor		x	
Missing outcome data	x		
Selective reporting			x
Other bias		x (15-days follow-up)	
Altındiş 2016 [2]	**Cochrane's collaboration tool for assessing the risk of bias**		
Items	**Low risk**	**High risk**	**Unclear risk of bias**
Randomisation	x		
Allocation			x
Blinding participant and personnel		x	
Blinding outcome assessor		x	
Missing outcome data	x		
Selective reporting			x
Other bias	3-month follow-up	x (age of 12.6 years)	x (absence of skeletal maturation indicators)
Altorkat 2016 [21]	**Newcastle-Ottawa Quality Assessment Scale**		
	0 star	**1 star**	**2 stars**
Representativeness	x		
Selection	x		
Sample size		x	
Non-respondent		x	
Exposure	x		
Comparability	x		
Outcome assessment	x		
Statistical test	x		

Study: stereophotogrammetry is the most versatile method for quantitative longitudinal assessment of craniofacial dimensions and shapes in children [40 41]. It is a noninvasive method that allows a routine clinical assessment of facial changes induced by orthodontic appliances. The versatility of this technique offers the opportunity to have a longitudinal monitoring of the facial soft-tissue development [41]. Accordingly, we would strengthen the importance to obtain 3-D images following a standardised protocol: image acquisition should be performed after the active phase of RME, after the retention period and one-two years thereafter, in order to have a clear idea of the soft-tissue remodeling in growing patients.

Conflict of interest statement

None declared.

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Supplementary material

Supplementary material 1. Full electronic search strategy.

Database	Search strategy
Pubmed (free text words)	((((((((orthodontics*[All Fields]) OR jaw*[All Fields]) OR face*[All Fields]) OR (growth and development*[All Fields])) OR malocclusion*[All Fields]))) AND (((((((female*[All Fields]) OR male*[All Fields]) OR child*[All Fields]) OR adult*[All Fields]) OR adolescent*[All Fields]) OR epidemiologic studies*[All Fields]))) AND (((((diagnosis*[All Fields]) OR determination*[All Fields]) OR assessment*[All Fields]) OR evaluation*[All Fields]) OR treatment outcomes*[All Fields]))) AND (photogrammetry*[All Fields])
Pubmed MeSh	((((((((orthodontics*[MeSh]) OR jaw*[MeSh]) OR face*[MeSh]) OR (growth and development*[MeSh])) OR malocclusion*[MeSh]))) AND (((((((female*[MeSh]) OR male*[MeSh]) OR child*[MeSh]) OR adult*[MeSh]) OR adolescent*[MeSh]) OR epidemiologic studies*[MeSh]))) AND (((((diagnosis*[MeSh]) OR determination*[MeSh]) OR assessment*[MeSh]) OR evaluation*[MeSh]) OR treatment outcomes*[MeSh]))) AND (photogrammetry*[MeSh])
Scopus	((TITLE-ABS-KEY (orthodontics*)) OR (TITLE-ABS-KEY (jaw*)) OR (TITLE-ABS-KEY (face*)) OR (TITLE-ABS-KEY (growth AND development*)) OR (TITLE-ABS-KEY (malocclusion*))) AND ((TITLE-ABS-KEY (female*)) OR (TITLE-ABS-KEY (male*)) OR (TITLE-ABS-KEY (child*)) OR (TITLE-ABS-KEY (adolescent*)) OR (TITLE-ABS-KEY (epidemiologic AND studies*))) AND ((TITLE-ABS-KEY (diagnosis*)) OR (TITLE-ABS-KEY (assessment*)) OR (TITLE-ABS-KEY (evaluation*)) OR (TITLE-ABS-KEY (determination*)) OR (TITLE-ABS-KEY (treatment AND outcomes*))) AND (TITLE-ABS-KEY (photogrammetry*))
Cochrane Central (Free Text Words)	(orthodontics* OR jaw* OR face* OR growth and development* OR malocclusion*) AND (male* OR female* OR child* OR adult* OR adolescent* OR epidemiologic studies*) AND (diagnosis* OR assessment* OR evaluation OR determination* OR treatment outcomes*) AND photogrammetry*
Cochrane Central MeSh	((MeSH orthodontics) OR (MeSH jaw) OR (MeSH face) OR (MeSH Growth AND Development) OR (MeSH Malocclusion)) AND ((MeSH diagnosis) OR (MeSH Outcomes AND Process Assessment) OR (MeSH Evaluation Studies as Topic) OR (MeSH Treatment outcome)) AND ((MeSH male) OR (MeSH female) OR (MeSH child) OR (MeSH adult) OR (MeSH Adolescent) OR (MeSH Epidemiologic Studies)) AND (MeSH Photogrammetry)
Web of Science	(TS=(orthodontics*) OR TS=(jaw*) OR TS=(face*) OR TS=(growth and development*) OR TS=(malocclusion*)) AND (TS=(male*) OR TS=(female*) OR TS=(child*) OR TS=(adult*) OR TS=(adolescent*) OR TS=(epidemiologic studies*)) AND (TS=(diagnosis*) OR TS=(assessment*) OR TS=(evaluation) OR TS=(determination*) OR TS=(treatment outcomes*)) AND (TS=(photogrammetry*))
EBSCO MeSh	(MH orthodontics* OR MH jaw* OR MH face* OR MH jaw diseases* OR MH (growth and embryonic development*) OR MH malocclusion*) AND (MH Photogrammetry*) AND (MH male* OR MH female* OR MH child* OR MH adult* OR MH child development: 5 years* OR MH child development: 6-11 years* OR MH child development: 11-17 years* OR MH experimental studies*) AND (MH diagnosis* OR MH outcome assessment* OR MH evaluation* OR MH treatment outcomes*)

Supplementary material 2. Table showing references of excluded studies with rationale for exclusion.

References	Rationale for exclusion
Bishara et al., 1995	3D analysis not performed
Cummins et al., 1995	3D analysis not performed
Kamonji, 1980	3D analysis not performed
Kim et al., 2016	Patients not treated with RME
Matzler et al., 2014	Patients not treated with RME
Rune et al., 1980	3D analysis on hard tissue and not on soft tissue
Singh, 2002	Patients not treated with RME