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Evaluation of surgically assisted rapid maxillary expansion and orthodontic treatment

Effects on dental, skeletal and nasal structures and rhinological findings

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To Helen, Cajsa, Måns and Maja

"To everything there is a season, and a time for every purpose under the heaven"

Contents

Abstract

Surgically Assisted Rapid Maxillary Expansion (SARME) is frequently used to treat skeletal maxillary transverse deficiency (MTD) in skeletally mature and non-growing individuals. Despite previous research in the field, questions remain with respect to the long-term stability of SARME and its effects on hard and soft tissue.

The overall aim of the present doctoral work was to achieve a greater understanding of SARME, using modern image technology and a multidisciplinary approach, with special reference to effects on the hard and soft tissues and respiration. A more specific aim was to evaluate the long-term stability in a retrospective sample of patients treated with SARME and orthodontic treatment and to compare the results with a matched, untreated control group. The studies in this doctoral project are thus based on two different samples and study designs.

The first sample, Study I (Paper I), is a retrospective, consecutive, long-term follow-up material of study models from 31 patients (17 males and 14 females) treated with SARME and orthodontic treatment between 1991 and 2000. The mean pre-treatment age was 25.9 years (SD 9.6) with a mean follow-up time of 6.4 years (SD 3.3). Direct measurements on study models were made with a digital sliding caliper at reference points on molars and canines. To evaluate treatment outcome and long-term stability, the results were compared with study models from an untreated control group, matched for age, gender and follow-up time.

The second sample, Study II (Papers II-IV), is a prospective consecutive, longitudinal material of 40 patients scheduled to undergo SARME and orthodontic treatment between 2006 and 2009.

In Paper II, one patient was excluded because of a planned adenoidectomy. The final sample comprised 39 patients (16 males and 23 females). The mean age at treatment start was 19.9 years (range 15.9 – 43.9). Acoustic rhinometry, rhinomanometry and a questionnaire were used to assess the degree of nasal obstruction at three time-points; pre-treatment, three months after expansion and after completed treatment (mean 18 months).

In Papers III–IV, three patients declined to participate and two had to be excluded because their CT-records were incomplete. The final sample comprised 35 patients (14 males and 21 females). The mean age at treatment start was 19.7 years (range 16.1 – 43.9). Helical CT-images were taken pre treatment and eighteen months' post-expansion. 3D models were registered and superimposed at the anterior cranial base. The automated voxel-based image registration method allows precise, accurate measurements in all areas of the maxilla. In Papers II–IV, the treatment groups constituted their own control groups.

The main findings in the retrospective, long-term follow-up study were that SARME and orthodontic treatment normalized the transverse discrepancy and was stable for a mean of 6 years post-treatment. Pterygoid detachment did not entirely eliminate the side effect of buccal tipping of the posterior molars. Relapse is time-related and is most pronounced during the first 3 years after treatment. Thus the retention period should be extended and should be considered for this period.

The main rhinological findings in the prospective longitudinal study were that SARME had a short-term, favourable effect on nasal respiration, but the effect did not persist in the long-term. However, subjects with pre-treatment nasal obstruction reported a lasting sensation of improved nasal function.

SARME and orthodontic treatment had a significant but non-uniform skeletal treatment effect, with significantly greater expansion posteriorly than anteriorly. The expansion was parallel anteriorly but not posteriorly. The lateral tipping of the posterior segment was significant, despite careful surgical separation. No correlation was found between tipping and the patient's age. Furthermore, SARME and orthodontic treatment significantly affected all dimensions of the external features of the nose. The most obvious changes were at the most lateral alar-bases. The difference in lateral displacement profoundly influenced the perception of a more rounded nose. There were no predictive correlations between the changes. Patients with narrow and constrained nostrils can benefit from these changes with respect to the subjective experience of nasal obstruction. It is questionable whether an alar-cinch suture will prevent widening at the alar-base.

The 3D superimposition applied in Study II is a reliable method, circumventing projection and measurement errors. In conclusion, SARME and orthodontic treatment normalize the transverse deficiency, with long-term stability. SARME has a favourable effect on the subjective perception of nasal respiration. SARME significantly affects dental, skeletal and nasal structures.

List of papers

This thesis is based on the following papers, which are referred to by their Roman numerals in the text.

I
Magnusson A, Bjerklin K, Nilsson P, Marcusson A. Surgically assisted rapid maxillary expansion: long-term stability. Eur J Orthod 2009; 31: 142-149.
II
Magnusson A, Bjerklin K, Nilsson P, Jönsson F, Marcusson A. Nasal cavity size, airway resistance, and subjective sensation after surgically assisted rapid maxillary expansion: A prospective longitudinal study. Am J Orthod Dentofacial Orthop 2011; 140: 641-651.
III
Magnusson A, Bjerklin K, Kim H, Nilsson P, Marcusson A. Three-dimensional assessment of transverse skeletal changes after surgically assisted rapid maxillary expansion and orthodontic treatment: A prospective computerized tomography study. Am J Orthod Dentofacial Orthop 2012; 142: 825-833.
IV
Magnusson A, Bjerklin K, Kim H, Nilsson P, Marcusson A. Three-dimensional computed tomographic analysis of changes to the external features of the nose after surgically assisted rapid maxillary expansion and orthodontic treatment: A prospective longitudinal study. Am J Orthod Dentofacial Orthop, 2013 submitted, manuscript number: AJODO-D-13-00060R1. Accepted 2013-04-24.

Abbreviations

AR	Acoustic rhinometry
CBCT	Cone beam computed tomography
DO	Distraction osteogenesis
FEM	Finite element method
GBI	Glasgow benefit inventory questionnaire
GUI	Graphical user interface
MCA	Minimum cross-sectional area
MTD	Maxillary transverse deficiency
NAR	Nasal airway resistance
NARexp	Nasal airway resistance / expiration
NARinsp	Nasal airway resistance /inspiration
PA	Postero-anterior
QOF	Quality of life
R	Resistance
RME	Rapid maxillary expansion
RMM	Rhinomanometry
SARME	Surgically assisted rapid maxillary expansion
TPS	Thin-plate spline model
TPS-CPM	Thin-plate spline-closest point matching
VAS	Visual analogue scale

Introduction

General Introduction

A correct transverse skeletal relationship between the jaws is essential for stable and functional occlusion (Vanarsdall, Jr. 1999, Wertz 1970). Maxillary transverse hypoplasia is associated primarily with functional impairments, such as posterior uni- or bilateral cross bite, dental crowding, reduced nasal respiratory function or anterior-posterior skeletal anomalies (Betts *et al.* 1995, Haas 1980, Warren *et al.* 1987b).

Surgically Assisted Rapid Maxillary Expansion (SARME) is a frequently used method to treat skeletal maxillary transverse deficiency in skeletally mature and non-growing individuals. SARME is a further development of Rapid maxillary expansion (RME), an orthopaedic method to expand the maxilla. SARME is a combination of orthodontics and surgical procedures and by separating the surrounding sutures, offers substantial enlargement of the dental arch, the maxillary apical base and the palatal vault.

The narrow palate in growing individuals has been associated with impaired nasal respiratory function (Harvold *et al.* 1972, Linder-Aronson 1979, Lofstrand-Tidestrom *et al.* 1999, McNamara 1981, Vig 1998). Several studies have reported improvement in nasal patency in children after orthopaedic maxillary expansion; it can be hypothesized that similar associations exist after maxillary expansion in non-growing individuals (Warren *et al.* 1987b, Wriedt *et al.* 2001).

McNamara,Jr *et al.* (2003) suggested maxillary transverse expansion as a tool to correct crowding and space deficiency.

Despite previous research in the field, questions remain with respect to the effects and long-term stability of SARME and orthodontic treatment. In the present thesis, new technology and a multidisciplinary approach are applied in the quest for new scientific knowledge about SARME.

Definition and classification

Maxillary transverse deficiency (MTD) is one of the most pervasive and common skeletal problems in the craniofacial region, often combined with a simultaneous vertical or antero-posterior skeletal discrepancy (Betts *et al.* 1995). MTD is prevalent in both syndromic and non-syndromic patients (Menon *et al.* 2010).

The most frequently reported clinical manifestations are uni- or bilateral posterior crossbites, palatal inclination of teeth, dental crowding, high palatal arch, narrow, tapering arch form and problems associated with nasal breathing (Pereira *et al.* 2010). Unlike vertical or sagittal discrepancies, MTD is difficult to diagnose extraorally. The extraoral manifestations are often discrete, uncertain and limited to narrow alar bases, paranasal hollowing and a deep nasolabial groove. Vertical and sagittal anomalies often exist concomitantly; as they are more recognizable they will clinically mask the extraoral appearance of a MTD (Fig 1).

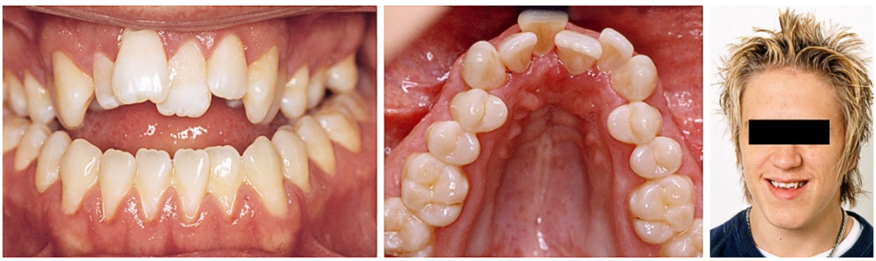


Figure 1. *Clinical intra- and extra-oral manifestations of maxillary transverse deficiency (MTD).*

The etiology of MTD is multifactorial, including congenital, genetic, developmental, traumatic or iatrogenic factors (Betts *et al.* 1995, Haas 1970, Harvold *et al.* 1972, Larsson 2001, Ogaard *et al.* 1994). Examples of causative factors are different syndromes, thumb and finger-sucking habits, mouth-breathing during critical growth periods, trauma or iatrogenic injuries after cleft palate repair. The prevalence of MTD is reported to be 8.5 to 22 per cent. The wide range of prevalence can be attributed to lack of uniformity in classification of maxillary transverse deficiency, such as magnitude of the skeletal discrepancy and the severity of dental components (da Silva Filho *et al.* 1991, da Silva Filho *et al.* 2007, Egermark-Eriksson *et al.* 1990, Harrison and Ashby 2001, Ingervall *et al.* 1978, Thilander and Myrberg 1973, Thilander *et al.* 1984). There is no difference in prevalence with respect to gender or ethnicity (Allen *et al.* 2003) and no available data in the literature on prevalence in an adult skeletally mature population.

It is essential to distinguish between skeletal and dental components of the deformity in order to select the treatment modality which will achieve a stable, functional result (Haas 1965). The maxillary constriction can be purely skeletal, purely dental or a combination of both (Bishara and Staley 1987). Some cases have an apparent maxillary deficiency due to the palatal inclination of one or two posterior teeth. These maxillary transverse deficiencies with purely dental components are, in most cases, simple orthodontic problems and do not require extensive orthodontic or surgical treatment.

Bishara and Staley (1987) advocated a clinical examination of MTD. The examination takes into account the magnitude of the transverse discrepancy between maxilla and mandible, the number of teeth involved and the initial angulation of the maxillary molars and premolars. A transverse discrepancy exceeding 4mm and/ or buccally inclined maxillary molars and premolars indicate a true skeletal MTD

There are several indices for evaluating transverse dental deficiencies on study models such as Pont´s Index, Korkhaus Index and Howe´s Analysis, but these cannot be applied to determine the extent of a skeletal discrepancy (Dause *et al.* 2010, Howe 1947, Joondeph *et al.* 1970). Since most cases of MTD comprise a combination of dental and skeletal components, the delineation can be problematic.

Ricketts (1998) and Ricketts and Grummons (2004) proposed the use of frontal cephalometric analysis to distinguish between discrepancies in the widths of the dental arch, alveolar arch and skeletal base. The analysis was also an attempt to stratify skeletal MTD into different maxillomandibular combinations, such as narrow or normal maxilla and normal or wide mandible, in order to determine the severity of the deficiency (Ricketts 1981). MTD in patients exhibiting a narrow maxilla and wide mandible was expected to be the most difficult to correct and the most susceptible to relapse. A disadvantage of this method is major measurement error based on two dimensional analysis of radiographs.

Jacobs *et al.* (1980) stated that skeletal MTD can be divided into two categories; real and relative. Relative MTD implies that a transverse discrepancy exists clinically, but is attributable to a sagittal discrepancy between the jaws, i.e. in a relative MTD no transverse deficiency exists when the study models are examined in a Class I relationship. This is a common phenomenon in Angle Class III skeletal malocclusions.

Real MTD implies a true transverse maxillary insufficiency. Clinically there may or may not be a posterior crossbite. In contrast to relative MTD, true MTD shows a uni- or bilateral posterior crossbite when the study models are positioned in a Class I relationship. Real MTD is frequently associated with skeletal Class II malocclusions and skeletal open bites.

Although relative MDT can be treated with midpalatal suture opening, dental maxillary transverse deficiency and relative MTD require no orthopaedic or surgical transverse expansion (Jacobs *et al.* 1980). In such cases, the transverse discrepancy can be corrected by conventional orthodontics, with or without extractions. In surgical treatment of skeletal sagittal anomalies, relative MTD will be corrected by the following sagittal displacement.

Real MTD, however, requires opening of the midpalatal suture and separation of the maxilla to normalize the transverse deficiency and cannot be achieved by conventional orthodontics alone (Vanarsdall and White 1994). Once the diagnosis has been made and a need for expansion is ascertained, other factors must be addressed, such as the magnitude of the transverse discrepancy, the age of patient, whether the expansion should be achieved orthopaedically and/or by surgical intervention.

MTD in growing individuals

The concept of correcting MTD in growing individuals by midpalatal suture opening and a separation of the maxilla was first described in 1860 by Angell (1860). The patient, a 14-year old girl with a narrow maxillary arch, was fitted with an appliance that featured two contra-rotating screws. The screws were threaded left and right and placed against the necks of the posterior maxillary teeth. According to Angell, correction of the narrow arch was achieved in two weeks by separation of the maxilla along the midpalatal suture. Unfortunately, those responsible for the most influential dental journals and the scientific establishment could not see beyond the limitations of accepted science and believed that the method was either impossible or too dangerous to be used and Angell's report was revised.

During the early 1900´s numerous papers, mostly based on subjective findings, referred to the procedure and its favourable implications for nasal respiration (Brown 1903, Dean 1909). The procedure was, however, attempted in orthodontics with varying success. In 1893, Goddard (1893) showed that an appliance connected only to the maxillary first molar and premolar could separate the maxilla into halves in order to relieve dental irregularities caused by a narrow upper jaw. In 1913, Schoeder-Benseler (1913) presented the non spring-loaded jackscrew, a hygienic all-wire frame appliance.

The method was, however highly criticised and opponents pointed out the risk of such complex separation of the maxilla and possible serious disturbances to the surrounding hard and soft tissues. The irregularity of teeth could be treated in a more simple manner.

At this time, at the end of the 1920´s, the functional concept of development gained popularity among orthodontists, based on the theory that if the teeth were gently moved into their proper positions, bone would grow to support them. The increase in the dental arch width after conventional orthodontics would result in an increase in the width of the nasal passage. With the acceptance of this concept, maxillary expansion was almost abandoned.

However, Korkhaus and Haas reintroduced the concept in the early 1960´s as Rapid Maxillary Expansion (RME) and showed its effectiveness in adjusting real and relative MTD in growing and non- skeletally mature patients (Haas 1961, Korkhaus 1960). Haas recognized, more specifically, six indications for RME: real and relative MTD, nasal stenosis, all Class III malocclusion cases, the mature cleft patient, antero-posterior maxillary deficiency and arch length problems. The appliance consisted of orthodontic bands on the first permanent maxillary molars and either the first premolars or the deciduous first molars and connected with soldered lingual and buccal bars. The jackscrew was placed in the center of the midpalatal suture and attached to the lingual bars with an acrylic baseplate. Heavy orthopaedic forces, up to 45 N were used to separate the two maxillary halves at the midpalatal suture (Isaacson 1964). These forces were not limited to the maxilla and the midpalatal suture, but affected also adjacent structures, directly or indirectly (Bell 1982, Davis and Kronman 1969, Timms 1980). To ensure adequate separation in the midpalatal suture, separation was documented with an occlusal radiograph and the development of an inter-incisal diastema.

Haas documented 10 clinical cases with skeletal changes after RME in both transverse, vertical and antero-posterior dimensions (Haas 1961). Krebs (1964) supported these findings and in implant studies with a mean of 7 years, showed stable long-term expansion in the maxillary base and nasal cavity. Thorne (1960) found a gain in nasal width from 0.4mm to 5.7 mm, with an average increase of 1.7mm, and noted that without retention the effects would be lost. The main finding was however, that the ideal timing for expansion was before and during the growth spurt period (Haas 1970, Proffit 2013, Wertz 1970). Treatment after this period was found to result in alveolar bending, periodontal compression, lateral tooth displacement, tooth extrusion, relapse, and pain, and fewer true skeletal changes (Lines 1975, Menon *et al.* 2010). These sequelae were attributed to increased rigidity of the facial bones and the closure of cranial sutures (Isaacson 1964, Kokich 1976). Once skeletal maturity has been reached, RME alone does not achieve a stable widening of the maxilla (Proffit 2013). Skeletal maturity was based on anatomical studies of the maturing face and especially the midpalatal suture and adjacent circum-maxillary articulations (Korn and Baumrind 1990, Silverstein and Quinn 1997, Wertz 1970, Zimring and Isaacson 1965).

In an autopsy material, Persson and Thilander (1977) found evidence of bony union in the midpalatal suture in late adolescence, but also open sections in the mid-twenties. Melsen (1975) concluded that growth at the midpalatal suture continues until around the age of 13–15 and is then followed by continuation of apposition until the age of 18 years. The sutural growth was assumed to coincide with the end of somatic growth (Isaacson 1964).

Thus, sutural closure diminishes the potential to achieve an adequate stable skeletal expansion of the maxilla. Determination of the skeletal maturity is crucial. The literature presents conflicting views about the age limit for achieving orthopaedic sutural opening of the maxilla. Timms and Vero (1981) suggested 25 years as an upper limit for orthopaedic expansion; this is supported by the findings of Mossaz *et al* (1992). In contrast, Mommaerts (1999) found limited orthopaedic sutural opening in the maxilla of individuals older than 12 years. A further complication is gender differences: Alpern and Yurosko (1987) found a mean age difference of five years for closure of the maxillary suture in males and females. All these variations are however, consistent with reports by Persson and Thilander (1977) of a wide difference in midpalatal suture ossification in various age groups. Since the skeletal outcome of expansion depends on the sutural patency and flexibility of the craniofacial skeleton, orthopaedic opening of the midpalatal suture is successful when initiated before the pubertal peak in skeletal growth i.e. until the age of approximately 14–15 years (Baccetti *et al.* 2001, Bailey *et al.* 1997, da Silva Filho *et al.* 1995, Ghoneima *et al.* 2011, Lione *et al.* 2008, Ramieri *et al.* 2005, Suri and Taneja 2008, Weissheimer *et al.* 2011).

MTD in non-growing individuals

Adequate transverse maxillary dimensions are equally important in non-growing and skeletally mature patients. Activation of an expansion appliance against mature sutures can lead to the sensation of pressure, pain, periodontal defects, root resorption, dental tipping, minimal skeletal effects and major relapse (Alpern and Yurosko 1987, Barber and Sims 1981, Greenbaum and Zachrisson 1982, Haas 1980, Krebs 1958, Mommaerts 1999, Wertz 1970).

The magnitude of the skeletal component in MTD is an important factor. It is generally accepted that it is possible to achieve limited expansion of the maxilla without any separation of the midpalatal suture (Baydas *et al.* 2006, Betts *et al.* 1995, Silverstein and Quinn 1997). Handelman (1997) presented stable long-term expansion up to 5 mm in skeletally mature patients without any sutural opening and cited the work of Krebs (1958), showing that 50% of the expansion after RME in children consisted of maxillary alveolar bending. Iseri *et al.* (1998) advocated slow orthopaedic expansion to overcome the resistance and diminish the side effects and the degree of relapse. The slower expansion would, according to Iseri, stimulate the adaptation processes in the nasomaxillary structures and result in less tissue resistance. Still, the stability is directly related to the skeletal maturity of the suture lines and the long-term effects of such procedures have been questioned (Northway and Meade 1997, Shetty *et al.* 1994).

In non-growing and skeletally mature patients, most orthodontists and maxillofacial surgeons currently recommend a combined surgical and orthodontic treatment approach, in order to achieve stable and functional long-term results, with minimal side effects (Alpern and Yurosko 1987, Barber and Sims 1981, Bell and Jacobs 1979, Haas 1980, Kennedy *et al.* 1976, Krebs 1958, Mommaerts 1999, Zimring and Isaacson 1965).

The most common treatment options for skeletally mature patients with MTD are Surgically Assisted Rapid Maxillary Expansion and segmental LeFort I osteotomies, but the long-term effects of such procedures have been questioned (Proffit *et al.* 1996). In comparison with segmental LeFort I osteotomies and non-surgical orthopaedic maxillary expansion, SARME has been advocated to improve stability (Pogrel *et al.* 1992).

Areas of skeletal resistance

Various surgical procedures have been developed for SARME in proportion to the primary areas of resistance in the craniofacial skeleton (Figure 2).

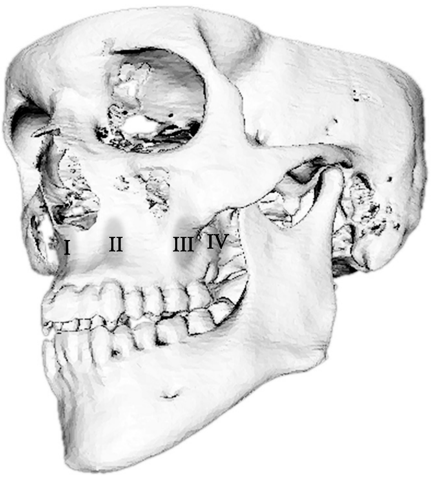


Figure 2. *Different areas of skeletal resistance in the maxilla. (I) midpalatal synostosed suture, (II) piriform aperture pillars, (III) zygomatic buttresses, (IV) pterygoid junction.*

It was early assumed that the mid-palatal suture was the main area of resistance. Surgical techniques favouring midpalatal osteotomies are derived from Timms´ (1968) histological studies in the sixties. Isaccsson (1964) and Kennedy *et al.* (1976) concluded that the major resistance to maxillary expansion was not the midpalatal suture but the remainder of the maxillary articulations. Wertz (1970) stated that resistance of the zygomatic arch prevented parallel opening of the midpalatal suture, which was highlighted by Lines (1975) and Bell and Epker's (1976) results. On the basis of photoelastic observations, Shetty *et al.* (1994) insisted that the mid-palatal suture and the pterygomaxillary region were the most resistant areas and exclusive use of bilateral zygomatic buttress osteotomies was inadequate. In three-dimensional FEM studies Jafari *et al.* (2003) showed high resistance posteriorly, and particularity at the sphenoid and zygomatic bones and concluded a need for surgical release in this area. Holberg and Rudzki-Janson (2006) reported lateral bending of the pterygoid process and increased stress in the sphenoidal area in adulthood, after maxillary expansion.

Principles of treatment

Various combinations of lateral and palatal osteotomies and corticotomies have been proposed and the decision to choose one procedure over another has led to controversies (Figure 3). Procedures are frequently based on uncertain hypotheses and comparisons with orthopaedic expansion in non-growing individuals. The diversity of empirically proposed techniques reflects the lack of consensus about the primary areas of resistance in the craniofacial skeleton (Bays and Greco 1992, Bell and Epker 1976, Glassman *et al.* 1984, Kennedy *et al.* 1976, Kraut 1984, Lehman *et al.* 1984).

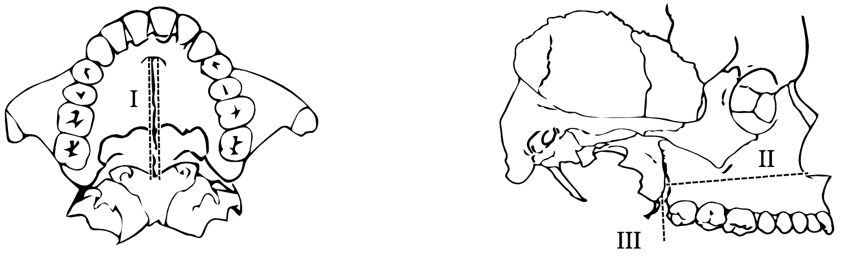


Figure 3. *(I) Paramedial osteotomies from posterior nasal spine to a point posteriorly to the incisive canal. (II) Osteotomies from the piriform rim to the pterygomaxillary junction. (III) Osteotomies and separation of the pterygoid fissure.*

Despite variations, each technique seeks to promote optimal separation of the maxillary halves, while curtailing dentoalveolar side-effects. Choice of maxillary osteotomies is a critical determinant of whether the effects of the expansion appliance are predominantly orthopaedic or orthodontic in nature (Shetty *et al.* 1994). The dilemma is to combine the degree of surgical intervention with an expected optimal therapeutic outcome, with respect to long-term stability, dentoalveolar side effects and minimum morbidity. Thus there are opposing interests. One approach is more invasive surgery with separation of all articulating bones, associated with less stress in the craniomaxillary skeleton, but with higher risks of complications. On the other hand, less invasive surgery makes the procedure more clinically accessible, with fewer surgical complications, but greater skeletal stress and dentoalveolar side effects.

Segmented LeFort I osteotomy

The segmented Le Fort I osteotomy has been the procedure of choice when a single surgical procedure is planned to correct all maxillo-mandibular discrepancies. Obwegeser (1969) suggested splitting the maxilla to correct a retroplaced, narrow maxilla. Steinhauser (1972) reported a procedure comprising a multiple-piece maxillary osteotomy with a stabilizing iliac graft in the midline split. The aim of this extensive procedure was to separate all major areas of maxillary support i.e. anterior (piriform aperture pillars), lateral (zygomatic buttresses), posterior (pterygoid junction) and median (midpalatal synostosed suture). Besides risks and increased morbidity with such major surgical procedures, it is difficult to provide stable, parallel expansion. The dens palatal tissue will hamper parallel expansion and result in tipping and major relapse of the buccal segments. Phillips *et al.* (1992) reported a transverse relapse of 40 per cent after a multi-piece LeFort I osteotomy. Moreover, too much expansion at one time will compromise the vascularity and the success of the procedure (Northway and Meade 1997, Silverstein and Quinn 1997).

Surgically assisted rapid maxillary expansion

Surgically assisted rapid maxillary expansion SARME is a form of distraction osteogenesis (DO). In the purest sense, craniofacial DO was first reported in the early 1860’s by Angell (1860) long before the biological healing principles of DO were known. DO involves the process of generating new bone in a gap between two bone segments, in which new bone is a result of tensile stress across the bone gap (Swennen et al. 2001, Yen 1997). The technique was first described in 1905 by Codivilla (1905) but remained undeveloped until Ilizarov (1988) “rediscovered” the technique in the 1950’s. The unique feature of DO is stability and the biological concept of simultaneous expansion of a soft tissue matrix, including blood vessels, nerves, muscles, mucosa and periosteum (Cope et al. 1999, Al-Daghreer et al. 2008).

The principle of DO is based on four phases; osteotomy or surgical phase, a latency period, a distraction period and finally a consolidation period.

The initial surgery and osteotomy is followed by a latency period of between five and seven days. This is a period of rest and formation of a fibrovascular haematoma; newly formed capillaries and granulation tissue infiltrate into the fibrin clot. Shorter latency periods are generally associated with decreased callus formation and inadequate osteogenesis, whereas longer latency periods are usually associated with premature consolidations (Kojimoto *et al.* 1988).

In the following distraction phase, collagen fibres are formed parallel to the distraction vector; intramembranous ossification starts and follows the collagens fibres towards the midline. Further mineralisation and remodelling of the immature soft bone takes place during the consolidation phase. Bone remodelling begins during the consolidation phase and continues over 1–2 years, eventually transforming the regenerated tissue into a mature osseous structure, similar in size and shape to the adjacent bone (Bell *et al.* 1997, Koudstaal *et al.* 2005, McCarthy *et al.* 2001).

SARME is far from a standardized procedure. When first described by Brown (1938), as a method to correct MTD in non- growing individuals, only midpalatal splitting was involved. The rationale for choosing a particular osteotomy technique is, as mentioned above, based on the assumption of different skeletal resistance in the maxillae (Figure 2, page 12). Those who consider the intermaxillary suture to be the essential area of resistance recommend paramedial palatal osteotomies (Bierenbroodspot et al. 2002, MacIntosh 1974, Timms and Vero 1981), whereas those who regard the zygomaticomaxillary buttress as the main area of resistance advocate osteotomy solely in the lateral areas of the maxilla (Bays and Greco 1992, Glassman et al. 1984). Some include the pterygomaxillary complex in the lateral osteotomies (Byloff and Mossaz 2004, Kraut 1984). Many clinicians advocate combined osteotomies in the palatal, anterior and lateral maxilla and especially posteriorly at the pterygomaxillary complex (Bell and Epker 1976, Han et al. 2009, Kennedy et al. 1976, Stromberg and Holm 1995). Thus, there is no gold standard for optimal surgical procedures and no general consensus in the literature with respect to skeletal effects after SARME.

SARME requires a stable, firm orthodontic expansion device. Removable appliances are not recommended. The most common appliance consists of a tooth-borne expander with a soldered framework and a jackscrew in the midline (Figure 4). When a tooth-borne device is used, the mechanical stress is applied via the teeth. Haas (1961) advocated acrylic palatal coverage to distribute the expansion force evenly on the teeth and the alveolar process. The Hyrax expander has excluded palatal coverage on hygienic grounds. Both devices are anchored on the premolars and or molars.

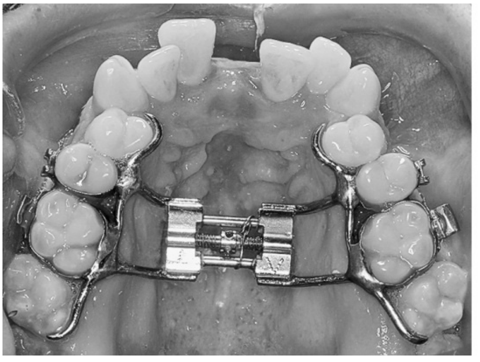


Figure 4. *Tooth-borne hyrax appliance consists of a soldered framework and a jackscrew in the midline tooth-born device activated by means of a conventional Hyrax expander (Hyrax II, Dentaurum, Ispringen, Germany) with a soldered framework and orthodontic bands*

It has been reported that tooth-borne expanders cause dentoalveolar side effects such as dental tipping, cortical fenestration and root resorption (Asanza *et al.* 1997, Betts *et al.* 1995, Langford and Sims 1982;, Sarver and Johnston 1989). These effects are probably attributable to remaining skeletal resistance and loss of anchorage (Anttila *et al.* 2004). Mommaerts (1999) introduced the bone-borne device to minimize dental side effects. The proposed advantages are more parallel skeletal expansion of the maxilla, the potential to treat periodontally compromised patients and the fact that the device does not interfere with orthodontic treatment (Neyt *et al.* 2002, Charezinski *et al.* 2009, Pinto *et al.* 2001). Several bone-borne distractors have been introduced, such as the Dresden distractor, the Magdeburg palatal distractor and the Rotterdam palatal distractor (Hansen *et al.* 2007, Gerlach and Zahl 2003, Koudstaal *et al.* 2006). However, the disadvantages of bone-borne expansion are not negligible. Recent studies report complications including mucosal infections, loosening of abutments and the risks of damage to roots by osteosynthesis screws (Neyt *et al.* 2002, Ramieri *et al.* 2005).

The pitch of the jackscrew is 0.25 mm and after the latency period the daily activation rates range from 0.25 mm to 1 mm (Bays and Greco 1992, Glassman *et al.* 1984). However, the significance of the latency period has been questioned (Aronson 1994). Bays and Greco (1992) suggested peri-operative expansion of 1.5– 2.0 mm.

Despite the reduced skeletal resistance after SARME, tipping of the anchor teeth can occur and transverse relapses of 5–25 per cent have been reported (Phillips *et al.* 1992). Chung and Goldman (2003) advocated overexpansion to compensate for this tendency.

Treatment effects on hard tissue

There is some debate over the relative degree of skeletal and dental effects and whether or not expansion occurs evenly throughout the maxilla. Differentiation of dental and skeletal components in the treatment outcome is crucial with respect to stability and relapse (Capelozza Filho *et al.* 1996, Chung *et al.* 2001, do Egito Vasconcelos *et al.* 2006, Hino *et al.* 2008, Loddi *et al.* 2008, Shetty *et al.* 1994). Study models provide limited information about the skeletal effects (Laudemann *et al.* 2010). Using postero-anterior radiographs, Berger *et al.* (1998), Byloff and Mossaz (2004) reported respectively 52 per cent and 24 per cent skeletal effects for SARME and orthodontic treatment.

In a radiographic implant study in growing individuals, Krebs (1958) reported different effects in various zones of the maxilla after non - surgical orthopaedic expansion. Dental expansion was greater than skeletal expansion and more pronounced anteriorly than posteriorly. Furthermore, there was more expansion in the alveolar process than in the maxillary base. However, Krebs´ results should be extrapolated with caution with respect to SARME, because of differences in study populations, age and the additional surgical procedures. Many investigators have tried to verify Krebs´ results, but their findings have been contradictory. (Anttila *et al.* 2004, Chung *et al.* 2001, Goldenberg *et al.* 2007, Oliveira *et al.* 2004, Zemann *et al.* 2009).

Although a number of reports of the treatment effects of SARME have been published, surprisingly little detailed information exists with reference to long-term stability. In a review of the literature, Koudstaal *et al.* (2005) found no consensus with respect to long-term stability and relapse. Furthermore, apart from the diversity of the surgical and orthodontic procedures, which complicates comparison of treatment outcomes, the sample sizes in previous studies were often too small and/ or the follow-up periods were too short (Anttila *et al.* 2004, Berger *et al.* 1998, Byloff and Mossaz 2004, Sokucu *et al.* 2009). Swennen *et al.* (2001) concluded that there is a lack of appropriate data on long-term follow-up and relapse. In a review of the literature, Lagravere *et al.* (2006a) found six long-term studies with follow-up of more than one year.

Treatment effects on soft tissue

Consistent clinical findings after maxillary osteotomies and SARME are changes in soft tissue and a widening of the nose (O'Ryan and Schendel 1989) (Figure 5).

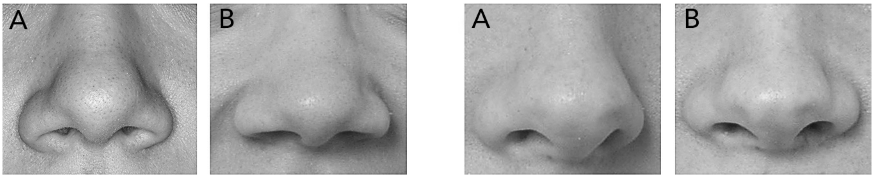


Figure 5. *Changes in soft tissue in the nose (A) pre treatment, (B) post treatment*

Previous studies on SARME and its effects on soft tissue have been limited by the methods available at the time for quantifying soft tissue changes; hence the reported findings are doubtful. Ngan *et al.* (1996) and Filho *et al.* (2002) used traditional two-dimensional (2-D) lateral cephalograms. Berger *et al.* (1999) used serial frontal photographs and Ramieri *et al.* (2006, 2008) utilized laser scanning and 3D morphometry. The major disadvantage of the methods applied in all the above-cited studies is the potential for errors associated with uncertain superimposition.

Treatment effects on nasal respiration

During the early 1900´s, numerous papers, mostly based on subjective findings, referred to maxillary expansion and its favourable implications for nasal respiration (Dean 1909, Schroeder 1904). Brown (1903) described the first case in which nasal blockage was “cured” by rapid maxillary expansion.

This favourable effect of RME on nasal respiration was later associated with Krebs’ (1958) radiological findings of an outward displacement of the lateral walls of the nasal cavity. Furthermore, Babacan *et al.* (2006) observed lowering of the palatal vault, lengthening of the nasal septum and lateralization of the inferior nasal turbinates and thereby an improved respiratory pattern. Hershey *et al* (1976) stated that RME was an effective method of widening the nasal passages and reducing nasal resistance (NAR) from levels associated with mouth-breathing to levels compatible with normal respiration.

Timms (1986) argued that the anatomical changes at the nostrils correlated with the patients’ subjective perception of improved nasal respiration. Niinemma *et al.* (1980) and Subtelny (1980) hypothesized that there is a defined breakpoint of nasal resistance which will lead to either nose breathing or to mouth-breathing. Vig (1998) however, questioned a direct association between nasal obstruction and mouth-breathing and assumed that mouth-breathing might be a learned phenomenon that is not attributable solely to nasal obstruction and a narrow maxilla. Timms (1987) evaluated the occurrence of respiratory symptoms, albeit in a limited retrospective study of patients with MTD, and found an increase in respiratory disease and an improvement in nasal blockage after palatal expansion. It has been suggested that long-faced individuals with MTD are candidates for respiratory disturbances (Fields *et al.* 1991).

A number of studies report that RME can affect the size of the nasal passages and airway resistance, favouring improved nasal respiration (Basciftci *et al.* 2002, Doruk *et al.* 2004, Linder-Aronson 1979, Oliveira De Felippe *et al.* 2008, Warren *et al.* 1987a, Wriedt *et al.* 2001). There is a lack of consensus with respect to RME in terms of mode of action, long-term effects and justification as a modality for the treatment of nasal blockage (Compadretti *et al.* 2006, Gordon *et al.* 2009, McDonald 1995, Neeley *et al.* 2007).

However, the results of improved respiration after RME should be extrapolated with caution with respect to SARME. Although many RME studies have implied improvement in nasal respiration, the reports did not take into account confounding factors such as growth, age and the effects of the surgical intervention (Gray 1975). Few studies have investigated variables related to nasal obstruction in non- growing individuals with MTD or the effects of SARME on nasal patency (Babacan *et al.* 2006, Baraldi *et al.* 2007, Berretin-Felix *et al.* 2006, Kunkel *et al.* 1999, Spalding *et al.* 1991, Wriedt *et al.* 2001). Wriedt *et al.* (2001) showed a tendency toward increased nasal volume after SARME and their findings were supported by Babacan *et al.* (2006). However the findings were not significant. Furthermore, the sample sizes were small and there is some uncertainty regarding the methodology.

Methodological background: rhinology

Various methods have been proposed for measurement of nasal airway dimensions and function (Hilberg 2002). The methods range from minor clinical examinations and questionnaires to major radiological examinations (Cole 1992, Gleeson *et al.* 1986, Hilberg and Pedersen 2000, Hirschberg 2002, Jones *et al.* 1991, Muto *et al.* 2006, Roithmann *et al.* 1994, Solow and Sandham 2002). The simplest way to assess nasal patency is to analyse exhalation on a cooled mirror surface. However there is a diversity of rhinological examinations, some are more accurate and some are considered to be more objective than others. In general, rhinological examinations are sensitive to bias and there is no gold standard for assessing and measuring nasal airway function (Lam *et al.* 2006). Different methods of assessment capture different aspects of the nasal airway and should be considered complementary rather than alternatives (Lam *et al.* 2006). The ideal would be a quantifiable, reproducible objective test closely correlated with the subjective perception of nasal airflow (Roithmann *et al.* 1994, Semeraro and De Colle 1989).

Clinical examination and nasal endoscopy are the most common methods and offer exceptional visualisation of the area of interest, but cannot provide exact quantitative data (Kuhn 2004).

Studies on SARME and respiration have focused primarily on dimensions and structural changes in the cross-sectional areas of the nasal apparatus (Bicakci *et al.* 2005, Erbe *et al.* 2001, Gordon *et al.* 2009). Acoustic rhinometry (AR) is a frequently used method, because the cross-sectional areas and nasal volume are assumed to be important factors in airway resistance and ultimately, in nasal function (Hinton *et al.* 1987).

AR is simple and non-invasive and requires minimal patient collaboration (Figure 6a). AR reflects the anatomic profile along the length of the nasal cavity (Cakmak *et al.* 2005, Hilberg 2002, Roithmann *et al.* 1995) and can more specifically localize the level and sites of an obstruction (Grymer *et al.* 1991).

Nasal respiratory function can be measured in different ways. It can be measured in an active and dynamic manner while the patient is breathing or in a passive or static manner, by applying a flow at a given pressure through the nasal passages while the patient is in apnoea.

Active anterior rhinomanometry (RMM) (Figure 6b) is an accepted direct, dynamic method for measuring transnasal pressure and nasal airflow within the nose during respiration and thereby calculates the nasal airway resistance (NAR) or nasal obstruction. In active anterior RMM NAR can be assessed separately in each nasal cavity. In a consensus document, the International Committee on Standardization of Rhinomanometry defined this method as the method of choice for measuring nasal ventilation (Clement 1984, Clement and Gordts 2005, Hirschberg 2002).

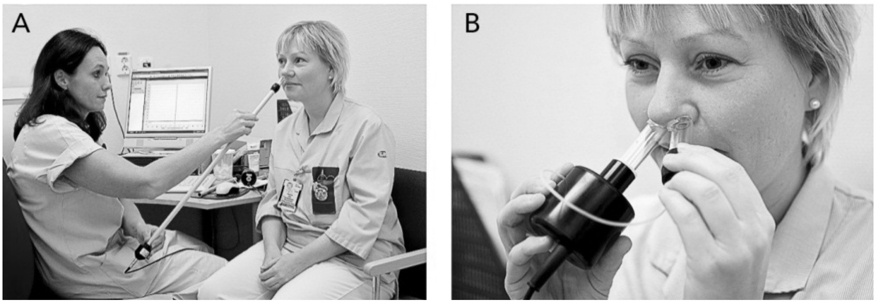


Figure 6A. *Acoustic rhinometry (AR) is simple and non-invasive method and reflects the anatomic profile along the length of the nasal cavity.* ***Figure 6B.*** *Active anterior rhinomanometry (RMM) is an accepted direct, dynamic method for measuring transnasal pressure and nasal airflow within the nose during respiration and thereby calculates the nasal airway resistance (NAR) or nasal obstruction.*

Although most studies have evaluated nasal function using quantitative data such as cross-sectional areas, volumes and resistance, the question of the subjective sensation of nasal obstruction remains. The perception can vary considerably and correlations between objective and subjective findings are often contradictory (Cole 1989; Fairley *et al.* 1993, Roithmann *et al.* 1994, Semeraro and De Colle 1989, Wang *et al.* 2004). However, the overall success of a treatment cannot be assessed from technical, quantitative measurements alone and changes in the patient's perception of nasal blockage must also be considered. The Glasgow Benefit Inventory questionnaire (GBI) (Benninger and Senior 1997) is an otorhinolaryngologic sensitive tool which assesses the effect of an intervention on the health status of the patients. Other indices include Chronic Sinusitis Survey , SNOT -20, Rhinosinusitis Disability Index and NOSE-scale (Piccirillo *et al.* 2002, Fairley *et al.* 1993, Stewart *et al.* 2004).

Methodological background: radiology

Conventional standard procedures for evaluating skeletal and soft tissue changes after SARME and orthodontic treatment have comprised two-dimensional (2D) lateral or posterior-anterior cephalometric radiographs. The major limitations are a distorted view of the skull and projection errors (Athanasiou *et al.* 1999). Traditionally, serial cephalometric radiographs have been taken at different time points to evaluate treatment outcome (Baumrind *et al.* 1976). Different stable structures have been suggested in order to superimpose and register and orientate the two cephalograms (Bjork and Skieller 1972). These structures can be more or less accurate. Traditionally the anterior cranial base and nasion-sella have been used to superimpose two lateral cephalograms. However lateral cephalograms are not optimal for transverse measurements. In postero-anterior (PA) cephalograms, stable landmarks are difficult to identify and analyses are associated with measurement error (Athanasiou *et al.* 1999 Leonardi *et al.* 2008) (Figure 7).

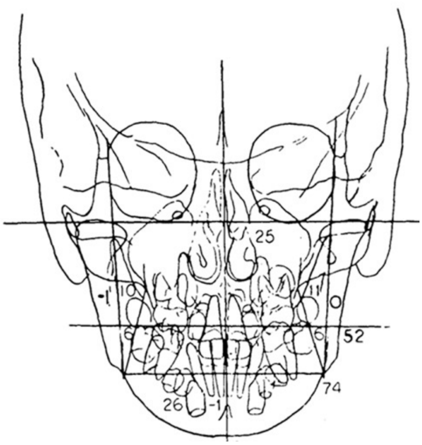


Figure 7. *In postero-anterior (PA) cephalograms, stable landmarks are difficult to identify and analyses are associated with measurement error*

In recent years there have been great advances in computed tomography. Podesser *et al.* (2004) investigated the reproducibility of maxillary structures using computerized tomography and concluded that the patient's position in the scanner was a crucial factor for projection and measurements errors. Tausche *et al.* (2007) found that 3-dimensional (3D) CT analysis had major advantages for determining craniofacial changes associated with maxillary expansion, but emphasised the importance of reliable landmarks for superimposition. Various landmarks and coordinate systems have been proposed to minimize projection errors (Lagravere *et al.* 2006b), but the potential errors associated with such constructions are not acceptable for superimposition and treatment analysis (Cevidanes *et al.* 2011, Lagravere *et al.* 2011). Recent progress in registering 3D models on stable structures offers a more precise, accurate superimposition method for visualizing and measuring changes (Cevidanes *et al.* 2005, Cevidanes *et al.* 2006).

Aims

Although SARME is a widely accepted treatment modality in modern orthodontics, there is a lack of evidence-based data and no consensus in the literature with respect to the optimal surgical technique or to the treatment outcome (Proffit *et al.* 1996). The most contentious issues are the long-term stability, the effects on hard and soft tissue and on respiration. Studies to date have been limited by the available methods and the existing scientific data are based on small, retrospective samples without adequate long-term follow-up.

General aim

The overall aim of the research underlying the present thesis was to acquire new evidence-based knowledge about the short- and long-term outcomes of the procedure, with a multidisciplinary approach, applying the most recent technological advances, and using larger patient samples and longer follow-up.

The specific objectives were

- to evaluate the effect on and the degree of long-term stability of the transverse dimensions of subjects who had undergone SARME and orthodontic treatment, in comparison with a matched control group of untreated subjects. (Paper I)

- to evaluate prospectively short- and long-term changes in the nasal airway after SARME and orthodontic treatment, using two objective methods, acoustic rhinometry and rhinomanometry and to compare and correlate these findings with the patient's subjective sensation of nasal obstruction. (Paper II)

- to evaluate prospectively the transverse skeletal treatment effects of SARME and orthodontic treatment , using a 3D imaging technique and registration based on superimposition on the anterior cranial base. (Paper III)

- to evaluate prospectively nasal soft tissue changes after SARME and orthodontic treatment , using a 3D imaging technique and registration based on superimposition on the anterior cranial base. (Paper IV)

Materials

The studies in this doctoral project are based on two different samples and study designs (Figure 8).

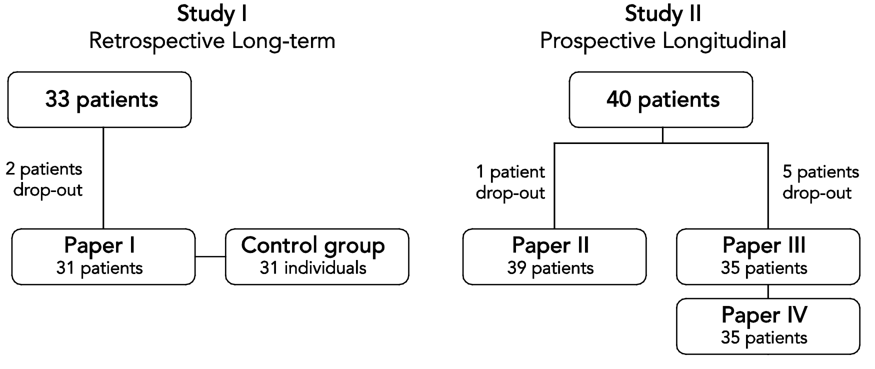


Figure 8. *Study I, is a retrospective, consecutive, long-term follow-up material of study models from patients treated with SARME and orthodontic treatment at the Institute for Postgraduate Dental Education, Jönköping, Sweden, between 1991 and 2000. The results were compared with study models from an untreated control group of Norwegian dental students, matched for age, gender and follow-up time. Study II is a prospective consecutive, longitudinal material of patients scheduled to undergo SARME and orthodontic treatment at two centres, Jönköping and Linköping, between 2006 and 2009.*

The first sample, Study I, is a retrospective, consecutive, long-term follow-up material of study models from patients treated with SARME and orthodontic treatment at the Institute for Postgraduate Dental Education, Jönköping, Sweden, between 1991 and 2000. The second sample, Study II, comprised a prospective consecutive, longitudinal material of patients scheduled to undergo SARME and orthodontic treatment at two centres, Jönköping and Linköping, between 2006 and 2009.

In Study I (Paper I) study models were made before treatment and after completed treatment and retention. The total number of patients treated with SARME and orthodontic treatment during this period, 1991–2000, was 33. Two patients were excluded from the study, one because of the incorrect registration date of the post-treatment model and one because the quality of the study model was inadequate. Follow-up models were taken in January 2006.

To evaluate treatment outcome and long-term stability, the results were compared with study models from an untreated control group of Norwegian dental students, matched for age, gender and follow-up time.

The final material thus comprised matched study models from 31 patients (14 females and 17 males) at Baseline (T0), at three months post-expansion examination (T1) and at follow-up (T2) mean 6.4 years.

Study II (papers II–IV) comprised a consecutive sample of patients who were scheduled to undergo SARME and orthodontic treatment. According to the power calculation, *a priori*, the minimum sample size was set at 34 patients. In order to avoid sample size not in accordance with the power calculation, 40 patients were recruited.

To ensure the required sample size within a reasonable time-period, the patients were recruited at two centres in Sweden, the Department of Orthodontics at the Institute for Postgraduate Dental Education, Jönköping and the Department of Dentofacial Orthopaedics, Maxillofacial Unit, Linköping, between June 2006 and October 2009.

Prior to treatment start, all patients in Study II received printed and oral information about the survey and were invited to participate. The voluntary basis of participation in the extra examinations was highlighted and emphasized.

In Paper II, all 40 patients consented to participate. One patient was however excluded because of a planned adenoidectomy which might jeopardize the result. The final sample thus comprised 39 patients (16 males and 23 females). The mean age at treatment start was 19.9 years (range 15.9 – 43.9).

In papers III–IV, three patients declined to participate and two had to be excluded because their CT-records were incomplete. The final sample comprised 35 patients (14 males and 21 females). The mean age at treatment start was 19.7 years (range 16.1 – 43.9).

In papers II–IV, the treatment groups constituted their own control groups.

Methods

A summary of the methods is presented below. Details are presented in papers I–IV.

Orthodontic and surgical procedures

All treatment procedures in the present doctoral project, orthodontic and surgical, were approved at treatment start by an interdisciplinary team of orthodontists and oral and maxillofacial surgeons in Jönköping and Linköping, Sweden.

The orthodontic procedure in the retrospective study, Study I, was undertaken at the Institute for Postgraduate Dental Education, Jönköping, and in the prospective study, Study II, at the local orthodontic clinics in three counties in Southeast Sweden, under the supervision of the orthodontic departments in Jönköping and Linköping. In the prospective study, detailed printed information was sent to the local orthodontists in order to standardize the treatment process.

Despite efforts to standardize the protocols, differences nonetheless arose between Study I and in Study II. The differences are primarily related to the surgical procedures, but some were also associated with the orthodontic procedures.

The pre-surgical orthodontic preparation was the same in the two studies and consisted of a tooth-borne device activated by means of a conventional Hyrax expander (Hyrax II, Dentaurum, Ispringen, Germany) with a soldered framework and orthodontic bands (Figure 9).

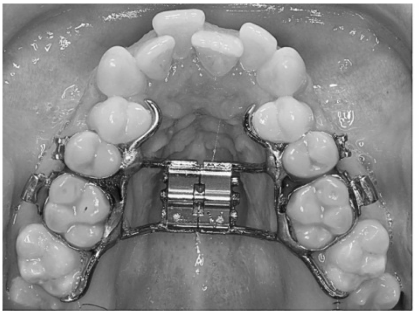


***Figure 9.** Tooth-born device activated by means of a conventional Hyrax expander (Hyrax II, Dentaurum, Ispringen, Germany) with a soldered framework and orthodontic bands.*

The degree of expansion was calculated for each individual, including a general bilateral overexpansion of half a molar-cusp width. The patients were instructed to activate the jack-screw (0.25 mm) twice a day. In Study I, the patients were instructed to start activating the appliance with one turn twice a day (0.5 mm) on the first day after surgery and the patients in Study II after a latency period of five days. Post-operative control was scheduled for seven days post-expansion start and included a periapical radiograph to ensure clinically symmetrical interdental separation and a medial diastema (Cureton and Cuenin 1999). At that time the amount of additional expansion was calculated. The expansion device was scheduled for insertion as close as possible to the date of the surgery.

The surgical treatment in Study I followed a technique described by Kraut (1984) and in Study II a technique described by Glassman *et al.* (1984). Both techniques are considered to be minor surgical procedures, but differ with respect to pterygomaxillary detachment. Kraut advocated separation at the pterygoid buttress to diminish skeletal resistance in the maxillofacial complex, in order to enable parallel antero-posterior expansion and to prevent transverse maxillary relapse. Glassman *et al.* on the other hand opposed this separation, in order minimize the surgery and the risks and questioned the probability of an increased relapse.

The surgical interventions in the present studies are all minor in comparison with other major osteotomies such as Le Fort I. The procedure can be carried out under sedation and local anaesthesia on an outpatient basis (Bays and Greco 1992), as was done in five patients in Study I. In our experience, however, it was preferable to do it under general anaesthesia.

The surgical treatment in the retrospective Study I was undertaken by three experienced senior oral and maxillofacial surgeons according to Kraut(1984). In the prospective Study II the surgical procedures were standardized and the two senior oral and maxillofacial surgeons in Jönköping and Linköping were calibrated according to Glassman *et al.* (1984).

The mucoperiosteal incisions were made in the same way in in both studies. Incisions were made from the second right premolar to the second left premolar and bilateral osteotomies from the piriform aperture to the pterygoid plates. In Study I the pterygoid fissures were separated on both sides with a curved osteotome, but kept intact in Study II. In both protocols, the lining on the floor and lateral walls of the nasal passage was reflected and a vertical osteotomy according to Cureton and Cuenin (1999) was done at the anterior nasal spine and the median palatal suture, in order to ensure separation of the maxillary halves (Figure 10).

Figure 10. *(Left) Bilateral osteotomies from the piriform aperture to the pterygoid plates. (Right) Vertical osteotomy according to Cureton and Cuenin (1999) was done at the anterior nasal spine and the median palatal suture in order to ensure separation of the maxillary halves.*

The hyrax expander was activated twelve turns peri-operatively to verify the success of the osteotomy and to ensure symmetrical separation and then deactivated by the same amount. Depending on their physical condition and post-operative swelling, the patients were discharged from the hospital on the same day or the day after surgery.

After the active expansion period mean 15 days, range 14-22, in Study I and mean 15 days, range 11-17, in Study II, the appliance was used as a passive retainer for 90 days. The hyrax expander was replaced by a modified transpalatal arch and fixed appliance treatment began (Figure11 a-c).

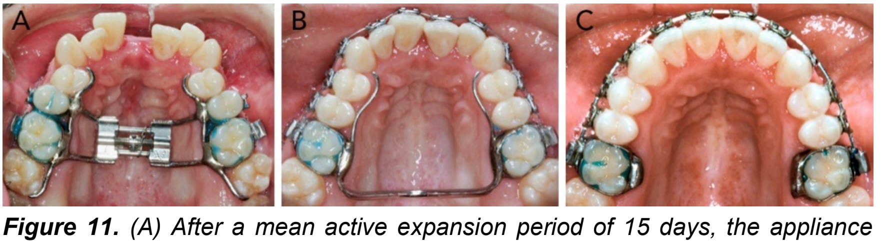


Figure 11. *(A) After a mean active expansion period of 15 days, the appliance was left in situ as a passive retainer. (B) Ninety days after the active expansion period, the hyrax expander was replaced by a modified transpalatal arch, and fixed appliance treatment was started. (C) On completion of alignment, the transpalatal arch was removed, and fixed appliance treatment continued with stiff rectangular arch wires to adjust the transverse width and to control and correct the buccal root torque of the molars.*

On completion of the active treatment phase, the transpalatal arch was removed and fixed appliance treatment continued with stiff rectangular arch-wires, in order to adjust the transverse width and to control and correct the buccal root torque of the molars. All transverse discrepancies were corrected by the end of treatment and the orthodontic treatment period was then concluded. At this point, 26 patients in Study II were referred for second stage orthognathic surgery. In the remaining patients (31 patients in Study I and nine in Study II) the fixed appliance was debonded and a Hawley plate was provided as a retainer. In study I the Hawley plate was used full time for six months and at night for the following six months and treatment was then concluded.

In Study II the Hawley plate was used full time for one year and at least at night for the following two years.

Measurements on study models

Direct measurements on study models were made with a digital sliding caliper (model Mitutoyo 500-171, Kanagawa, Japan). According to the manufacturer, the instrument has a resolution of 0.01 mm and an accuracy of 0.025 mm. Measurements in the present retrospective Study I were taken to the nearest 0.01 mm.

Measurements were taken at two reference points on the canines and the first molars respectively, according to Moorrees (1959), to measure intermaxillary distance anteriorly and posteriorly and to assess dental tipping. As shown in figure 12, CI denotes the distance between the cusp tips of the canines and CII the distance between the most prominent cervical point of the palatal ridge on the canines. MI represents the distance measured between the mesiobuccal cusp tips of the maxillary first molars and MII the distance between the most cervical points of the palatal fissure of the maxillary first molars.

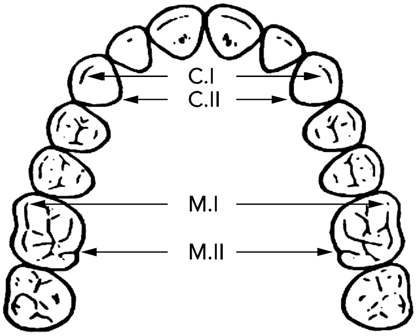


Figure 12. *Direct measurements on the study models were made to the nearest 0.01mm with a digital sliding caliper at two reference points on the canines and the maxillary first molars respectively.*

In order to assess post-treatment changes over time, the treatment group was divided into two groups: those with less than five years' follow-up and those with more (15 patients, mean 3.7 years, and 16 patients, mean 9.3 years, respectively).

The results were compared with an untreated control group of Norwegian dental students to evaluate treatment outcome and long-term stability. The control group was matched with the test group for age, gender and follow-up time.

Questionnaire and rhinological examination

In this study, the subjective parameters were assessed by a questionnaire approved by the Swedish Rhinologic Society (Loth *et al.* 2001). This questionnaire is a disability index used to evaluate the impact of nasal obstruction from the subject's perspective (Benninger and Senior 1997 Stewart *et al.* 2004). It is based on ten anamnestic "yes" or "no" questions and ten questions on a visual analogue scale (VAS). The anamnestic questions were constructed to reveal current medication, earlier experiences of ENT illness/treatment, nasal obstruction and expectations of the planned treatment.

The VAS-scale is useful in evaluating nasal blockage and discharge, facial pain or pressure, headache and overall symptoms (Kruse *et al.* 2010, Jones *et al.* 1989 Price *et al.* 1983). The first eight VAS rated the subject's symptoms on a scale of 0 to 10, where 0 = "never" and 10 = "constantly" regarding nasal blockage, nasal congestion, running nose, snoring, facial pain, headache, nose breathing, and sense of smell. The last two VAS were also on a scale of 0 to 10 where 0 = "good" and 10 = "bad", concerning quality of life in general and quality of life from a rhinological perspective respectively. All subjects scored their subjective symptoms of nasal obstruction at three time points in conjunction with the rhinological examinations: before treatment start and then three and 18 months after SARME.

The rhinological examination was carried out by two calibrated rhinologists at the ENT-Department, Ryhov County Hospital, Sweden and at the ENT-Department, University Hospital, Linköping, Sweden. The examination comprised clinical examination, acoustic rhinometry (AR), and anterior rhinomanometry (RMM). For inter-examiner calibration, the two examiners were supplied with the same equipment (Rhinoscan, RhinoStream) and trained together.

The patient was allowed to rest for 15 minutes before the examinations and recordings were commenced. The presence of an adequate nasal cavity space was assessed by anterior rhinoscopic examination. The technical procedures and data calculations were carried out in accordance with guidelines developed by the International Standardization Committee for Rhinomanometry (Clement and Gordts 2005).

AR measures the nasal airway dimensions by emitting wide-band noise into the nose. A standard probe for adults and tailored nose adapters to fit right and left nostrils were used in accordance with the recommendations of the Standardization Committee on Acoustic Rhinometry (Hilberg and Pedersen 2000, Hilberg 2002). AR and RMM were performed with a digital platform, SRE 2000 Digital Signal Unit (Interacoustics A/S Assens Denmark) (Figure 13). A RhinoScan software module was used for AR and RhinoStream for RMM.

Figure 13. *Acoustic rhinometry and rhinomanometry performed with a digital platform, SRE 2000 Digital Signal Unit (Interacoustics A/S Assens Denmark)*

The front portion of the nasal cavity is the narrowest and most resistant area to nasal airflow and comprises the inner valve, the anterior part of the turbinate and isthmus nasi (Nigro *et al.* 2005).

AR (RhinoScan) (Figure 6a, page 21) measures the minimum cross sectional area (MCA) at the front portion at two distances: MCA I (the structural valve), from the nostril rim to approximately the anterior border of the inferior turbinate (0.0 - 2.2cm) and MCA II (the functional valve), from the anterior border of the inferior turbinate to isthmus nasi (2.2 - 5.4cm). The five recordings on each side were registered and displayed both graphically and as a chart (Figure 14). The mean values for MCA I and MCA II were calculated for left and right sides respectively (Figure 14).

RMM (RhinoStream) (Figure 6b, page 21) gives a dynamic assessment of nasal patency by measuring trans-nasal pressure and flow during respiration and on this basis calculates the nasal airway resistance (NAR). The RhinoStream module expresses nasal airway resistance at 75 Pa. The manometer-probe attached to the tailored nose adapter registered values for inspiration and expiration on each side. The instrument was calibrated before each test, and each side was registered separately. The recordings were registered and displayed both graphically and as a chart (Figure 14 A-C). The NAR-value was calculated for inspiration (NARinsp) and expiration (NARexp) according to the formula Rinsp/exp= Rleft*Rright/Rleft +Rright. In order to reduce the mucosal swelling of the nasal valve the registrations were made after administration of a decongestant (Otrivin 1mg/ml) (Cole 2000, Larsson *et al.* 2001).

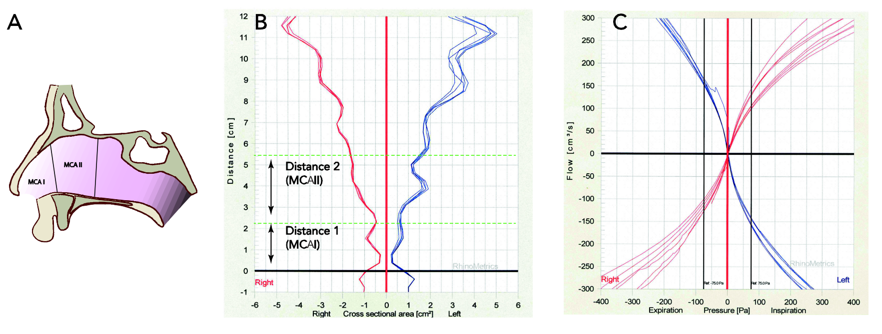


Figure14A. *MCA I (the structural valve), from the nostril rim to approximately the anterior border of the inferior turbinate (0.0 - 2.2cm) and MCA II (the functional valve), from the anterior border of the inferior turbinate to isthmus nasi (2.2 - 5.4cm).* ***Figure 14B.*** *Minimum cross sectional areas, MCA, were registered at two distances from the nostril, MCA I and MCA II. The five recordings on each side were recorded and displayed both graphically and as a chart.* ***Figure 14C.*** *Nasal airway resistance (NAR) was registered and displayed both graphically and as a chart. The NAR-value was calculated for inspiration (NAR insp) and expiration (NAR exp).*

CT-examination and image analysis

The CT-examinations were undertaken at the Center for Medical Image Science and Visualization (CMIV) University Hospital, Linköping, and at the Department of Radiology, Ryhov County Hospital, Jönköping, one week prior to surgery, and at the end of the active orthodontic treatment phase (mean 18 months postoperatively).

A helical CT machine (Siemens Somatome Sensation 64 CT-scanner, Erlangen, Germany) with a low dose protocol (CARE Dose 4D/Siemens Medical Solutions) was used at 120 kV and 55 mAs. The rotation time was 1 sec and the pitch factor was 0.9, with a collimation of 0.6 mm. The increment was 0.3 mm. According to the manufacturer, the isotopic resolution/voxel size was 0.33 mm. The patient's head was positioned so that the Frankfurt plane was vertical.

The scanned area comprised the anterior cranial base to the mandibular base. After examination, the images were processed at a radiological workstation (Sectra Imtec AB, Linköping, Sweden) with slice thicknesses of 0.75 mm and slice increments of 0.3 mm in Kernel H 60s sharp FR, to allow further segmentation and registration.

The data were processed to visualise and measure changes caused by SARME and orthodontic treatment, using a modified version of a technique described by Cervidanes *et al.* (Cevidanes *et al.* 2006, Cevidanes *et al.* 2010). This process involves image segmentation, registration and visualisation (Figure 15, page 37). In Paper III, lateral skeletal displacements were assessed in the maxilla and in Paper IV, three-dimensional changes of nasal soft tissue were measured.

The image registration and superimposition of the pre- and post-operative 3D models were done prior to segmentation with a volumetric registration method, specifically normalized mutual information, based on the anterior cranial base. The cranial fossae and the ethmoid bone surfaces are regarded as stable areas, with growth completed before puberty (Belden 1998, Melsen 1969). Once the pre- and post-operative volumes are registered, they share the same coordinate system, which compensates for any discrepancies between pre- and post-volumes and diminishes the risks of projection and measurement errors.

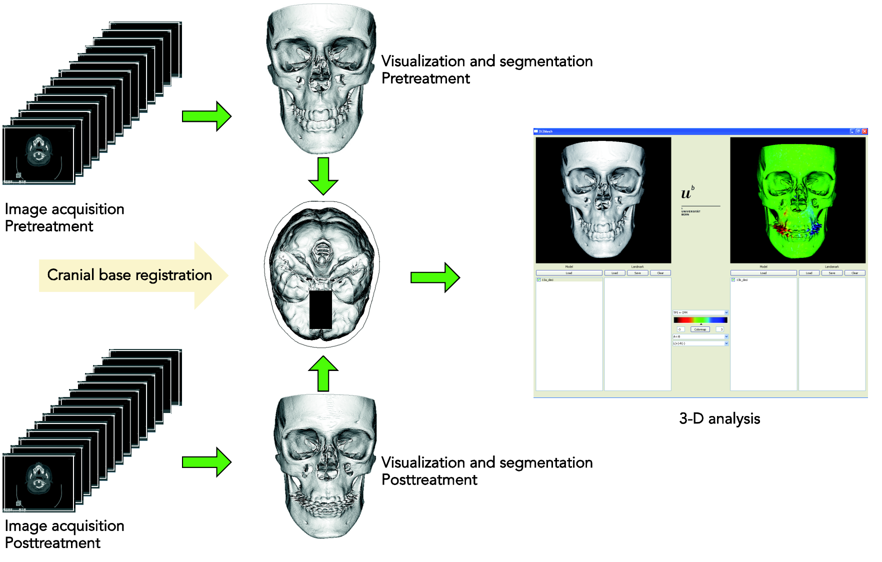


Figure 15. *Helical CT's were taken for each patient before and after treatment. Visualization and segmentation involves creation of 3D models and delineation of anatomical structures of interest. The 3D models were superimposed on the anterior cranial base by means of a volumetric registration method. A Graphical User Interface (GUI) based application (Di2Mesh) was used for 3D analysis and measurements.*

Segmentation is the process of outlining the shape of a structure. The segmentation was performed semi-automatically in AMIRA (Mercury Computer System, Germany). In the semi-automatic segmentation technique, the region of interest is outlined with mouse-clicks in the cross-sections of a data set and algorithms (simple thresholding and region-growing) are applied, so that the path that best fits the edge of the image is shown, i.e. with simple thresholding it is possible, in areas of interest, to select a lower range of Hounsfield units (HU) and values above this level will automatically be selected. In some images the threshold value was adjusted interactively to achieve better contours.

A landmark-based, non-rigid mapping technique, Thin-Plate Spline (TPS), was used to determine the corresponding landmarks between the pre- and post-surgery 3D models (Bookstein 1989). This was done by a pipeline procedure according to Kim *et al.* (2010).

Di2Mesh software is a Graphical User Interface (GUI) -based application, allowing the user to compute surface-to-surface distances in any specified direction and visualise them using a colour-map.

Various validated landmarks were used in Papers III-IV for measurements of skeletal and soft tissue displacements (Baik and Kim 2010, Moore-Jansen 1994, Swennen 2006a, Yamada *et al.* 1999).

The landmarks were identified and digitized and the non-rigid transformation model was used for measurements. Thin-Plate-Spline deformation and Closest Point Matching (TPS-CPM) (Kim *et al.* 2010), were used to show displacements in color maps. The software (Di2Mesh) computed the closest-point relationship between the pre- and post landmarks in a 3D Euclidean space coordinate system.

The displacement vectors were normalized with the Frankfurt Horizontal Plane coordinate system (FHP) according to Xia et al. (2000). Transversal plane is defined by right and left Porion and average coordinate of right and left Orbitale. Frontal plane is perpendicular to the transversal plane and through right and left Porion. The sagittal plane is perpendicular the transversal plane and frontal plane, and through Nasion.

In Paper III, seven pairs of bony landmarks were selected (Lagravere *et al.* 2006a, Moore-Jansen 1994, Swennen G R J, Schutyser F, Hausamen J-E. 2006b) for measurements and to show the lateral skeletal displacements in the maxilla from both sagittal and coronal aspects (Figure 16).

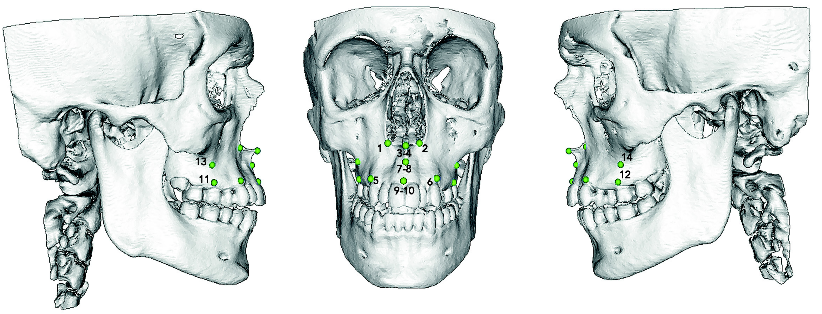


Figure 16. *Landmarks in Paper III. 1 and 2, alare, left and right: the most lateral and inferior point of the nasal aperture in a transverse plane; 3 and 4, spina nasalis anterior: the tip of the anterior nasal spine; 5 and 6, ectocanine, left and right: the most lateral and inferior point on the alveolar ridge opposite the center of the maxillary canine; 7 and 8, A-point: the most posterior and deepest point on the anterior contour of the maxillary alveolar process in the midsagittal plane; 9 and 10, prosthion: the most anteroinferior point on the maxillary alveolar margin in the midsagittal plane; 11 and 12, ectomolare, left and right: the most lateral and inferior point on the alveolar ridge opposite the center of the maxillary first molar; 13 and 14, processus zygomaticus, left and right: the most inferior and lateral point of the processus zygomaticus.*

In Paper IV, 15 validated landmarks were used for three-dimensional measurements (Figure 17). (Baik and Kim 2010, Swennen 2006a, Yamada *et al.* 1999)

As shown in Figure 18, lateral displacement on the X-axis, superior displacement on the Y- axis and anterior displacement on the Z-axis were recorded as positive values.

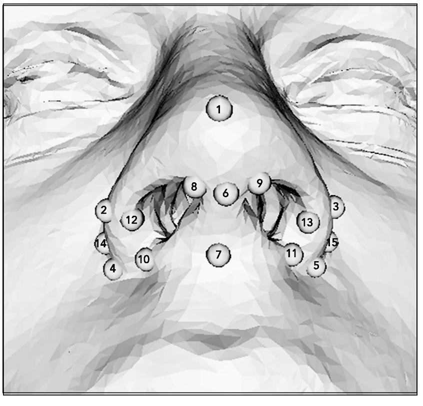


Figure 17. *(1) Pronasale: the most anterior midpoint of the nasal tip, (2-3) Alar right, left: the most lateral point on each alar contour,(4-5) Alar curvature right, left: The point located at the facial insertion of each alar base, (6) Columella: The midpoint on the columella at the level of the superior nostrils (landmark 8-9), (7) Subnasale: the mid-point on the nasolabial soft-tissue contour between the columella crest and the upper lip, (8-9) Nostril superior right, left: the most superior point of the nostril, (10-11) Nostril inferior right, left: the most inferior point of the nostril, (12-13) Nostril lateral right, left: the most lateral point of the nostril (14-15) Alar base right, left: the most lateral point of the alar base.*

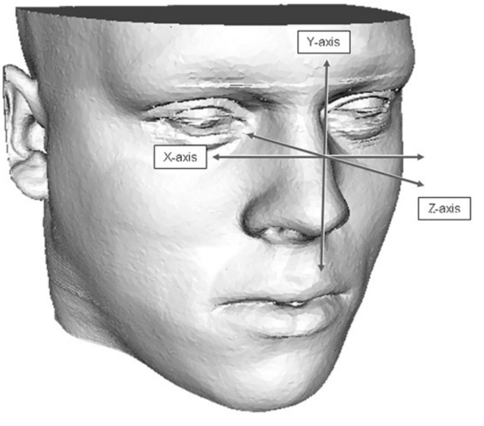
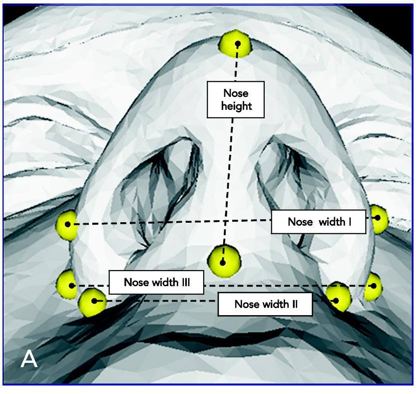


Figure 18. *The displacement vectors were normalized with the Frankfurt Horizontal Plane coordinate system and recorded as positive values laterally on the X-axis, superiorly on the Y- axis and anteriorly on the Z-axis.*

The Euclidean distances, i.e. the shortest distances between two landmarks, were measured to evaluate the height and width of the nose and nostrils (Figure 19 A, B).



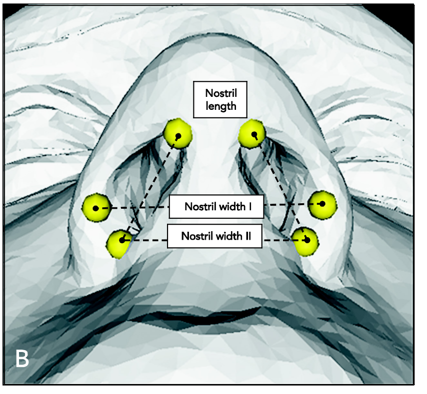


Figure 19A. *The shortest distance without orientation in space, was measured for nose-height (landmark 1-7), nose-width I (landmark 2-3), nose-width II (landmark 4-5) and nose-width III (landmark 14-15)* ***Figure 19B.*** *The shortest distance without orientation in space, was measured for nostril-lengths (landmark 8-10, 9-11), nostril width I (landmark 12-13) and nostril-width II (landmark 10-11).*

A colour-map scheme was applied to disclose outward lateral displacement on the right side in red and on the left side in blue. The absence of displacement was indicated in green (Figure 20).

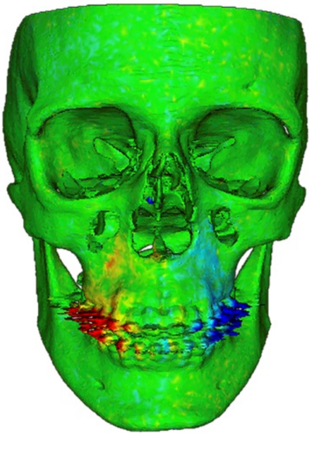


Figure 20. *The color map scheme shows transverse displacement: transverse outward displacement is shown in red on the right side and in blue on the left side. Green indicates no displacement.(in skeletal or soft tissue)*

Statistical analyses

Power and sample size calculation

The material in Study I comprised all consecutive patients treated in Jönköping between 1990-2000.

In Study II, the power and sample size calculation, *a priori*, was made in IBM SPSS Sample Power trial version (Ludvigsson 2004) according to skeletal displacements and based on a significance level of α 0.05 and a power (1-β) of 80%, to detect a mean difference in displacement of 0.75 mm (SD 0.5). The accuracy of the measuring method warrants such a small mean difference. The standard deviation was an appraisal from the literature (Tausche *et al.* 2007). According to this power calculation, Study II would require a minimum sample size of 34 patients. Thus in order to ensure an adequate sample size, 40 patients were recruited.

Descriptive statistics

Statistical analyses were undertaken using Statistical Package for the Social Sciences version 13.0 (Paper I-II), 15.0 (Paper III) and 20.0 (Paper IV) (SPSS Inc, Chicago, Illinois, USA). Descriptive statistics such as mean value, median value, standard deviation, range and percentiles were used to describe the changes and ranges. The distribution of data was tested with the 1-sample Kolmogorov-Smirnov Test and showed non-normal distribution of the data in Papers I - II and normal distribution in Papers III-IV.

Differences and correlations

As the data were not normally distributed in Papers I-II, non-parametric tests, Mann-Whitney U, Spearman´s rho and Wilcoxon´s signed-rank tests were used.

The data in Papers III-IV showed normal distribution. Because of the sample size, non-parametric tests were also warranted and Wilcoxon´s signed–rank test was used to evaluate pre-and post-treatment differences.

Spearman rho was applied to assess the correlations. All statistical tests were two-tailed and the level of significance was $P<0.05$.

Error of measurements

Paper I. Ten study models from the treatment group were randomly selected and re-measured by the same observer after an interval of 4 weeks. The measurement error was calculated by intraclass correlation coefficients (ICCs) for single measurements, which is an expression of intraobserver reliability. The ICCs were between 0.995 and 0.999.

Paper II. The interexamination measurement errors for acoustic rhinometry and rhinomanometry were calculated by intraclass correlation coefficients, which are an expression of interobserver reliability. These were measured at six examinations and were above 0.75.

Papers III-IV. The same procedure was undertaken in Papers III-IV to assess the error of measurements. Fifteen computerized tomography volumes in Paper III and 10 in Paper IV were randomly selected. The anatomical landmarks were located and digitized in each 3D model. The same observer repeated the procedure after an interval of 4 weeks and the displacements of the landmarks were calculated. The error of measurements was calculated by intraclass correlation coefficient (ICC) for single measurements.

In Paper III, the ICC were between 0.810 and 0.971, with the exception of alare left and right (ICC, 0.701) and in Paper IV between 0.851 and 0.992.

In Paper IV, landmarks in the midline showed the weakest ICC.

Ethical considerations

The ethical principles for medical research involving human subjects according to the Helsinki Declaration (1997) were followed and all studies were approved by the Regional Ethical Review Board in Linköping, Sweden 2006-03-08 (diary number M746-04).

In the retrospective Study I, 33 participants received, by post, a printed letter of information about the investigation and the need for follow-up study models. In order to minimise attrition and to maintain a complete consecutive material, patients were offered travel allowances. The study was reported to The Swedish Data Inspection Board as required by The Personal Data Act.

Individuals in the prospective Study II received an invitation to participate in the study prior to treatment start. This invitation comprised detailed information about a questionnaire and radiological - rhinological examinations. The information was also presented by the orthodontist at the first visit. The voluntary basis of participation in the study was emphasized and patients were assured that they could withdraw from the study at any time without any personal consequences. Consent to participate was signed by each participant. The study was reported to The Swedish Data Inspection Board according to The Personal Data Act.

Results

Long-term stability after SARME

AT BASELINE

Table I. At baseline there were significant differences between the treatment and control groups with respect to the transverse dimensions. This applied to all four distances measured: *CI*, *CII*, *MI* and *MII* (Figure 12, page 33).

Table I. *Comparison between maxillary intercanine and intermolar distances for treatment and control groups at baseline, before start of observation.*

	Treatment group			Control group			
Distance	n	Mean (mm)	SD	n	Mean (mm)	SD	p
CI	31	30.45	3.11	31	34.32	2.28	***
CII	31	21.04	2.53	31	24.56	2.22	***
MI	31	44.02	3.87	31	52.26	3.34	***
MII	31	30.48	3.44	31	36.43	3.08	***

*** = P< 0.001

The mean age at treatment start was 25.9 years (range 15.7 - 48.9) and the indications for treatment, according to the earlier definition, were real MTD in 16 subjects, relative MTD in 11 subjects and anterior crowding in four subjects.

AT COMPLETED TREATMENT AND RETENTION

All posterior crossbites were corrected and the expansion was statistically significant (Table II). The mean treatment and retention period was 2.8 years (SD 0.73, range 2.2-3.8) Depending on the clinical need for expansion, there was a major interindividual variance in the degree of expansion. The greatest expansion was recorded for *MI*, the distance between the tips of the buccal cusps of the maxillary first molars (Figure 12, page 33).

Table II. *Comparison between maxillary intercanine and intermolar distances for the treated subjects at baseline and after completed treatment and retention*

	Base line			Completed treatment			
Distance	n	Mean (mm)	SD	n	Mean (mm)	SD	p
CI	31	30.45	3.11	31	33.69	2.83	***
CII	31	21.04	2.53	31	24.93	2.18	***
MI	31	44.02	3.87	31	49.82	3.60	***
MII	31	30.48	3.44	31	35.03	3.23	***

*** = P< 0.001

AT FOLLOW-UP

Table III. After completed treatment and retention, the posterior crossbites remained corrected, mean 6.4 years (SD 3.3, range 3.1–13.9 years). There was, however, a significant decrease in all the distances measured: *CI*, *CII*, *MI* and *MII*.

Table III. *Comparison between the maxillary intercanine distances (CI CII) and intermolar distances (MI, MII) for the treatment group at completed treatment and at follow-up.*

	Completed treatment			Follow-up			
Distance	n	Mean (mm)	SD	n	Mean (mm)	SD	p
CI	31	33.69	2.83	31	32.85	3.08	*
CII	31	24.93	2.18	31	24.03	2.32	*
MI	31	49.82	3.60	31	48.28	3.67	***
MII	31	35.03	3.23	31	34.33	3.39	*

*** = P< 0.001, *= P 0.05

With respect to transverse measurements (Table IV), there were no statistically significant differences between the treatment and control groups, except for the distance *MI* (Figure 12, page 33).

Table IV. *Comparison between the intercanine distances and intermolar distances at follow-up for the treatment group and the last registration for the control group.*

	Treatment group			Control group			
Distance	n	Mean (mm)	SD	n	Mean (mm)	SD	p
CI	31	32.85	3.08	31	33.95	2.45	n.s
CII	31	24.03	2.32	31	24.56	2.24	n.s
MI	31	48.28	3.67	31	52.43	3.45	*
MII	31	34.33	3.39	31	36.30	3.12	n.s

n.s = non significant, * = P< 0.05

Post-treatment changes over time (Table V) were assessed in two subgroups: those with less than five years' follow-up (15 individuals, mean 3.7 years' follow-up) and those with more (16 subjects, mean 9.3 years' follow-up). No statistically significant differences were found.

Table V. *Comparison between post-treatment changes over time. Follow-up ≤ 5 years compared with follow-up > 5 years*

	Follow-up ≤5 years			**Follow-up > 5 years**			
Distance	n	Mean (mm)	SD	n	Mean (mm)	SD	p
CI	15	0.77	0.94	16	0.92	1.02	n.s
CII	15	1.02	0.59	16	0.78	0.97	n.s
MI	15	1.67	1.10	16	1.40	1.92	n.s
MII	15	0.62	1.04	16	0.77	1.02	n.s

n.s = non significant

Furthermore, no significant correlation was found between the age of the patient and the reduction in transverse dimensions, or between intercanine and intermolar expansion. No significant correlation was found between the initial expansion achieved and the severity of the transverse decrease post-treatment. No statistically significant differences were found between gender with respect to the severity of the changes.

Changes in the nasal airway

BASELINE (T1)

The main reason for seeking treatment was to correct a malocclusion, but 10 patients (1 male, 9 female) also expressed a need for treatment for aesthetics, and 9 patients (3 male, 6 female) had expectations of improved nasal patency.

With respect to nasal obstruction, 23 subjects reported problems of varying severity: 9 (3 male, 6 female) had occasional problems, 9 (4 male, 5 female) had frequent problems, and 5 (3 male, 2 female) had constant problems. Sixteen subjects had never perceived any nasal obstruction problems. Eight subjects (5 male, 3 female) had a mouth-breathing posture, 2 (both females) had a nose-breathing posture, and 29 (11 male, 18 female) had a mixed-breathing posture.

Table VI shows the median values and percentiles for minimum cross-sectional areas, nasal airway resistance, and subjective sensation of nasal obstruction at baseline and three months after SARME.

The 23 subjects who reported experiencing nasal obstruction at baseline were analyzed separately. Table VII shows the median values and percentiles for minimum cross-sectional areas (MCA I, MCA II), nasal airway resistance (NARinsp, NARexp) and subjective sensation of nasal obstruction at baseline and three months after SARME. The minimum cross-sectional area, nasal airway resistance, and subjective sensation for this subgroup were analyzed and compared with the rest of the sample. There were no significant differences in minimum cross-sectional area or nasal airway resistance between subjects with and without a sensation of nasal obstruction at baseline.

THREE MONTHS POST-EXPANSION (T2)

Three months after SARME (Table VI), the total sample reported subjective improvement ($P<0.001$). There were increases in MCA I ($P<0.01$) and MCA II ($P<0.01$). There was no correlation between either the cross-sectional area or in the change of minimum cross-sectional area and the perception of nasal obstruction. There were also decreases in nasal airway resistance on expiration (NARexp) ($P<0.01$) and inspiration (NARinsp) ($P<0.01$), but the analysis showed no correlation between either NARexp and NARinsp, or in changes of NARexp and NARinsp and the perception of nasal obstruction.

The 23 subjects (Table VII) who reported experiencing nasal obstruction at baseline were analyzed and compared with the rest of the sample. The improvement in subjective experience three months´ post expansion (T2) was almost the same ($P<0.001$) as in the rest of the sample, but the changes in MCA I ($P<0.001$) and MCA II ($P<0.001$) were more pronounced and differed significantly from the rest of the sample. With respect to NARexp and NARinsp, no major differences were disclosed between this group and the rest of the sample

Table VI. *Comparisons between median values, percentiles for minimum cross-sectional areas, nasal airway resistance, and subjective sensation of nasal obstruction at baseline and three months after SARME*

		Baseline			**3 months post-exp**			
		(T1)			(T2)			(T1-T2)
	n	Median	P10	P90	Median	P10	P90	Wilcox.
Subj. VAS	39	**2.0**	0.0	8.2	**0.9**	0.0	6.2	***
MCA I	39	**0.36**	0.23	0.49	**0.41**	0.26	0.55	**
MCA II	39	**0.45**	0.28	0.72	**0.52**	0.36	0.88	**
NAR Insp	39	**0.19**	0.14	0.36	**0.15**	0.11	0.20	**
NAR Exp	39	**0.17**	0.11	0.28	**0.14**	0.04	0.19	**

Wilcox., Wilcoxon test; P10, the 10th percentile; P90, the 90th percentile; MCA, minimum cross-sectional area; I, anterior; II, posterior; NAR, nasal airway resistance; insp, inspiration; exp, expiration. **P<0.01;*** P<0.001.

Table VII. *23 subjects experiencing nasal obstruction at baseline. Comparisons between median values, percentiles for minimum cross-sectional areas, nasal airway resistance, and subjective sensation of nasal obstruction at baseline and three months after SARME.*

		Baseline			**3 months post-exp**			
		(T1)			(T2)			(T1-T2)
	n	Median	P10	P90	Median	P10	P90	Wilcox.
Subj. VAS	23	**5.1**	1.3	8.5	**2.0**	0.0	6.5	***
MCA I	23	**0.35**	0.23	0.48	**0.41**	0.27	0.52	***
MCA II	23	**0.41**	0.26	0.70	**0.54**	0.36	0.89	***
NAR Insp	23	**0.20**	0.13	0.40	**0.14**	0.11	0.23	**
NAR Exp	23	**0.17**	0.13	0.28	**0.14**	0.02	0.22	**

Wilcox., Wilcoxon test; P10, the 10th percentile; P90, the 90th percentile; MCA, minimum cross-sectional area; I, anterior; II, posterior; NAR, nasal airway resistance; insp, inspiration; exp, expiration. **P<0.01;*** P<0.001.

However, of the above 23 subjects reporting a preoperative sensation of nasal obstruction, at T2, 1 subject had deteriorated, 3 were unchanged, and 19 reported improvement. For this subgroup of 19 subjects, there was a correlation ($P<0.001$, $r = 0.68$) between narrow MCA I at T1 and a moderate increase in MCA I at T2. Furthermore, there was a correlation ($P< 0.05$, $r = -0.42$) between a small decrease in NARexp and significant subjective improvement, which was not evident in the total sample.

The responses to the questions about quality of life related to nasal function showed an improvement in the whole sample (P<0.05) that was not apparent in the subgroup of 23 with subjective nasal obstruction.

EIGHTEEN MONTHS POST EXPANSION (T3)

In the total sample (Table VIII), there were no differences between the examinations at baseline (T1) and 18 months later (T3) with respect to the subjective experience of nasal obstruction, minimum cross-sectional areas I and II, NARexp, and NARinsp. Nor were there any correlations between minimum cross-sectional area I and II, the changes in minimum cross-sectional area I and II and the experience of nasal obstruction, or NARexp and NARinsp. The responses to the question about quality of life related to nasal function showed no significant improvement.

Table VIII. *Total sample. Comparisons between median values, percentiles for minimum cross-sectional areas, nasal airway resistance, and subjective sensation of nasal obstruction at baseline and eighteen months after SARME, total sample.*

		Baseline			**18 months post-exp**			
			(T1)			(T3)		(T1-T3)
	n	Median	P10	P90	Median	P10	P90	Wilcox.
Subj. VAS	39	**2.0**	0.0	8.2	**1.5**	0.0	6.2	**ns**
MCA I	39	**0.36**	0.23	0.49	**0.35**	0.26	0.54	**ns**
MCA II	39	**0.45**	0.28	0.72	**0.50**	0.34	0.70	**ns**
NAR Insp	39	**0.19**	0.14	0.36	**0.18**	0.12	0.25	**ns**
NAR Exp	39	**0.17**	0.11	0.28	**0.17**	0.10	0.25	**ns**

Wilcox., Wilcoxon test; P10, the 10th percentile; P90, the 90th percentile; MCA, minimum cross-sectional area; I, anterior; II, posterior; NAR, nasal airway resistance; insp, inspiration; exp, expiration. NS, Nonsignificant

However, the subgroup of 23 subjects initially reporting a sensation of nasal obstruction (Table IX) showed significant improvement in this regard. Twenty subjects had experienced improvement, two had deteriorated and 1 was unchanged (P<0.01). There was an increase in minimum cross-sectional area II from baseline (T1) to eighteen months post expansion (T3) (P<0.01) but no correlation with the subjective experience.

Table IX. *23 subjects experiencing nasal obstruction at baseline. Comparisons between median values, percentiles for minimum cross-sectional areas, nasal airway resistance, and subjective sensation of nasal obstruction at baseline and eighteen months after SARME.*

		Baseline			**18 months post-exp**			
		(T1)			(T3)			(T1-T3)
	n	Median	P10	P90	Median	P10	P90	Wilcox.
Subj. VAS	23	**5.1**	1.3	8.5	**2.0**	0.0	7.0	**
MCA I	23	**0.35**	0.23	0.48	**0.35**	0.28	0.54	**ns**
MCA II	23	**0.41**	0.26	0.70	**0.52**	0.34	0.75	**
NAR Insp	23	**0.20**	0.13	0.40	**0.16**	0.12	0.24	**ns**
NAR Exp	23	**0.17**	0.13	0.28	**0.16**	0.01	0.25	**ns**

Wilcox., Wilcoxon test; P10, the 10th percentile; P90, the 90th percentile; MCA, minimum cross-sectional area; I, anterior; II, posterior; NAR, nasal airway resistance; insp, inspiration; exp, expiration. NS, Nonsignificant; **P<0.01.

Skeletal treatment effects

After SARME and orthodontic treatment, there were significant transverse skeletal displacements in all measured landmarks, except for right spina nasalis anterior (Table X). The displacements varied in size and distributions.

Table X. *Median transverse displacements in landmarks, with outward displacements shown as positive values and inward displacements shown as negative values.*

Landmark	***Median****(mm)*	***Wilcox.***	***P*** ^{10}	***P*** ^{90}	***Min***	***Max***
Arlare-right (1)	1.29	*	0.16	2.20	-0.52	3,24
Arlare-left (2)	1.23	*	-0.32	2.62	-0.69	3,28
Spina nasalis right (3)	0.86	NS	-0.92	2.48	-2.17	2,99
Spina nasalis left (4)	1.49	*	-0.30	2.64	-2.04	4,89
Ectocanine right (5)	1.71	**	0.20	2.98	-0.06	3,86
Ectocanine left (6)	1.73	**	0.21	2.38	-0.79	4,93
A-point right (7)	2.34	**	1.41	3.15	-0.88	4,81
A-point left (8)	1.95	**	0.92	3.18	-1.44	5,85
Prosthion right (9)	1.79	**	0.59	2.77	-0.48	3,91
Prosthion left (10)	1.51	**	0.25	3.16	-0.50	3,53
Ectomolare right (11)	2.37	***	0.85	3.83	0.15	5,04
Ectomolare left (12)	2.04	***	0.76	4.17	0.00	4,95
Proc zygomaticus right (13)	1.57	*	0.00	2.74	-0.25	3,82
Proc zygomaticus left (14)	1.23	*	0.08	2.66	-0.37	3,57

Wilcox., Wilcoxon test; P10, 10th percentile; P90, 90th percentile. NS, Nonsignificant *P<0.05; **P<0.01; ***P<0.001

There was no significant difference in displacement between corresponding landmarks on the left and right sides, except for spina nasalis anterior, which showed significantly more outward or transverse displacement on the left side. There were no significant differences in displacement with respect to sex or age.

The total change was calculated as the sum of the transverse displacement of the seven pairs of corresponding landmarks on the left and right sides (Figure 16, page 38). The median, probability and percentile values for each variable are shown in Table XI.

Table XI. *Total median transverse expansion in the maxilla, measured at 7 pairs of corresponding landmarks.*

Landmarks	***Median.*** *(mm)*	***Wilcox.***	P^{10}	P^{90}
Arlare right/left (1-2)	2.62mm	*	0.63	4.17
Spina nasalis anterior right/left (3-4)	2.17mm	*	0.00	4.79
Ectocanine right/left (5-6)	3.38mm	**	1.54	5.13
A-point right/left (7-8)	4.14mm	**	3.07	5.49
Prosthion right/left (9-10)	3.70mm	**	1.19	5.20
Ectomolare right/left (11-12)	4.72mm	***	2.01	7.17
Processus zygomaticus right/left (13-14)	2.63mm	*	0.49	4.79

Wilcox., Wilcoxon test; P10, 10th percentile; P90, 90th percentile. *P<0.05; **P<0.01; ***P<0.001.

The expansion was not uniform and the variations were pronounced. Significantly more expansion was seen posteriorly, in the molar area (11 and 12), than laterally, in the canine area (5 and 6). There was no significant difference between lateral expansion in the canine area (5 and 6) and anterior expansion at prosthion (9 and 10). Expansion was more pronounced superiorly at the A-point (7 and 8) than at prosthion (9 and 10), but the difference was not statistically significant. There was significantly less expansion at processus zygomaticus (13 and 14) than in the ectomolare region (11 and 12). We found no significant difference in expansion in the ectocanine (5 and 6) and alare areas (1 and 2).

There was significantly less expansion at spina nasalis anterior (3 and 4) than at A-point (7 and 8) and prosthion (9 and 10). There were no correlations between the various transverse displacements, anterior, posterior, lateral, or inferior, except for the significant correlation between expansion in the ectomolare area (11 and 12) and processus zygomaticus (13 and 14) ($P<0.001$; $r = 0.732$). No correlation was found between the severity of posterior tipping and the age of the patients.

Changes to the external features of the nose

There was in general significant widening and overall anterior and inferior displacement of the nose.

X-AXIS (LATERAL DISPLACEMENT LEFT AND RIGHT)
All landmarks at alar-wings showed lateral displacement (Table XII). The displacements on the left and right sides were symmetrical and most obvious at the lateral alar bases (landmarks 14, 15).

Table XII. *Median displacements on the X-axis at the nose measured at 15 landmarks (Figure 17, page 39). Displacement was recorded as positive values laterally.*

X-axis

Landmark	Median	p^{10}	p^{90}	Wilcox.
1 Pronasale	0.11	-0.64	0.86	NS
2 Alar right	1.10	0.06	1.89	***
3 Alar left	0.70	-0.13	1.91	***
4 Alar curvature right	0.59	-0.62	2.16	**
5 Alar curvature left	0.58	-1.22	1.85	*
6 Columella	0.10	-0.54	1.38	NS
7 Subnasale	0.09	-1.22	1.20	NS
8 Nostrile sup.right	0.42	-0.47	1.67	NS
9 Nostrile sup. left	-0.10	-1.44	1.00	NS
10 Nostrile inf. right	0.35	-1.32	2.26	NS
11 Nostrile inf. left	0.29	-1.04	1.87	NS
12 Nostrile lat. right	0.81	-0.42	2.40	***
13 Nostrile lat. left	0.67	-0.33	1.76	***
14 Alar base right	1.47	0.30	2.90	***
15 Alar base left	1.41	0.46	2.60	***

Wilcox., Wilcoxon test; p10, 10th percentile; p90, 90th percentile. Wilcoxon test. NS, Nonsignificant; *$P< 0.05$; **$P< 0.01$; ***$P< 0.001$.

Displacement at lateral alar bases decreased gradually, both anteriorly and inferiorly. The most pronounced lateral change to the nostrils was at the utmost lateral point of the inner contour of the nostrils (Landmarks: 12, 13), which decreased both anteriorly and inferiorly. Landmarks 1, 6 and 7, in the midline, did not show any significant lateral displacement; neither did Landmarks 10 and 11, at the most inferior point of the nostrils. There were significant correlations ($P<0.001$) between lateral displacements at the alar wings and between lateral displacements in the nostrils.

Y-AXIS (INFERIOR-SUPERIOR DISPLACEMENT)

Most landmarks showed moderate inferior displacement (Table XIII). The most significant displacement, albeit minor, was found at pronasale and subnasale (Landmarks 1, 7) and decreased gradually both posteriorly and laterally.

Table XIII. *Median displacements on the Y-axis at the nose measured at 15 landmarks (Figure 17, page 39). Displacement was recorded as positive values superiorly.*

Y-axis

Landmark	Median	p^{10}	p^{90}	Wilcox.
1 Pronasale	-0.26	-1.40	0.28	***
2 Alar right	-0.25	-1.34	1.23	NS
3 Alar left	-0.04	-1.85	1.04	NS
4 Alar curvature right	-0.27	-1.84	1.06	NS
5 Alar curvature left	-0.48	-1.91	1.11	*
6 Columella	-0.11	-1.20	0.61	NS
7 Subnasale	-0.51	-2.28	0.59	**
8 Nostrile sup.right	-0.20	-1.52	1.00	NS
9 Nostrile sup. left	-0.35	-1.29	0.62	*
10 Nostrile inf. right	-0.19	-1.49	1.23	NS
11 Nostrile inf. left	-0.12	-1.47	0.76	NS
12 Nostrile lat. right	0.48	-1.79	0.71	**
13 Nostrile lat. left	0.47	-1.43	1.10	*
14 Alar base right	0.10	-1.12	1.66	NS
15 Alar base left	-0.04	-1.62	1.03	NS

Wilcox., Wilcoxon test; p10, 10th percentile; p90, 90th percentile. Wilcoxon test. NS, Nonsignificant; *$P< 0.05$; **$P< 0.01$; ***$P< 0.001$

Z-AXIS (ANTERIOR-POSTERIOR DISPLACEMENT)

The most significant and obvious displacement of all occurred anteriorly, particularly at landmarks near the facial insertion (landmarks 4, 5, 10 11, 14, 15) (Table XIV). This anterior displacement was however, not evident at subnasale (landmark 7) which showed a contrasting, posterior displacement.

Table XIV. *Median displacements on the Z-axis at the nose measured at 15 landmarks (Figure 17, page 39). Displacement was recorded as positive values anteriorly.*

Z-axis

Landmark	Median	p^{10}	p^{90}	Wilcox.
1 Pronasale	0.03	-0.14	0.80	**
2 Alar right	0.46	-1.23	2.28	*
3 Alar left	0.63	-0.72	2.39	***
4 Alar curvature right	1.14	-0.17	2.82	***
5 Alar curvature left	1.18	-0.40	3.45	***
6 Columella	0.41	-0.59	2.04	**
7 Subnasale	0.07	-1.32	1.41	NS
8 Nostrile sup.right	0.26	-0.36	1.57	**
9 Nostrile sup. left	0.22	-0.50	1.31	*
10 Nostrile inf. right	0.85	-0.85	1.94	***
11 Nostrile inf. left	1.07	-0.23	2.37	***
12 Nostrile lat. right	0.18	-2.06	1.44	NS
13 Nostrile lat. left	0.43	-0.94	2.12	**
14 Alar base right	1.36	0.05	2.76	***
15 Alar base left	1.98	0.37	3.25	***

Wilcox., Wilcoxon test; p10, 10th percentile; p90, 90th percentile. Wilcoxon test. NS, Nonsignificant; *P< 0.05; **P< 0.01; ***P< 0.001

EUCLIDEAN DISTANCES

The Euclidean distance, *i.e.* the shortest distance between two landmarks, was analysed and calculated for height and width of the nose and nostrils (Table XV).

Nose height, measured between pronasale and subnasale, remained unchanged, but a significant and evident widening was apparent at the alar wings and alar base. The nose width at the facial insertion persisted unchanged. A significant widening of the nostrils was obvious at the lateral alar wings but not at the lowest point. The nostril length remained unchanged.

No correlation was disclosed between the initial and final widths of the nose, nor between the initial and final widths of the nostrils.

Table XV. *Median changes between landmarks without orientation in space (Figure 19, page 40)*

		Median	p^{10}	p^{90}	Wilcox.
Nose height	(Landmark 1-7)	0.18	-1.38	2.15	NS
Nose width I	(Landmark 2-3)	1.66	0.27	3.13	**
Nose width II	(Landmark 4-5)	1.01	-0.65	2.72	NS
Nose width III	(Landmark 14-15)	3.09	1.56	4.70	***
Nostril height	(Landmark 8-10, 9-11)	-0.47	-1.12	0.83	NS
Nostril width I	(Landmark 12-13)	1.47	-0.08	3.19	***
Nostril width II	(Landmark 10-11)	0.68	-1.51	2.29	NS

Wilcox., Wilcoxon test; p10, 10th percentile; p90, 90th percentile. Wilcoxon test. NS, Nonsignificant; **P< 0.01; ***P< 0.001.

Discussion

Background to current thesis

Over time, treatment procedures have developed, changed and sometimes also ceased to exist. SARME became an overall accepted and common strategy for treatment of MTD in non-growing individuals in the late 1980's and early 1990's.

In Sweden, SARME was adopted as a routine clinical procedure in the 1990's and was based on prevailing knowledge and scientific reports.

Various treatment protocols were proposed, all focusing on different aspects of the procedure. The lack of consensus from scientific studies puts clinicians in the challenging position of having to choose and balance between factors such as the complexity of the surgery, risks for the patient, expected long-term stability, the effect on soft tissue, effect on respiration, clinical accessibility for the procedure, etc.

Over the past decade there has been increased interest in SARME, its effects on hard and soft tissues and its impact on respiration. The even distribution of expansion in the maxilla has been questioned, and there is now greater focus on the variation of displacement in different parts of the maxilla and how these changes affect the soft tissue and respiration.

The immediate effects after SARME are often obvious and can be encouraging and optimistic. The long-term effects are however, more difficult to assess. When a patient reports an instant subjectively improved perception of nasal respiration after SARME, this can be this related empirically to a widening of the nasal cavity (Babacan *et al.* 2006) and be supported by previous studies on nasal respiration and maxillary expansion after RME (Baccetti *et al.* 2001, Wriedt *et al.* 2001). However, such an assumption is hazardous. Although the relationships seem obvious, it is easy to draw hasty conclusions. The assessment of any complex treatment is challenged by many factors. What kind of widening is the improvement related to and in which area? Is an expansion in growing individuals comparable to an expansion in non-growing individuals? Is the improved subjective perception a valid measurable variable and will it persist long-term? Such questions are fundamental and have to be answered before any conclusions can be drawn about the effect of a treatment in the short- or long-term.

In 2005, at the beginning of the present doctoral project, a literature review of SARME and orthodontic treatment was done as a pilot study. Although many studies and conclusions about the method were available, most of the findings were approximations of RME; hence the scientific support for SARME was rather weak (Lagravere *et al.* 2005). Moreover, the studies were limited by the methods of investigation available at the time.

The main findings from this review were, however, the wide variety of methods, indications and treatment outcomes. Furthermore, the findings were ambiguous, with inaccurate interpretations and a number of confounding factors. Crucial factors for reliable scientific results are sample selection and sample size, valid instruments for measurements and proper long-term follow-up periods. The studies reviewed were lacking one or more of these factors.

The lack of long-term follow-up studies and the availability of a well-documented material of study models prompted the retrospective long-term follow-up study which initiated the present doctoral project. Collaboration with the Maxillofacial Unit at the University Hospital in Linköping provided the conditions necessary to achieve sufficient material for a prospective study and professional supervision. The multidisciplinary approach in the study design was accomplished by involving professional teams, such as The Center for Medical Image Science and Visualization, Linköping Sweden (CMIV), The Ear, Nose and Throat Departments in Jönköping and Linköping, Sweden, The Institute for Surgical Technology & Biomechanics, University of Bern, Switzerland and foremost Dr Hyungmin Kim at Harvard Medical School, Boston USA.

Methodological considerations

Samples and study designs

The studies in the present doctoral project are based on two different samples and study designs. The first sample is a retrospective, consecutive, long-term follow-up of material comprising study models from patients treated with SARME and orthodontic treatment at the Institute for Postgraduate Dental Education, Jönköping, Sweden, between 1991 and 2000. The second sample is a prospective consecutive, longitudinal material of patients scheduled to undergo SARME and orthodontic treatment at two centres, Jönköping and Linköping, between 2006 and 2009.

Previous studies of SAME have been compromised by small, retrospective samples and short follow-up periods (Lione *et al.* 2013, Vilani *et al.* 2012). In general, retrospective investigations are often criticised: errors due to confounding factors and bias are more common in these studies. Confounding factors may be the varying experience of the operators, non-consecutive patient selection or differences in treatment protocols. Randomized controlled trials (RCTs) are regarded as the gold standard for a clinical trial and are often used to test the efficacy and/or effectiveness of various types of treatment within a patient population. However, in clinical trials where only one treatment option is available, blinding can be difficult to achieve in an RCT.

Prospective cohort studies are alternatives to RCTs. In a prospective study it is possible to limit bias and confounding factors. In both prospective and retrospective studies, the outcome of interest should be obvious; otherwise, the number of outcomes observed will be too small for meaningful statistical analysis. In a prospective study, all efforts should be made to avoid sources of bias such as the loss of individuals to follow-up.

The material in the retrospective study (Paper I) comprised study models of 33 consecutive patients treated in Jönköping between 1990 and 2000. Study models were available from treatment start, at the end of the active expansion phase and at the end of the retention period. It would have been interesting to measure the immediate dental changes after the surgical expansion. Study models were available for that period of treatment, but the persisting bulky palatal Hyrax expander precluded measurement of expansion.

The distribution of data was tested and showed non-normal distribution. In a larger sample, normal distribution might be expected. Despite these disadvantages, the sample size was larger than in previous studies.

Retrospective materials and studies are associated with errors due to bias and confounding factors. Potential sources of bias in the present retrospective study are selection bias and operator bias. Selection bias can be linked to an incorrect diagnosis. The inclusion criterion for eligible subjects specified "patients with skeletal MTD, treated with SARME". Assessment of MTD was made on study models in an Angle Class I relationship, according to Bishara and Staley's (1987) recommendations. This is a simple and reliable method for estimating a transverse discrepancy between jaws. While it would have been advantageous to verify the diagnosis by measuring the skeletal component versus the dental component, this would have required radiographs. Grummons and Ricketts (2004) claimed that postero-anterior radiographs (PA) are necessary for differential diagnosis of true skeletal

MTD, relative MTD and dentoalveolar MTD. The validity of the prevailing PA radiographic analyses has however, been questioned and PAs were not used in this retrospective study. Consequently clinical assessment of MTD based on study models might at the time have been more relevant than PA radiographs.

Operator bias refers to errors related to variations in experience, skills or techniques of the operators in a study. When SARME was introduced in Jönköping in the 1990's, it was based on a strict orthodontic and surgical treatment protocol according to Kraut (1984). All treatment plans were made and confirmed by an interdisciplinary team of orthodontists and oral/ maxillofacial surgeons. The orthodontic procedure was undertaken at a single orthodontic clinic and the surgery was carried out by two experienced senior oral and maxillofacial surgeons. The two surgeons were calibrated and undertook the same number of procedures. These conditions minimised the risk for major operator bias.

The longitudinal prospective studies (Papers II-IV) comprised a consecutive sample of patients who were to undergo SARME and orthodontic treatment. A mandatory question in the start-up of a prospective study is statistical power and sample size. The power of a statistical test (1-β) is the probability that the test will reject the null hypothesis when the null hypothesis is false, i.e. the probability of not committing a Type II error (Kirkwood 1988). Power analysis can also be used to calculate the minimum sample size required.

The statistical power is in general a function of the magnitude of the effects, the statistical significance, and the sample size. The magnitude of the effect can be quantified in terms of an effect size, which requires information about the variability and distribution of the measurements. The variability and distribution of the effects on respiration have not been analyzed and were therefore unknown. With respect to the CT-measurements on hard and soft tissues, the effect size and variance were based on previous studies (Tausche *et al.* 2007).

The minimum sample size of 34 patients was based on a level of significance of 0.05 and with a power (1-β) of 80 per cent to detect a mean difference in displacement of 0.75 mm. Higher statistical power could have been achieved in the present study, but to the detriment of the significance level. A larger sample size would have increased the statistical power. By convention, 80 per cent is an acceptable level of power (Kirkwood 1988) and it would have been difficult to ensure a much larger sample within a reasonable time-frame. In a consecutive material, the likelihood of attrition must be addressed. Thus in order to ensure the minimum sample size required to fulfil the power calculation, 40 patients were recruited.

Rigorous accuracy was used in the construction of the study protocol in order to avoid confounders and bias. A multi-centre study is however, more sensitive to some kinds of bias than others. As treatment was carried out at more than one centre, it was important that potential operator bias was analyzed and minimized.

Measurements on study models

The aim of the retrospective study (Paper I) was to evaluate long-term transverse dental changes after SARME and orthodontic treatment. The stability was assessed on a consecutive material of study models. Although the material was well-documented, long-term it is difficult to assess anything other than the dental effects. The dental changes may reflect skeletal displacements, but it is hazardous to draw any major conclusions of skeletal effect on study models alone.

There are several accepted indices for evaluating transverse dental deficiencies on study models, such as Pont´s Index, Korkhaus Index and Howe´s Analysis (Dause *et al.* 2010, Howe 1947, Joondeph *et al.* 1970). All these indices are based on direct measurements on study models, using calipers. By 2005-2006, when the present study was initiated, several authors had reported methods for digital scanning of study models and measurements on 3D study models (Hirogaki *et al.* 2001, Bell *et al.* 2003, Santoro *et al.* 2003). Quimby *et al* (2004) and others (Stevens *et al.* 2006) reported acceptable accuracy but greater variance for measurements made from computer-based models. Thus, the method selected for the present study was direct measurement on study models, using digital calipers.

To measure intermaxillary distance anteriorly and posteriorly and to assess dental tipping, measurements were taken at two reference points on the canines and the first molars respectively, as described by Moorrees (1959). However the choice of the canines for reference points is a potential source of error. Some patients present with buccally tipped or buccally positioned maxillary canines, which are subsequently normalized by the fixed appliance therapy. An alternative reference point would have been the upper first premolars. However, first premolars were in most cases anchor teeth in the hyrax appliance and fitted with orthodontic bands.

Questionnaire

The effect of a treatment or surgical intervention can be measured in lengths, areas, volumes, degrees and so forth. However, the overall success of a treatment cannot be assessed from technical, quantitative measurements alone: subjective parameters such as changes in quality of life as a result of treatment must also be considered (Robinson *et al.* 1996).

In rhinology, patient-based outcomes have been studied extensively. This is highly relevant, because the symptoms associated with many rhinological conditions have a negative impact on quality of life (QOL) (Stewart and Smith 2005, Eccles 1992).

It is generally accepted that there is only a weak correlation between subjective experience of nasal obstruction and objective findings (Cole 1989, Fairley *et al.* 1993, Jones *et al.* 1989, Larsson *et al.* 2001, Roithmann *et al.* 1994, Semeraro and De Colle 1989, Wang *et al.* 2004). Several validated instruments have been proposed to assess the patient's subjective perception of nasal patency and QOL (Levy *et al.* 2006, van Oene *et al.* 2007). These include the Glasgow Benefit Inventory questionnaire (GBI), the Chronic Sinusitis Survey, SNOT -20, the Rhinosinusitis Disability Index, the NOSE scale, FNQ questionnaires and SNAQ-11 (Benninger and Senior 1997, Piccirillo *et al.* 2002, Robinson *et al.* 1996, Stewart *et al.* 2004, Fahmy *et al.* 2002, Fairley *et al.* 1993).

In Paper II, the subjective parameters were assessed by a questionnaire approved by the Swedish Rhinologic Society (Loth *et al.* 2001). It is based on ten anamnestic "yes" or "no" questions and ten visual analogue scales (VAS). The questionnaire was intended primarily to assess the disease-specific effects of rhinological conditions, but can also be used to evaluate treatment outcome in terms of nasal obstruction.

Visual analogue scales were used to assess subjective experience. It may be argued that VAS lack validity and reliability. However, these are common instruments and have been extensively and independently validated with respect to patients' subjective experiences (Jones *et al.* 1989, Price *et al.* 1983, Grant *et al.* 1999, Krouse *et al.* 2010).

The VAS in the present questionnaire was based on the patient's rating of current overall nasal obstruction on a linear scale, where 0 mm represents "never" and 100 mm represents "constantly". In order to evaluate consistency, the initial VAS rating was analysed and classified and compared with the anamnestic questions about the patients' initial subjective perception of nasal obstruction (Aitken 1969).

The differences in VAS ratings at pre-treatment, post expansion and at the 18 month follow-up were analysed. In order to evaluate the consistency between the outcome from VAS scales and anamnestic questions, the VAS differences were classified and compared with the anamnestic questions about changes in the subjective perception of nasal obstruction (Aitken 1969).

Acoustic Rhinometry and Rhinomanometry

Nasal geometry and physiology were assessed with a Rhinometrics model SRE 2000 acoustic rhinometry/rhinomanometry device. (RhinoMetrics, Interacoustics A/S Assens, Denmark). These measurements are sensitive to bias. In order to reduce bias, the two ENT departments were equipped with identical devices; throughout the study, these were handled by two trained operators according to the International Committee on Standardization of Rhinomanometry (Clement 1984, Clement and Gordts 2005). However, some weaknesses remain, because of the multi-centre design and difficulty maintaining optimal calibration.

It is generally accepted that AR is accurate for measurements within the first 5 cm of the nasal cavity (Nigro *et al.* 2009, Hilberg 2002) and particularly in the region anterior to the narrowing areas, up to 2.5 cm from the nostril (Min and Jang 1995). However, there is a lack of consensus. While most AR studies affirm that the first notch (approx. 2.5 cm from the nostril) is the nasal valve and the second notch (approx. 5.0 cm from the nostril) is the anterior end of the inferior turbinate (Eduardo Nigro *et al.* 2009), other studies claim that the first notch is the nostril and the second is the nasal valve as a whole (Corey *et al.* 1999, Roithmann *et al.* 1997).

All registrations, structural as well as functional, were made after administration of a decongestant (Otrivin, 1mg/ml; Novartis Pharma AG, Basel, Switzerland) (Cole 2000, Larsson *et al.* 2001).

In the present study the minimum cross sectional areas (MCA I-II) were measured at two sites on the anterior nose. MCS I represents the structural valve, from the nostril rim to approximately the anterior border of the inferior turbinate (0.0-2.2 cm) and MCS II represents the functional valve, from the anterior border of the inferior turbinate to the isthmus nasi (Figure 14, page 35). Five recordings were taken in each nostril and a mean value was calculated after exclusion of outliers. Regardless of left- or right nostril, the narrowest area in MCS I and MCS II was chosen for analysis. This simplification was made on the assumption that the narrowest area, regardless of nostril, was the most interesting area.

Active anterior rhinomanometry (RMM) is the most common method for assessing nasal airway resistance (NAR). Determination of NAR is a useful objective aid in evaluation of nasal function and the patency of the nose (Broms *et al.* 1982, Clement and Gordts 2005, Cole 2000, Gordon *et al.* 1989, Nathan *et al.* 2005). In active anterior rhinomanometry**,** one nasal cavity is occluded while the other is left open for measurements.

The resistance was measured for inspiration and expiration for left and right nostril respectively at a default transnasal pressure of 75 Pa. and the total resistance analysed according to the formula $R_{insp/exp} = R_{left} * R_{right} / R_{left} + R_{right}$. It would also have been possible to analyse the total NAR for left and right nostrils separately. However, the results can be affected by the "nasal cycle", i.e. reciprocal and periodical changes in NAR between left and right nasal cavity during respiration (Stoksted 1953, Numminen *et al.* 2003). The mechanisms underlying the "nasal cycle" are unclear (Flanagan and Eccles 1997) but Gilbert and Rosenwasser (1987), applying the most stringent criteria, reported that 13 per cent of all individuals displayed the classical nasal cycle. In order to avoid such errors, the analyses were made on the total NAR for inspiration and expiration.

CT-examination

The CT examinations were performed with a helical CT-machine (Siemens Somatome Sensation 16/64, Forchheim Germany) equipped with automatic exposure control (AEC) (Mulkens *et al.* 2005 Soderberg and Gunnarsson 2010). To reduce the radiation dosage and optimize image quality, Siemens Care Dose 4D was utilized to regulate mAs (Lee *et al.* 2008). The maximum value was set to 120 kV and 55 mAs. The scanned area comprised the anterior cranial base to the mandibular base. After examination, the images were processed at a radiological workstation with slice thicknesses of 0.75 mm and increments of 0.3 mm in Kernel H 60s sharp FR, to allow further segmentation and registration.

When the study was initiated in 2005, the risk of radiation exposure was weighed against achieving the required information i.e. a three dimensional assessment of skeletal and soft tissue changes.

The standard radiographic protocol for a preoperative examination includes panoramic radiographs, cephalograms, intraoral radiographs and sometimes antero-posterior radiographs. The radiation physicist calculated the radiation dosage for these modalities to be an effective dose of 0.05 mS. The diagnostic outcome from these modalities is however, not sufficient for exact treatment planning, particularly in soft tissue. To increase the diagnostic advantage in treatment planning a helical CT machine was used. The helical CT machine offers high quality images of both soft and hard tissue. The total radiation dose for this modality was calculated to be an effective dose of 0.5 mS. The increased radiation dosage was weighed against an expected superior diagnostic outcome. The sample comprised non-growing individuals and additional two-dimensional images would have increased radiation dose, but provided only limited, partial diagnostic information. Magnetic Resonance Imaging (MRI) could have been an alternative. MRI poses no radiation risk to the patient and provides good soft tissue contrast, but is associated with major artefacts around fixed orthodontic appliances. Today, in 2013, the method of choice would be cone beam computed tomography (CBCT), but it was not available at the time the study was undertaken.

With respect to radiation exposure, it is important that ethical aspects are addressed, not only in the context of clinical studies, but also in routine practice. Radiation exposure should always follow the ALARA-principle; as low as reasonably achievable (Anonymous 2001).

Superimposition of 3D models and analyses

New and advanced methods of 3D superimposition were introduced when this doctoral project was initiated in 2005 (Cevidanes *et al.* 2005, Cevidanes *et al.* 2006). These methods were considered to be very precise and accurate, but very time consuming to perform (Cevidanes *et al.* 2009, De Clerck *et al.* 2009, Nada *et al.* 2011). While earlier studies were limited to prevailing 2D methods, the new methods had the potential to evaluate 3D changes more accurately. In the present study a modified version of an automated voxel-based image registration was utilized. The precision and reproducibility of an automated voxel-based image registration has been evaluated and confirmed by Nada *et al* (2011). The examiner manually selects the area of interest (anterior cranial base) and performs a preliminary superimposition. The software computes a more precise and accurate alignment of the constructed 3D models, based on the maximization of mutual information. This means that images are superimposed by comparing the Hounsfield unit for each voxel in the anterior cranial base.

The segmentation process of the 3D images was accelerated with simple thresholding, which allows selection of a range of Hounsfield units (HU). In the present study, the lower threshold for bony tissue was set at 300 HU. Values above this were automatically selected. However, in some images the HU value had to be adjusted interactively to achieve better contours. Still, this simplified segmentation process has markedly accelerated the procedure. There are other methods for cranial base registrations, but their accuracy relies on the precision of landmark identification and the accuracy of surface models (Grauer *et al.* 2009, Nada *et al.* 2011, Plooij *et al.* 2009).

A landmark-based, non-rigid mapping technique, Thin-Plate Spline (TPS), was used to determine corresponding landmarks on the pre- and post-surgery 3D models. Once the two volumes were registered, the displacement vectors for each landmark were calculated. The Frankfurt horizontal plane (FHP) was used for the normalization of displacement vector according to Xia *et al.* (2000).This means that zero point of FHP will be in the centre of the left and right Porion. TPS+CPM were used only for defining corresponding points other than digitized landmarks and to show continuous changes of distances between two surfaces i.e. in a color-map display. The post registrations were made eighteen months after SARME. This means that the healing process in the midline made it difficult to identify reliable landmarks for lateral displacement. Thus, in 11 cases, TSP-CPM were used to define midline lateral skeletal displacements.

Voxel-based superimposition offers new potential in science to assess and to quantify changes in various anatomical areas. The color maps make it possible to measure changes in both hard and soft tissue in all directions with high accuracy and reproducibility.

Reflections on results

The visible and clinical findings vary during the different phases of treatment. The most immediate and significant postoperative change was the medial diastema. This diastema represents a skeletal effect in the maxilla (Bishara and Staley 1987). However, the subsequent orthodontic treatment and diastema closure will obscure the signs of skeletal effects. Moreover the immediate post-operative swelling after SARME will affect the soft tissue and the patient's perception of nasal respiration (Nooreyazdan *et al.* 2004). These immediate changes are interesting, but should not be extrapolated to long-term interpretations and conclusions. Therefore it is vital to analyse the time-points of measurements and follow-up periods and to use more sophisticated methods in order to understand the treatment outcome in a longer perspective.

Long-term stability

The aim of Study I was to assess the long-term stability of SARME and orthodontic treatment based on measurements on study models. Although analyses of study models are limited in many ways, they are suitable and useful for assessing dental changes, such as transverse measurements and dental tipping. The analyses showed that SARME and orthodontic treatment normalized the transverse discrepancy and was stable for a mean of 6.4 years (Figure 21A, B).

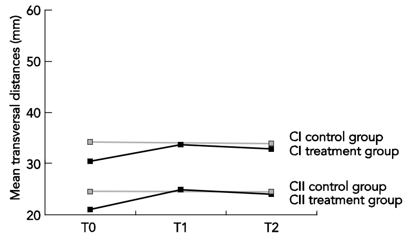


***Figure 21A.** Mean transverse distances (black) in the treatment group at the maxillary canines before treatment (T0), after completed treatment (T1) and at follow-up (T2), and at the first and last registration (grey) for the control group.*

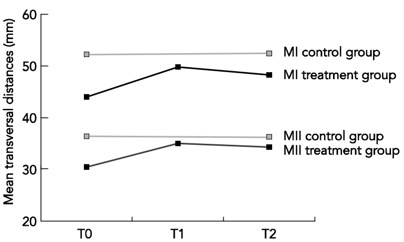


***Figure 21B.** Mean transverse distances (black) in the treatment group at the maxillary molars before treatment (T0), after completed treatment (T1) and at follow-up (T2), and at the first and last registration*

The mean expansion after completed treatment and a retention period of 6 months (T1) (Figure 21) was somewhat less, but corresponds well with previous findings (Bays and Greco 1992 Berger *et al.* 1998, Northway and Meade 1997, Pogrel *et al.* 1992).

On average, there was greater expansion posteriorly, at the molars, than anteriorly, at the canines. This finding is in agreement with current studies on study models (Byloff and Mossaz 2004, Wriedt *et al.* 2001, Anttila *et al.* 2004). A number of older studies however, have reported the opposite, greater expansion anteriorly than posteriorly (Bays and Greco 1992, Berger *et al.* 1998, 1992, Northway and Meade 1997, Pogrel *et al.* 1992, Stromberg and Holm 1995). There are many proposed explanations for these variations in results. A common interpretation is related to the surgical technique applied and the skeletal maturity/age of the patients. It would be logical to assume that in the present study, pterygoid detachment was a contributing factor to the greater posterior expansion (Bays and Greco 1992, Jafari *et al.* 2003, Laudemann *et al.* 2009, Matteini and Mommaerts 2001). This conclusion might be correct, but it cannot be drawn on the basis of study models alone. Moreover, analyses did not show any correlation between age and dental tipping, despite the wide age range in the study group.

Another explanation for the difference in posterior and anterior expansion is the initial buccal tipping of the canines. In MTD, buccally tipped and buccally placed canines are a common feature; this condition, is normalized during fixed appliance therapy after SARME. This uprighting effect on the canines was measurable and evident at the two levels on the canine and can thus obscure the real skeletal effect in this area. Had the upper first premolar not been part of the bulky palatal Hyrax expander, it would have been more correct to analyse the anterior transverse dimension in this area.

Buccal dental tipping after SARME is associated with transverse relapse; hence its control and reduction are vital (Bays and Greco 1992, Byloff and Mossaz 2004, Chung and Goldman 2003, Koudstaal *et al.* 2009a, Koudstaal *et al.* 2009b, Kurt *et al.* 2010a, Lehman and Haas 1989, Phillips *et al.* 1992, Seeberger *et al.* 2010a, Stromberg and Holm 1995).

An obvious effect in the present study was the buccal tipping at the maxillary first molars. According to a previous study (Byloff and Mossaz 2004), the buccal tipping of the anchor will be normalized during the period of fixed appliance therapy. The bilateral overexpansion was done according to previous studies, to compensate for transverse relapse following the process of uprighting the anchor-teeth (Jacobs *et al.* 1980, Kraut 1984, Wertz 1970). Even after completed treatment and retention, the molars exhibited on average 25 per cent more expansion at the mesiobuccal cusp tips. Our first assumption of this persisting buccal tipping of molars was to emphasise the importance of proper subsequent orthodontic treatment The assumption that a proper orthodontic alignment is necessary to achieve stable results is of course correct, but may perhaps be somewhat too hasty, given that tipping of molars can be a result of both skeletal and dental components.

While some studies measure the transverse expansion immediately after surgical expansion (Berger *et al.* 1998, Byloff and Mossaz 2004), in other studies the measurement is made at the end of active treatment and in others, after completed retention (Anttila *et al.* 2004, Bays and Greco 1992). This variation in time-point of measurement is reflected in the disparity in conclusions about the stability. Byloff and Mossaz (2004), who measured transverse changes immediately after surgical expansion reported relapse in 36 per cent of cases after 1 year, compared to a relapse of 5-8 per cent in other studies (Lagravere *et al.* 2006a, Suri and Taneja 2008). This is a misinterpretation of relapse. If as has been shown, SARME and subsequent orthodontic treatment normalize the transverse discrepancy, then relapse and long-term stability should be assessed after completed treatment and retention.

It is unclear whether the present molar tipping is attributable to the appliance or the surgical technique. When tooth-borne devices are used, the mechanical stress is applied via the teeth, with an increased risk of dental side effects. Application of the force directly to the bone via a bone-borne distractor will decrease the risks of such effects (Laudemann *et al.* 2010, Mommaerts 1999, Tausche *et al.* 2007, Verstraaten *et al.* 2010). However, in the literature, there is lack of consensus on the effects of bone-borne distractors (Pinto *et al.* 2001, Ramieri *et al.* 2005). Bone-borne devices often produce greater skeletal expansion anteriorly and less posteriorly and more asymmetries in the widening (Landes *et al.* 2009). Moreover, the associated risks of ulceration, infection and palatal abscesses are not inconsiderable.

The pterygoid processes and the pterygomaxillary junction are considered to be areas of major resistance (Bays and Greco 1992, Holberg *et al.* 2007, Jiang *et al.* 2009, Lima *et al.* 2011). Some studies show that pterygoid disjunction should be determined on the basis of the patient's age i.e. patients under 20 years of age should not require separation (Anttila *et al.* 2004, Laudemann *et al.* 2009). In the retrospective material of study models (Study I), with a mean patient age of 25.9 years, careful separation was made at the pterygoid fissures to increase the posterior skeletal expansion and to decrease the tipping of the molars. Although the procedure is considered to reduce posterior resistance sites, the tipping at the molars was obvious. The question is whether separation at the pterygoid fissures was radical enough to reduce the posterior resistance. There is no overall consensus regarding this separation (Han *et al.* 2009). Some surgeons prefer not to separate the pterygoid fissures, despite the major resistance in the area, because of the risk of injury to the pterygoid plexus by the osteotomy (Koudstaal *et al.* 2009a, Lanigan and Mintz 2002, Politis 2012).

The long-term stability at a mean of 6.4 years was compared with an untreated, matched control group. This is to date the longest follow-up study after SARME and orthodontic treatment, with a consecutive sample of

33 patients (Vilani *et al.* 2012). There was a significant decrease in all measured transverse dimensions but the crossbites remained corrected at T2 and there were no significant differences from the control group, except for the distance between mesiobuccal cusp tips of the maxillary first molars *(MI)*. In the control group, an increase in the maxillary intermolar width would be expected between T1 and T2 (Bondevik 1998), and thus a greater difference between the groups, but this was not evident.

The follow-up range in the sample made it possible to study two groups: those with a follow-up of less than five years (mean 3.7 years) or more than 5 years (mean 9.3 years), with 15 cases in the first group and 16 cases in the second (Figure 22). There were no significant differences between these two groups with respect to the degree of expansion, dental tipping or retention time. The major finding of this analysis was that there was no significant difference between these two groups with respect to the decrease in transverse dimension. This indicates that the relapse is most pronounced during the first 3 years. Whether these changes were related to dental or skeletal factors could not be determined from study models. This means that the retention period after SARME and orthodontic treatment should be prolonged from the current six months to at least three years.

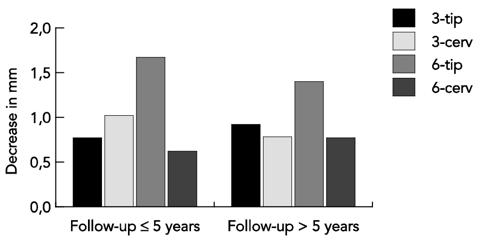


Figure 22. *In order to evaluate post-treatment changes over time, the treatment group was divided into two groups: those with less than five years follow-up and those with more (15 samples, mean 3.7 years, and 16 samples, mean 9.3 years respectively). No statistically significant differences were found between these two groups with respect to post-treatment changes.*

Nasal respiration

Maxillary expansion is associated with enlargement of the nasal cavity and nasal airways (Suri and Taneja 2008). Most of the previously described effects of SARME on nasal patency are based on technical, quantitative measurements (Babacan *et al.* 2006, Baraldi *et al.* 2007, Berretin-Felix *et al.* 2006, Kurt *et al.* 2010b, Mitsuda *et al.* 2010, Schwarz *et al.* 1985, Seeberger *et al.* 2010b, Sokucu *et al.* 2009, Wriedt *et al.* 2001). The specific aim of the present study was to investigate whether changes in patients' subjective perception of nasal patency after SARME can be related to or correlated with changes in nasal "volume" (MCA I, MCA II) and changes in nasal airway resistance (NAR).

The objective findings at three months after the surgical expansion (T2) were in accordance with previous studies (Babacan *et al.* 2006, Baraldi *et al.* 2007, Berretin-Felix *et al.* 2006, Kurt *et al.* 2010b, Mitsuda *et al.* 2010, Schwarz *et al.* 1985, Seeberger *et al.* 2010b, Sokucu *et al.* 2009, Wriedt *et al.* 2001). Analysis of the results showed significant improvements in all variables, but no significant correlations. The highly significant improvement in the subjective experience of nasal patency was confusing, because 16 subjects had reported no nasal obstruction at treatment start (T1). This might be attributable to sampling bias, or a placebo effect. The remaining 23 patients with nasal obstruction at T1 were analysed separately and compared with the 16 patients without nasal obstruction. The analysis did not disclose any significant differences with respect to MCA or NAR. This absence of significant difference at T1 can be related to small sample sizes, but also to a low correlation between "objective" and "subjective" variables (Jones *et al.* 1989, Roithmann *et al.* 1994, Sipila *et al.* 1994, Sipila *et al.* 1995).

The 23 subjects with initial nasal obstruction at T1 showed significant improvements in all variables at T2, but no correlations between "objective" and "subjective" variables. However, minor change in an initial narrow anterior part of the nose (MCA I) in these patients showed significant correlation with an improved subjective perception of nasal patency at T2 ($P<0.001$, $r = 0.68$). Moreover, a small decrease in the expiratory NAR correlated ($P<0.05$, $r = -0.42$) well with an improved subjective perception of nasal patency at T2. These findings were somewhat unexpected, as only minor changes in the most anterior parts of the nose correlated with subjective improvements. The nostrils and nasal vestibule are regarded as the areas responsible for sensing airflow and stuffiness (Aldren and Tolley 1991, Clarke and Jones 1994, Eccles *et al.* 1988). It is likely that factors other than the amount of widening of the nasal passage or the degree of decrease in NAR are responsible for the improvements. Guenthner *et al.* (1984) associated changes in the shape of the external nares to an improved subjective experience of nasal patency. More studies of this topic are warranted.

Eighteen months after the surgical expansion, no changes were found from pre-treatment values for subjective nasal obstruction, minimum cross-sectional areas (MCA I MCA II) or nasal airway resistance (NAR Insp / Exp) and there were no correlations. These results are in accordance with previous studies (Mitsuda *et al.* 2010, Wriedt *et al.* 2001, Zambon *et al.* 2012). Nasal obstruction is probably more closely related to other rhinologic factors than a narrow maxilla, such as inferior turbinate hypertrophy, nasal septum deviations and inflammatation (Goode 1978, Jessen and Malm 1997, Dahlstrom *et al.* 2006).

However, 23 subjects with sensations of nasal obstruction at treatment start reported a lasting significant subjective improvement. This subjective improvement could not be correlated with either MCA or NAR. It seems that other factors such as the shape of the nares are crucial to the subjective sensation of nasal patency (Turvey *et al.* 1984, Petruson and Theman 1992). The clinical appearance of the external nares after SARME is familiar (Figure 5, page 18). The change from narrow slits to more ovoid forms is often obvious and must be considered closely in this context. In what way and to what extent SARME influences the shape of the nose and the nares is discussed later in this doctoral project.

Skeletal changes

There were significant skeletal treatment effects after SARME and orthodontic treatment in all landmarks measured, except for the right anterior nasal spine. The skeletal effects were not uniform and differed between posterior-, lateral-, anterior-, superior- and inferior areas (Figure 23). In previous studies, quite contradictory results have been reported (Bretos *et al.* 2007, Byloff and Mossaz 2004, Chung *et al.* 2001, Gilon *et al.* 2000, Loddi *et al.* 2008, Nada *et al.* 2012). The discrepancies in results can be related to various factors such as surgical technique, the type of expansion device, the area of measurement, the time-points for measurements and methodological weaknesses in the studies.

To our knowledge, this is the first study investigating lateral skeletal displacements in the entire maxilla, not only in the sagittal plane but also in a coronal plane. These changes and displacements can now be measured using 3D models superimposed on the anterior cranial base. The automated voxel-based image registration method used in this study allows precise, accurate measurements in all areas of the maxilla.

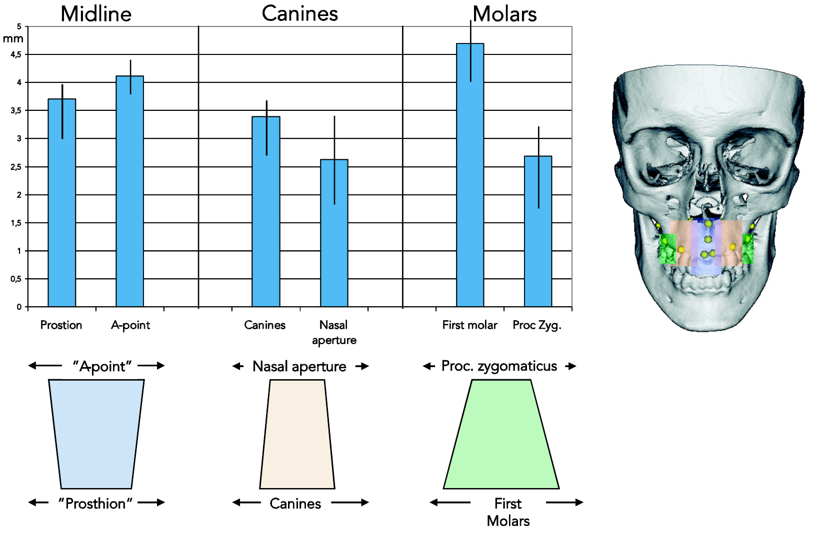


Figure 23. *Mean transverse change following SARME and orthodontic treatment at the maxillary outer skeletal surface in the coronal and sagittal planes. Midline (blue), canine area (orange) and molar area (green).*

In general, sagittal skeletal displacement was greater posteriorly than anteriorly and this finding is in accordance with similar studies on a tooth-borne expansion device (Anttila *et al.* 2004, Byloff and Mossaz 2004, Koudstaal *et al.* 2009b, Nada *et al.* 2012). Berger *et al* (1998) and Byloff and Mossaz (2004) concluded that the skeletal effects after SARME ranged from 24 to 52 per cent of the total expansion, which is consistent with our findings. Inconsistent results have been reported for the sagittal plane (Landes *et al.* 2009, Goldenberg *et al.* 2007, Laudemann *et al.* 2010, Zemann *et al.* 2009). These differences are most likely related to the use of a bone-borne expansion device, which exerts a greater effect anteriorly.

Lateral displacements following SARME and orthodontic treatment at the maxillary outer skeletal surface in a coronal plane have not previously been evaluated; thus there are no comparable reference data available. In general, more skeletal displacements were found inferiorly than superiorly and more posteriorly than anteriorly, with the exception of the midline. The superior landmarks in the maxilla were located at the zygomatic processes, and at the most lateral and inferior point of the nasal aperture and at the anterior nasal spine. All these landmarks are validated and reliable for measurements in the maxilla (Moore-Jansen 1994, Swennen, Schutyser, Hausamen 2006b). It would however, have been desirable to have been able to use another landmark than the lateral nasal aperture to correspond with the landmark at the canine, as there is a sagittal discrepancy between these two landmarks.

Expansion at the midline was greater than at the canines and significantly more pronounced superiorly than inferiorly. An explanation for this divergence is the vertical osteotomy procedure anteriorly. This procedure might have varied, despite a strict treatment protocol, and affected the results in this area. Another plausible explanation is the difficulty in measuring lateral changes anteriorly i.e. the healing process in the midline made it difficult to identify reliable landmarks for TPS analyses. Thus, in 11 cases TSP-CPM were used to define lateral skeletal displacements in color maps (Figure 20, page 40).

A significant and notable finding was the lateral outward tilting of the posterior bony segment. Byloff and Mossaz (2004) considered the "molar tipping" to be an undesirable dental side effect. In our study, the marked posterior tipping at the molars seems to be related primarily to tipping of the whole posterior bony segment and to a lesser extent a "dental side effect". Under these conditions, it is questionable whether skeletal overexpansion as recommended by Chung and Goldman (2003) would help to reduce the molar tipping.

Pterygoid disjunction has been proposed to reduce posterior resistance. However, this is a hazardous procedure, associated with complications. In this study, mobilization of the maxillary halves was ensured by chiselling in the anterior midline to avoid the risk of injury to the pterygoid plexus. Our earlier findings (Paper I), had shown that pterygoid disjunction did not eliminate posterior tipping. More extensive surgery, including pterygoid separation, might have diminished the risks for posterior tipping, but at the expense of increased risks of complications and limited accessibility to treatment.

There was no significant difference between the changes in the corresponding landmarks on left and right side, although there was a marked distribution. This may indicate less uniform expansion.

Furthermore, it would be beneficial to be able to correlate the various intramaxillary changes, in order to predict the effects in different areas. Statistical analysis failed to disclose any such correlations, apart from the posterior outward tilting ($P<0.001$; $r = 0.732$).

The time-points for measurements are crucial to understanding the treatment outcome of SARME. The procedure has been criticised as unstable and unpredictable (Proffit *et al.* 1996). The CT-registrations in this study were made before treatment start and at the end of active treatment. This means that findings in the present study reflect the combined results of surgical and orthodontic interventions. The skeletal effects would certainly have been different immediately post-operatively. Measurements made at that time-point, would have yielded highly questionable results with respect to both the procedure and the stability of the outcome.

The main purpose of combining SARME with orthodontics is to provide proper conditions for establishing a correct maxillomandibular transverse dental relationship, without dental tipping, at the end of treatment. Whether there is a decrease or "relapse" after the initial surgical procedure is of minor interest

Shape of the nose

Changes to the nose following SARME have been a problem for many clinicians. While in some cases this change can be regarded as an unwanted side effect, in other cases it may be an improvement in facial aesthetics. After SARME and orthodontic treatment, there is a true three-dimensional change in the nose: anteriorly, laterally and inferiorly (Figure 17, page 39). The most pronounced changes were found at the most lateral alar base and particularly in lateral and anterior directions. These changes are somewhat greater than in previous reports (Berger *et al.* 1999, Ramieri *et al.* 2008). A logical and rational explanation is the occurrence of corresponding displacement in soft and hard tissue (Bretos *et al.* 2007, Chung *et al.* 2001). There are conflicting reports about the displacement of the underlying skeletal structure following SARME (Lagravere *et al.* 2006a). Using CBCT scans and 3D photographs Nada *et al* (2013) investigated changes to the nose after SARME and 2 years´ treatment with a bone-borne distractor. They concluded that soft tissue changes following SARME included posterior repositioning of the upper lip and an increased projection of the cheek area. To resolve contradictory findings, further studies are warranted, applying appropriate 3D techniques and modern surgery planning systems (Swennen *et al* 2009).

The findings in the present study indicate that soft tissue changes are more likely to be multifactorial, involving surgical technique, the amount of soft tissue and facial type (Ramieri *et al.* 2006, Ramieri *et al.* 2008). It is nevertheless important that the clinician is aware of the soft tissue changes associated with SARME. The ideal would be to be able to predict and correlate these changes, as a poor aesthetic treatment outcome must be avoided. The present study did not reveal any such correlations, neither between initial and final nose widths, nor between initial and final nostril widths. However, this is a research field in progress.

Many of the 3D displacements in the nose were small and perhaps not clinically relevant, but the overall change is still interesting. The whole soft nasomaxillary complex moves outward, forward and downward. In candidates for SARME, it would be logical to expect most changes to occur in the transverse direction. However, the single most significant changes were found to be in an anterior direction at the alar base, which was unexpected and notable.

The lateral displacements decreased gradually anteriorly and inferiorly at the nose. The difference in lateral displacement at lateral landmarks played an essential role in the perception of a more rounded shape and increased size of the nose. In this situation, alar base suturing might be considered, to reduce the widening of the nose (Westermark *et al.* 1991). The effect of this procedure will however, be the opposite and should be avoided, as the widening of the nose is mostly related to widening at the alar bases (Landmarks 12 and 13) and not to the applied alar base sutures at the facial insertion of the nose (Landmarks 4 and 5).

The significant changes to the nostril shape, from narrow slits to more ovoid form, is notable and should be analysed in the context of previous findings in this doctoral project (Paper II). It is of interest to note that narrow nostrils are associated with nasal obstruction (Hinton *et al.* 1987) and widening is associated with a subjective perception of improved nasal function (Magnusson *et al.* 2011). Consequently, patients with narrow and constrained nostrils benefit from the soft tissue changes.

Conclusions

This series of investigations has shown that

- In the long-term, SARME and orthodontic treatment is a reliable and safe method for correcting and normalizing skeletal maxillary transverse deficiencies in non-growing individuals. Relapse is time related and is most pronounced during the first 3 years after treatment. Retention should be considered for this period.

- In the short-term, SARME and orthodontic treatment has a favourable effect on nasal respiration but these effects do not persist long-term. No correlation was found between objective and subjective findings. Patients with pre-treatment nasal obstruction, however, reported a lasting sensation of improved nasal function at the final registration, eighteen months after surgically assisted rapid maxillary expansion.

- SARME and orthodontic treatment had a significant but non-uniform skeletal treatment effect. There was significantly greater transverse expansion posteriorly than anteriorly. The expansion was parallel anteriorly but not posteriorly. The lateral tipping of the posterior segment was significant, despite careful surgical separation. No correlation was found between tipping and the patient's age.

- SARME and orthodontic treatment significantly affects all dimensions of the external features of the nose. The most obvious changes are at the most lateral alar-bases. The difference in lateral displacement profoundly influences the perception of a more rounded nose. There were no predictive correlations between the changes. Patients with narrow and constrained nostrils can benefit from these changes with respect to the subjective experience of nasal obstruction. It is questionable whether an alar-cinch suture will prevent widening at the alar-base.

- The 3D superimposition applied in this study is a reliable method, circumventing projection and measurement errors.

Tomorrow

Evaluation and assurance of the quality of health care is a prerequisite for appropriate, correct treatment. This must be a continuous and ongoing process, in order to increase patient safety and to achieve the expected results. The introduction of a new treatment approach raises curiosity and interest among clinicians. However, not all new methods to be introduced have an adequately comprehensive scientific base; when treatment outcomes vary and the expected result is not achieved, the method is questioned. In this context, the questions must be addressed and further research undertaken before the method is accepted or rejected.

SARME is not a new modality and has been a part of orthodontic therapy for many years. Although the advantages of the method are acknowledged, there is lack of consensus with respect to skeletal efficiency, effect on respiration and stability. These inconsistencies have made clinicians reluctant to accept SARME into their treatment arsenal.

The comparative advantages of SARME over other treatment modalities for correcting true skeletal MTD are however, indisputable and efforts must be made to implement SARME more widely in everyday practice.

The focus in continuing research must now be directed towards the mechanisms underlying SARME and orthodontic treatment, which affect the soft tissues and respiration. With the major advances in computerized tomography and imaging techniques in recent years, it is now possible to achieve very precise and accurate data about all tissues. The importance of predicting skeletal as well as soft tissue alterations must be emphasised. The most recent imaging techniques allow simulation of soft tissue changes, which will enable very precise and accurate soft tissue prediction. Moreover, the indications in the present study that the shape of the nostril plays an important role in the perception of nasal patency warrants further investigation.

The latest imaging techniques applied in the present doctoral project will be used in coming projects on orthognathic surgery and apnea and predictions in orthognathic treatment planning.

Summary in Swedish

Avvikelser i käkarnas storlek och relation har kopplats till en försämrad oral hälsa. Ett flertal studier har visat att en smal och avvikande överkäke kan orsaka nedsatt tugg funktion, näsandningssvårigheter, smärtproblematik och psykosociala problem.

På unga, växande individer, behandlas dessa transversella bettavvikelser med en tandställning som vidgar överkäken ortopediskt.

På vuxna individer krävs ett kirurgiskt ingrepp för att vidga överkäken. Det kirurgiska ingreppets omfattning kan variera och det finns flera metoder beskrivna. Surgically assisted rapid maxillary expansion (SARME) är en metod. Alltsedan metoden introducerades har den dock varit ifrågasatt. Oenigheten har främst rört frågor såsom varaktigheten av behandlingen, effekten på skelett och mjukvävnad och dess inverkan på näsandningen. Tidigare studier har begränsats av de rådande undersökningsmetoderna och av små, retrospektiva material med kort uppföljningstid.

Syftet med denna avhandling har varit att, med hjälp av modern rhinologisk utrustning och kunskap, mäta objektiva och subjektiva effekter på näsandningsfunktionen efter behandling med SARME samt att, med hjälp av en avancerad CT- och bildbehandlingsteknik, tredimensionellt mäta förändringar i mjukvävnad och skelett.

31 patienter har också följts upp (medel 6.4 år efter avslutad behandling) för att bedöma långtidsstabiliteten.

Resultaten i avhandlingen visar att SARME är en stabil och tillförlitlig metod som normaliserar och återskapar god bettfunktion. Avgörande för stabiliteten är dock att en enklare natt tandställning användes under de tre första åren efter avslutad behandling.

Det fanns en signifikant förbättrad näsandningsfunktion, både objektivt och subjektivt direkt efter behandlingen. Denna förbättring var dock ej bestående. Emellertid upplevde patienter med nästäppa innan behandlingsstart en bestående subjektiv förbättring. En möjlig förklaring till den subjektiva förbättringen kan vara ett förändrat utseende på näsöppningarna.

De skelettala transversella förändringarna i överkäken efter SARME var signifikanta men varierade stort. Den största skelettala effekten fanns i den bakre och nedre delen av överkäken. Tippning av det bakre segmentet kan relateras till det ökade skelettala motståndet i området.

Behandlingen påverkar näsans utseende i alla dimensioner. Den mest uppenbara förändringen finns vid de laterala näsvingarna. Skillnaderna i näsans förändringar gör att näsan uppfattas som mer rund.

Den använda CT- och bildbehandlingstekniken reducerar projektions- och mätfel och är en exakt och reproducerbar metod för att mäta och jämföra tredimensionella förändringar i skelett och mjukvävnad.

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