Opponent

Krister Bjerklin, Associate Professor, Faculty of Odontology, Malmö University, Malmö, Sweden

Examining Committee

Heidrun Kjellberg, Associate Professor, Specialist Dental Care Centre/Orthodontics, Lund, Sweden

Gunilla Klingberg, Associate Professor, Mun-H-Center, Public Dental Service, Västra Götalandsregionen, Göteborg, Sweden

Rune Lindsten, Associate Professor, Institute for Postgraduate Dental Education, Jönköping, Sweden

Main supervisor

Jan Huggare, Professor, Karolinska Institutet, Department of Dental Medicine, Division of Orthodontics and Pediatric dentistry, Huddinge, Sweden

Co-supervisors

Bertil Lennartsson, Associate Professor, Postgraduate Dental Education Center, Public Dental Service, Örebro County Council, Örebro, Sweden

Kristina Arnrup, PhD, Postgraduate Dental Education Center, Public Dental Service, Örebro County Council, Örebro, Sweden

CONTENTS

SUMMARY

Interception of crowding, by extraction of deciduous and permanent teeth, to eliminate or at least facilitate orthodontic treatment has a long tradition. This treatment procedure, know as "guided eruption" or "serial extraction" was re-introduced by Robert Hotz and Birger Kjellgren in 1947-48. The sequential extraction procedure begins with the removal of the deciduous canines in the early mixed dentition and additional extractions of deciduous first molars and permanent bicuspids are considered after careful monitoring of dental arch development.

Few studies have evaluated the entire treatment procedure, especially the first phase including extraction of the deciduous canines. Dentists have therefore had to rely mainly on clinical experience and consequently this established procedure has become controversial.

The general aim of this work has been to evaluate the effects on incisor alignment and dental arch dimensions after interceptive deciduous canine extractions. Furthermore, patient's reactions to these extractions regarding pain, discomfort and dental fear are described.

Paper I examined the reproducibility of and agreement between a conventional (using plaster casts) and a 3D virtual technique for recordings used in orthodontic study cast analysis.

Paper II and III were randomized controlled trials involving 73 and 71 children respectively, stratified for gender. Paper II evaluated the early effects on mandibular incisor irregularity and rotation together with changes in dental arch dimensions, overjet and overbite. Paper III evaluated the long-term effects on mandibular and maxillary incisor irregularity and rotation together with changes in dental arch dimensions, overjet and overbite. Paper IV explored procedural and postoperative pain and discomfort among child dental patients undergoing orthodontic extractions of four deciduous canines. Changes in dental fear ratings from pre- to post-treatment were also investigated.

The conclusions based on the results from the studies are that:

The conventional method showed better reproducibility for angular variables, but no clear pattern was found for differences between the two methods in reproducibility of

linear variables. Reproducibility was considered clinically acceptable for both methods, although systematic errors indicated that the two methods should not be used interchangeably.

Extraction of deciduous canines can not be expected to improve maxillary or mandibular incisor alignment in a significant way and should therefore not be recommended for the relieve of incisor crowding. The congruent results between professional visual assessment and conventional measurements concerning alignment strengthen the validity of the treatment outcome results. No major effect was seen on arch dimensions, overjet or overbite. The extraction of four deciduous canines was not found to trigger or increase dental fear and should not cause major post-operative inconvenience. A small number of individuals though had very high ratings of pain and discomfort at several occasions, revealing a need for updating clinical routines for pain management.

PREFACE

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

I. Orthodontic study cast analysis – reproducibility of recordings and agreement between conventional and 3D virtual measurements.
    Sjögren AP, Lindgren JE, Huggare JA
    J Digit Imaging. 2010;23:482-492

II. Mandibular incisor alignment and dental arch changes 1 year after serial extraction of deciduous canines.
    Sjögren A, Arnrup K, Lennartsson B, Huggare J
    Eur J Orthod. 2011;doi:10.1093/ejo/cjr028

III. Incisor alignment and dental arch changes 2.5 years after serial extraction of deciduous canines.
    Sjögren A, Arnrup K, Lennartsson B, Huggare J
    Manuscript

IV. Pain and fear in connection to orthodontic extractions of deciduous canines.
    Sjögren A, Arnrup K, Jensen C, Knutsson I, Huggare J
    Int J Paediatr Dent. 2010;20:193-200

DEFINITIONS AND ABBREVIATIONS

Agreement	Analysis of coherence between two methods (if one can replace the other).
Angular variables	Attribute measured in degrees between to lines.
ANOVA	Analysis of Variance
Arch circumference	The distance between the buccal centre of the first permanent molars around the dental arch measured at the gingival-enamel junction.
Arch length	The perpendicular distance from the contact points of the central incisors and a line drawn between the mesiolingual cusptips of the first molars in the mandible and between the mesio-palatal cusptips of the first molars in the maxilla, respectively.
Arch width	The distance between the mesiolingual cusp tips of the first permanent molars in the mandible, and between the mesio-palatal cusp tips of the first permanent molars in the maxilla, respectively.
Baseline	At the time in dental stage I, when the first impressions were taken.
Contact point (cp)	Anatomical contact point of the tooth.
Chronbach's alfa	Measures internal consistency, i.e. how well the single items in a survey answers the question of interest (range 0-1).
Conventional measurements	Linear measurement made on plaster casts with digital calliper and angular measurement with the Facad® program from digital photos.
CFSS-DS	Children's Fear Survey Schedule- Dental Subscale.
Endpoint	Dental stage III, when at least one first upper premolar had penetrated the gingival surface, but both not yet reached occlusion.
Dental anxiety	Fear related to more general and anticipatory state of apprehension. In this thesis described as dental fear.
Dental fear	Fear related to a specific threatening dental situation.

Dental stage	Dental development stage according to Björk et al. (1964) based on eruption of primary and permanent teeth.
Discomfort	Mental or bodily distress, inconvenience, something that disturbs or deprives of ease.
Guided eruption	Interceptive extraction procedure in order to eliminate or at least facilitate future orthodontic treatment of crowding.
Incisor retrusion	Bodily posterior migration of the incisors crown and root.
Incisor retroclination	Lingual tipping of the incisor crown.
Interceptive extractions	Early extractions aiming at constraining a negative dental development.
Invasive treatment	Injection, slicing, drilling and extraction.
Irregularity index	After Little's irregularity index [1]. An expression of the amount of incisor crowding based on a summation of the total magnitude of tooth displacement at each contact point in the anterior region of the dental arch. In this thesis; sum of displacement at the three cp's from the lateral incisor to lateral incisor.
Leeway space	Space occupied by the primary canine and first and second primary molars, which exceeds that occupied by the canine and premolar teeth of the secondary dentition. Approximately 1.9 mm in the maxilla and 3.4 in the mandible.
Linear variables	Attribute measured in mm between two points or summation of sections.
Learned response	A way that a person reacts to a situation. The response may be learned through intentional teaching, or may be learned through interaction with the environment.
Occlusal plane (mandible)	Defined by points at the anatomical mesial contact point of the lower left incisor and the mesiolingual cusptips of the first molars.
Occlusal plane (maxilla)	Defined by points at the anatomical mesial contact point of the upper right incisor and the mesiopalatal cusptips of the first molars.
Overbite	Average value of the vertical distance between the incisal edges of incisors 11 and 41 and 21 and 31, respectively.

Overjet	Average value of the horizontal distance between incisors 11 and 41 and 21 and 31, respectively, measured from the incisal edge of the upper incisor to the buccal surfaces to the lower incisor.
Pain	An unpleasant sensory and/or emotional experience associated with actual or potential tissue damage or described in terms of such damage.
Procedural pain	Pain experienced during treatment.
Parental assessment	Evaluation of guardian/parent.
Professional evaluation	Assessment of rotation, irregularity and general alignment by an orthodontist.
Random error	Inherently unpredictable fluctuations in the readings of a measurement apparatus or in the experimenter's interpretation of the instrumental reading.
RCT	Randomized Controlled Trial.
Recovery time	Time from treatment completion to first intake (drinking or eating).
ROC- analysis	Receiver Operating Characteristic analysis (used for determining cut offs for detection).
Rotation	Angle between the incisal edge of the incisor and a perpendicular to a line between the mesiolingual/palatal cusp tips of the first permanent molars, assessed from an occlusal view.
Serial extraction	See guided eruption.
Randomized stratified for gender	The participants in the extraction and control group were appointed randomly and so that an equal number of boys and girls should be present in the two groups.
Systematic error	Error, which is typically constant or proportional to the true value. Could be caused by imperfect calibration of instruments or methods of observations.
Virtual 3D model	Laser scanned plaster model presented as a virtual digital model on a monitor with the aid of a soft ware program.

INTRODUCTION

HISTORIC BACKGROUND

Interceptive extractions, including deciduous and permanent teeth, with the aim to correct dental crowding has already been described in the 18th century, when Robert Bunon made references to early extractions in his "Essay on Diseases of the Teeth" (cited by Mayne[2]). Nearly hundred years later 1851, Linderer described means to provide space for lateral incisors by proximal enamel reduction or extraction of deciduous canines and subsequently removal of first premolars (cited by Mayne [2]).

These ideas were much disregarded by the orthodontic community until 1947-48 when Robert Hotz from Switzerland and Birger Kjellgren from Sweden presented similar treatment protocols for interceptive extractions in order to eliminate or at least facilitate orthodontic treatment of crowding. The procedures were presented as "Active supervision of the eruption of teeth by extraction" [3] and "Serial extraction as a corrective procedure in dental orthopedic therapy" [4] and comprised of planned sequential deciduous and permanent tooth extractions, starting with the removal of the deciduous canines in the early mixed dentition [3-4]. In this treatment protocol tooth eruption and dental arch development should be carefully monitored during the mixed dentition and a cautious approach to decisions regarding additional extractions of first primary molars and the first bicuspids was recommended [3-4].

Much in the same spirit prominent American orthodontists, such as Dewel, Nance and Tweed, advocated extractions for crowded cases in terms of "serial extraction", "progressive extraction" and "pre-orthodontic guidance" during the 1940's and forth [5-7].

Serial extraction/guided eruption has become an established but controversial treatment method over the years [8-10] much depending on sparse documentation of favorable treatment outcome. Despite this, a substantial amount of primary tooth extractions have been carried out over the years. Bradbury found that the greatest proportion of primary teeth prescribed for extractions within the British Orthodontic Hospital Service were canines (40%) with 96 per cent free from caries or restoration [11] and Kau et al. (2004) calculated a yearly cost of over £250,000 for primary canine extractions in the British National Health Service system [9].

STATE OF THE ART

Considerations and suggestions concerning interceptive extraction procedures and other means of producing or maintaining space for incisors, such as discing and use of orthodontic appliances, have been extensively described in the literature [3-8, 12-25].

However, a limited number of studies have evaluated treatment outcome for the entire or later part of the serial extraction procedure [27-33] and even fewer studies have focused on the first part of serial extraction, the removal of the deciduous canines [9, 34].

Although positive results have been reported for the entire treatment sequence including bicuspid extractions [29, 31], prediction of spontaneous incisor correction is considered uncertain [9, 23, 26, 28, 35-36]. Hagberg have demonstrated that mandibular intercanine distance of less than 26 mm among 7-, 9- and 10-year old children were associated with mandibular incisor crowding [37]. Favourable growth in the alveolar process and palatal suture along with lee-way space may, however, eliminate quite substantial crowding, with an acceptable anterior and posterior occlusion as a result [23, 38].

Besides the expected improvement in alignment, other benefits of interceptive deciduous canine extractions have been pointed out. Incisors, blocked-out, in a buccal position are reported to constitute a risk for gingival recession [39-41] and this risk could be reduced along with unwanted incisal wear that might occur in a crowded incisor segment.

Drawbacks connected to extractions of primary canines are reported as decrease in arch length, due to mesial movement of the first molars [9], increased mandibular incisor retrusion [33-34] and retroclination [33]. Space conditions for the permanent canines are compromised due to mesial molar migration according to Kau et al. [9], although questioned by Sayin and Türkkahraman [34].

Clinicians therefore have to rely much on anecdotal information and their own clinical experience in prediction and evaluation of treatment outcome. Thus it is understandable that the orthodontic profession has been divided into those who are in favour and those who are against removal of the deciduous canines in order to promote spontaneous incisor alignment.

In clinical practice the dentist has to evaluate not only the anticipated orthodontic treatment outcome, but also to predict if the child can cope with extraction of four deciduous

canines without becoming inducted with a negative attitude to dental treatment. An important part in evaluation of treatment success should therefore be to include patient experiences from these treatment procedures.

Patient perspective on invasive treatment

Since most children, at the age when the deciduous canines are extracted, presumably have limited previous dental experience [42-43], this invasive treatment procedure may become their first encounter with dental care. Tooth extractions may cause pain and/or discomfort and thereby constitute a risk of inducing dental fear [44-51].

Pain has been defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage [52].

Due to its complex aetiology of past experiences, learned responses, and expectations besides physiological responses measurement and interpretation of pain experiences are difficult [53-55].

Minor medical procedures can produce significant pain and distress for some children, as pain response is unique to each child and each procedural situation and depends on several determinants. Inadequate prevention and treatment of children's pain and distress responses may have long-term negative effects on the child's future pain response [55]. Painful early invasive dental treatment has also been reported to have a negative effect on pain perception during subsequent treatment sessions [56] and later in life [57]. Despite this, few studies have been made on pain in connection to extractions of deciduous teeth in an every day clinical situation [58-61]. Descriptions of procedural pain are more commonly presented in relation to other types of invasive treatment procedures such as pediatric medical care, restorative dentistry or dental treatment in connection to sedation [53, 56, 62-63].

A recent study on adolescent patient recovery after orthodontic premolar extractions reported that the number of extractions performed at the same appointment had no effect on post-treatment recovery. A dramatic decline was seen in severe pain (17% to 3%) and analgesic consumption (70% to 13%) from day one to day two postoperatively [64].

Still, discomfort experienced in association with tooth extraction is not only influenced by pain [46-47, 63], but also by dental fear/anxiety and feelings of lack of control [44, 47, 63, 65-68]. Sensation of numbness and unfamiliar or unpleasant taste can also contribute to a feel-

ing of discomfort [63, 69]. Assessment of disturbances in everyday routines, such as recovery time for drinking and eating should be a valuable indicator of post-treatment discomfort in combination with analysis of analgesic consumption [64].

Insufficient use of medical pain alleviation (analgesics, local anaesthesia, and sedatives) seems to be common in dental treatment of children [54, 58-60, 70]. Analgesics were administered to only half of those reporting post-extraction pain in studies among North American children (aged 2–10 years) [59-60]. This indicates that dentists believe that young children report pain with uncertainty which also has been demonstrated for Swedish and Danish dentists [70-71].

The importance of minimizing pain experiences in early years not only to avoid discomfort, but also to prevent the risk of triggering dental fear, is often emphasized [44-50], because dental fear constitutes a risk for future avoidance of dental treatment and poorer oral health [49, 72-78].

Although, associations between tooth extraction and dental fear have been found in Finnish [65] and Dutch [66, 79] children, a lot of patients with no dental fear have had negative dental experiences, and some with considerable fear fail to recall any traumatic incidents [44, 51]. Perceptions regarding loss of control, unpredictability and feelings of dangerousness, and disgustingness might be equally or even more important predictors of dental fear than negative dental experiences [44, 58, 80-81]. This clearly demonstrates the complexity in exploring the origin of dental fear.

Little is known about children's experiences of pain and discomfort in connection to interceptive extractions of deciduous canines. It is reasonable to presume that these early extractions should be performed with great efforts to minimize pain and discomfort. It was therefore our ambition to gain more knowledge and to be able to weigh assumed benefits in alignment against possible negative reports on pain and discomfort.

TREATMENT OUTCOME AND MEASUREMENT RELIABILITY

In evaluation of treatment outcome, study design plays an essential role [82-83]. Randomized controlled trials are considered as the most appropriate for comparative studies in that it minimises allocation bias, balancing both known and unknown prognostic factors, in the assignment of treatments [84-86]. In exploring areas where little previous research have been

made a descriptive approach is suitable and might help to generate new hypotheses [84]. Among the few studies covering the first step in serial extraction; the removal of the deciduous canines [9, 28, 30, 32-34], only one is a randomized controlled trial (RCT) [9]. Substantial differences in follow up time together with variations in measurement technique also hamper comparison of results regarding treatment outcome. The common praxis of including both primary and permanent canines in longitudinal evaluation of incisor alignment constitutes a risk of involving a confounding factor.

Crowding is quantified in two main ways with a variety of different techniques: Measurement of contact point discrepancies [1, 87-92] and arch length tooth size discrepancy [6, 87, 89-90, 93-97].

Little's irregularity index [1] is probably the most common method for expressing the amount of incisor crowding. It is based on a summation of the magnitude of tooth displacement at each contact point in the anterior region of the dental arch. This procedure can thereby conceal differences between lateral and central incisors [98] and might also underestimate rotation when mandibular incisor alignment is evaluated [99]. On the other hand, this index can be assumed to generate unusually high scores due to severe labio-lingual displacement of a single tooth [99-100].

Measurement accuracy is crucial for correct evaluation of orthodontic treatment outcome. Improvements in this field should be possible by the use of computer-assisted techniques on virtual 3-dimensional models.

A majority of studies performed with the aid of digitized virtual models [101-114] investigates linear variables and recent studies on reproducibility and reliability have shown promising results with equal or better accuracy compared to more traditional measurements techniques on plaster casts [103, 110, 114-116].

Despite the fact that relief of tooth rotation is a vital part of alignment and assumed to play an important role in post-retention stability [98, 117], studies on angular measurements, using virtual models, have been performed mainly for evaluation of accuracy regarding implants [118-119], but so far not for regular orthodontic treatment planning or evaluation of treatment outcome.

Regardless of all efforts to produce new techniques there still is a need for validation in assessment of crowding [96, 100]. Treatment outcome measures, such as Little's irregularity index, are seldom validated against a clinical evaluation. A mathematically constructed

cut off, such as a 50 per cent reduction in initial crowding, has so far been a rare example for appraisal of success [9].

Professional assessments associated to cut off's for clinically detectable changes would surely improve validation and interpretation of results produced with contemporary techniques.

Although a certain amount of inaccuracy has been demonstrated when producing plaster models [115, 120], greater errors are probably caused during assessment of intermaxillary relations [121] and might seriously affect evaluation of overbite and overjet.

One of the most commonly used questionnaires for assessing dental fear among children is the Dental Subscale of the Children's Fear Survey Schedule (CFSS-DS) [122]. It has been found to measure dental fear more precisely and cover more aspects of the dental situation compared to other questionnaires and normative values are available [123]. Test-retest reliability is considered high [123] and has been found to have a moderate to good correlation with other psychometric measures [68] indicating reasonable validity. Recent research has suggested age and gender related cut-off's for dental fear in favor of the earlier established level of >38 [127].

AIMS

GENERAL AIM

The general aim of this thesis was to evaluate the effect on incisor alignment and dental arch dimensions caused by interceptive deciduous canine extractions. Furthermore, patient reactions to these extractions regarding pain, discomfort and dental fear are described.

SPECIFIC AIMS

The specific aims of the individual papers were as follows:

Paper I
- To examine the reproducibility of and agreement between a conventional and a 3D virtual technique for recordings used in orthodontic study cast analysis.

Paper II
- To evaluate the early effects on mandibular incisor irregularity and rotation together with changes in dental arch dimensions of the extraction of the deciduous canines using conventional measurements methods and a professional evaluation of alignment.
- To establish cut off scores for clinically detectable changes in rotation and irregularity.

Paper III
- To evaluate the long-term effects on mandibular and maxillary incisor irregularity and rotation together with changes in dental arch dimensions of the extraction of the deciduous canines using conventional measurements methods and a professional evaluation of alignment.

Paper IV
- To describe reported procedural and postoperative pain and discomfort among child dental patients undergoing orthodontic extractions of four deciduous canines.
- To explore changes in dental fear from pre- to post-treatment.

HYPOTHESES

The null hypotheses were:

Paper I
Reliability for recordings of orthodontic variables will show no significant differences between measurements on plaster casts and on virtual 3D models.

Paper II and III
Incisor alignment and dental arch dimensions are not significantly affected by extraction of the deciduous canines on a short or a long time basis.

Paper IV
Dental fear levels do not change due to extractions of deciduous canines.

MATERIALS AND METHODS

SUBJECTS

The study participants were recruited from children attending 250 orthodontic consultation appointments in Örebro County, Sweden from November 2005 to June 2007. To meet the inclusion criteria, children had to be in the early mixed dentition stage (dental stage DS 1 according to Björk et al.) [124] with a lower intercanine distance of < 26 mm and bimaxillary moderate to severe anterior space deficit representing the amount of half the width of the maxillary central incisor and 2/3 of mandibular central incisor width, respectively. Exclusion criteria were diseases affecting somatic growth, neuro-psychiatric disabilities, and/or learning disabilities. Children diagnosed with agenesis and/or having previous tooth extractions and/or earlier or ongoing orthodontic treatment were excluded. Children or parents in need of an interpreter during the treatment dialogue were also excluded.

The sample size was based on calculations of mean values and standard deviations (SDs) for displacement of contact points from the only study with a control group [9] and indicated that a sample of 70 subjects was needed using a 5% significance level with a power of 90%. Drop out rate was estimated to 17% due to the long follow-up period (2.5 years), thus an initial total number of 82 subjects would be sufficient.

One hundred and ten children and their accompanying parents were invited to participate in a randomized controlled trial investigating the effects of serial extraction on incisor alignment. Sixteen children /parents declined participation without giving a specific reason, 11 requested either extraction or non-extraction treatment and were therefore not included.

Eighty-three children were randomized stratified for gender into one extraction and one control group. Of the 40 children randomized to the extraction group, 4 girls and 2 boys were excluded after being randomized because of recordings of increased mobility of the deciduous canines. One girl /parent changed their mind about participating and another girl was referred to paediatric specialist care for extractions of the first molar together with the deciduous canines, leaving 32 children in the extraction group.

Fortythree children were randomized to the control group, where one boy and one girl were excluded due to lack of cooperation and change in preference to extraction treat-

ment. Thus, in paper II and IV, the extraction group consisted of 14 boys and 18 girls with mean ages of 8.8 and 8.5 years, respectively, and the control group of 16 boys and 25 girls had mean ages of 8.8 and 8.4 years, respectively, at baseline. Two girls in the control group were not able to attend in the endpoint follow up as one moved from the area and the other one started orthodontic treatment (Fig.1).

In paper I the plaster models from the 20 first subjects participating in the study were used for analysis.
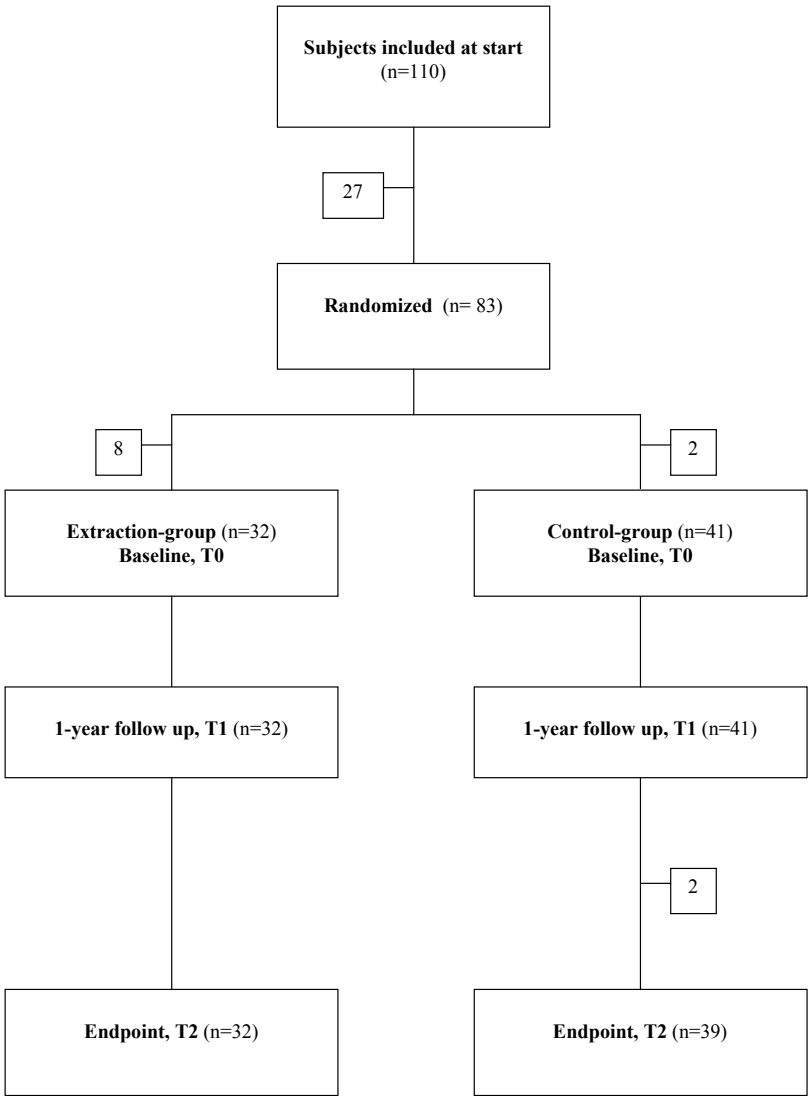
Figure 1. Flow chart

METHODS

Paper I

To determine measurement accuracy for variables representing incisor alignment and dental arch dimensions, two different methods were tested for reproducibility and agreement between the two. Twenty sets of plaster models were consecutively sampled from subjects in the early mixed dentitions.

The patients' general practitioners took alginate impressions of the dental arches and all plaster models were made by the same orthodontic dental laboratory using white BESV gypsum plaster to make the models.

The plaster models were sent to ORTOLAB®, Czestochowa, Poland for scanning and conversion into 3D virtual models in the O3DM® basic version 1.4.00 software program. The file format of the O3DM®, Aarhus C, Denmark software program was proprietary and closed.

Variables of interest were the rotation, angulation and irregularity of maxillary and mandibular incisors, and arch circumference, arch width and the overjet and overbite. Two orthodontists (AS, JL) carried out recordings of variables using both a conventional and a virtual digital technique (O3DM). Both examiners underwent an eight-hour introduction and calibration of the measuring techniques. After that the recording procedure was carried out with at least 2 weeks between measurement sessions.

Instrumentation

Linear variables were measured directly on the plaster casts with a digital calliper and recorded to the nearest 0.01 mm. A multithreaded wire (Coaxial) of .0175 inch diameter was used for arch circumference measurements. For angular measurements, digital photographs were taken of the plaster models with the camera in a fixed position. The occlusal plane served as reference plane and was adjusted to the camera in a rig with help of a metal plate and a spirit level. Reference points on the plaster models and the spirit level were matched to the outer focus frame of the camera in order to get standardized photographs. The digital photographs were imported to a customized software program and

magnified approximately 2.5 times. Standard computers with 17-inch monitors with 96 DPI, resolution 1024x768 and 32-bit colours were used for measurements with the software programs.

The digital models in the O3DM software program could be magnified, re-positioned, and rotated around one point making inspection of the model from any angle possible. Desired reference planes could be determined by selecting any three points. Sagittal and transversal planes perpendicular to the reference plane were constructed at any point defined by the user. By placing red dot markers on suitable reference points, distances and angles were automatically calculated and recorded with an accuracy of 0.01 degree and 0.01 mm (Fig. 2).

Fig. 2.
Measurement technique regarding of overjet (point to plane), arch circumference (summation of point to point measurements) and rotation (angle measurement) with the O3DM system.
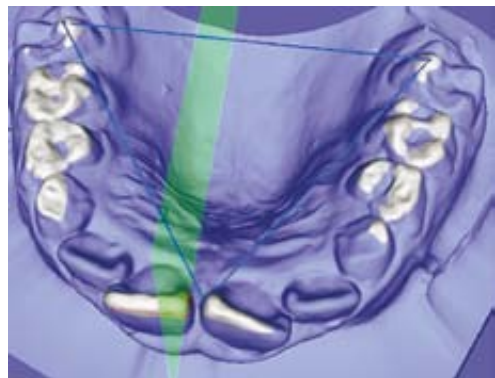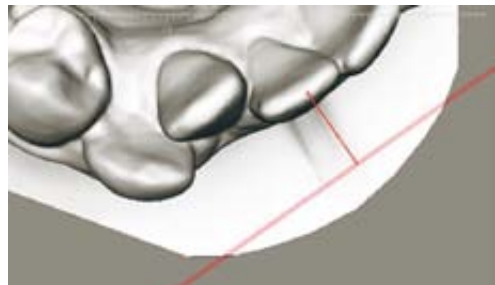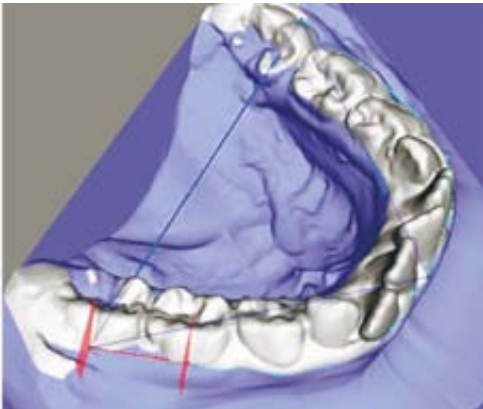
Paper II

To evaluate early changes in mandibular incisor alignment (contact point discrepancies and rotation) and dental arch dimensions (arch width, -length, -circumference), overjet and overbite, one orthodontist (ASj) recorded the variables of interest on plaster models from baseline and the 1-year follow up. These measurements were made in accordance to the conventional technique described in paper I with the exception of a slightly different definition of overjet described in definitions and abbreviations. Irregularity index was defined as the sum of contact point discrepancies at 3 sites, between the contact points of the lateral and central incisors (see Appendices).

Subjective evaluations of changes during the same time period (1-year after baseline) in rotation for each incisor and general alignment of the mandibular frontal segment were made by a second orthodontist (ASv). The visual assessments were performed from an occlusal view and categorized as positive change, no change or negative change. Cut-offs for clinically detectable changes in mandibular rotation and irregularity index were computed.

Parental opinion of change in alignment of the mandibular incisors was also recorded approximately one year after baseline. Parents were interviewed on telephone if they had noticed changes in alignment of their children's lower front teeth. The response alternatives were; fully aligned, improved, no change and worse.

Paper III

Changes in mandibular and maxillary incisor alignment, dental arch dimensions, overjet and overbite were recorded, as described in paper II, on plaster models from baseline, the 1-year follow up and endpoint approximately 2.5 years after baseline. Records of maxillary incisor alignment were limited to plaster models from the 1-year follow up and endpoint since all children did not have sufficiently erupted lateral incisors at baseline. Subjective evaluations of changes in maxillary and mandibular incisor rotation and contact point displacement were made for each incisor and as overall alignment of the frontal segments. These evaluations were performed from both an occlusal and a frontal view and changes were categorized as; fully aligned, (minor, major) positive change, no change or (minor, major) negative change. Conventional measurements (ASj) and subjective assess-

ments (ASv) of alignment were made by the same orthodontists as in paper II. Cut-off's for clinically detectable changes in maxillary and mandibular rotation and irregularity index were computed. Correlation between irregularity measurements and subjective assessments was analyzed.

Paper IV

All interventions took place at public dental clinics, and the child's usual dentist performed the extractions following clinical routine procedures. The deciduous canines were though removed in a specific order over three occasions. At the first appointment the lower left canine (73) was extracted, at the next visit the two canines on the right side (53 and 83) were removed, and at the last visit the upper left canine (63) was extracted.

The children, with guidance of their parents, recorded pain and discomfort during sessions with extractions of one or two deciduous canines and pain at bedtime six days following the extractions in a diary. Visual analogue scales (VAS) of 100 mm length was used with 'no pain' and 'worst imaginable pain' and 'no discomfort' and 'worst imaginable discomfort' as the respective endpoints (Appendices).
We used 30 mm on the VAS as the cut-off point for considerable pain, based on standards for offering pain alleviation at Karolinska University Hospital in Huddinge/Solna, Sweden [125].
The parents were also asked to report after how many hours their child started to drink and eat for the first time and when he/she ate as usual. Analgesics consumption was reported as type of drug and dose on the day of the extraction and the following six days. The child's dentist and/or dental assistant evaluated cooperation on a 4-graded modified Frankl scale [126] at appointments when impressions were taken and for injections and extractions (Appendices).
Dental records were retrieved for all children regarding earlier treatment experiences recorded as present or not at any time from the age of four to the time of randomization. Of the 32 children included, 10 had previous experience of invasive treatment with (n=8) or without (n=2) injection of local anaesthesia. For two children, invasive dental treatment had been performed as emergency care.
Parental ratings of child dental fear (DF), pre- and post-extraction in the study group,

were performed using the Swedish version of the Children's Fear Survey Schedule-Dental Subscale (CFSS-DS [122]). The questionnaire uses a 5-point Likert scale consisting of 15 items giving possible sum-scores of 15-75 (Appendices). A cut-off for dental fear of ≥38 was used in paper IV, but recently suggested age and gender differentiated cut-off scores are also used for comparison [127].

Additional information was available on dental fear ratings in the control group and ratings 1 year after baseline and at endpoint. At endpoint self-ratings were added to the parental ratings.

STATISTICAL ANALYSES

Paper I

Reproducibility of the angular and linear measurements was presented as the standard deviation SD of duplicated measurements according to Dahlberg's formula ($s = \pm \sqrt{(\Sigma d^2/2n)}$ and the coefficient of variation $COV = (SD/mean) \times 100$ for each examiner and method. The mean of the duplicated measurements for each patient under each condition (method and examiner) was calculated and used in the subsequent analyses.

Differences in the angular and linear measurements between methods were described and analysed using mean, standard deviation, and 95% confidence interval. The Pearson correlation coefficient with p-values, testing the null hypothesis that the correlation is zero, was calculated between these differences and the means of the two methods. This calculation was made in order to evaluate whether the estimated differences between methods were homogeneous over the range of measurements; 95% limits of agreement (mean difference $\pm$ 2*SD diff) was calculated to describe the variation on an individual level [128].

Paper II, III and IV

Descriptive statistics (i.e., mean, SD, 95% Confidence Interval, median, interquartile range, min, and max) were used to report the data. The distributions for background and outcome variables were tested using the detrended normal Q-Q plot and the Shapiro-Wilks test, which did not indicate a symmetric normal distribution for all measurements.

Subsequently, irregularity was described with both mean and median values. Pain, discomfort and dental fear were described using median, interquartile range, and min. and max. values due to the non-parametric character of the variables.

Differences between groups were analysed using the Independent-Samples T-test and Mann-Whitney U test, while categorical data were analysed using the χ^2test, McNemar's test and Fischer's exact test.

Changes over time were analysed using the Paired-Samples T-test and Wilcoxon signed-rank test.

Interaction effects between group and time were analysed with ANOVA for repeated measurement (general linear model; with Huynh-Feldt post hoc test).

For analysis of correlation between variables Spearman's rank correlation (r_S) was used.

ROC (Receiver Operating Characteristic) analysis was used to compute cut-off values for "clinically detectable changes" in rotation angle and reduction of irregularity. The combined highest values for sensitivity and specificity were selected and professional assessment of change/no change was used as the state variable. Analysis of maxillary incisor irregularity from baseline (T0) was made on a subgroup with adequately erupted maxillary lateral incisors at T0, consisting of 21 of the 32 subjects from the extraction group and 27 of the 39 subjects in the control group.

Analysis of internal consistency showed that Cronbach's alphas were 0.85 and 0.87 for the pre- and post-extraction measurements with the CFSS-DS.

P-values less than 0.05 were considered statistically significant. Statistical analyses were performed using version 15.0 of the SPSS and version 17.0 of the PASW software packages (SPSS Inc., Chicago, Illinois, USA).

ETHICAL APPROVAL

Studies I, II, III and IV were all pre-approved by the local ethics committee, Regionala etikprövningsnämnden Stockholm, Sweden (Dnr: 2005/960-31/1)

Prior to participation, all participants, children and parents, received oral and written information about the study. A signed informed consent was provided by an adult with parental responsibilities and rights in accordance with the Declaration of Helsinki.

RESULTS

Reproducibility of recordings and agreement between measurements (Paper I)

Intraexaminer variation (reproducibility)
The conventional method showed a higher reproducibility overall in that both examiners had less variation for all variables of maxillary and mandibular incisor rotation, and for all but one of the angular variables (see paper I, Table 1). The differences between the two methods in reproducibility of linear variables did not show any clear pattern except for overbite, which showed less variability when measured with the 03DM system (paper I, Table 1).

Variation between the two measurements (ASj) was 0.9 to 1.5 degrees on plaster models regarding rotation and equal to or below 0.20 mm for irregularity. Arch dimensions (including arch length, not reported in the article), overjet and overbite displayed a variation of 0.18 to 0.43 mm. Both incisor rotation and angulation measurement errors were <2.5% of the variable mean. The corresponding values for irregularity had a range of 6.5 to 27.0% and for dental arch dimensions, overjet and overbite measurement errors were <7% (paper I, Table 1).

Intermethod variation
The O3DM method expressed a tendency for higher values for measurement of rotation. Angular and linear variables exhibited poor 95% limits of agreement.

Interexaminer variation
Regardless of the method the measurements made by examiner 1 displayed significantly lower values than examiner 2 for mandibular arch width but greater for mandibular arch circumference. Angular and linear variables both showed poor 95% limits of agreement.

Mandibular incisor alignment (paper II and III)

Mandibular incisor irregularity showed a significant decrease from baseline to endpoint in both groups, with different patterns between groups. Median values at T0, T1 and T2 were

4.15, 2.25 and 2.96 mm in the extraction group vs. 3.62, 2.94 and 2.73 mm in the control group (paper III, Fig. 2, Table 1; Table 1 a, b, pages 32, 33). Reduction in the initial mandibular incisor irregularity index of >21% and >50% was recorded for comparable proportions in the extraction and control group (16/32 vs.18/39 and 6/32 vs. 6/39, respectively). Contact point discrepancies between the two central incisors accounted for 20% of the three site irregularity index at T0, but did not contribute to the decrease in irregularity index from T0 to T2 in the extraction or the control groups.

Mandibular lateral and central incisor rotation demonstrated wide ranges at baseline in both the extraction and control groups. Lateral incisor rotation displayed a significant reduction from T0 to T2 in both groups ($P<0.001$), while central incisor rotation remained unchanged (paper III, Fig. 4; Table 1 a, b, pages 32, 33). Fifty-eight percent of the lateral incisors in the extraction group showed a change >10° vs. 63% in the control group (paper III, Fig. 4, Table 3).

Professional assessments of mandibular incisor alignment from T0 to T2 revealed no significant differences between the two groups in number of subjects rated as having a positive change. Seventy percent of the subjects were regarded as improved, less than 40% as major improvement and no one as fully aligned in either of the two groups (paper III, Table 4). Fifty-two percent of the lateral incisors in the extraction group were considered as improved compare to 42% in the control group. The corresponding numbers for the central incisors were 11% and <5% respectively. Less than 7% of lateral and central incisor rotation in both groups was categorized as having minor or major deterioration except for central incisors in the control group (11,5%).

More parents of children in the extraction group rated changes of mandibular incisor alignment as improved after 1 year (13/32 vs. 7/41; $P=0.03$).

At endpoint, no significant difference was detected between the extraction and control group for maxillary or mandibular incisor irregularity. Analysis of variances revealed a significant interaction effect (group*time) for mandibular incisor irregularity and rotation of lateral incisors ($P<0.001$ and $P=0.035$, respectively) .

Correlation between change in irregularity index and sum of absolute change in rotation for maxillary incisors (T1 to T2) and mandibular incisors (T0 to T1 and T0 to T2) was found to be weak in both groups ($r_S \leq 0.3$; not significant). Subjects divided into groups showing mandibular rotation index changes below or above 9° and <21% or ≥21% of irregularity index change revealed no significant relation.

Professional assessment of alignment showed the following correlation with change in maxillary (T1 to T2) and mandibular (T0 to T2) irregularity index r_S=0.45; P<0.01 and r_S=0.68; P<0.01 respectively.
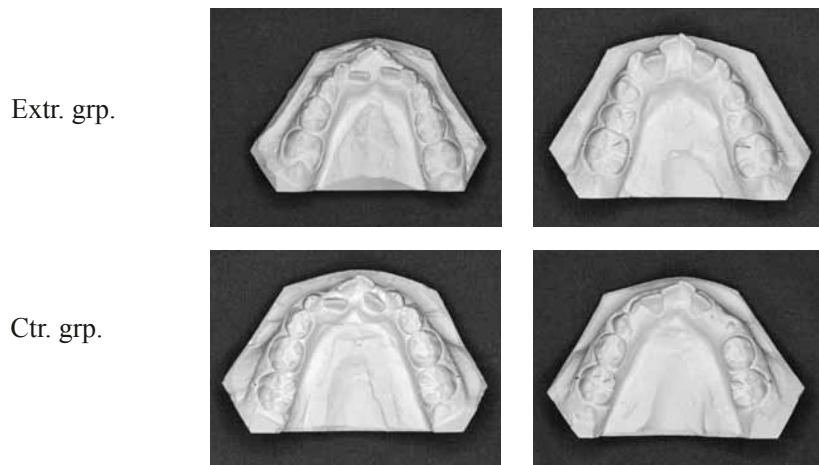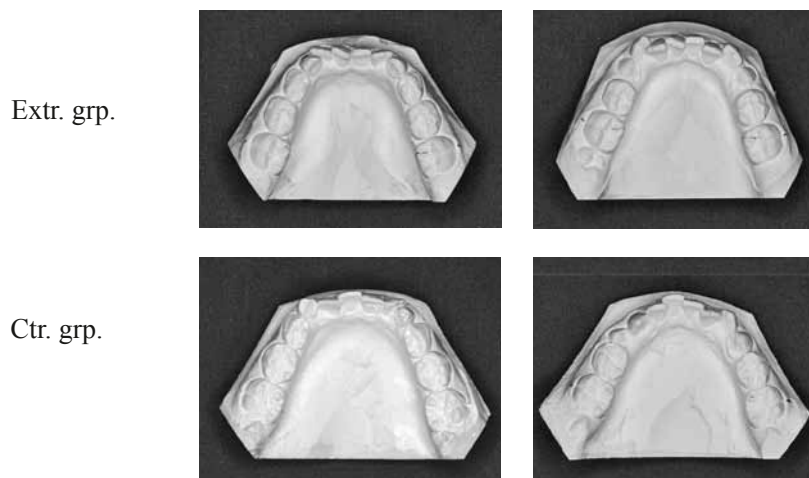
Extr. grp.

Ctr. grp.

Fig. 3. Examples of the largest improvements in mandibular irregularity from baseline (left) to endpoint (right) in the extraction and control group.

Extr. grp.

Ctr. grp.

Examples of smallest or no improvement in mandibular irregularity from baseline (left) to endpoint (right) in the extraction and control group.

Table 1a. Differences in outcome variables T1 to T0, T2 to T1 and T2 to T0 in the extraction group.

		Differences T1-T0		Differences T2-T1		Differences T2-T0	
		Mean	95% Confidence Interval[1]	Mean	95% Confidence Interval[1]	Mean	95% Confidence Interval[1]
Irregularity	Max	-1.88	*-2.68 to -1.07*	0.31	-0.15 to 0.77	-1.03	*-1.77 to -0.29*
	Mand			0.85	*0.52 to 1.18*		
Rotation	12			-0.91	-3.80 to 1.98		
	11			0.69	-0.24 to 1.62		
	21			0.66	-0.74 to 2.06		
	22			-0.74	-2.64 to 1.16		
	32	-8.09	*-11.41 to -4.77*	-2.56	*-4.73 to -0.37*	-10.52	*-15.25 to -5.79*
	31	-0.60	*-2.23 to 1.03*	0.76	-1.97 to 0.45	-1.36	-3.36 to 0.63
	41	1.27	*-0.55 to 3.08*	-0.88	-2.51 to 0.75	0.39	-1.44 to 2.21
	42	-6.94	*-10.04 to -3.84*	-3.07	*-5.47 to -0.67*	-9.98	*-14.17 to -5.79*
Arch width	Max	-0.18	-0.35 to 0.01	0.17	-0.07 to 0.42	0.01	-0.31 to 0.29
	Mand	-0.18	*-0.35 to -0.01*	0.06	-0.14 to 0.26	-0.12	-0.40 to 0.16
Arch length	Max	-1.31	*-1.63 to -0.99*	0.01	-0.25 to 0.28	-1.30	*-1.75 to -0.85*
	Mand	-1.05	*-1.33 to -0.77*	0.35	-0.27 to 0.97	-0.70	-1.48 to 0.08
Arch circf.	Max	-2.43	*-2.86 to -1.99*	0.00	-0.55 to 0.54	-2.43	*-3.13 to -1.73*
	Mand	-2.02	*-2.64 to -1.39*	1.11	*0.43 to 1.79*	-0.90	*-1.73 to -0.09*
Overjet		*-0.35*	*-0.66 to -0.03*	0.13	-0.10 to 0.36	-0.22	-0.52 to 0.09
Overbite		*0.58*	*0.19 to 0.97*	*0.83*	*0.53 to 1.12*	*1.40*	*0.97 to 1.84*

[1] Statistically significant differences printed in italics

Table 1b. Differences in outcome variables T1 to T0, T2 to T1 and T2 to T0 in the control group.

		Differences T1-T0		Differences T2-T1		Differences T2-T0	
		Mean	95% Confidence Interval[1]	Mean	95% Confidence Interval[1]	Mean	95% Confidence Interval[1]
Irregularity	Max	-0.55	*-0.90 to -0.19*	-0.71	*-1.32 to -0.10*	-0.65	*-1.23 to -0.08*
	Mand			-0.10	-0.49 to 0.28		
Rotation	12			-5.04	-6.96 to -3.12		
	11			-1.08	-2.25 to 0.09		
	21			-0.62	-1.78 to 0.55		
	22			-3.30	-5.66 to -0.95		
	32	-6.00	*-8.30 to -3.70*	-6.44	*-8.77 to -4.11*	-12.44	*-16.19 to -8.68*
	31	0.56	-0.42 to 1.55	-1.87	-3.40 to -0.35	-1.31	-3.18 to 0.56
	41	0.07	-0.94 to 1.05	-1.69	-3.05 to -0.34	-1.63	*-3.12 to -0.13*
	42	-5.63	*-8.43 to -2.83*	-7.93	-10.80 to -5.05	-13.56	*-17.72 to -9.39*
Arch width	Max	0.15	-0.03 to 0.33	0.26	*0.01 to 0.51*	0.41	*0.07 to 0.75*
	Mand	0.25	*0.10 to 0.39*	0.06	-0.29 to 0.17	0.19	-0.13 to 0.51
Arch length	Max	0.29	0.04 to 0.61	-0.21	-0.65 to 0.24	0.08	-0.29 to 0.45
	Mand	0.05	-0.16 to 0.27	-0.48	*-0.80 to -0.16*	-0.43	*-0.81 to -0.05*
Arch circf.	Max	0.52	*0.14 to 0.90*	-0.43	-1.00 to 0.13	0.09	-0.52 to 0.70
	Mand	0.45	*0.10 to 0.80*	-1.02	*-1.63 to -0.41*	-0.60	-1.18 to 0.04
Overjet		0.16	-0.10 to 0.41	0.05	-0.20 to 0.30	0.21	-0.07 to 0.48
Overbite		0.07	-0.29 to 0.43	0.96	*0.66 to 1.26*	1.03	*0.65 to 1.42*

[1] Statistically significant differences printed in italics

Maxillary incisor alignment (paper III)

Due to few erupted lateral incisors at baseline, change in maxillary irregularity index was evaluated only at the one-year follow up and then at endpoint. A significant difference between groups (P=0.01), with increased median values in the extraction group (2.49 to 2.96 mm; not significant) in contrast to decreased median values in the control group (4.53 to 3.47 mm; not significant), see paper III (Fig. 1, Table 1) and Table 1 a, b (pages 32, 33). Less subjects in the extraction group than in the control group showed a >20% and >50% reduction of maxillary incisors irregularity index from T1 to T2 (7/32 and 2/32 vs. 14/39 and 8/39; not significant).

A subgroup, consisting of subjects with lateral incisors sufficiently erupted for measurement already at T0, showed a significant decrease from baseline to endpoint in both the extraction and control groups (P<0.001), though showing different patterns with median irregularity values at T0, T1 and T2 of 5.57, 2.59 and 3.41 mm in the extraction group vs. 5.71, 4.53 and 3.83 mm in the control group. The interaction effect (group*time) was significant at P=0.049.

Rotation of maxillary incisors varied widely at the start of measurements (T1) in both groups. Minor reductions in lateral incisor rotation angle were displayed from T1 to T2 in the control group (range 3.3° to 5.0°; p<0.001), while no significant change in rotation was seen for central incisors in either of the two groups. (Table 1 a, b, pages 32, 33). Less than 5% of the lateral incisors in the extraction group showed a change >10° vs. 18 % in the control group and only one central incisor in the control group changed rotation >10° from T1 to T2 (paper III, Table 3).

Professional assessments of maxillary incisor alignment from T1 to T2 from an occlusal and a frontal view showed significantly less subjects assessed as having positive change in the extraction group compared to the control group (6/32 vs. 20/39; P<0.01; paper III, Table 4).

Arch dimensions, overjet and overbite (paper II and III)

Maxillary and mandibular arch circumference and maxillary arch length decreased significantly in the extraction group from T0 to T2 ($P<0.001$, $P=0.034$ and $P<0.001$; Table 1 a, b, pages 32, 33). Mandibular arch length decreased in the control group ($P=0.027$), while maxillary arch width increased ($P=0.020$). Mandibular arch width remained unchanged in both groups from T0 to T2 (Table 1, a, b, pages 32, 33) No significant differences in arch dimensions were observed between groups at endpoint except for a significant larger maxillary arch circumference in the control group (92.60 vs. 90.17; $P=0.018$).
Overjet remained unchanged, while overbite increased significantly in both groups ($P<0.001$; Table 1, a, b, pages 32, 33).
Analysis of variances revealed a significant interaction effect (group*time) for maxillary and mandibular arch length and circumference ($P<0.01$) and overjet ($P=0.020$), but not for maxillary and mandibular arch width or overbite.

Procedural pain and discomfort (paper IV)

Procedural pain was reported at low median levels on all three extraction occasions (6, 8 , and 2 on the 0-100 VAS, respectively). High values were seen for some individuals as the total ranges were 0–59, 0–83, and 0–99 (Fig. 4 a, page 36). Boys reported a significantly higher pain level when two teeth were extracted compared with the occasions when a single tooth was extracted (23.5 vs. 6 and 3; $P=0.02$ and $P=0.03$, respectively) in opposite to girls who reported low median levels on all three occasions (Fig. 4 a, page 36). Seven children (six boys, one girl) had pain scores exceeding 30 on the VAS at least once during the three appointments.
Discomfort scores showed median levels of 7, 8, and 10, with wide ranges of 0–89, 0–95, and 0–95, respectively (Fig. 4 b, page 36). Differences between boys and girls were non-significant (Fig. 4 b, page 36).
Fifteen (5 boys, 10 girls) of the 32 children were categorized as fully acceptant for both injection and extraction at all three treatment occasions, whereas 11 children (6 boys, 5 girls) showed reluctant acceptance and 6 children (3 boys, 3 girls) were non-acceptant at any of the three occasions.
When alginate impressions were taken at baseline, 27 of the 32 children in the extraction group were rated as fully acceptant vs. 31 of the 41 children in the control group.
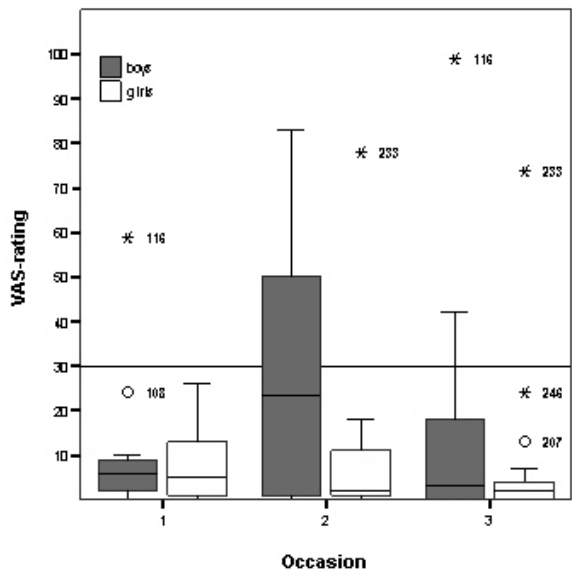
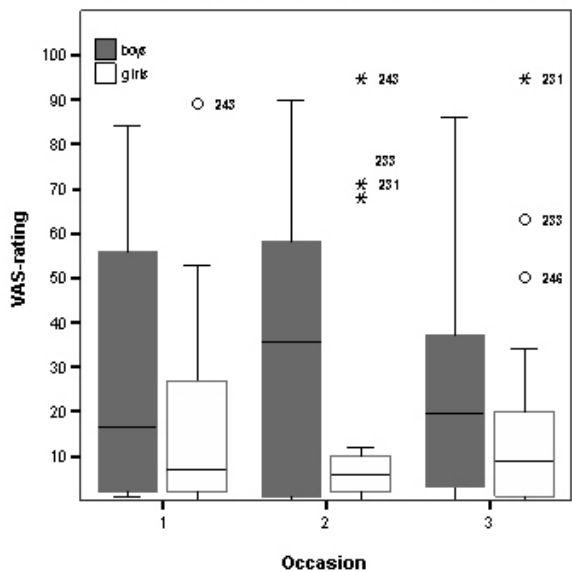*Fig. 4 a. Procedural pain*

Fig. 4 b. Discomfort

Fig. 4 a, b. Ratings of procedural pain and discomfort at extraction occasions 1, 2, and 3. The vertical axis represents the 100 mm visual analogue scale, with "no pain/discomfort" and "worst imaginable pain/discomfort" as endpoints. (Box plots showing median, interquartile range, and min and max values for boys and girls. Whiskers less than 1.5 box lengths from either end of the box show min and max values).

Postoperative pain and discomfort (paper IV)

Median VAS ratings for postoperative pain at bedtime after each of the three occasions ranged from 0 to 3.5 and did not differ between boys and girls (paper IV, Fig. 2). Individual maximum scores for pain reported at bedtime were 59 on the first evening, 33 on the second, and 21 on the third, and decreased thereafter. Two boys and two girls reported pain exceeding the clinically accepted cut-off (>30 on the VAS) during the first two evenings after the extractions at occasion 2.

Use of analgesics was reported for 7 children (4 boys, 3 girls), as a single dose for all but one. One child used analgesics at all three occasions, and was the only one to use analgesics at occasion 3.

Recovery time ranged from 0.5 to 6 h (first drinking) and 1 to 18 h (first eating) after the three occasions (Table 2). Median time for eating as usual after the three appointments were 3.5, 3.8, and 2.8 h with a total range from 1 to 24 h. There was significantly longer recovery time at occasion 2 for first eating when compared with occasion 1 (P=0.02) and for eating as usual when compared with occasion 3 (P<0.01).

Dental fear changes (paper IV)

Pre-extraction ratings (before randomization) of child dental fear paralleled population norm values [129] for both boys and girls (median 22.0; range 15–40; paper IV, Fig. 3). CFSS-DS median scores decreased from pre to post-extraction for boys (23.5–21.5; P=0.02) and girls (20.0–18.0; NS; Fig. 3). No one exceeded the cut-off of ≥38 for dental fear, post-extraction.

Analysis of long term changes in CFSS-DS scores (data not shown) in the extraction and the control group showed that both groups paralleled population values over a 2,5 year period after extractions (Fig. 5, page 38).

Six children (3 boys and 3 girls) in the extraction group had self-rating scores exceeding an estimated age and gender related cut off at endpoint [127]. These children showed no clear pattern of increased dental fear.
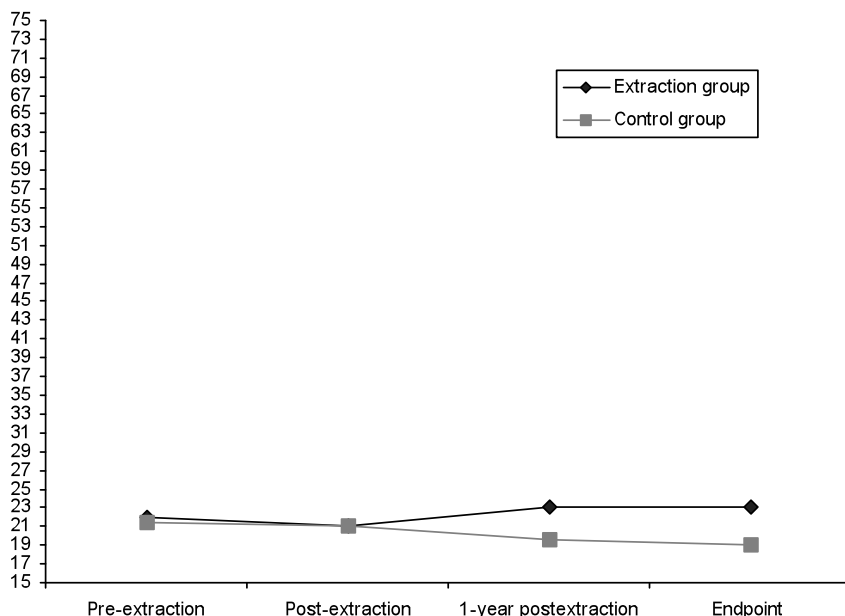
Fig. 5. Description of parental dental fear ratings from start to endpoint. Median values for CFSS-DS sum score in the extraction and control group pre- and post-extraction, 1-year post-extraction and at endpoint.

Analysis of bivariate relationships and subgroups (paper IV)

There was a strong relationship between pain and discomfort reports at the three occasions (r_S=0.70–0.78). Furthermore, both pain and discomfort reports showed a moderate relationship with the post-extraction CFSS-DS ratings (r_S=0.47 and 0.54, respectively). Children rating procedural pain >30 on the VAS scale had no significantly different pre- or post-extraction median CFSS-DS rating compare with the others (23.0 and 23.0 vs. 22.0 and 19.0).

Children categorized as fully acceptant, when compared with those who were reluctant or non-acceptant, rated discomfort lower at the second occasion (median 4.5 vs. 22.0; P=0.049), whereas no significant differences were seen for procedural pain at any of the three occasions. The fully acceptant group showed a lower (median 17.5 vs. 24.0; P<0.01) post-extraction dental fear score compared with a group of reluctant and non-acceptant children.

DISCUSSION

The general aim of this thesis was to evaluate spontaneous incisor alignment and change in dental arch dimensions in children subjected to deciduous canine extractions. Furthermore, patient response to these extractions regarding pain, discomfort and dental fear was examined.

Measurement reliability

Reproducibility

With the ambition to improve measurement accuracy we started out comparing a new technique for measuring virtual digital models with a conventional technique using plaster models. The conventional method became the method of choice, due to slightly better reproducibility for angular measurements and comparable results for linear variables. Reproducibility was though considered clinically acceptable for both methods, although measuring procedures were very time consuming for both techniques, and not adjusted to clinical routines. The O3DM concept has since the study been upgraded several times and tools for registration of angular variables have been improved.

Interexaminer variation was probably caused by differences in experience with the O3DM method, related to as "a learning curve" in earlier studies [104, 108, 110, 112, 116]. The examiner having a lower level of variation was therefore performing all linear and angular measurements in paper II and III. Evaluation of incisor angulations was omitted in paper II and III because many lateral incisors were located in such a position, that no registration was possible with the techniques at hand.

Measurement error levels should not impose difficulties in evaluation of rotation, irregularity or dental arch dimension changes. The substantial Coefficient of Variation ((SD/mean)×100) in central incisor irregularity should be explained by the corresponding low mean value [128]. Variation for linear variables was in line with earlier studies [102, 105, 110, 112, 114]. The wide intervals for 95% limits of agreement in respect to angular and linear variables clearly indicate that comparing results on an individual basis would cause problems. This was seen in both intermethod and interexaminer analysis.

Validity

Arch length tooth size analysis is, although preferred by many orthodontists in quantifying crowding, associated with problems such as differences in individual dental arch form and a certain amount of subjective judgement involved [100]. Surbeck and Årtun (1998) found contact point discrepancies and rotation in a group chosen as being perfectly aligned, which indicates that this type of computer-generated arch form might not reflect the actual dental arch [98]. Furthermore, discrimination between treatment effect and growth is considered dubious [9, 23, 26, 28, 35-36]. We therefore chose to describe alignment and dental arch dimension changes separately and compared these results with professional visual assessments of alignment for validation. The irregularity index also enabled us to compare our results with earlier studies, despite its tendency to overestimate crowding scores in some cases and inherent weakness in identifying rotation [99-100].

This was compensated by separate analyses of lateral and central incisor rotation and contact point discrepancy changes. To minimize confounding effects of a mix of primary and permanent canines we used a 3-site index instead of the more traditional 5-site index. The inclusion criteria based on professional evaluation of space deficit together with the professional evaluation of treatment outcome should also contribute to increased validity. Categories for professional evaluation were adapted to cut-off's defined in an earlier study [9] to make comparisons easier. Cut-offs for detecting changes in maxillary and mandibular incisor rotation and irregularity changes were developed and should be essential for estimation of the clinical value of small changes despite elements of subjectivity.

The congruent levels for cut off's assessed on different sets of models strengthen the validity of such procedure although only one observer was used. Professional assessments of alignment were made from an occlusal and a frontal view to get both a professional and a more patient oriented perspective on alignment, showing minor differences between the two. This might imply that either perspective could be used though further research is needed for validation.

Treatment outcome

Alignment

Besides our general aim to evaluate outcome of spontaneous alignment and dental arch changes, we wanted to enhance knowledge regarding possible patterns of changes over

time. Our working hypothesis was that an early improvement in incisor alignment from deciduous canine extractions might deteriorate during eruption of the permanent canines. As expected, mandibular irregularity initially showed a larger reduction in the extraction group compared to the control group. During the latter observation period, the treatment effect was reversed, with increased irregularity in the extraction group, resulting in no significant difference between groups at endpoint. A similar pattern was seen for the maxillary incisors, although analyzed only for a subgroup.

A probable explanation to the late increase in irregularity could be that of a more mesial eruption path for the permanent canines due to the extracted primary canine. The lack of alignment effect on the central incisors in both groups implies that any distal movement of the lateral incisors was not enough to eliminate irregularity among the central incisors and that Little's irregularity index can conceal differences between lateral and central incisors. For methodological purposes, a comparison between mandibular irregularity, based on measurements at 3 and 5 sites was made. Neither index showed statistically significant differences between groups at baseline or endpoint. This implicates that the 3-site index could be used for monitoring changes in irregularity in the mixed dentition.

Due to lack of golden standard for incisor position with regard to rotation, analysis was made with professional assessment of no, negative and positive changes. An interaction between changes in irregularity and rotation could be suspected, though correlation between these to variables was weak and correlation between professional assessment and the irregularity index was moderate at best. This strengthens our findings and our assumption that Little's irregularity index underestimates rotation when mandibular incisor alignment is evaluated [130].

Overall clinical evaluation of alignment showed discouraging signs in that less than 40% were categorized as having major improvement in alignment and no one was considered as fully aligned in either of the two groups.

A survey regarding parental assessments of mandibular alignment after one year showed significantly more children regarded as improved in the extraction group. However, 41% of the parents in both groups expressed uncertainty about accurately remembering the initial status and/or correctly reporting changes in alignment. This substantial recall bias together with an expected treatment bias makes the results unreliable.

Dental arch dimensions, overjet and overbite

It seems unlikely that permanent tooth eruption should be impeded by the deciduous canine extractions, due to the modest decrease (<4%) in maxillary and mandibular dental arch length and circumference recorded from baseline to endpoint. However, the initial decrease caused by either mesial movement of the first molars and/or increased mandibular incisor retrusion/retroclination, might induce a change in eruption path for the permanent canines and bicuspids, resulting in secondary crowding.

Results for arch length and circumference from the early phase and the non-significant differences between groups for arch width, overbite and overjet are in line with the recordings from Kau et al. (2004). The congruent results between arch length and arch circumference changes and modest differences between groups for overjet and overbite changes indicate that the early changes in arch length were not entirely due to retroclined incisors.

The differences between the extraction and the control group in early and later changes in irregularity, rotation, arch length, circumference and overjet together with large individual differences illustrate the complexity in tooth alignment and dental arch changes. Differences in opinion among clinicians concerning treatment outcome from deciduous canine extractions and the divergent results between the few studies available could very well be a result of the different patterns for changes over time demonstrated in this thesis. Evaluation of patient experiences were included in this thesis to be weighted against assumed benefits in incisor alignment.

Patient experiences

Procedural and postoperative pain and discomfort

Although 1 out of 5 children reported procedural pain scores indicating a need for additional pain alleviation in connection to the deciduous canine extractions these ratings demonstrated a low median level. This is in line with earlier studies by Tate and Acs (2002)[54] and Wondimu and Dahllöf (2005)[70] pointing out the importance of individually adapted care and recommending preparatory use of analgesics. Despite the fact that these studies did not exclusively explore orthodontically induced extractions and that prediction of individual pain experiences is difficult, routine use of preoperative medication could be a way to reduce the risk of inadequate pain control.

No common characteristics such as negative earlier dental experience or different dental fear levels were found for the children reporting pain at levels in need of additional pain alleviation. This could though be due to the small sample.

Single tooth extraction seems to be preferable to extractions of two teeth at the same appointment at least for boys, as implied by the reported higher procedural pain ratings and the distribution of postoperative pain ratings exceeding the cut-off for offering pain alleviation. This contrasts to the findings regarding orthodontic extractions of first bicuspids [64] and could be age related. The small study group did not allow for analyses of gender difference.

Discomfort represents factors that, besides pain probably are important for the child's perception of good empathic care. In fact, ratings of procedural discomfort were higher than pain ratings in our study. The experience of having a wide numbness area may be more unpleasant than the sensation of pain in connection to the removal of deciduous canines [131]. As a complement to pain and discomfort ratings, acceptance rated by the treating dentist was explored. A higher frequency of non-acceptance (19%) was found in our study compared to population-based Swedish studies by Holst and Crossner (8%) [132] and Klingberg (10%) [133] probably because acceptance rating in our study was focused on treatment steps of injection and extraction. Furthermore, ratings of acceptance when impressions for plaster models were taken showed that 1 one out of the 32 children was categorized as non-acceptant.

Postoperative pain and discomfort ratings indicated that most of the children experienced only a limited amount of inconvenience. The low level of analgesic consumption and the short recovery time in drinking and eating strengthen this assumption. One explanation may be the presumably uncomplicated extractions, although the same pattern for post-extraction pain and analgesic consumption was seen after orthodontically induced bicuspid extractions [64].

Dental fear

We assumed that the CFSS-DS level would increase from pre- to post-extraction and then return to the initial values after one or two years. However, median dental fear score decreased from pre- to post-extractions and remained at population mean values throughout the entire observation period for the extraction group, similar to scores in the control

group. This indicates that dental fear was not triggered or increased, but an element of uncertainty remains as the use of parental ratings of their children's dental fear can been questioned [127].

The moderate relationship between dental fear and pain and/or discomfort ratings further adds to the impression that orthodontic extractions of deciduous canines have no or little impact on dental fear levels. However, lower levels of post-extraction dental fear were associated with the fully acceptance group, which calls for attention on individual dental fear levels in clinical practice.

Strengths and limitations

The major strength of this study is the randomized control design, with early intervention and substantial follow up time. To minimize influence of differences in dental development between genders and between subjects, baseline and endpoint were defined by dental development stages (DS 1 and 3) and not by chronological age.

The main purpose of the thesis was to study alignment and dental arch dimensions after deciduous canine extractions and power analysis was performed for that purpose.

The relatively small number of subjects participating has limited analysis of gender differences and earlier dental experiences in paper IV as well as analysis of maxillary incisors in paper II and III.

Those 16 children/parents that declined participation might have done so because of anxiety of dental fear and contributed to selection bias. Of the remaining 11 excluded before randomization, 6 parents requested the non-extraction alternative and 5 the extraction alternative indicating at least partially a parental positive attitude to extractions. Initial CFSS-DS scores for the 12 children excluded after randomization revealed a median score similar to that for the investigated children (median 18.5, range17 to 29).

No lateral cephalograms were available and thus no proper evaluation of incisor position/ inclination or first molar movements was possible.

The quality and accuracy of the plaster models in our studies should not be compromised by the routines for storage and tray design (as summarized in a recent study) [115], contradictory to earlier findings by Eriksson et al. (1998) [120]. Errors could though be caused by variation in mixing techniques [120] and in clinical registration of intermaxillary relation [121], which was out of our control.

Clinical implications

The idea of eliminating or at least to facilitate future orthodontic treatment of crowding by serial extractions has been attractive, especially in times of shortage of orthodontic resources [3]. This treatment modality has been promoted for a long time, based mainly on encouraging clinical results for the entire procedure. No well designed scientific evaluation of the first part of this procedure was made until 2004, when Kau et al. published their article "Extractions as a form of interception in the developing dentition: a randomized controlled trial" [9]. The present thesis supports and strengthens the conclusions made by Kau and co-workers that the benefits from lower deciduous canine extractions in order to relieve lower incisor crowding are questionable [9]. Furthermore, no benefits can be expected regarding improvement of maxillary incisor crowding by removing the primary canines.

Although, the extractions were performed relatively early, during the eruption of the maxillary and mandibular lateral incisors, one could speculate if an even earlier intervention would have made a difference. This seems unlikely for the mandibular incisors, as a result of the early decrease in arch length and late decrease in alignment in the extraction group. A positive side effect of such early intervention might though be that of enhanced eruption of permanent teeth, less risk for gingival recession for buccal positioned incisors and less maxillary lateral incisors in inverted positions. Evaluation of these effects was though beyond the scope of this thesis.

Fortunately, the assumed and previously reported shortening of the dental arch, due to primary canine extractions [9, 33-34], was demonstrated to be of minor magnitude, when evaluated in the late mixed dentition. This implies that early extraction of deciduous canines is of minor importance in the development of the dental arch.

Despite low median levels of pain and short duration of discomfort, some children experienced considerable procedural pain. Revised recommendations of pain management routines focusing on providing preoperative analgesics in connection to invasive procedures of this kind might therefore be advisable.

To summarize, extractions of deciduous canines could not be recommended as evidence based treatment to relieve crowding and/or malalignment of permanent incisors.

Suggestions for future research

A major problem when evaluating changes measured on two different models is the construction of reliable reference points and planes. Using the x, y, z coordinates in CBCT images and superimpositions on the anterior cranial base might resolve this problem, if an acceptable level of radiation exposure can be reached.

Considering patient/parental assessment of treatment outcome combined with evaluation of the residual treatment need would add valuable information to the studies of interceptive treatment procedures.

Studies on children's reactions on dental standard procedures are few and more knowledge regarding gender and age related experiences of pain and discomfort in connection to common invasive procedures would improve the quality of dental care.

CONCLUSIONS

In the methodological study of reproducibility and agreement of orthodontic study cast analysis

- The conventional method showed better reproducibility for angular variables.
- No clear pattern was found for differences between the two methods in reproducibility of linear variables.
- Reproducibility was considered clinically acceptable for both methods.
- Systematic errors indicated that the two methods should not be used interchangeably.

In the evaluation of treatment outcome regarding alignment, dental arch dimensions, overjet and overbite after extraction of the deciduous canines it was concluded that:

- Extraction of deciduous canines cannot be expected to improve maxillary or mandibular incisor alignment significantly and should therefore not be recommended for relieve of incisor crowding.
- The congruent results for professional visual assessment and conventional measurements regarding alignment strengthen the validity of the interpretation of the treatment results.
- No major effect was seen on arch dimensions overjet or overbite due to extraction of the deciduous canines.

Regarding the study of procedural and postoperative pain and discomfort and changes in dental fear levels over time the following conclusions were made.
Extraction of the deciduous canines:

- Did not trigger or increase dental fear.
- Should not cause major post-operative inconvenience.
- Revealed a need for updating clinical routines for pain management.

POPULÄRVETENSKAPLIG SAMMANFATTNING

"Serie-extraktion" har en lång tradition och har varit baserad mera på klinisk erfarenhet än på vetenskapligt stöd. Idén om att förebygga platsbrist och snedställda tänder genom att ta bort (extrahera) mjölktänder och permanenta tänder i förtid beskrevs redan på 1700-talet, men metoden blev populär först under senare delen av 1940-talet.

Första steget i den här behandlingstekniken är att avlägsna samtliga fyra mjölkhörntänder, då de permanenta sidoframtänderna är under frambrott. Senare avlägsnas flera tänder, vanligtvis de permanenta första kindtänderna, för att ge plats åt de permanenta hörntänderna. På grund av att det saknas studier, som entydigt visar att det första steget av behandlingen är effektiv går åsikterna, bland tandregleringsspecialister, isär om lämpligheten med åtgärden.

Syftet med avhandlingen var att utvärdera vilken effekt avlägsnandet av mjölkhörntänderna har på utjämning av framtänder som står trångt och oregelbundet.

Vi har också utvärderat om extraktionerna påverkar utrymmet för de permanenta tänder som skall komma senare. Vi undersökte dessutom hur barnen vars mjölkhörntänder togs bort upplevde smärta och obehag i samband med och efter ingreppen och om tandvårdsrädsla påverkades.

Projektet genomfördes med en studiegrupp (som fick tänderna borttagna) och en kontrollgrupp (som fick tappa dem naturligt) och grupperna lottades fram för att kunna tolka resultaten på bästa sätt vetenskapligt. Mättekniker som användes testades och visade god tillförlitlighet.

Utjämningseffekten hos framtänderna i över och underkäken, förändringar i utrymme i tandbågarna och tandvårdsrädsla utvärderades över en 2,5-års period och grupperna jämfördes vid start och vid projektets slut. En tandregleringsspecialist fick bedöma förändringar i utjämningseffekt hos de båda grupperna och föräldrar tillfrågades om de tyckte att framtänderna blivit jämnare eller inte.

Resultat

Vi fann att extraktionsgruppen hade en tidig större utjämning av framtänderna i över och underkäken jämfört med kontrollgruppen, men båda grupperna var jämförbara vid slutkontrollen. Detta kan förklara varför åsikterna beträffande behandlingseffekt går isär hos tandregleringsspecialisterna.

Samma mönster av förändring sågs också för utrymmet i käkarna. Tandreglerings-specialistens bedömning av utjämningseffekt stämde väl överens med de uppmätta värdena, vilket styrker resultaten.

En femtedel av barnen rapporterade betydande smärta i samband med tandborttag-ningarna, men mycket lite besvär rapporterades i efterförloppet.

Ingen ökning av tandvårdsrädsla kunde konstateras.

Slutsatser

Man bör inte regelmässigt avlägsna mjölkhörntänder i syfte att åstadkomma en spontan förbättring av trångställda och/eller snedställda framtänder.

Åtgärder för att minimera smärtupplevelser i samband med tandborttagningar bör över-vägas.

ACKNOWLEDGEMENTS

My colleagues and friends at the Department of Dental Medicine, Karolinska Institutet for sharing their stimulating enthusiasm and genuine scholarship always available for discussions and advice.

All the personnel in Folktandvården, Örebro County Council engaged in collecting data with such accuracy and great enthusiasm, although with a tight time schedule.

The children and their parents for participated in this study with such endurance, especially regarding taking impressions and filling out "the same" surveys repeatedly.

My closest and dearest friends Tommy Johansson, Ola Fernberg and Anders Nylander with families who never fail to surprise me in offering invaluable companionship and delicious dinners.

My wonderful daughters, AnnaMaria and Ebba, for your endless patience with an impatient father and for all your love and support.

References

1.   Little RM. The irregularity index: a quantitative score of mandibular anterior alignment.
     Am J Orthod. 1975; 68: 554-63.

2.   Mayne WR. Serial extraction-orthodontics at the crossroads.
     Dent Clin North Am. 1968: 341-62.

3.   Hotz RP. Active supervision of the eruption of teeth by extraction.
     Trans Eur Orthod Soc. 1947: 34-47.

4.   Kjellgren B. Serial extraction as a corrective procedure in dental orthopedic therapy.
     Acta Odontol Scand. 1948; 8: 17-43.

5.   Dewel B. Serial extractions in orthodontics: Indications, objectives and treatment
     procedures. Am J Orthod. 1954; 40: 906-26.

6.   Nance HN. The limitations of orthodontic treatment; mixed dentition diagnosis and
     treatment. Am J Orthod. 1947; 33: 177-223.

7.   Tweed CH. Indications for the extraction of teeth in orthodontic procedure.
     Am J Orthod Oral Surg. 1944; 42: 22-45.

8.   Dale JG, Brandt S. Dr. Jack G. Dale on serial extraction.
     J Clin Orthod. 1976; 10: 44-60.

9.   Kau CH, Durning P, Richmond S, Miotti FA, Harzer W. Extractions as a form of
     interception in the developing dentition: a randomized controlled trial.
     J Orthod. 2004; 31: 107-14.

10. Little RM. The effects of eruption guidance and serial extraction on the developing
     dentition. Pediatr Dent. 1987; 9: 65-70.

11. Bradbury AJ. A current view on patterns of extraction therapy in British health
     service orthodontics. Br Dent J. 1985;159: 47-50.

12. Dale JG. Interceptive guidance of occlusion with emphasis on diagnosis.
     Alpha Omegan. 1999; 92: 36-43.

13. Dale JG, Brandt S. Dr. Jack G. Dale on serial extraction. 3.
     J Clin Orthod. 1976; 10: 196-217.

14. Dale JG, Brandt S. Dr. Jack G. Dale on serial extraction. 2.
     J Clin Orthod. 1976 ; 10: 116-36.

15. Dewel BF. Serial extraction: Precautions, limitations, and alternatives.
     Am J Orthod. 1976; 69: 95-7.

16. Foley TF, Wright GZ, Weinberger SJ. Management of lower incisor crowding in the early
     mixed dentition. ASDC J Dent Child. 1996; 63: 169-74.

17. Gianelly AA. Treatment of crowding in the mixed dentition.
     Am J Orthod Dentofacial Orthop. 2002; 121: 569-71.

18. Graber TM. Serial extraction: a continuous diagnostic and decisional process.
     Am J Orthod. 1971; 60: 541-75.

19. Heath J. The interception of malocclusion by planned serial extraction.
N Z Dent J. 1953; 49: 77-88.

20. Hotz RP. Guidance of eruption versus serial extraction. Am J Orthod. 1970; 58: 1-20.

21. Lloyd Z. Serial extraction as a treatment procedure. Am J Orthod. 1956; 42: 728-39.

22. McKeown M. The diagnosis of incipient arch crowding in children.
N Z Dent J. 1981; 77: 93-6.

23. Moorrees CFA, Fanning EA, Grön A-M. The consideration of dental development in serial extraction. Angle Orthod. 1963; 33: 44-59.

24. Ngan PW, Kao EC, Wei SH. Guidance of eruption for general practitioners.
Int Dent J. 2003; 53: 100-13.

25. Proffit WR, Bennett IC. Space maintenance, serial extraction, and the general practitioner. J Am Dent Assn. 1967; 74: 411-9.

26. Henrikson J, Persson M, Thilander B. Long-term stability of dental arch form in normal occlusion from 13 to 31 years of age. Eur J Orthod. 2001; 23: 51-61.

27. Little RM, Riedel RA, Engst ED. Serial extraction of first premolars-postretention evaluation of stability and relapse. Angle Orthod. 1990; 60: 255-62.

28. Odenrick L, Trocmé M. Facial, dentoalveolar and dental morphology in serial or early extraction. Angle Orthod. 1985; 55: 206-14.

29. Persson M, Persson EC, Skagius S. Long-term spontaneous changes following removal of all first premolars in Class I cases with crowding. Eur J Orthod. 1989; 11: 271-82.

30. Ringenberg QM. Influence of serial extraction on growth and development of the maxilla and mandible. Am J Orthod. 1967; 53: 19-26.

31. Wagner M, Berg R. Serial extraction or premolar extraction in the permanent dentition? Comparison of duration and outcome of orthodontic treatment.
J Orofac Orthop. 2000; 61: 207-16.

32. Yoshihara T, Matsumoto Y, Suzuki J, Sato N, Oguchi H. Effect of serial extraction alone on crowding: relationships between tooth width, arch length, and crowding.
Am J Orthod Dentofacial Orthop. 1999; 116: 691-6.

33. Yoshihara T, Matsumoto Y, Suzuki J, Sato N, Oguchi H. Effect of serial extraction alone on crowding: spontaneous changes in dentition after serial extraction.
Am J Orthod Dentofacial Orthop. 2000; 118: 611-6.

34. Sayin MO, Türkkahraman H. Effects of lower primary canine extraction on the mandibular dentition. Angle Orthod. 2006; 76: 31-5.

35. Bishara SE, Khadivi P, Jakobsen JR. Changes in tooth size-arch length relationships from the deciduous to the permanent dentition: a longitudinal study.
Am J Orthod Dentofacial Orthop. 1995; 108: 607-13.

36. Sampson WJ, Richards LC. Prediction of mandibular incisor and canine crowding changes in the mixed dentition. Am J Orthod. 1985; 88: 47-63.

37. Hagberg C. The alignment of permanent mandibular incisors in children. A longitudinal prospective study. Eur J Orthod. 1994; 16: 121-9.

38. Moorrees CFA, Chadna JM. Avaliable space for the incisors during dental development - A growth study based on physiologic age. Angle Orthod. 1965; 35: 12-22.

39. Andlin-Sobocki A, Bodin L. Dimensional alterations of the gingiva related to changes of facial/lingual tooth position in permanent anterior teeth of children. A 2-year longitudinal study. J Clin Periodontol. 1993; 20: 219-24.

40. Andlin-Sobocki A, Persson M. The association between spontaneous reversal of gingival recession in mandibular incisors and dentofacial changes in children. A 3-year longitudinal study. Eur J Orthod. 1994; 16: 229-39.

41. Joss-Vassalli I, Grebenstein C, Topouzelis N, Sculean A, Katsaros C. Orthodontic therapy and gingival recession: a systematic review. Orthod Craniofac Res. 2010; 13: 127-41.

42. Hugoson A, Koch G, Helkimo AN, Lundin SA. Caries prevalence and distribution in individuals aged 3-20 years in Jonkoping, Sweden, over a 30-year period (1973-2003). Int J Paediatr Dent. 2008; 18: 18-26.

43. Sundberg H. Changes in the prevalence of caries in children and adolescents in Sweden 1985-1994. Eur J Oral Sci. 1996; 104: 470-6.

44. Armfield JM. Towards a better understanding of dental anxiety and fear: cognitions vs. experiences. Eur J Oral Sci. 2010; 118: 259-64.

45. Holst A, Schroder U, Ek L, Hallonsten AL, Crossner CG. Prediction of behavior management problems in children. Scand J Dent Res. 1988; 96: 457-65.

46. Liddell A, Locker D. Changes in levels of dental anxiety as a function of dental experience. Behav Modif. 2000; 24: 57-68.

47. McNeil DW, Helfer AJ, Weaver BD, Graves RW, Kyle BN, Davis AM. Memory of pain and anxiety associated with tooth extraction. J Dent Res. 2011; 90: 220-4.

48. Milgrom P, Vignehsa H, Weinstein P. Adolescent dental fear and control: prevalence and theoretical implications. Behav Res Ther. 1992; 30: 367-73.

49. Raadal M, Strand GV, Amarante EC, Kvale G. Relationship between caries prevalence at 5 years of age and dental anxiety at 10. Eur J Paediatr Dent. 2002; 3: 22-6.

50. Skaret E, Raadal M, Berg E, Kvale G. Dental anxiety among 18-yr-olds in Norway. Prevalence and related factors. Eur J Oral Sci. 1998; 106: 835-43.

51. Oosterink FM, de Jongh A, Aartman IH. Negative events and their potential risk of precipitating pathological forms of dental anxiety. J Anxiety Disord. 2009; 23: 451-7.

52. Loeser JD, Treede RD. The Kyoto protocol of IASP Basic Pain Terminology. Pain. 2008; 137: 473-7.

53. McGrath PA. An assessment of children's pain: a review of behavioral, physiological and direct scaling techniques. Pain. 1987; 31: 147-76.

54. Tate AR, Acs G. Dental postoperative pain management in children. Dent Clin North Am. 2002; 46: 707-17.

55.   Young KD. Pediatric procedural pain. Ann Emerg Med. 2005; 45: 160-71.

56.   Versloot J, Veerkamp JS, Hoogstraten J. Children's self-reported pain at the dentist. Pain. 2008; 137: 389-94.

57.   Maggirias J, Locker D. Psychological factors and perceptions of pain associated with dental treatment. Community Dent Oral Epidemiol. 2002; 30: 151-9.

58.   Acs G, Drazner E. The incidence of postoperative pain and analgesic usage in children. ASDC J Dent Child. 1992; 59: 48-52.

59.   Acs G, Moore PA, Needleman HL, Shusterman S. The incidence of post-extraction pain and analgesic usage in children. Anesth Prog. 1986; 33: 147-51.

60.   Primosch RE, Nichols DL, Courts FJ. Comparison of preoperative ibuprofen, acetaminophen, and placebo administration on the parental report of postextraction pain in children. Pediatr Dent. 1995; 17: 187-91.

61.   Primosch RE, Nichols DL, Courts FJ. Risk factors associated with acute dental pain in children. ASDC J Dent Child. 1996; 63: 257-60.

62.   Brown SC, Hart G, Chastain DP, Schneeweiss S, McGrath PA. Reducing distress for children during invasive procedures: randomized clinical trial of effectiveness of the PediSedate. Paediatr Anaesth. 2009; 19: 725-31.

63.   van Wijk AJ, Hoogstraten J. Anxiety and pain during dental injections. J Dent. 2009; 37: 700-4.

64.   Chaushu G, Becker A, Zeltser R, Vasker N, Branski S, Chaushu S. Patients' perceptions of recovery after routine extraction of healthy premolars. Am J Orthod Dentofacial Orthop. 2007; 131: 170-5.

65.   Karjalainen S, Olak J, Soderling E, Pienihakkinen K, Simell O. Frequent exposure to invasive medical care in early childhood and operative dental treatment associated with dental apprehension of children at 9 years of age. Eur J Paediatr Dent. 2003; 4: 186-90.

66.   Klaassen MA, Veerkamp JS, Hoogstraten J. Changes in children's dental fear: a longitudinal study. Eur Arch Paediatr Dent. 2008; 9: 29-35.

67.   ten Berge M, Veerkamp JS, Hoogstraten J, Prins PJ. Childhood dental fear in the Netherlands: prevalence and normative data. Community Dent Oral Epidemiol. 2002; 30: 101-7.

68.   Klingberg G, Broberg AG. Dental fear/anxiety and dental behaviour management problems in children and adolescents: a review of prevalence and concomitant psychological factors. Int J Paediatr Dent. 2007; 17: 391-406.

69.   Meechan JG. Pain control in local analgesia. Eur Arch Paediatr Dent. 2009; 10: 71-6.

70.   Wondimu B, Dahllöf G. Attitudes of Swedish dentists to pain and pain management during dental treatment of children and adolescents. Eur J Paediatr Dent. 2005; 6: 66-72.

71.   Rasmussen JK, Frederiksen JA, Hallonsten AL, Poulsen S. Danish dentists' knowledge, attitudes and management of procedural dental pain in children: association with demographic characteristics, structural factors, perceived stress during the administration of local analgesia and their tolerance towards pain. Int J Paediatr Dent. 2005; 15: 159-68.

72. Armfield JM, Stewart JF, Spencer AJ. The vicious cycle of dental fear: exploring the interplay between oral health, service utilization and dental fear. BMC Oral Health. 2007; 7: 1. doi:10.1186/1472-6831-7-1.

73. Schuller AA, Willumsen T, Holst D. Are there differences in oral health and oral health behavior between individuals with high and low dental fear? Community Dent Oral Epidemiol. 2003; 31: 116-21.

74. Skaret E, Raadal M, Berg E, Kvale G. Dental anxiety and dental avoidance among 12 to 18 year olds in Norway. Eur J Oral Sci. 1999; 107: 422-8.

75. Skaret E, Raadal M, Kvale G, Berg E. Factors related to missed and cancelled dental appointments among adolescents in Norway. Eur J Oral Sci. 2000; 108: 175-83.

76. Sohn W, Ismail AI. Regular dental visits and dental anxiety in an adult dentate population. J Am Dent Assoc. 2005; 136: 58-66.

77. Vika M, Raadal M, Skaret E, Kvale G. Dental and medical injections: prevalence of self-reported problems among 18-yr-old subjects in Norway. Eur J Oral Sci. 2006; 114: 122-7.

78. Vika M, Skaret E, Raadal M, Ost LG, Kvale G. Fear of blood, injury, and injections, and its relationship to dental anxiety and probability of avoiding dental treatment among 18-year-olds in Norway. Int J Paediatr Dent. 2008; 18: 163-9.

79. ten Berge M, Veerkamp JS, Hoogstraten J. The etiology of childhood dental fear: the role of dental and conditioning experiences. J Anxiety Disord. 2002; 16: 321-9.

80. Thomson WM, Broadbent JM, Locker D, Poulton R. Trajectories of dental anxiety in a birth cohort. Community Dent Oral Epidemiol. 2009; 37: 209-19.

81. Thomson WM, Locker D, Poulton R. Incidence of dental anxiety in young adults in relation to dental treatment experience. Community Dent Oral Epidemiol. 2000; 28: 289-94.

82. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA. 1992; 268: 2420-5.

83. Ackerman M. Evidence-based orthodontics for the 21st century. J Am Dent Assoc. 2004; 135: 162-7.

84. Altman D. Principles of statistical analysis. In: Practical Statistics for Medical Research. Altman D (editor) Boca Raton, Florida Chapman& Hall / CRC; 1999; pp 152-178.

85. Antczak AA, Tang J, Chalmers TC. Quality assessment of randomized control trials in dental research. II. Results: periodontal research. J Periodontal Res. 1986; 21: 315-21.

86. Colditz GA, Miller JN, Mosteller F. How study design affects outcomes in comparisons of therapy. I: Medical. Stat Med. 1989; 8: 441-54.

87. Moorrees CF, Reed RB. Biometrics of crowding and spacing of the teeth in the mandible. Am J Phys Anthropol. 1954; 12: 77-88.

88. Norderval K, Wisth PJ, Boe OE. Mandibular anterior crowding in relation to tooth size and craniofacial morphology. Scand J Dent Res. 1975; 83: 267-73.

89. Richardson ME. The relationship between the relative amount of space present in the deciduous dental arch and the rate and degree of space closure subsequent to the extraction of a deciduous molar. Dent Rec. 1965; 16: 111-8.

90. Richmond S. Recording the dental cast in three dimensions. Am J Orthod Dentofacial Orthop. 1987; 92: 199-206.

91. Van Kirk LE, Jr. Assessment of malocclusion in population groups. Am J Public Health Nations Health. 1959; 49: 1157-63.

92. Mew J. Relapse following maxillary expansion. A study of twenty-five consecutive cases. Am J Orthod. 1983; 83: 56-61.

93. Beazley WW. Assessment of mandibular arch length discrepancy utilizing an individualized arch form. Angle Orthod. 1971; 41: 45-54.

94. Betteridge MA. Index for measurement of lower labial segment crowding. Br J Orthod. 1976; 3: 113-6.

95. Herren P, Schmoker R, Jordi T. Arch shape and space balance determined by arcogramme technique. Trans Eur Orthod Soc. 1973: 61-73.

96. Musich DR, Ackerman JL. The catenometer: a reliable device for estimating dental arch perimeter. Am J Orthod. 1973; 63: 366-75.

97. Pepe SH. Polynomial and catenary curve fits to human dental arches. J Dent Res. 1975; 54: 1124-32.

98. Naraghi S, Andren A, Kjellberg H, Mohlin BO. Relapse tendency after orthodontic correction of upper front teeth retained with a bonded retainer. Angle Orthod. 2006; 76: 570-6.

99. Harris EF, Vaden JL, Williams RA. Lower incisor space analysis: a contrast of methods. Am J Orthod Dentofacial Orthop. 1987; 92: 375-80.

100. Johal AS, Battagel JM. Dental crowding: a comparison of three methods of assessment. Eur J Orthod. 1997; 19: 543-51.

101. Alcan T, Ceylanoglu C, Baysal B. The relationship between digital model accuracy and time-dependent deformation of alginate impressions. Angle Orthod. 2009; 79: 30-6.

102. Asquith J, Gillgrass T, Mossey P. Three-dimensional imaging of orthodontic models: a pilot study. Eur J Orthod. 2007; 29: 517-22.

103. Bootvong K, Liu Z, McGrath C, Hagg U, Wong RW, Bendeus M, et al. Virtual model analysis as an alternative approach to plaster model analysis: reliability and validity. Eur J Orthod. 2010; 32: 589-95.

104. Costalos PA, Sarraf K, Cangialosi TJ, Efstratiadis S. Evaluation of the accuracy of digital model analysis for the American Board of Orthodontics objective grading system for dental casts. Am J Orthod Dentofacial Orthop. 2005; 128: 624-9.

105. Gracco A, Buranello M, Cozzani M, Siciliani G. Digital and plaster models: a comparison of measurements and times. Prog Orthod. 2007; 8: 252-9.

106. Leifert MF, Leifert MM, Efstratiadis SS, Cangialosi TJ. Comparison of space analysis evaluations with digital models and plaster dental casts. Am J Orthod Dentofacial Orthop. 2009; 136: 1-4.

107. Mok CW, Zhou L, McGrath C, Hagg U, Bendeus M. Digital images as an alternative to orthodontic casts in assessing malocclusion and orthodontic treatment need. Acta Odontol Scand. 2007; 65: 362-8.

108. Mullen SR, Martin CA, Ngan P, Gladwin M. Accuracy of space analysis with emodels and plaster models. Am J Orthod Dentofacial Orthop. 2007; 132: 346-52.

109. Paredes V, Gandia JL, Cibrian R. New, fast, and accurate procedure to calibrate a 2-dimensional digital measurement method. Am J Orthod Dentofacial Orthop. 2005; 127: 518-9.

110. Quimby ML, Vig KW, Rashid RG, Firestone AR. The accuracy and reliability of measurements made on computer-based digital models. Angle Orthod. 2004; 74: 298-303.

111. Rossouw PE, Benatar M, Stander I, Wynchank S. A critical comparison of three methods for measuring dental models. J Dent Assoc S Afr. 1991; 46: 223-6.

112. Stevens DR, Flores-Mir C, Nebbe B, Raboud DW, Heo G, Major PW. Validity, reliability, and reproducibility of plaster vs digital study models: comparison of peer assessment rating and Bolton analysis and their constituent measurements. Am J Orthod Dentofacial Orthop. 2006; 129: 794-803.

113. Tomassetti JJ, Taloumis LJ, Denny JM, Fischer JR, Jr. A comparison of 3 computerized Bolton tooth-size analyses with a commonly used method. Angle Orthod. 2001; 71: 351-7.

114. Zilberman O, Huggare JA, Parikakis KA. Evaluation of the validity of tooth size and arch width measurements using conventional and three-dimensional virtual orthodontic models. Angle Orthod. 2003; 73: 301-6.

115. Dalstra M, Melsen B. From alginate impressions to digital virtual models: accuracy and reproducibility. J Orthod. 2009; 36: 36-41.

116. Santoro M, Galkin S, Teredesai M, Nicolay OF, Cangialosi TJ. Comparison of measurements made on digital and plaster models. Am J Orthod Dentofacial Orthop. 2003; 124: 101-5.

117. Surbeck B, Årtun J. Associations between initial, posttreatment and postretention alignment of maxillary anterior teeth. Am J Orthod. 1998; 113: 186-95.

118. Ewers R, Seemann R, Krennmair G, Schicho K, Kurdi AO, Kirsch A, et al. Planning implants crown down-a systematic quality control for proof of concept. J Oral Maxillofac Surg. 2010; 68: 2868-78.

119. Widmann G, Keiler M, Zangerl A, Stoffner R, Longato S, Bale R, et al. Computer-assisted surgery in the edentulous jaw based on 3 fixed intraoral reference points. J Oral Maxillofac Surg. 2010; 68: 1140-7.

120. Eriksson A, Ockert-Eriksson G, Lockowandt P. Accuracy of irreversible hydrocolloids (alginates) for fixed prosthodontics. A comparison between irreversible hydrocolloid, reversible hydrocolloid, and addition silicone for use in the syringe-tray technique. Eur J Oral Sci. 1998; 106: 651-60.

121. Utz KH, Muller F, Luckerath W, Fuss E, Koeck B. Accuracy of check-bite registration and centric condylar position. J Oral Rehabil. 2002; 29: 458-66.

122. Cuthbert MI, Melamed BG. A screening device: children at risk for dental fears and management problems. ASDC J Dent Child. 1982; 49: 432-6.

123. Aartman IH, van Everdingen T, Hoogstraten J, Schuurs AH. Self-report measurements of dental anxiety and fear in children: a critical assessment. ASDC J Dent Child. 1998; 65: 252-8.

124. Björk A, Krebs A, Solow B. A method for epidemiological registration of malocclusion. Acta Odontol Scand. 1964; 22: 27-41.

125. Karolinska University Hospital ANOPIVA-kliniken. Riktlinjer vid smärta. Solna, Sweden; 2009.

126. Frankl SS, FR, Fogels H. Should the parent remain with the child in the dental operatory? ASDC J Dent Child. 1962; 29: 150-63.

127. Gustafsson A, Arnrup K, Broberg A, Bodin L, Berggren U. Child dental fear as measured with the CFSS-DS; the impact of referral staus and type of informant (child vs. parent). Community Dent Oral Epidemiol. 2010 Jan 14. [Epub ahead of print].

128. Altman D. Some common problems in medical researc. In: Practical Statistics for Medical Research. Altman D (editor) Boca Raton, Florida Chapman& Hall / CRC; 1999; pp 398-432.

129. Klingberg G, Berggren U, Noren JG. Dental fear in an urban Swedish child population: prevalence and concomitant factors. Community Dent Health. 1994; 11: 208-14.

130. Sjögren A, Arnrup K, Lennartsson B, Huggare J. Mandibular incisor alignment and dental arch changes 1 year after extraction of deciduous canines. Eur J Orthod. 2011 Feb 23. doi:10.1093/ejo/cjr028.

131. Armfield JM, Milgrom P, Armfield J. A clinician guide to patients afraid of dental injections and numbness. SAAD Dig. 2011; 27: 33-9.

132. Holst A, Ek L. Effect of systematized "behavior shaping" on acceptance of dental treatment in children. Community Dent Oral Epidemiol. 1988; 16: 349-55.

133. Klingberg G. Dental fear and behavior management problems in children. A study of measurement, prevalence, concomitant factors, and clinical effects. Swed Dent J Suppl. 1995; 103: 1-78.