

INTERCEPTIVE TREATMENT OF PALATALLY DISPLACED CANINES

*Studies of treatment effect and patients' perception and
methodological evaluation of 3D measurements of CBCT*

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The cover page illustration: Clinical photo and cone beam computed tomography image of bilateral palatally displaced canines. This patient was randomized for extraction of the right deciduous canine also shown on the clinical photo.

Interceptive treatment of palatally displaced canines- *Studies of treatment effect and patients' perception and methodological evaluation of 3D measurements of CBCT*

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To Halil, Teoman, Melisa
&
Saniye, Mehmet

“Science is the most reliable guide in life”

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ABSTRACT

Interceptive Treatment Of Palatally Displaced Canines

Studies of treatment effect and patients' perception and methodological evaluation of 3D measurements of CBCT

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Background: In 2 % of the Swedish population the canine fails to erupt and in 85 % of the cases the canine is palatally displaced. The most common interceptive treatment of palatally displaced canines (PDCs) is extraction of the deciduous canine at the age of 10-13 years and follow-up of the canine for 12 months to monitor whether its eruption path will normalize. In case the canine does not erupt spontaneously, a surgical exposure and orthodontic treatment is commonly considered. However, an early and easy interceptive treatment is preferable both from a health economic perspective as well as to reduce the risk of root resorption of the adjacent teeth and to avoid later comprehensive treatment/s.

Objective: The aims of this thesis were: to develop a reliable and valid method to measure the position of PDCs on 3D images (Cone Beam Computed Tomography, CBCT) (paper I). To evaluate children's subjective experience before, during and after extraction of the deciduous canine (paper II). To compare whether extraction of the deciduous canine more often results in spontaneous eruption of the permanent canine compared to non extraction (paper III) and to find out which clinical cases benefit from interceptive extraction (paper IV).

Materials and Methods: In total 89 PDCs in 67 children (10-13 years of age) were randomly assigned to either have their deciduous canine extracted (extraction group, EG) or not extracted (control group, CG). Clinical and radiographic examinations were carried out at baseline (T0), after 6 (T1) and 12 months (T2) in both groups. 3D images of 20 patients out of 67 were randomly chosen and measured by two dentists at different occasions. The validity of the method to measure the displaced canines was assessed by comparing measurements on the 3D images with measurements on a dry skull. Children who had extraction of the deciduous canine were asked to answer a questionnaire before, the same day as and one week after the extraction.

Results:

- The radiographic method to measure and assess the position of the PDCs on 3D images was reliable and had a high validity (paper I).
- The reported pain and discomfort were in overall low. The injection was experienced as more painful compared to the extraction, and analgesics were taken the first evening by 42 % of the children (paper II).
- Extraction of the deciduous canine resulted in eruption of the PDCs in 69 % of the cases compared to 39% in the CG. Significantly more positional changes and a shorter mean eruption time were seen in the EG (paper III).
- PDCs with a mesioangular angle of 103°, distance of the canine cusp tip-dental arch plane of 2.5 mm and distance of the canine cusp tip-midline of 11 mm in patients < 11 years will likely erupt without interceptive extraction. However, PDCs with a less favourable position, i.e. a mesioangular angle of 116 degrees, canine cusp tip-dental arch plane of 5mm and canine cusp tip-midline of 6 mm, in patients > 11-12 years old, will not erupt spontaneously in spite of interceptive extraction of the deciduous canine (paper IV).

Conclusions: The radiographic method to measure and assess the position of the PDCs was reliable and valid and can be used in future studies. Adequate analgesics and dose should be given to children before and after extracting the deciduous canine. Interceptive extraction of the deciduous canine at 10-13 years of age was effective and will result in significantly more spontaneous eruptions of the permanent canine compared to a control group. The cut-off points may be a helpful tool for the clinician to choose whether the patient benefit from interceptive extraction of the deciduous canine or whether immediate surgical exposure should be performed.

Keywords: palatally displaced canines, orthodontics, interceptive treatment, extraction of deciduous canine, cone beam computed tomography, patient perception, pain, questionnaire

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SUMMARY IN SWEDISH

Bakgrund: I ca 2 % av en svensk population (ca 1900 nya fall/år) bryter hörntanden inte fram (retinerad) och i 85 % av fallen är tanden retinerad i gommen. Retention av hörntanden utgör en risk för att skada de permanenta framtändernas rötter och vid de allvarligaste formerna kan dessa skador orsaka förlust av en eller flera framtänder i överkäken. Den vanligast förebyggande behandlingen som utförs är att avlägsna mjölkhörntanden vid 10-13 års ålder och avvakta i 12 månader för att den permanenta tanden skall bryta fram. I de fall där hörntanden inte bryter fram, görs en kirurgisk exponering följt av tandreglering för aktiv framdragning av hörntanden. En tidig och enkel förebyggande behandling är att föredra både ur ett hälsoekonomiskt perspektiv men också för att minska risken för skador på de permanenta framtändernas rötter och minska behovet för ytterligare behandling.

Syfte: Syftet med denna avhandling var att utveckla en tillförlitlig mätmetod av retinerade hörntänder på 3D röntgenbilder (studie I). Att undersöka barnens subjektiva upplevelse inför, under och efter borttagning av mjölkhörntanden (studie II). Och att med en randomiserad kontrollerad studie undersöka om förebyggande borttagning av mjölkhörntanden är en effektiv behandling (studie III) samt i vilka fall denna behandling är gynnsamt (studie IV).

Material och metod: Sextiosju barn med 89 retinerade hörntänder i 10-13 års åldern, deltog i projektet och blev lottade till att antingen få sin mjölkhörntand borttagen (studiegrupp) eller inte (kontrollgrupp). Klinisk och röntgenologisk undersökning gjordes vid start, efter 6 respektive 12 månader på samtliga barn. Röntgenbilder på 20 av 67 barn mättes vid två olika tillfällen utav två tandläkare. Barnen som fick sina mjölkhörntänder borttagna fick svara på ett frågeformulär före, samma dag och en vecka efter borttagningen av tanden.

Resultat:

- Den mätmetod som utvecklades för att mäta positionen på 3D röntgenbilder av den retinerade hörntanden var tillförlitlig.
- Den rapporterade smärtan och obehaget vid och efter borttagning av mjölkhörntanden i överlag var låg. Trots det togs smärtlindring av 42 % av barnen första kvällen efter tandutdragningen. Injektionen upplevdes som mera smärtsam än borttagningen av tanden.
- Borttagning av mjölktdanden resulterade i att den permanenta tanden kom fram i 69 % av fallen jämfört med 39 % i kontrollgruppen.
- Retinerade hörntänder med 103° mesioangulär vinkel respektive 2.5 mm från hörntandskuspspets till tandbåge och 11 mm från hörntandskuspspets till mittlinjen hos patienter yngre än 11 år kommer mest troligen att eruptera utan förebyggande extraktion av mjölkhörntanden. Retinerade hörntänder med ogynnsammare position d.v.s med 116° mesioangulär vinkel respektive 5 mm från hörntandskuspspets till tandbåge och 6 mm från hörntandskuspspets till mittlinjen hos patienter äldre än 11-12 år kommer inte att spontant eruptera trots förebyggande extraktion av mjölkhörntanden.

Konklusion: Den radiologiska mätmetoden som utvecklades för att utvärdera positionen av retinerade hörntänder är tillförlitlig och kan användas i framtida studier. Lämplig smärtlindring och dos bör ges till barn- och ungdomar innan och efter utdragning av mjölkhörntanden. Borttagning av mjölkhörntanden vid 10-13 års ålder på barn som har en permanent hörntand i gommen är en effektiv förebyggande behandling utom i de allra lättaste och svåraste fallen. I gränsfall där hörntänderna som enligt bestämda mätvärden låg gynnsamt till kan man överväga om förebyggande borttagning av mjölktdanden är nödvändig medan man i de fall där hörntanden låg mycket ogynnsamt till kan överväga att frilägga tanden kirurgiskt och dra fram den aktivt utan föregående uttagning av mjölktdanden.

PREFACE

This thesis is based on following four papers, which will be referred in to the text by their Roman numerals I-IV:

- I **Naumova, J** Palm R, Kjellberg H. Cone-beam computed tomography for assessment of palatal displaced canine position - A methodological study. *The Angle Orthodontist* 2014 May; 84(3): 459-466

- II **Naumova J**, Kjellberg H, Kurol J, Mohlin B. Pain, discomfort, and use of analgesics following the extraction of primary canines in children with palatally displaced canines. *International Journal of Paediatric Dentistry* 2012 Jan; 22(1): 17-26

- III **Naumova J**, Kurol J, Kjellberg H. Extraction of the deciduous canine as an interceptive treatment in children with palatal displaced canines - Part I: Shall we extract the deciduous canine or not? *The European Journal of Orthodontics* 2014;doi: 10.1093/ejo/cju040

- IV **Naumova J**, Kurol J, Kjellberg H. Extraction of the deciduous canine as an interceptive treatment in children with palatal displaced canines - Part II: Possible predictors and cut-off points for a spontaneous eruption. *Accepted for publication to The European Journal of Orthodontics*

ABBREVIATIONS

ANOVA	Analyse of Variance
CBCT	Cone Beam Computed Tomography
CG	Control Group
CI	Confidence Interval
CT	Computed Tomography
DA	Dental Anxiety
DAS	Dental Anxiety Scale
DBMP	Dental Behaviour Management Problems
DF	Dental Fear
EG	Extraction of the deciduous Canine
ECMG	Extraction deciduous Canine and first Molar concomitant Group
EHG	Extraction/HeadGear
HG	HeadGear
PMC	Palpation of permanent Maxillary Canine bulge
ICC	Intraclass Correlation Coefficient
ITT	Intention-To-Treat
N	Number
NS	Not significant
p	Level of significance
PA	Postero-anterior cephalogram
PDC	Palatally Displaced Canine
RCT	Randomized Clinical Trial
RME	Rapid Maxillary Expansion
SBU	The Swedish Council on Health Technology Assessment
SD	Standard Deviation
SFSS-DS	Children's Fear Survey Schedule- Dental Subscale
SPSS	Statistical Package of Social Science
SAS	Statistical Analysis System
RME/HG	Rapid Maxillary Expansion/Headgear
RME/TPA/EG	Rapid Maxillary Expansion/TransPalatal Arch/Extraction of the deciduous Canine
TPA	TransPalatal Arch
TPA/EG	TransPalatal Arch/Extraction of the deciduous canine
VAS	Visual Analogue Scale
2D	Two-dimensional
3D	Three-dimensional
Sn	Sensitivity
Sp	Specificity
ROC	Receiver-operating characteristic
AUC	Area under the curve

INTRODUCTION

Diagnosis and treatment of palatally displaced canines (PDCs) are a challenge that requires coordination of care by several healthcare providers e.g. general dentists, orthodontists, pediatric dentists, oral surgeons and periodontologists. Clinical examination along with selective radiographs are required to assure early diagnosis of PDCs and timely interceptive therapy in the mixed dentition patients. Failure to diagnose and manage the displaced canine could result in more complex treatment and risk for damage to the adjacent teeth, which may lead to a loss of anterior teeth.

A Cochrane review was published some years ago (Parkin et al., 2009) evaluating the effect of extracting the deciduous canine on the eruption of the palatally displaced canine, since previous studies (Kurol and Ericson, 1988; Power and Short, 1993; Baccetti, 2008) had suggested that, if the deciduous canine is removed at the right time, palatal eruption of the canine might be avoided. However, the review group concluded that there is no evidence of the effect of extracting the deciduous canine as an interceptive treatment in the mixed dentition. The review also stated that there were no trials reporting the outcome of pain, patient satisfaction or incidence of root resorption following extraction of the deciduous canine. The Cochrane review became the inspiration for the four studies in this thesis.

Normal development of the maxillary permanent canine

The maxillary canines have the longest period of development: the calcification starts already at the age of 1 and around the age of 6-7 the calcification of the enamel is completed (Dewel, 1949). According to the Belfast Growth Study (Coulter and Richardson, 1997), the canine travels almost 22 mm between the age

of 5 and 15 years. The canine follows a mesial path from its point of formation, lateral to the piriform fossa, until it reaches the distal aspect of the lateral incisor root. The canine is guided by the lateral incisor root to erupt in a more vertical position until it fully erupts adjacent to the lateral. Almost three quarters of the root is formed before the canine erupts and the root formation is completed around 2 years after eruption (Nanda, 1983). The permanent canine is among the last teeth to erupt in the maxilla and the mean age of emergence varies depending on the population that has been studied. In American children, the mean age of eruption was 12.3 years for girls and 13.1 years for boys (Hurme, 1949). In a Swedish population, the mean eruption time in girls was 10.8 years and in boys 11.6 years (Hägg and Taranger, 1986), while in a Japanese study, the mean ages were somewhat earlier, 10.3 years and 10.8 years, respectively (Sato, 1990).

Definition of palatal displaced canine (PDC)

According to a newly published systematic review (Naoumova et al., 2011), there is still no uniform definition and/or classification of PDC available in the literature and consequently many authors have different ways to describe and define PDC. There is some confusion in the literature about the definition of PDC and some examples are given below:

- An impacted tooth is one *” whose eruption is considerable delayed, and for which there is clinical or radiographic evidence that further eruption may not take place”* (Thilander and Jakobsson, 1968).
- *”Unerupted canine after complete root development or if the contralateral tooth was erupted for at least 6 months with complete root formation”* (Lindauer et al., 1992).
- *”A condition in which a tooth is embedded in the alveolus so that its eruption is prevented or the tooth is locked in position by bone or by the adjacent teeth”* (Kuftinec et al., 1995).

- *“Developmental dislocation to a palatal site often resulting in tooth impaction requiring surgical and orthodontic treatments” (Peck et al., 1996).*
- *”Intraosseous palatal position of the maxillary permanent canines.” (Baccetti et al., 2008).*

Prevalence

The maxillary canine is the second most frequently displaced tooth in the dental arch, after the third molar. The reported prevalence rates of PDC vary from 0.9 % to 2.8 %, depending on the patient’s ethnic origin, gender, definition, and the diagnostic methods used (Rayne, 1969; Thilander and Myrberg, 1973; Shah et al., 1978; Grover and Lorton, 1985). Displacements of maxillary canines are 10 to 20 times more common than of mandibular canines, and palatal displacement of the maxillary canine occurs more frequently (85%) than labial displacement (15%) (Dachi and Howell, 1961; Thilander and Jakobsson, 1968; Ericson and Kuroi, 1988; Peck et al., 1994). PDCs occur also twice as frequently in females than in males and unilateral displacement is more common than bilateral (90-92% versus 8-10%) (Nordenram and Strömberg, 1966; Becker et al., 1981; Ericson and Kuroi, 1988; Peck et al., 1994). In a Caucasian population, maxillary canine displacement is 5 times more common than in an Asian population and, in addition, the majority of canines in Caucasian’s are palatally displaced, while buccal displacement is more common among Asians (Oliver et al., 1989).

Aetiology

The aetiology of PDCs is still unknown; however, two theories have most often been mentioned in the literature: the guidance and the genetic theory. The guidance theory suggests that the root of the lateral incisor serves as a guide for the eruption of the canine, and if different predisposing factors interfere with the eruption path of the canine, it will not erupt. The most commonly mentioned predisposing factors

in the literature are: congenitally missing maxillary lateral incisors, malformed or dilacerations of the lateral incisor root, peg-shaped later incisors, supernumerary teeth, prolonged retention or early loss of the deciduous canine, ankylosis of the permanent canine, odontomas, cyst or neoplasm, transposition of teeth and degree of dental crowding (Becker et al., 1981; Jacoby 1983; Becker et al., 1984; Brin et al., 1986; Oliver et al., 1989; Zilberman et al., 1990; Bishara 1992; Brin et al., 1993).

The genetic theory supports a genetic aetiology for canine displacement and is often present with other dental abnormalities including tooth size, shape, tooth number and structure, which have a hereditary background (Peck et al., 1994; Peck et al., 1995; Peck et al., 1996). In a family study, Pirinen and co-workers (1996), concluded that canine displacement has a genetic or familiar pattern of inheritance and belongs to the spectrum of dental anomalies related to incisor-premolar hypodontia. Different dental anomalies related to hypodontia have previously been described by many authors such as: small tooth size, peg shaped maxillary laterals, infraocclusion of primary molars, short root anomaly and invaginations in incisors (Alvesalo and Portin, 1969; Garn and Lewis, 1970; Svinhufvud et al., 1988; Bjerklin et al., 1992; Kjaer, 1995; Peck et al., 1996; Pirinen et al., 1996; Garib et al., 2010). These findings have also been supported by the family studies from Peck et al. (1994, 1995, 1996) who suggested a multifactorial genetic pattern of inheritance for displacement of maxillary canines.

Sequelae of canine impaction

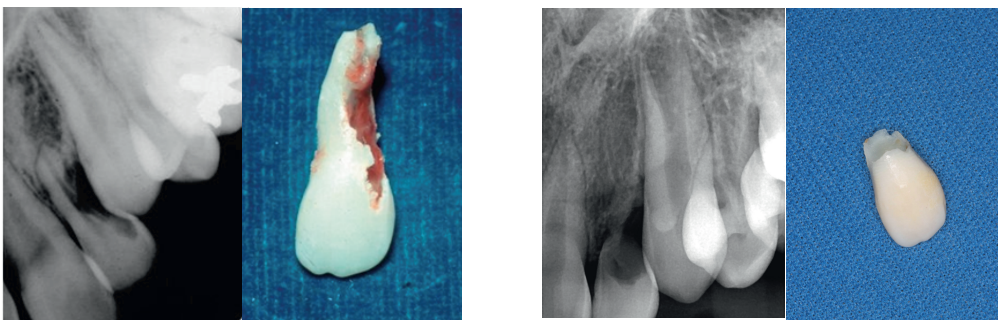
The most frequent consequence of PDC is impaction of the canine and the main risk of canine impaction is external root resorption of adjacent teeth with a potential result in tooth loss (Figure 1). Resorption of the lateral incisors is more common than of the central incisors (Arens, 1995; Rimes et al., 1997; Saldarriaga and Patiño, 2003). Ericson and Kurol (1987, 1987) found, using 2 periapical radiographs, lateral incisor root resorption in about 12 % of the buccally or

palatally displaced canine population. Using CT examination of the maxilla in 107 children with PDC, the rate of resorption of the lateral incisors increased to 38 % (Ericson and Kurol, 2000). Of the central incisors nine percent showed root resorption. Thus the amount of root resorption detected on CT images was 50% higher than on 2D radiographs. The frequency of root resorption caused by the PDCs has been reported by several studies in the literature to be around 50% (Bjerklin and Kurol, 2006; Walker et al., 2005; Liu et al., 2008).

The greatest risk to cause root resorption of the lateral incisor is when the ectopically erupting canine has a medial inclination with a well-developed root and shows an overlapping of more than 50 % of the lateral incisors on radiographs (Ericson and Kurol, 1987). The most common location of resorptions of the lateral incisors is the apical and middle third of the root, with a frequency of 13 % and 85 %, respectively (Ericson and Kurol, 1987; Ericson and Kurol, 2000). Incisor resorption is more common in females than in males: however, no gender differences were found regarding the severity or the location of the root resorption (Ericson and Kurol, 1987; Ericson and Kurol, 2000; Bjerklin and Ericson, 2006).

Other more rare complications with untreated impacted canines are: resorption of first premolars, formation of follicular cysts, canine ankylosis, loss of vitality of the incisors and poor aesthetics when the primary canine exfoliates (Shafer et al., 1984).

Figure 1. Two clinical cases with extracted lateral incisors that have been resorbed by ectopic erupting canines. (Courtesy of Professor Emeritus Jüri Kurol and associate professor Heidrun Kjellberg).



Diagnosis

Three diagnostic procedures can be used to evaluate whether a maxillary canine is erupting palatally or not. These methods are: inspection, palpation and radiographs.

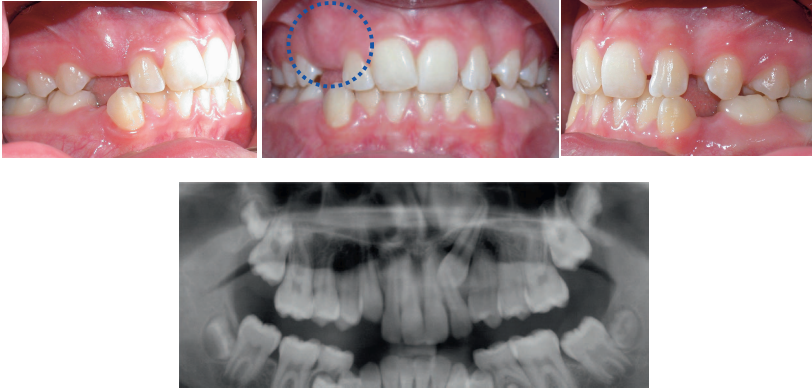
Inspection

Various clinical signs of canine displacement can be observed by inspection only. These signs include: delayed eruption of the permanent successor, persisting (overretained) deciduous canine, asymmetry in the exfoliation and eruption between the right and left side in the maxilla, absence of labial bulge or presence of a palatal bulge. Another clinical sign is the position of the adjacent lateral incisors. In cases where the maxillary canine is palatally placed, the lateral incisor might be retroclined in relation to the central incisor, since the canine causes the root to tip labially and the crown palatally and visa versa in buccally placed canines. In very rare cases, the crown of the central incisor can be malpositioned by the palatally positioned canine (Shapira and Kuftinec, 1998; Bishara, 1998; Jacobs, 1999; Ngan et al., 2005; Bedoya et al., 2009).

Palpation

A labial bulge is normally palpable about 1 to 1.5 years before the maxillary canine emerges: therefore the absence of the labial bulge after the age of 10 indicates that the canine might be displaced from its normal position and radiographs should be taken to confirm the diagnosis (Figure 2). An obvious palpable bilateral asymmetry in children older than 10 years indicates that the permanent canine is palatally displaced, while in children younger than 10 years, asymmetries in palpation are considered as a vertical difference in the eruption rate (Ericson and Kurol, 1986). One may also manipulate the deciduous canine to determine whether it is mobile. Non-significant mobility of the deciduous canine beyond the age of 13 years strongly indicates displacement of the permanent canine. (Shapira and Kuftinec, 1998; Bishara, 1998; Jacobs, 1999; Ngan et al., 2005; Bedoya et al., 2009).

Figure 2. On the right side in the maxilla a labial bulge is palpated; however, on the left side where a labial bulge is absent, the canine is palatally displaced. (Courtesy of Dr Helené Carlander-Lindén)



Radiographs

Accurate radiographs are essential in diagnosing the position of the canine and its relation to the adjacent teeth as well as assessing root resorption of the lateral and/or central incisors but they are also necessary to determine the prognosis and the best mode of treatment. In the past, several radiographic methods have been used. The most common methods can be divided into intraoral and extraoral techniques. The intraoral techniques include occlusal and periapical projections. Occlusal radiographs have been used to determine the buccolingual position of the displaced tooth and its relation to the midline (Jacobs, 1999). However, the traditional method of diagnosing maxillary canines has been the use of two periapical views, known as the buccal object rule or Clark's Rule (Clark, 1909). Ericson and Kuroi (1987) found the canine position was correctly evaluated that in 92 % of the cases when using this method.

The extraoral techniques include panoramic, posterior-anterior, lateral cephalometric radiographs and computed tomography (CT). In the panoramic technique, the tube of the machine moves in a standardized arch around the patient's head, resulting in a projection that is not always orthoradial. Therefore, the x-ray beam may not be perpendicular to the dental arch at all times. Because of

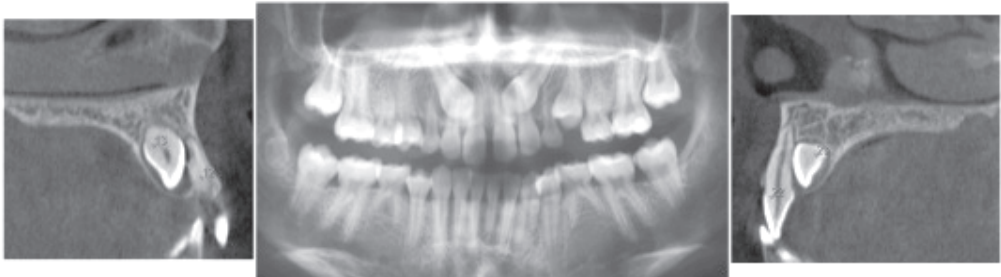
this uncertainty, a different relationship between the canine and the lateral incisor can be displaced compared to a posterior-anterior x-ray. Furthermore, structures closer to the x-ray source appear more magnified than those closer to the detector, which gives an indication to judge whether the canine position is buccal or palatal in relation to the dental arch. In posterior-anterior radiographs, Sambataro et al. (2005) found that “the closer the canine crowns are to the midsagittal plane and the larger the posterior portion of the hemimaxilla is, the higher the probability of canine impaction” by making two predictive measurements: “the distance from the center of the crown of the maxillary permanent canine to the midsagittal plane and the transverse width of the maxilla on the same side as the evaluated canine”.

Lateral cephalometric radiographs on the other hand are helpful in evaluating the anterior-posterior position of the canine, as well as its inclination and vertical location in the alveolus (Ericson and Kuroi, 1987; Jacobs, 1999; Bedoya et al., 2009; Algerban et al., 2009).

There are several disadvantages of conventional 2D images, such as: distortion, superimposition of structures, errors in projection, imaging artefacts and variation in magnification. Therefore, 2D radiographs lack the accuracy necessary for assessing resorption of lateral and/or central incisors, especially with mild or early resorption (Baumrind and Frantz, 1971; Major et al., 1994; Elefteriadis and Athanasiou, 1996). CT can detect the location of the displaced canine as well as diagnose associated lesions such as root resorption of adjacent teeth and the amount of bone surrounding each tooth. However, since the cost and radiation doses are high with CT, its clinical use has been limited (Ericson and Kuroi, 1978; Ericson and Bjerklind 2001; Bodner et al., 2001). In the 1990s, a new system, cone-beam computed tomography (CBCT), with reduced radiation exposure compared to conventional CT and 3D imaging was presented for studying of dental structures. This method not only identifies and localizes the canine and the condition of the surrounding teeth and structures but also gives the clinician helpful information for the surgical and orthodontic treatment of the displaced canine

(Figure 3). Different CBCT systems are available on the market, but they all use the same technology with slight differences in the detector type. The CBCT machines emit a conical-shaped X-ray beam and make it possible to reconstruct the area of interest in three dimensions. The digital data can then be exported to acquisition software to provide axial, frontal and sagittal views, which can be used for advanced analysis (Ziegler et al., 2002; Kau et al., 2005; Ludlow et al., 2006). CBCT has been proven in many studies to be superior to other radiographic methods in visualizing the craniofacial field and diagnosing displaced erupting canines and the adjacent teeth (Botticelli et al., 2010; Haney et al., 2010; Alqerban et al., 2011).

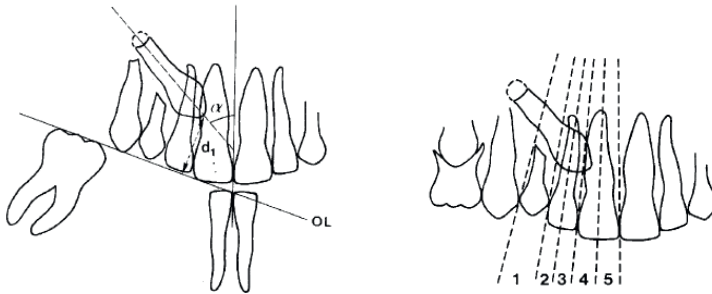
Figure 3. A 14-year-old girl with bilateral palatally displaced canines in the maxilla. On the 2D radiographs potential root resorption on the adjacent teeth is not visible, but on the 3D images severe root resorption into the pulp on the right lateral incisor can be diagnosed as well as minor root resorption on the left lateral incisor (Own patient of J.N).



Assessing the canine position on radiographs

Ericson and Kurol (1988) used linear, angular and sector measurements (Figure 4) to assess the effectiveness of interceptive extraction of the deciduous canine. Some researchers have thereafter tried to develop a method to predict the risks of impaction of the canine (Lindauer et al., 1992; Warford et al., 2003), to grade the severity of the impaction (Koutzoglou and Kostaki, 2013) and to assess the difficulty of the treatment (Kau et al., 2009; Dalessandri et al., 2013), which are all a modification of the measurement method of Ericson and Kurol (1988).

Figure 4. Inclination of the canine to the midline measured in alpha angle, distance (d_1) of the canine cusp to the occlusal plane (OL). Canine crown position in sectors 1-5. (Reprinted with permission of the publisher from Ericson and Kuroi, 1988.)



Lindauer et al. (1992), used four different sectors to localize the canine cusp tip on panoramic radiographs and its relationship to the adjacent lateral incisors (Figure 5). By using this method, the authors found that 78 % of the canines that are destined to become impacted can be identified. All of these canines were in sectors II-IV. Warford et al. (2003), used the method by Lindauer et al. (1992), and confirmed their results with their finding that 82 % of the impacted canines were in sectors II-IV.

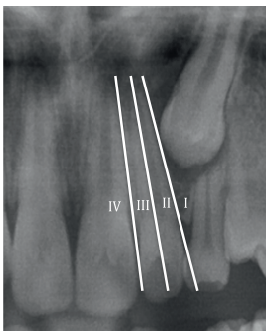


Figure 5. Sector definitions according to Lindauer et al., 1992. *Sector I:* “the area distal to the line tangential to the distal heights of contour of the lateral incisor crown and root”. *Sector II:* “mesial to sector I, but distal to the line bisecting the lateral incisor’s long axis”. *Sector III:* “mesial to sector II, but distal to the mesial heights of contour of the lateral incisor crown and root”. *Sector IV:* “all areas mesial to sector III”.

Koutzoglou and Kostaki (2013) used a grading system consisting of 7 grades to categorize the severity of canine impaction on panoramic radiographs in both jaws (Figures 6-7):



Figure 6. *Grade I:* “the canine cusp had no contact with the distal part of the lateral- mandibular left canine”. *Grade II:* “the canine cusp touches or reaches the distal part of the root canal of the lateral- maxillary right canine”. *Grade III:* “the canine cusp reaches as far as to the mesial aspect of the root canal of the lateral- maxillary left canine”. *Grade IV:* “the canine cusp can reach as far as the mesial aspect of the root canal of the central incisor- mandibular right canine”. (Reprinted with permission of the publisher from Koutzoglou and Kostaki, 2013.)



Figure 7. *Grade IV:* “the canine cusp can reach as far as the mesial aspect of the root canal of the central incisor- left canine”. *Grade V:* “the canine cusp tip appears on the x-ray through the root canal of the central incisor, can reach far as to its mesial part or even the midline of the contralateral side- right canine”. *Grade VI:* “the canine cusp is located above the border between the apical and coronal halves of the lateral or central incisors’ roots in the maxilla and below this border in the mandible”. *Grade VII:* “canines that are in transposition or transmigration in the maxilla or the mandible”. (Reprinted with permission of the publisher from Koutzoglou and Kostaki, 2013.)

Kau et al. (2009), developed a radiological 3 dimensional classification system to analyze maxillary canine impaction, termed the KPG index. The index classifies the canine position, based on its distance from the norm, giving a number on a 0-5 scale to both cusp and root tip along the x, y and z planes on CBCT images (Figures 8-11). The sum of these six scores would assess the anticipated difficulty of treatment, classified as:

- Easy (0-9 points)
- Moderate (10-14 points)
- Difficult (15-19 points)
- Extremely difficult (20 points and above)

Figure 8. “Mesiodistal position for cusp and root tips in *x-axis*”. (Reprinted with permission of the publisher from Dalessandri et al., 2013.)

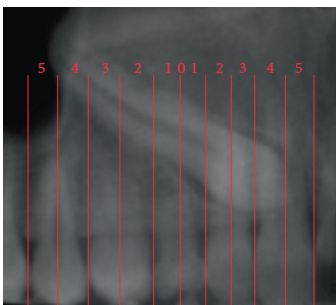


Figure 9. “Vertical position for cusp tip in *y-axis*”. (Reprinted with permission of the publisher from Dalessandri et al., 2013.)

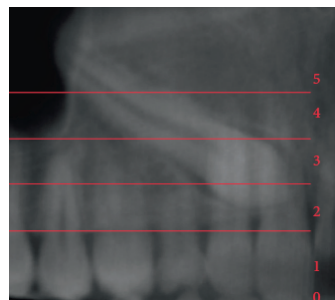


Figure 10. “Vertical position for root tip in *y-axis*”.
(Reprinted with permission of the publisher from
Dalessandri et al., 2013).

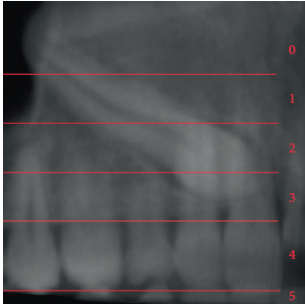
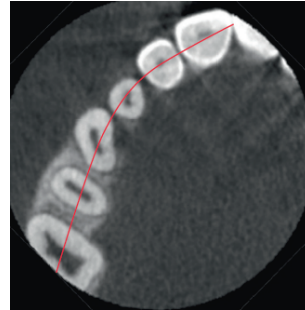


Figure 11. “Occlusal reference arch in *z-axis*”.
(Reprinted with permission of the publisher from
Dalessandri et al., 2013).



The KPG index has recently been evaluated for both intra-and inter-operator reliability for assessment of the degree of difficulty for orthodontic treatment of canine impaction (Dalessandri et al., 2013). The results of the study showed that almost a perfect intra-and interoperator agreement could be achieved when the operators were calibrated to each other. The use of different softwares however affected the reliability: the Kodak Dental Imaging 3D module software had better reliability in z-axis values, while the Planmeca Romexis software showed better reliability in x-and y-axis values (Dalessandri et al., 2013).

Validity and reliability of CBCT

Since CBCT is a rather new technique, it is important to evaluate its reliability and validity in measuring and localizing the canine positions and also the precision in making an accurate diagnosis and assessments of the treatment effects. Several studies have investigated the measurement accuracy in CBCT, and most of them studies are based on comparisons between measurements made on anatomical structures on human skulls and cephalometric analysis. The main conclusion is that CBCT gives high accuracy and validity of linear (Lagravère et al., 2008; Stratemann et al., 2008) and angular measurements (Kumar et al., 2007). In addition, results from in vitro studies made on a cube (Marmulla et al., 2005),

acrylic block (Pinsky et al., 2006) or Plexiglas plates with metal spheres (Lund et al., 2009) show that linear measurements can be made with high precision and accuracy. Linear and angular measurements of maxillary impacted canines using the NewTom software have previously been described (Walker et al., 2005; Liu et al., 2008). However, there are to our knowledge, no studies available in the literature that assess the validity or the intra and inter-examiner reliability in localizing PDC on 3D images.

Interceptive treatment

Interceptive extraction of the deciduous canine in order to improve the unfavourable position of the PDC and to prevent the canine from becoming impacted was already recommended in 1936 by Buchner HJ. This treatment was later evaluated in a prospective uncontrolled study by Ericson and Kurol, (1988), in patients 10-13 years of age. After extraction of the deciduous canine, the authors followed up the patients clinically and radiographically at 6-month intervals up to 1 year and recommended that if the eruption path of the permanent canine had not changed after 1 year, another treatment procedure should be considered. Furthermore, Ericson and Kurol, (1988), reported that extraction of the deciduous canine was effective only up to 11 years of age. Bruks and Lennartsson, (1999), showed that there was a reasonably good chance of spontaneous eruption of the permanent canine in 1/3 of the patients if they had been diagnosed and the deciduous canine had been extracted at an earlier age. These results have been confirmed in a newly published RCT study, showing that extraction of the deciduous canine results in significant more successful spontaneous eruption of the PDC in younger patients (10-11 years) than in older (12-14 years) (Bazargani et al., 2013). The position of the PDC is also another factor that influences the success rate of early extractions of deciduous canines. Ericson and Kurol, (1988), demonstrated that when the crown of the canine is distal to the midline of the

lateral incisors root, the eruption of the permanent canine is normalized in 91 % of the cases. However, this rate decreased to 64 % when the permanent canine crown was mesial to the midline of the lateral incisor root. Another factor mentioned in the literature that may influence the prognosis is the angulation of the canine, i.e. when the vertical angulation exceeds 31 %, the chance of normal eruption will significantly decrease (Power and Short, 1993). Furthermore, the initial vertical position of the canine is also crucial for spontaneous eruption; a distance of 12 mm from the crown tip of the displaced canine to its final position in the dental arch has been shown to be the borderline between successful and unsuccessful outcome in adolescent patients not older than 18 years (Smailienė et al., 2011). In an earlier RCT from Leonardi et al. (2004), a less beneficial conclusion was drawn for interceptive extraction. The authors found that extraction is successful in only 50 % of the cases, while the use of headgear (HG) in addition to extraction resulted in successful eruption in 80% of the cases. However, when the number of patients was increased, the same study design showed that extraction of the deciduous canine resulted in successful eruption of the canine in 65.2 % and in 87.5 % with additional use of headgear (Baccetti et al., 2008).

Previous research on extraction of the deciduous canine includes studies that are either retrospective (Power and Short, 1993; Bruks and Lennartsson, 1999) or prospective but with no control group (Ericson and Kurol, 1988; Smailienė et al., 2011) or RCT (Leonardi et al., 2004; Baccetti et al., 2008). The studies contain several weaknesses that give a limited quality of scientific evidence and ambiguous conclusions. This lack of evidence to support interceptive extraction in patients with PDC has been pointed out in two systematic reviews (Parkin et al., 2009, 2012; Naoumova et al., 2011). However, several studies have come since these review articles were published and therefore an updated literature search (until September 2014) was made in the same databases and with the same search terms, inclusion and exclusion criteria and quality assessment were the same as in the study by Naoumova et al. (2011). Eight new articles were included. A hand search

in the reference lists of the retrieved articles did not result in additional articles. The studies were graded with a score of A-C according to pre-determined criteria (Table 1) which were used as a template as the first step, and each study was then assessed in detail in order to gain a more fair judgement (Table 2).

Table 1 Criteria for grading of assessed studies.

<p>Grade A—high value of evidence <i>All criteria should be met</i> Randomized clinical study or a prospective study with a well-defined control group Defined diagnosis and endpoints* Diagnostic reliability tests and reproducibility tests described Blinded outcome assessment</p>
<p>Grade B—moderate value of evidence <i>All criteria should be met</i> Cohort study or retrospective case series with defined control or reference group Defined diagnosis and endpoints Diagnostic reliability tests and reproducibility tests described</p>
<p>Grade C—low value of evidence <i>One or more of the conditions below</i> Large attrition** Unclear diagnosis and endpoints Poorly defined patient material</p>

*Outcome of treatment.

**Patients that are lost during the trial and not included in the analysis.

The final level of evidence for each conclusion was judged according to the protocol of the Swedish Council on Technology Assessment in Health Care (SBU) 2005, which is based on the criteria for assessing study quality from the Centre for Reviews and Disseminations in York (2001). The evidence level was graded in four levels:

- **Level 1: strong evidence.** At least two studies assessed as level ‘A’ are needed to conclude that the evidence level is high.
- **Level 2: moderate evidence.** One study assessed as level ‘A’ and at least two studies as level ‘B’.
- **Level 3: limited evidence.** At least two studies assessed as level ‘B’.
- **Level 4: inconclusive evidence.** Fewer than two studies assessed as level ‘B’.

The assessed interceptive treatment methods, the success rates and the outcomes of the studies are summarized in Table 2. All studies were prospective and seven of them had a RCT design. One of the studies had moderate quality (Grade B) and the rest had low quality (grade C).

The main weaknesses of the studies were: missing power analysis or questionable power since explanation was not given to the underlying assumption that led to the number, unequal number of patients in the different groups despite the fact that an equal number of drop-outs were described in each groups, there were also questions on the randomization, and details about the randomization procedure and allocation concealment concerning uni- and bilateral PDCs were missing. Four studies lacked ethics approval (Baccetti et al., 2009; Silvolva et al., 2009; Bonetti et al., 2010; Bonetti et al., 2011). In one of the studies the untreated control group contained only canines that were judged by the investigators not to be at risk (Bonetti et al., 2011), i.e. no randomization of the subjects was performed. In one study, the inclusion criteria were 7-year-old patients with moderate crowding and CL II tendency who had headgear (HG) treatment and not displacement of the maxillary canine and, in addition, the patients in the control group received a mixed of interceptive treatment, such as: extraction of the maxillary or mandibular deciduous canine or interdental stripping (Silvolva et al., 2009). Thus it is impossible in that study to draw any conclusions on the effect that HG has on the eruption pattern in maxillary canines and if it will be beneficial on palatally displaced canines. Furthermore, the results of the 8-year follow-up show that there are no significant changes in the alpha angle between the HG and the CG group.

Other confounding factors in the articles were: the vagueness of diagnosing PDC from lateral cephalograms, panoramic radiographs or PA radiographs (Baccetti et al., 2009; Bonetti et al., 2011), the latter according to a method by Sambataro et al. (2005), who suggested that PA radiographs can be used at the age of 8 to predict

palatal displacement. However, they evaluated this method in only 12 patients. The validity of the method is therefore uncertain. Panoramic radiographs have also been suggested for predicting PDC in patients younger than 10 years (Sajani and King, 2012), however in this study as well, the examined group was too small to be able to draw any conclusions that may be generalized. Further confounding factors were: inclusion of centrally placed maxillary canines (Bonetti et al., 2010, 2011) or inclusion of too young patients in three of the studies (Baccetti et al., 2009; Silvolva et al., 2009; Armi et al., 2011), which can lead to a false diagnoses of PDC, as maxillary canine tends to move palatally between the age of 5 to 9, with substantial movement in a buccal direction between 10 and 12 years (Coulter and Richardson, 1997). Thus, it is unlikely that PDC can be detected before the age of 10 years (Ericson and Kurol, 1986). Furthermore, the definition of a PDC varied in all articles and one article gave no definition (Silvolva et al., 2009).

Descriptive data in the different groups before and after treatment were missing in two of the studies (Baccetti et al., 2009; Armi et al., 2011), which makes it difficult to assess the treatment effect of the applied methods. A reliability test was missing in one of the studies (Armi et al., 2011) and successful results in the control group were mentioned only in the abstract and not in the text. All articles measured the outcome variables by comparing the changes in the panoramic radiographs taken at different times after the interventions. Even though most of the articles had a reliability tests, the use of the panoramic radiographs is problematic in angular and linear measurements, especially in the canine region, due to the amount of distortion and magnification resulting in overestimation of the angulation of the misplaced canines and of the distance of the tooth from the midline (Tronje et al; 1981; Coupland, 1984; Alqerban et al., 2011). Bazargani et al. (2013), used a stainless steel wire placing it parallel to the lower arch in order to get a more precise calibration in the panoramic radiographs.

The baseline values between the treated groups and the control group was claimed to be equal according to the text in one of the studies but the table included in the article showed substantial differences (Baccetti et al., 2011).

Bonetti et al. (2010), compared the effect of extracting deciduous canine versus extraction of deciduous canine and primary molar, i.e. double extraction. However, the severity of the canine displacements at baseline was different between the two groups, despite the fact that the patients were randomized, giving uncertain results of the real treatment effect. No information was given as to whether there were significant differences between the groups at baseline. Furthermore, a mix of patients with centrally and palatally displaced canines was included in the trial, which explains the high success rates in both groups. Although statistically significant differences between the groups were not found, the authors concluded that double extraction is a more effective procedure.

Bazargani et al. (2013), assessed the PDC response of extraction depending on the zone in which the canine was located, but the response on the control side was lacking. In four of the studies (Baccetti et al., 2009; Armi et al., 2011; Baccetti et al., 2011; Sigler et al., 2011) RME treatment was assessed in patients with normal transversal relation, i.e. an absence of cross-bite, and patients were expanded 7 mm, but nothing is mentioned in the studies about the transversal relation after the treatment. The same four articles (Baccetti et al., 2009; Armi et al., 2010; Baccetti et al., 2011; Sigler et al., 2011) had also had the inclusion criteria CL II or CL III tendency but no explanation was given as to why these sagittal relationships were included and not CL I, which indicates that the material might be selected. The inclusion criterion of: *mild tooth size-arch length discrepancy* mentioned in four of the articles is not defined, which is of importance.

One of the studies is a 2-center study (Sigler et al., 2011), but this is questioned since the treated and the control group were assessed from different universities, thus a randomization and allocation concealment was not possible. In two of the studies it is written that the measurements were done blinded, however, the blinding procedure has not been described and is questioned since extraction of the deciduous canine is visible on the panoramic radiographs, unless the operator was unaware of the study (Baccetti et al., 2011; Sigler et al., 2011). The other studies did not have blinded measurements (Baccetti et al., 2009; Silvolva et al., 2009; Bonetti et al., 2010; Armi et al., 2011; Bonetti et al., 2011, Bazargani et al., 2013).

Six articles (Baccetti et al., 2009; Armi et al., 2010; Bonetti et al., 2010; Baccetti et al., 2011; Bonetti et al., 2011, Sigler et al., 2011) defined successful outcome as “full eruption of the canine thus permitting bracket positioning for final arch alignment when needed” and one article (Bazargani et al., 2013) did not give the definition of successful outcome in the method description. However, the authors mentioned in the results part that successful eruption was defined as eruption “above the gingival margin in an aesthetically acceptable location in the dental arch.” These definitions can be interpreted as that canines that have emerged through the gingiva but not in correct position are assessed as unsuccessful. One article had the change in alpha angle as the definition on successful outcome (Silvolva et al., 2009).

Due to the above mentioned weaknesses, the overall levels of evidence of these eight new articles are assessed as level 4, i.e. inconclusive evidence is available.

Table 2. Summarized *Published* Data of the Eight New Studies regarding interceptive treatment of PDCs

Article/ Design	Inclusion & Exclusion criteria	Participants/ Definition of PDC	Methods/Measurements/ Observation time	Success rate of canine eruption+ definition/ Side Effects/Cost/Patient satisfaction	Outcomes	Quality assessment/ Grade	
Baccetti T, Mucedero M, Leonardi M, Cozza P. Interceptive treatment of palatal impaction of maxillary canines with rapid maxillary expansion: a randomized clinical trial. <i>Am J Orthod Dentofacial Orthop</i> . 2009; 136(5): 657–661.	Inclusion criteria: White race; age at baseline: 7.6 to 9.6 years; prepubertal stage of skeletal growth (CS I or CS 2) as assessed on lateral cephalograms; Class II or Class III tendency, or mild tooth-size/arch-size discrepancy.	Σ 60 subjects RME: 35 (22 girls, 13 boys, 3 dropouts) Age: 8.8±9m. CG: 25 (17 girls, 8 boys, 3 dropouts) Age: 8.4±1yr.	RME: “expansion until the palatal cusps of the maxillary posterior teeth were in contact with the buccal cusps of the mandibular posterior teeth.” 6m passiv retention with the RME followed by retention plate for 1 yr. CG: non-treatment. PA cephalograms (method by Sambataro et al., 2005). Panoramic radiographs (method by Ericson and Kurol, 1988a, b). Dental casts (method by Tollaro et al., 1996) Observation: RME: mean duration-4.4 years. CG: mean duration-4.11 years.	RME: success rate - 65.7% CG: success rate- 13.6% <i>Success defined as:</i> “ Full eruption of the canine thus permitting bracket positioning for final arch alignment when needed” Side Effects/Cost/Patient satisfaction: Not declared	RME is significantly more effective in increasing the rate of eruption of PDC compared with CG. Method error-Yes Confounding factors-Yes Valid measurement method-Yes? Adequate statistics-Yes?	Grade C	
<i>Randomized clinical trial</i>	Exclusion criteria: Previous orthodontic treatment, supernumerary teeth, odontomas, cysts, craniofacial malformations, or sequelae of traumatic injuries.	<i>Definition:</i> Prediction of canine palatal impaction derived from analysis of PA films by Sambataro et al., 2005)	HG: outer bows bent 10° upwards, inner bow expanded 10 mm. Active treatment: 2 – years for 8–10hours/day. CG: (Extraction of maxillary (35%) and mandibular (38%) deciduous canine. Interdental stripping in 19% of the subjects). Active treatment time: 2 –years. Total follow-up for both groups: 8 years.	Alpha angle more vertically positioned on the right side in the HG compared to the CG after 1 and 2 yrs. On the left side no differences between the groups. At the 8-yr follow-up no differences of the alpha angle between HG and GC. <i>Success defined as:</i> Alpha angle of the maxillary canine. Side Effects/Cost/Patient satisfaction: Not declared	“The canine eruption pattern was significantly more vertical after HG use.” “The strongest influence was seen in the right side canines after 2 years of HG use.”	Randomisation- Yes Allocation concealment-Yes Assessor blinding- No Dropouts described-Yes Sample justified-No Baseline comparison-Yes Inclusion/Exclusion criteria-Yes/No Method error-Yes Confounding factors-Yes Valid measurement method-Yes? Adequate statistics-Yes	Grade C
Silvola AS, Arvonen P, Julku J, Lähdesmäki R, Kantamäa T, Pirttiniemi P. Early headgear effects on the eruption pattern of the maxillary canines. <i>Angle Orthod</i> . 2009; 79(3): 340–345.	Inclusion criteria: the need for orthodontic treatment due to moderate crowding and a Class II tendency. Exclusion criteria: Not declared	Σ 71 subjects, 3 dropouts (40 boys and 28 girls) aged 7.6 years (SD=0.3). Randomly divided into two groups (HG, CG) of equal size, matched according to gender. <i>Definition:</i> Not declared	Panoramic radiographs (Method by Ericson and Kurol, 1988a, b). Dental casts	Success rate of canine eruption+ definition/ Side Effects/Cost/Patient satisfaction: Not declared	“The canine eruption pattern was significantly more vertical after HG use.” “The strongest influence was seen in the right side canines after 2 years of HG use.”	Randomisation- Yes Allocation concealment-Yes Assessor blinding- No Dropouts described-Yes Sample justified-No Baseline comparison-Yes Inclusion/Exclusion criteria-Yes/No Method error-Yes Confounding factors-Yes Valid measurement method-Yes? Adequate statistics-Yes	Grade C
<i>Longitudinal randomized trial</i>							

Article/ Design	Inclusion & Exclusion criteria	Participants/ Definition of PDC	Methods/Measurements/ Observation time	Success rate of canine eruption + definition/ Side Effects/Cost/Patient satisfaction	Outcomes	Quality assessment/ Grade
Alessandri Bonetti G, Incerri Parenti S, Zanarini M, Marrini I. Double vs single primary teeth extraction approach as prevention of permanent maxillary canines ectopic eruption. <i>Pediatr Dent</i> . 2010; 32(5): 407-412.	Inclusion criteria: Caucasian race; maxillary deciduous canines and first molars in the dental arch; good-quality panoramic radiographs. Exclusion criteria: Previous orthodontic treatment; labially retained maxillary canines; aplasia or severe hypoplasia of the crown of the permanent lateral incisors; odontomas; cysts; traumatic injuries to the permanent incisors or to the face; multiple or advanced caries; systematic conditions that make children susceptible to PDC.	Σ 60 subjects, 1 dropout. EG: 29 (16 boys, 13 girls) with 52 PDCs. Age: mean 10.1±1.1. ECMG: 30 (14 boys, 16 girls) with 56 PDCs. Age: mean 10.2 ±0.9. Definition: Absence of palpation of permanent maxillary canine bulges (PMC); PMC bulge palatally; abnormal inclination and/or rotation of adjacent lateral incisor crown; PMCs inclination to the midline >25°; overlapping of the PMC crowns with the lateral incisor roots.	Single extraction (EG) versus double extraction (ECMG). Panoramic radiographs (method by Ericson and Kuroi, 1988a, b). EG: observation-18m ECMG: observation-18m	EG: success rate- 85% ECMG: success rate-96% <i>Success defined as:</i> “Surgical uncovering not required, full eruption of the canine thus permitting bracket positioning for final arch alignment when needed” Side Effects/Cost/ Patient satisfaction: Not declared	The double extraction approach is a more effective procedure that the single extraction approach.	Randomisation- Yes? Allocation concealment- Yes Assessor blinding- No Dropouts described- Yes Sample justified- No Baseline comparison- Unclear Inclusion/Exclusion criteria- Yes Method error- Yes Confounding factors- Yes Valid measurement method- Yes? Adequate statistics- Yes Grade C
Armi P, Cozza P, Baccetti T. Effect of RME and headgear treatment on the eruption of palatally displaced canines: a randomized clinical study. <i>Angle Orthod</i> . 2011; 81(5): 370-374.	Inclusion criteria: White ancestry; unilateral or bilateral PDC; dental age older than 8 yrs and younger than 13 yrs; skeletal age before CS 4, mild crowding and/or Class II molar tendency. Exclusion criteria: Previous orthodontic treatment; craniofacial syndromes, odontomas, cysts, cleft lip and/or palate, sequelae of traumatic injuries to the face, or multiple and/or advanced caries; aplasia or severe hypoplasia of the crown of upper lateral incisors.	Σ 64 subjects, 4 dropouts. HG: 17 (9 boys, 8 girls) with 25 PDCs. Age: mean 11.9. RME/HG: 21 (9 boys, 12 girls) with 30 PDCs. Age: mean 11.1. CG: 22 (9 boys, 13 girls) with 26 PDCs. Age: mean 11.6. Definition: Intraosseous palatal position of the maxillary permanent canines from panoramic radiographs and periapical radiographs (Clark's rule).	HG: 1 year for 12–14 hours a day versus RME (7 mm of active expansion, 6 m passive retention) followed by HG versus non-treatment (CG). Lateral cephalograms (method by Björk and Skieller, 1983). Panoramic radiographs (metodo by Ericson and Kuroi, 1988a, b). Dental casts (measurement-not declared) Observation period in all groups: 18 months.	HG: success rate- 82.3% RME/HG: success rate- 85.7% CG: success rate- 36% <i>Success defined as:</i> “ Full eruption of the canine thus permitting bracket positioning for final arch alignment when needed” Side Effects/Cost/ Patient satisfaction: Not declared	RME and HG (or HG alone) increases the success rate of eruption of the canine significantly (almost three times more than in CG). No significant difference between HG and RME/HG.	Randomisation- Yes Allocation concealment- Unclear Assessor blinding- No Dropouts described- Unclear Sample justified- Unclear Baseline comparison- No Inclusion/Exclusion criteria- Yes Method error- No Confounding factors- Yes Valid measurement method- Yes? Adequate statistics- Yes? Grade C
<i>Randomized clinical trial</i>						
<i>Randomized clinical trial</i>						

Article/ Design	Inclusion & Exclusion criteria	Participants/ Definition of PDC	Methods/Measurements/ Observation time	Success rate of canine eruption + definition/ Side Effects/Cost/Patient satisfaction	Outcomes	Quality assessment/ Grade
Baccetti T, Sigler M, Lauren, McNamara Jr James A. An RCT on treatment of palatally displaced canines with RME and/or a transpalatal arch. <i>Eur J Orthod.</i> 2011; 33(6): 601-607.	Inclusion criteria: Caucasian race; age 9.5-13.0 years; late mixed dentition stage; unilateral or bilateral PDC; stage of skeletal growth: CS I-CS 4 as assessed on lateral cephalograms; presence of Class II or Class III tendency or mild tooth-size/arch-size discrepancy.	Σ 120 subjects, 3 dropouts. RME/TPA/EG: 40 subjects (15 boys, 25 girls) with 66 PDCs. Age: 10y5m \pm 10m TPA/EG: 25 subjects (10 boys, 15 girls) with 36 PDCs. Age: 10y9m \pm 11m. EG: 25 subjects (11 boys, 14 girls) with 34 PDCs. Age: 11y1m \pm 11m. CG: 30 subjects, (12 boys, 18 girls) with 42 PDCs. Age: 10y5m \pm 10m.	RME/TPA/EG RME: (7 mm active expansion, 4-5m passive retention) followed by TPA and extraction of deciduous canines, versus TPA/EG: TPA followed by extraction of deciduous canine, versus EG: extraction of deciduous canine, versus non-treatment (CG) Panoramic radiographs (method by Ericson&Kuroi, 1988a, b and method by Nolla 1960). Lateral cephalograms (Baccetti et al., 2005). Observation: RME/TPA/EG: 3y6m \pm 16m. TPA/EG: 2y9m \pm 13m. EG: 2y2m \pm 10m CG: 3y1m \pm 14m	RME/TPA/EG: success rate- 80% TPA/EG: success rate-79.2% EG: success rate-62.5% CG: success rate-27.6% <i>Success defined as:</i> “Full eruption of the canine thus permitting bracket positioning for final arch alignment when needed” Side Effects/Cost/Patient satisfaction: Not declared	Significant differences between all the groups, with the exception between RME/TPA/EG and TPA/EG. TPA in absence of RME is equally effective than the RME/TPA combination.	Randomisation- Unclear Allocation concealment- Unclear Assessor blinding- No Dropouts described- Yes Sample justified- Unclear Baseline comparison-Yes Inclusion/Exclusion criteria-Yes Method error- Yes Confounding factors- Yes Valid measurement method-Yes ? Adequate statistics-Yes? Grade C
Sigler LM, Baccetti T, McNamara JA Jr. Effect of rapid maxillary expansion and transpalatal arch treatment associated with deciduous canine extraction on the eruption of palatally displaced canines: A 2-center prospective study. <i>Am J Orthop Dentofacial Orthop.</i> 2011; 139(3):e235-e244. <i>Prospective controlled clinical trial</i>	Inclusion criteria: White race; age 9.5- 13.0 yrs; late mixed dentition; unilateral or bilateral PDC, skeletal age:CS I-CS 4, Class II or III tendency or mild tooth size-arch length discrepancy.	Σ 70 subjects, 2 dropouts. RME/TPA/EG: 40 subjects, (15 boys, 25 girls) with 39 PDCs. Age: 10y5m \pm 10m. CG: 30 subjects, (12 boys, 18 girls) with 29 PDCs. Age: 10y5m \pm 10m. <i>Definition:</i> Intraosseous malposition, confirmed by lateral cephalogram and when necessary periapical radiographs (Clark's rule) PDC with alpha angle $\geq 15^\circ$ was included.	RME/TPA/EG: RME (7 mm active expansion, 4-5m passive retention)+ TPA+ extraction of deciduous canines, versus non-treatment (CG). Panoramic radiographs (method by Ericson & Kuroi, 1988a, b and Nolla, 1960). Lateral cephalo-grams (method by Baccetti et al., 2005). Dental casts (method by Tollaro et al., 1996). Observation: CG: 3y1m \pm 1y2m RME/TPA/EG: 3y7m \pm 1y5m	RME/TPA/EG: success rate- 79.5% CG: success rate-27.6% <i>Success defined as:</i> “ Full eruption of the canine thus permitting bracket positioning for final arch alignment when needed” Side Effects/Cost/Patient satisfaction: Not declared	RME followed by a TPA combined with extraction of the deciduous canine increases the success rate of eruption of the PDC compared to a control group.	Randomisation- No Allocation concealment-No Assessor blinding- Unclear Dropouts described-Yes Sample justified-Unclear Baseline comparison-Yes Inclusion/Exclusion criteria-Yes Method error- Yes Confounding factors- Yes Valid measurement method-Yes? Adequate statistics-Yes? Grade C

Article/ Design	Inclusion & Exclusion criteria	Participants/ Definition of PDC	Methods/Measurements/ Observation time	Success rate of canine eruption+ definition/ Side Effects/ Cost/Patient satisfaction	Outcomes	Quality assessment/ Grade
Bonetti G A, Zamarini M, Incerti Parenti S, Marini I, Gatto MR. Preventive treatment of ectopically erupting maxillary permanent canines by extraction of deciduous canines and first molars: A randomized clinical trial. <i>Am J Orthod Dentofacial Orthop</i> . 2011; 139(3): 316- 323.	Inclusion criteria: White ancestry; age 8-13 years; maxillary deciduous canines and first molars in the dental arch; good-quality panoramic x-ray. Exclusion criteria: Previous orthodontic treatment; premature loss of maxillary deciduous canines and first molars; labially retained permanent canines; aplasia or severe hypoplasia of the crown of the lateral incisors; craniofacial syndromes; odontomas; cysts; cleft lip or palate; traumatic injuries to the permanent incisors or the face; multiple or advanced caries.	Σ 71 subjects with 123 PDCs, 3 drop-outs. EG: 17 subjects (9 boys, 8 girls). Mean age: 9.8y. ECMG: 20 subjects (9 boys, 11 girls). Mean age: 10.2y. CG: 31 subjects (16 boys, 15 girls). Mean age: 9.0y Definition: Absence canine bulge palpation, canine bulge palpable palatally, no abnormal inclination and/or rotation of adjacent lateral incisor crown, inclination of canine to vertical line passing through midline > 25° and overlapping canine crown with the lateral incisor roots.	EG: deciduous canine extraction alone versus, ECMG: deciduous canine and first molars concomitant extraction versus, CG: control group. Panoramic radiographs (method by Ericson and Kuroi, 1988a, b). EG: observation time-18m ECMG: observation time-18m CG: observation time- 18m	EG: success rate- 78.6% ECMG: success rate- 97.3% CG: success rate- not declared. <i>Success defined as:</i> “ Full eruption of the canine thus permitting bracket positioning for final arch alignment when needed” Side Effects/Cost/Patient satisfaction: Not declared EG: success rate- 67% CG: success rate- 42 % <i>Success defined as:</i> “ Eruption above the gingival margin in an aesthetically acceptable location in the dental arch” Side Effects/Cost/Patient satisfaction: Not declared	EMCG is significantly more effective in increasing the eruption of PDCs or centrally positioned maxillary canines compared to extraction of the deciduous canine alone.	Randomisation- Yes? Allocation concealment- Yes? Assessor blinding- No Dropouts described- Yes Sample justified- Yes Baseline comparison- Yes Inclusion/Exclusion criteria- Yes Method error- Yes Confounding factors- Yes Valid measurement method- Yes? Adequate statistics- Yes Grade C
Bazargani F, Magnusson A, Lennartsson B. Effect of interceptive extraction of deciduous canine on palatally displaced maxillary canine: A prospective randomized controlled study <i>Angle Orthod</i> . 2014; 84(1): 3-10.	Inclusion criteria: Inability to locate the canines by palpation; bilateral PDCs; age 10-14 years with dental stage in the late mixed dentition. Exclusion criteria: Previous or ongoing orthodontic treatment; aplasia of lateral incisors; moderate to severe crowding in the upper arch (>3 mm); and/or craniofacial syndromes; odontomas; cysts; or cleft lip and/or palate.	Σ 24 subjects with 48 bilateral PDCs, no drop-outs. EG: 24 subjects (8 boys, 16 girls). Mean age: 11.6 y. CG: 24 subjects (8 boys, 16 girls). Mean age: 11.6 y. Definition: Canine within sector 2-5 (Method by Ericson and Kuroi 1988 a,b) and intraosseous position within the palate observed on panoramic and intraoral occlusal radiographs.	EG: deciduous canine extraction versus non-extraction, CG: control group on the same patients. Panoramic radiographs (method by Ericson and Kuroi, 1988a, b). Observation time-18m	Extraction of the deciduous canine is effective compare to the control group and is preferably done on younger patients (10-11 y).	Randomisation- Yes Allocation concealment- Yes Assessor blinding- No Dropouts described- Yes Sample justified- Yes Baseline comparison- Yes Inclusion/Exclusion criteria- Yes Method error- Yes Confounding factors- Yes Valid measurement method- Yes? Adequate statistics- Yes Grade B	
<i>Randomized clinical trial</i>						
<i>Randomized clinical trial</i>						

EG, extraction group; CG, control group; PDC, palatally displaced canine; PA, posterior-anterior cephalograms; TPA, transpalatal arch; RME, rapid maxillary expansion; TPA/EG, rapid maxillary expansion followed by transpalatal arch and extraction; TPA/EG, transpalatal arch followed by extraction; ECMG, extraction deciduous canine and first molar group; PDC, palpation of permanent maxillary canine bulges; ? (in the quality assessment column), questionable.

Other treatment alternatives

Early diagnosis and interception represent the most desirable approach in managing palatally displaced canines. However, in cases when the diagnosis has been set too late or the outcome of the interceptive treatment has not been successful, alternative treatment modalities are needed. The most common procedure is then surgical exposure followed by orthodontic treatment to bring the canine into the dental arch. The surgical exposure can be performed by either by an open or closed techniques. There are no differences in operating time or patient reported outcomes between the two procedures according to the study by Parkin et al. (2012). The patient reported outcomes were assessed with a questionnaire that was given to the patients 10 days after the surgery. Questions dealt with: pain or soreness in the palate, pain duration, usage of pain killer and difficulties eating, speaking, brushing the palatal surface of the teeth, or having a bad taste in the mouth. Parkin et al. (2013) could also not find any significant differences for the periodontal health, assessed 3 months after removal of the fixed appliance, between the two surgical techniques. However, a statistical difference in mean attachment loss between the operated and unoperated canines was observed. The authors concluded that: “this is unlikely to be of clinical relevance in the short term; however, the long-term significance is still unknown”. The effect of age on the success rate and the duration of treatment of palatally impacted canines after surgical exposure have been studied by Becker and Chaushu (2003). The authors found that the prognosis of successful resolution of the canine impaction in an adult (mean age: 28 ± 8.6 years) is lower than in a younger patient (mean age 13.7 ± 1.3). The duration of the fixed appliance treatment is also influenced by the initial positions of the PDC, i.e. alpha angle, higher zone of impaction (Figure 3) and a greater than 14 mm of distance of the canine cusp to the occlusal plane result in longer treatment (Stewart et al., 2001; Smailienė et al., 2011; Olive, 2005; Nieri et al., 2010; Bazargani et al., 2012). Treatment of impacted canines with surgical

exposure followed by fixed appliance is an expensive treatment. A recent study in Sweden (Bazargani et al., 2012) estimated the average cost to be \$4300 per case.

In some rare cases, the impacted canine is extracted due to ankylosis, external root resorption, displacements that are severe or the root of the canine being severely dilacerated. Other rare alternatives are: autotransplantation or prosthetic replacement of the canine, i.e. implants or bridges. In some cases when the patient is not interested in treatment and there is no evidence of resorption of adjacent teeth and the deciduous canine has a good aesthetic and prognosis, it may be better not to give any active treatment except regularly monitoring the tooth with radiographs (Bishara, 1998; Ngan et al., 2005). No guidance currently exists on how often radiographic check-ups should be carried out, and there are no long-term follow-up studies on the prognosis of the deciduous canine when it is left in situ.

Patients' experiences of tooth extraction

In the past, treatment methods in orthodontics have mainly assessed their objective effectiveness, without evaluating the patient's response. The patient's acceptance and experience are important when extraction of the deciduous canine as an interceptive approach in children with PDC is performed, since this is often the child's first experience of invasive dental treatment. If the child experiences a negative dental event, this may lead to dental anxiety and in the long run to deteriorated oral health, as children with dental anxiety are more fearful, react stronger and earlier to pain, have higher numbers of missed/cancelled appointments, but also more dental treatments due to toothache (Milgrom et al., 1992; Locker et al., 1999; Maggiriias and Locker 2002; Wogelius and Poulsen, 2005). Negative dental experiences in childhood are often the reason for dental fear in adults (Berggren and Meynert, 1984; Locker et al., 1999).

The International Association for the Study of Pain defines **pain** as "*an unpleasant*

sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (IASP Subcommittee on Taxonomy 1979). “Pain is always subjective and it is constructed by an individual’s past experiences, learned responses and expectations in addition to physiologic responses” (IASP Subcommittee on Taxonomy 1979; Tate and Acs, 2002). It is also important to distinguish between the below mentioned definitions when reading about pain and fear (Klingberg and Broberg, 2007):

- **Dental fear (DF)**: “is a normal emotional reaction to one or more specific threatening stimuli in the dental situation. DF is defined by what the patient feels”.
- **Dental anxiety (DA)**: “denotes a state of apprehension that something dreadful is going to happen in relation to dental treatment, and it is coupled with a sense of loosing control. DA is defined by what the patient feels”.
- **Dental behaviour management problems (DBMP)**, “is *uncooperative* and disruptive behaviours, which result in delay of treatment or render treatment impossible, regardless of the type of behaviour or its underlying mechanism(s). DBMP is defined by the dentist’s experience when treating the patient”.

The prevalence of DF and DA in children varies from 3% to 21% and the reasons for this wide range are: different criteria for definition of DF and DA, differences in age, sample, study design, culture, and society and different systems for dental care (Alvesalo et al., 1993; Klingberg et al., 1994; Skaret et al., 1998; Klingberg and Raadal, 2001; Wogelius et al., 2003; Milsom et al., 2003). In a Swedish population-based study of 4-7 and 9-11-year olds, Klingberg et al. (1994) found the prevalence of DF to be 6.7 % and DBMP of 10.5 %. Pain perception and response are unique and different for each child. However, some factors have been shown to have a significant impact on the child’s dental fear and behaviour, e.g. age, gender, previous negative dental experience, environment, temperamental aspects, parental interactions and attitudes towards dental care, and socio-economic standards

(Berggren and Meynert 1984; Klingberg et al., 1994; Skaret et al., 1998; Arnrup et al., 2002; Young, 2005).

Few studies have assessed the pain children report at the extraction of deciduous teeth (Acs et al., 1986; Acs and Drazner, 1992; Primosch et al., 1996; Sjögren et al., 2010) and, in our search of the literature, only one study was found (Sjögren et al., 2010) that described the procedural and postoperative pain and discomfort among 7-9- year-old children, who had extractions of four deciduous teeth as an interceptive treatment to resolve dental crowding in the permanent dentition. The study revealed that the procedural pain level was low, as was also postoperative pain, and that the DF did not increase from pre-to post-extraction. Furthermore, single tooth extraction was preferable in comparison to double extraction at the same appointment.

A population study in healthy Swedish 8-19-years-olds has shown that the highest ranked painful dental treatment event is dental injection. Children with high dental anxiety rated dental pain higher than other children (Krekmanova et al., 2009). There is unfortunately still a persisting attitude among dentists worldwide who do not believe that the pain children reports is real or that children have difficulties telling the difference between pain and discomfort: therefore some dentists do not use local anaesthetics during restorations or extractions in children (Milgrom et al., 1994; Wondimu and Dahllöf, 2005; Krekmanova et al., 2009). Klingberg et al. (1994), found that children with DBMP received restorative treatment without local anaesthetics to a higher extent compared to children without DBMP. Furthermore, dentists do not recommend postoperative analgesics to children, since they believe that children do not experience postoperative pain, even though many studies have concluded that the majority of children are in need of analgesics postoperatively due to pain. The greatest need for postoperative analgesia is immediately after tooth extraction, before the loss of analgesia (Acs et al., 1986; Acs and Drazner, 1992; Atan et al., 2004; Wondimu and Dahllöf, 2005). Topical anaesthetics, slow injection

technique and a psychological approach, i.e. tell-show-do method, are easy techniques to use, in order to reduce the child's anxiety and fear (Holst and Crossner, 1987; Barrett, 1997). Pharmacological treatment approaches are also available and include: sedative, conscious sedation with nitrous oxide and general anaesthesia (Klingberg, 1995).

Accurate measurement of pain is very difficult since pain is a personal and subjective experience. Therefore the assessment instruments used should be reliable, valid and appropriate for the child's age (Young, 2005). Two main methods are commonly used to measure DA and DF: observation and rating of behaviours during treatment, assessed by the dental staff and psychometric scales, rated by the child him/herself or by the parents if the child is very young. The most frequently used behaviour rating scale in Scandinavia is the method developed by Rud and Kisling, (1973), which consists of four levels of acceptance (see page 57).

Many different anxiety and pain measures in dentistry are available; some examples are: The Dental Subscale of the Children's Fear Survey Schedule (CFSS-DS), which consists of fifteen items, where each item gives 5 different scores and the Dental Anxiety Scale (DAS) developed by Corah (1969), consists of 4 items on 4 dentally related situations. The respondents are asked to indicate which one out of the 4 responses is closest to there likely to that situation. The total score range is from 4 to 20, and population normative mean scores are between 8 and 9. Scores greater than 15 are indicative a high level of dental anxiety. DAS has been used both for adults and children, and the internal reliability and test-retest reliability of the scale are high (Newton and Buck, 2000).

AIMS

GENERAL AIM

The present thesis aimed to evaluate the effect of interceptive extraction of the deciduous canines on patients with PDCs and to describe the patient's experience of the tooth extraction.

SPECIFIC AIMS

PAPER I

- To evaluate the intra and inter-examiner error and the validity of a method for measuring the position of PDCs on CBCT.

PAPER II

- To evaluate pain intensity and discomfort, analgesics consumption, limitations in daily activities, and functional jaw impairment following extraction of a deciduous canine, as an interceptive treatment in patients with PDCs.
- To investigate whether pre-extraction dental anxiety influences post-extraction pain intensity and discomfort.
- To explore whether there are any differences in children's own assessments of previous experiences and pain in conjunction with dental treatment between children with a PDC, compared to a matched reference group without a PDC.

PAPER III

- To evaluate the effect of extracting the deciduous canine in children with PDCs compared to a control group.
- To assess the radiographic changes in eruption between the extraction and the control group in time, i.e. between 0 to 6 and 6 to 12 months after extraction.
- To analyse root resorption on adjacent teeth caused by the PDCs.

PAPER IV

- To analyse how factors as: initial angulations and positions of the PDC, extraction of the deciduous canine affect the success rate and influence the length of time it takes for the canine to erupt in successful cases.
- To assess whether age affects the success rate.
- To find a cut-off point for cases in which interceptive extraction is effective and should be recommended and those cases where exposure of the impacted canine should be considered without preceding interceptive extraction of the deciduous canine.

HYPOTHESIS

The hypotheses of the papers in this thesis were:

PAPER I

That inter- and intra-examiner reliability and validity of angles and distances of the PDC on CBCT are low.

PAPER II

That extraction of the deciduous canine as an interceptive treatment in patients with PDC does not cause high levels of pain and discomfort and that the dental anxiety scale is higher in patients with PDC.

PAPER III

That there are no differences between the extraction and the control groups regarding:

- 1) the success rate of spontaneous eruption of the PDC
- 2) change in eruption pattern or
- 3) for the number of root resorptions of adjacent teeth, after interceptive extraction of the deciduous canine.

PAPER IV

That there is no difference in the initial angulation and position of the PDC regarding the success rate and the time it takes for the canine to erupt.

That there is no age difference between the successful and unsuccessful group.

MATERIALS AND METHODS

Subjects (Studies I-IV)

The subjects in papers I-IV were consecutively recruited from 15 public dental clinics in Gothenburg, Region Västra Götaland, Sweden, during September 2008 to January 2011. Orthodontists from the clinic of orthodontics, University Clinics of Odontology, Gothenburg, Sweden recruited the patients during their consultation visits at the public dental clinics. Patients and parents had the opportunity before the first visit to enter a website explaining the aim and the design of the study (<http://www.odontologi.gu.se/horntand.html>).

Another website (http://www.odontologi.gu.se/horntand_tdl) was prepared for the general dentists and for the orthodontists, where they could easily access the inclusion and exclusion criteria of the study.

The inclusion criteria were as follows:

- Caucasians at age 10-13 years with either maxillary unilateral or bilateral PDC
- Persisting deciduous canines
- No previous experience of orthodontic treatment

The canine was considered palatally displaced, when clinical palpation of a labial canine bulge was absent and when the canine crown was diagnosed on intraoral radiographs as palatally positioned (Ericson and Kurol, 1988), using the Clark's rule (Clark, 1909).

Criteria for exclusion were:

- Crowding in the maxilla exceeding 2 mm
- Ongoing orthodontic treatment
- Craniofacial syndromes
- Odontomas, cysts

- Cleft lip and/or palate
- Resorption of the adjacent teeth, grades 3 and 4 according to Ericson and Kurol, (2000), either at the start of or during the trial.

The Ericson and Kurol, (2000), classification of root resorption severity was used³⁶:

- (1) no resorption, intact root surfaces and the cementum layer may be lost
- (2) slight resorption, resorption up to half of the dentine thickness to the pulp
- (3) moderate resorption, resorption midway to the pulp or more, the pulp lining being unbroken
- (4) severe resorption, the pulp is exposed by the resorption

The total group of participants in the study was 70 patients. Before the randomization procedure, 3 patients (mean age \pm SD: 11.5 \pm 0.7) declined participation in the study: all these patients were girls and had bilateral PDC. Two out of 3 patients declined due to fear for extraction and one patient thought it was too far to travel to the orthodontics clinic, University Clinics of Odontology, Gothenburg, Sweden for the check-ups. No patients dropped out after the randomization or during the study. Thus, in total, 67 patients (40 girls, mean age \pm SD: 11.3 \pm 1.1, 27 boys, mean age \pm SD: 11.4 \pm 0.9) were randomly allocated into the *extraction group* (EG) or the *control group* (CG). Figure 12 presents a flow chart of the patients in papers I-IV.

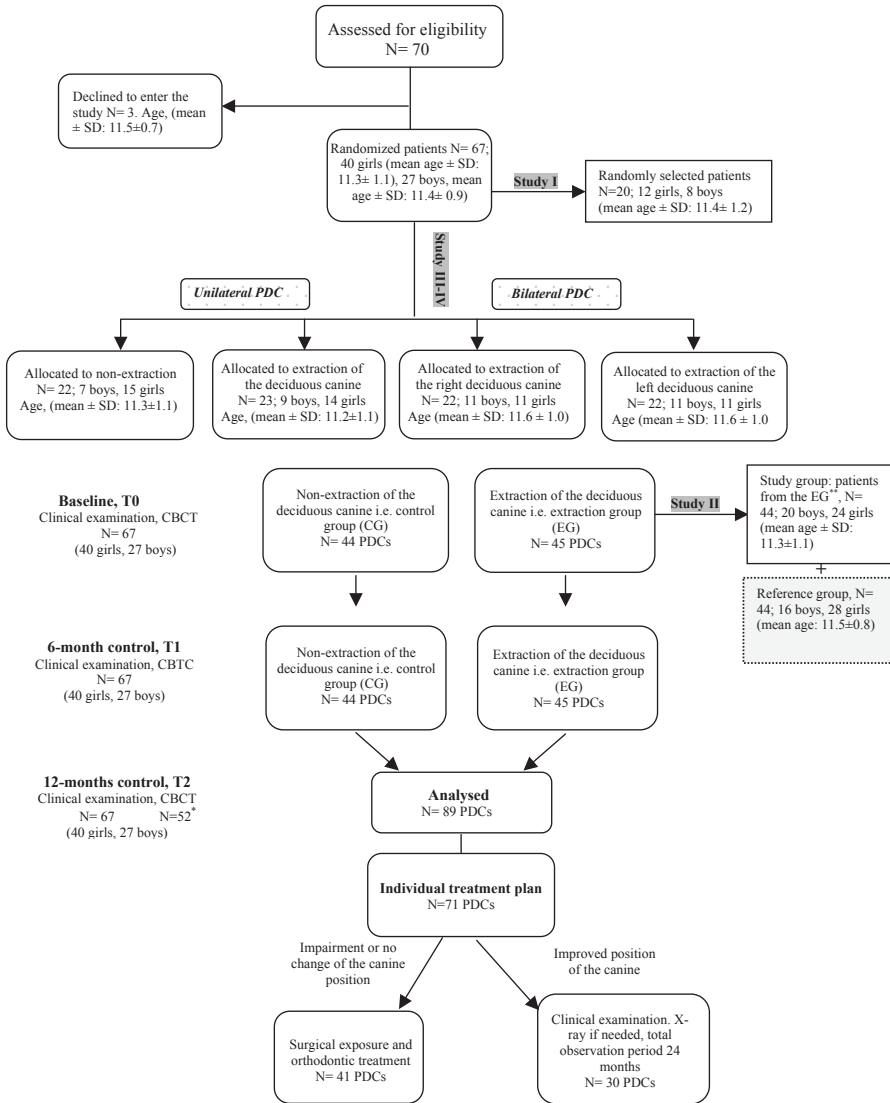
In **paper I**: Twenty patients, 8 boys and 12 girls (mean age \pm SD: 11.4 \pm 1.2 years) were randomly selected from the total group of participants. In total, 60 CBCT images were evaluated for the methodological analysis.

In **paper II**: Patients who had extraction of the deciduous canine from September 2008-October 2010 were included in a group referred to as the *study group*, which consisted of 44 children: 20 boys (11.5 \pm 1.2) and 24 girls (11.2 \pm 1.2). A *reference group* with an absence of PDC was recruited from the same public dental clinics in Gothenburg, of the same gender, living area, and nearest in birth date (\pm 10 days) to

the study group. Two “reference children” were indentified for each “study child”. Our aim was to have at least one reference child for each study child. Written information about the study and the questionnaire was sent to the parents. The children and parents were asked to sign the informed consent form and send it back with the questionnaire. Eighty-eight children were asked to participate and when 44 children (16 boys, mean age: 11.2 ± 0.7 , 28 girls, mean age: 11.6 ± 0.9) accepted to participation in the study, no attempt was made to send further mail reminders.

In **papers III-IV**: Patients with unilateral PDC (n=45) were randomized either to have extraction of the deciduous canine or non-extraction and patients with bilateral PDCs (n=22) were randomized to have either the right or the left deciduous canine extracted. For randomization, block randomization method was used and the allocations were concealed in consecutively numbered, sealed envelopes. An intention-to-treat (ITT) approach was also applied i.e. all randomized patients were included in the groups to which they were randomly assigned, regardless of the treatment they actually received and regardless of a deviation from the protocol as they were randomized.

Figure 12. Flowchart describing the patient sample in papers I-IV and the protocol used in papers III-IV.



* Number of patients that had CBCT images taken. ** Patients in the EG collected until October 2010.

Methods

Radiographic procedure (papers I, III, IV)

The CBCT examination (papers I, III, IV) was performed at the Department of Oral and Maxillofacial Radiology at the Faculty of Odontology at Sahlgrenska Academy, Gothenburg, with the 3D Accuitomo FPD (J. Morita, Kyoto, Japan) with a 360-degree rotation (Figure 13). The volume used was 60x60mm. The examination was performed at three stages: baseline, after 6 months and 12 months. The examinations depict from the incisors to the first molars in one volume. Primary data reconstructions were made by acquisition software (i-Dixel-3DX, 3D Version 1.691, J Morita Mfg Corp) at the Accuitomo workstation, providing axial, frontal and sagittal views. Secondary reconstruction was then made using the i-Dixel software. Using DICOM export, axial slices were sent to PACS for later reformatting.

Figure 13. 3D Accuitomo FPD.



Figure 14. Workstation for reformatting, viewing and measuring.

Reformatting and viewing the axial slices was performed at a workstation with the Sectra IDSS (Sectra Imtec AB, Linköping, Sweden) PACS Multi Planar Reconstructions program (Figure 14). Measurements were made on one of two monochromatic screens (OLXXXXRIN Medic Line ML 187D TFT-LCD, Olorin AB, Kungsbacka, Sweden) with a resolution of 1280x1024 pixels. Two calibrated examiners, one oral radiologist



(R.P.) and one orthodontist (J.N.), measured the reformatted images in 20 patients in paper I. The same oral radiologist carried out all the measurements in the 67 patients in papers III-IV and was unaware of the group to which the patients belonged.

Measurements

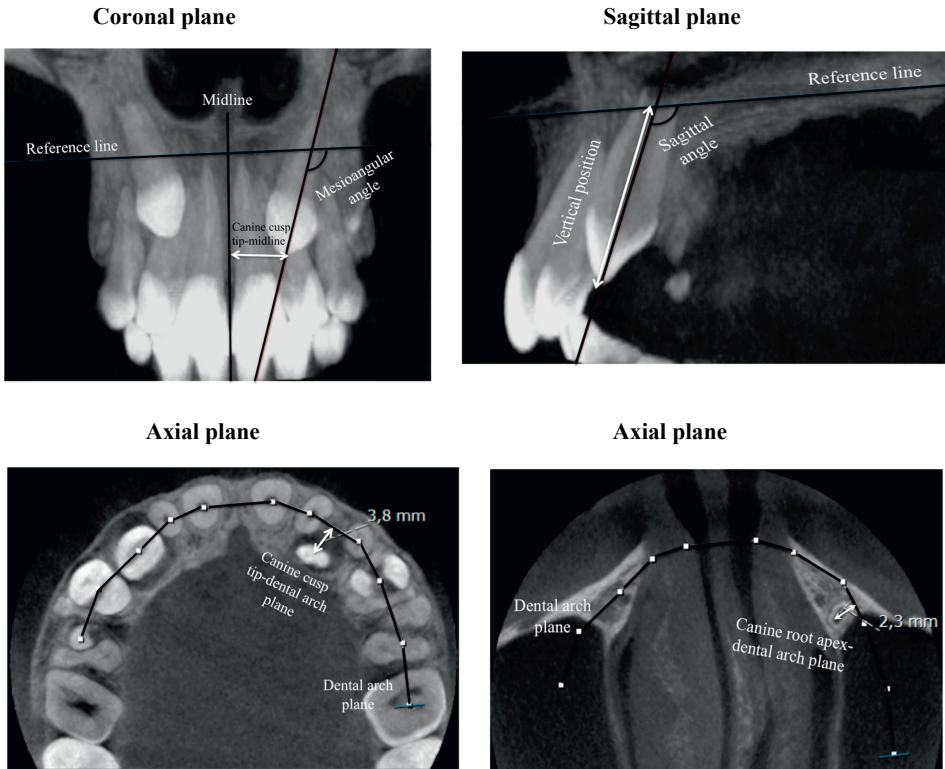
Angular and linear measurements were made in relation to either a) the reference line, b) the dental arch plane or c) to the midline (Figure 15). A *reference line* was drawn through the hard palate from spina nasalis anterior to spina nasalis posterior (written as pterygomaxillare in paper I). The reference line was fixed and thus never changed, irrespective of which view (sagittal or coronal) the measurements were performed in. A line centrally along the canine's longitudinal axis was drawn and angular and linear measurements were made to the reference line (Figure 15). The *dental arch plane* was drawn in the centre of the dental arch from tooth number 4 (54/14, 64/24) at the axial level, where the marginal bone was visible interdentially at 11/21. A positive radiographic value for the linear measurements of canine cusp tip-dental arch plane and canine root apex- dental arch plane indicates a palatal position of the cusp-tip or apex and a negative value a buccal position in relation to the dental arch plane. The *midline* was drawn in the centre of the two maxillary central incisors on the coronal images.

Coronal image: measurement of the *mesioangular angle* relative to the reference line and measurement of the distance from the *canine cusp-tip to the midline*.

Sagittal image: measurement of the *sagittal angle* to the reference line and of the distance i.e. *vertical position* from the reference line to the canine cusp tip.

Axial image: measurement of the bucco-lingual distance of the *canine cusp tip to dental arch plane* and the *canine apex to the dental arch plane*.

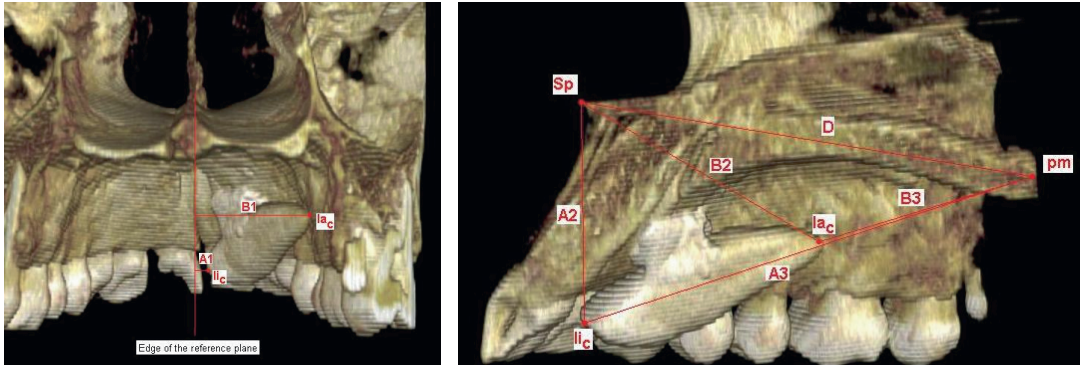
Figure 15. Radiographic measurements of the PDCs assessed in coronal, sagittal and axial plane on CBCT images used in papers I, III and IV.



Validity and reliability of radiographic procedures (paper I)

The validity of the mesioangular and sagittal angle was tested by using an extracted canine that was placed in the palate of a dry skull in three different locations and thus with 3 different angulations and positions, mimicking the PDC examined in the patients. CBCT images were then taken by placing the dry skull on a stand so it could be positioned, as though it was a patient's head. The dry skull measurements and the related measurements on the CBCT images were assessed by one observer (J.N.).

Figure 16. Direct measurements made on the dry skull. Definitions are explained in detail in the table to the right.



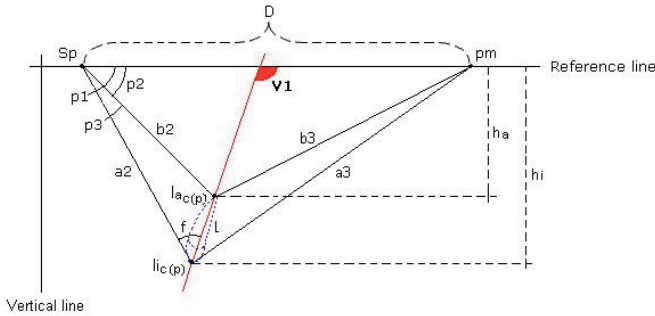
Measurements	Abbreviation	Definition
Reference line: spina nasalis anterior (sp) to spina nasalis posterior (pm)	sp-pm (D)	Distance in mm from spina nasalis anterior to spina nasalis posterior (written as pterygomaxillare in paper I).
Ii _c (incisal edge of the canine) to the reference plane (corresponds to midsagittal plane)	Ii _c -RP (A1)	Perpendicular distance in mm from Ii _c and reference plane (corresponds to midsagittal plane).
Ii _c to spina nasalis anterior	Ii _c -sp (A2)	Distance in mm from Ii _c to spina nasalis anterior.
Ii _c to spina nasalis posterior	Ii _c -pm (A3)	Distance in mm from Ii _c to spina nasalis posterior .
Ia _c (apex of the canine) to the reference plane (corresponds to midsagittal plane)	Ia _c -RP (B1)	Perpendicular distance in mm from Ia _c and reference plane.
Ia _c to spina nasalis anterior	Ia _c -sp (B2)	Distance in mm from Ia _c to spina nasalis anterior.
Ia _c to spina nasalis posterior	Ia _c -pm (B3)	Distance in mm from Ia _c to spina nasalis posterior.

In total, seven direct measurements (Figure 16) were measured on the dry skull using a digital calliper (Cocraft, Sweden AB, resolution 0.01 mm; accuracy ± 0.03 mm). The direct measurements were used to calculate the angles in Microsoft Excel with following methods:

- **Sagittal angle calculation**

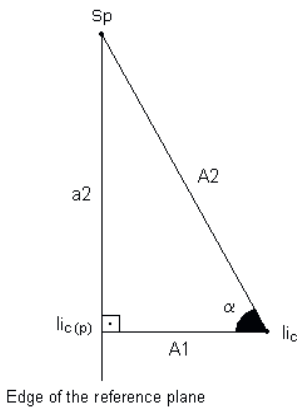
Several mathematical formulations were needed to calculate the sagittal angle. These are briefly described in the legends of Figure 17 and 18 and thoroughly in paper I.

Figure 17. Geometrical illustration of how the sagittal angle (V1), corresponding to the sagittal angle in Figure 15, was determined by projecting the canine (dotted drawing) on the reference line in a 2D plane. To find the sagittal angle, the angles “p1”, “p2”, “p3” and “f” and the distance x ($I_{ic(p)}-I_{a_c(p)}$) had first to be determined. The angles “p1”, “p2”, “f” and “x” were calculated using the Law of Cosines. Angle p3 was obtained by subtracting p2 from p1. The sagittal angle was obtained by summing the angles p1 and f. Abbreviations and definitions are shown on the right side.



ABBREVIATIONS AND DEFINITIONS	
$I_{ic(p)}$	projected incisal edge of the canine
$I_{a_c(p)}$	projected apex of the canine
V1	sagittal angle
Sp	spina nasalis anterior
pm	spina nasalis posterior
Reference line	a line between sp-pm
D	sp-pm
a2	distance between $I_{ic(p)}$ -sp
a3	distance between $I_{ic(p)}$ -pm
b2	distance between $I_{a_c(p)}$ -sp
b3	distance between $I_{a_c(p)}$ -pm
L	distance between $I_{ic(p)}$ - $I_{a_c(p)}$
hi	distance between $I_{ic(p)}$ - reference line
ha	distance between $I_{a_c(p)}$ - reference line
p1	angle between $I_{ic(p)}$ -sp and sp-pm
p2	angle between $I_{a_c(p)}$ -sp and sp-pm
p3	angle between $I_{ic(p)}$ -sp and $I_{a_c(p)}$ -sp
f	angle between $I_{ic(p)}$ -sp and $I_{ic(p)}$ - $I_{a_c(p)}$.

Figure 18. The triangle illustrates how the projection of line “a2” on the reference plane was determined. Distance a2y was found using the α angle in the equation $\tan(\alpha) = (a2/ A1)$. Abbreviations and definitions are shown on the right side.

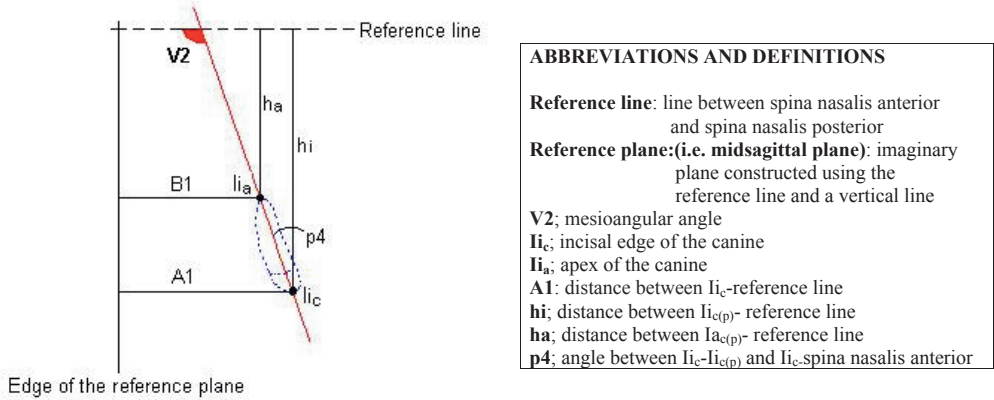


ABBREVIATIONS AND DEFINITIONS	
Sp	spina nasalis anterior
Reference plane (i.e. midsagittal plane)	imaginary plane constructed using the reference line and a vertical line
I_{ic}	incisal edge of the canine
$I_{ic(p)}$	projected incisal edge of the canine
A1	distance between I_{ic} -reference plane
A2	distance between I_{ic} -sp
a2	distance between $I_{ic(p)}$ - sp
α	angle between A1 and A2

• **Mesioangular angle calculation**

A brief explanation of how the mesioangular angle was determined is shown in Figure 19, and a stepwise detailed explanation is given in paper I.

Figure 19. Illustration of how the mesioangular angle (V2), corresponding to the mesioangular angle in Figure 15, was obtained. The dotted drawing indicates the canine. The mesioangular angle was obtained by summing the angle “p4” with 90 degrees. Abbreviations and definitions are shown on the right side



Repeat measurements

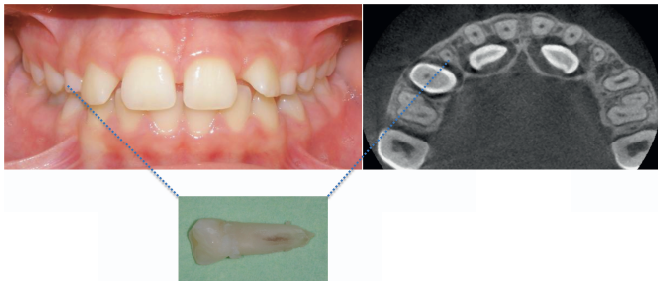
All 60 images were re-measured by the two examiners at an interval of at least 2 weeks in order to determine the intra- and inter-examiner error and the reproducibility of the 3D images. To avoid operator fatigue, no more than 10 images were analyzed at one time. Lines and reference planes were redrawn between the first and the second measurements. The direct measurements on the dry skull were made before the radiographs were taken, and the dry skull was measured 3 times at intervals of at least 2 days.

Patients’ perception (paper II)

At the *first visit*, before extracting the deciduous canine, children in the study group were asked to fulfil in a questionnaire (T1) measuring the level of anxiety using the dental anxiety scale (DAS) and questions about earlier dental treatment experiences (Appendices). DAS consists of 4 questions, each with a 1-5 scale response alternative. Population normative scores are between 8 and 9 and scores ≥ 15 are related to high levels of dental anxiety (Berggren and Carlsson, 1984). Previous experience of dental treatment was assessed with questions about: dental

injection, tooth drilling, tooth restoration and tooth extraction. Children in the reference group also answered the T1 questionnaire, which they received by mail. At the *second visit*, the deciduous canine was extracted. All deciduous canines were extracted by the same orthodontist (J.N.) at the orthodontics clinic, University Clinics of Odontology, Gothenburg, Sweden (Figure 20).

Figure 20. The right deciduous canine with a slightly resorbed root has been extracted in a patient with bilateral PDCs. The PDCs can be seen on the cone beam computed tomography image to the right.



Before the extraction, the children were given topical anaesthetics (2% lidocaine with 1:100,000 epinephrine) for 2 min and a buccal and palatal infiltration of local anaesthetics (20 mg/mL lidocaine with 12.5 g/mL epinephrine) with a dose of 1.8 mL. The children's acceptance of the treatment was rated during injection and extraction by the treating orthodontist (J.N.). The Rud & Kisling, (1973), rating of acceptance scale was used:

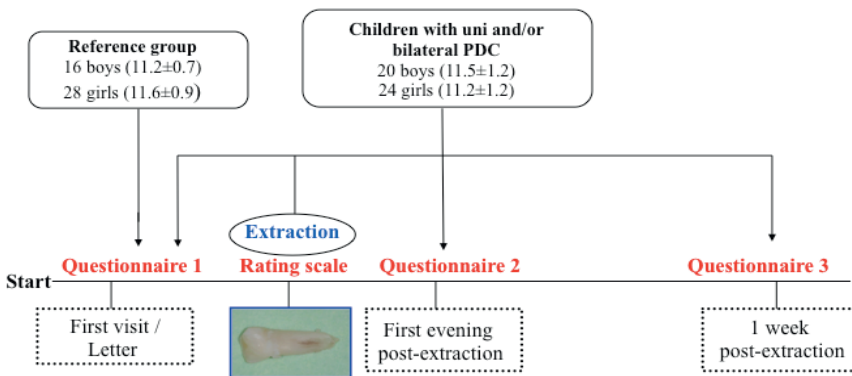
Rating scale	Level of acceptance
0	No acceptance
1	Reluctant acceptance
2	Indifferent acceptance
3	Full acceptance

Postoperative care information was given to the child and the parent/s, including a recommendation to use non-prescription analgesics at their own discretion. When the extraction was done, the children were given a post-extraction questionnaire to fill in at home and which they would return by mail. Figure 21 presents a flowchart

of the method used in this study. The post-extraction questionnaire consisted of 2 parts: the first part should be answered on the same evening as the day the extraction was done (T2) and the second part should be answered 1 week post-extraction (T3) (Appendices). The questions measured:

- pain & discomfort
- limitations in activities and jaw impairment
- use of analgesics
- children's acceptance of treatment

Figure 21. Flowchart of the method used in paper II.



Clinical procedure and follow-ups (papers III-IV)

At **baseline (T0)**, patients in the extracted group (EG) and in the control group (CG) had a radiographic examination consisting of CBCT images on the same day as the deciduous canine in the EG was extracted in order to get a precise timing of the start of the intervention. At the **6-months control (T1)**, all patients regardless of the group to which they belonged were clinically examined, followed by a new radiographic examination on the same day. At the **12-months control (T2)**, the above mentioned procedure was repeated. In cases where the canine had erupted at T2, imputation values were used i.e. by measuring the mean angular and linear measurements of 10 unilateral patients (8 girls mean age \pm SD: 11.2 \pm 0.9, 2 boys 11.7 and 10.6 years of age at baseline) whose contralateral non-palatal displaced

canine had fully erupted. Imputation values were used in 15 out of 67 patients (3 bilateral PDCs and 12 unilateral PDC: 3 from the CG and 9 from the EG).

After T2, an individual treatment plan was made for those patients with unerupted PDCs. If the unerupted canine in the EG had improved its position on the radiographic examination, continuous check-ups were made until the canine emerged through the gingiva. In the CG, the deciduous canine was extracted if it was not mobile. In cases in which the canine had impaired or no changes of its position at T2, surgical exposure followed by orthodontic treatment was done, regardless of the group to which the canine belonged. Figure 12 describes the patient sample and the protocol used in papers III and IV. The following outcome measures were assessed in paper III:

Primary outcome

- Eruption of the permanent canine (defined as canine emerged through the gingiva) during the total observation time, i.e. 24 months.

Secondary outcome

- Positional changes of the permanent canine over time (T1-T0 and T2-T1) observed by radiographic means and changes between T1-T0 and T2-T1 within and between the EG and the CG.
- Root resorption of adjacent teeth.

The following outcome measures were assessed in paper IV:

Primary outcome

- Differences in radiographic means of erupted and non-erupted canines.
- Radiographic variables that might influence the duration of the canine eruption between T1 and T2 and after T2.

Secondary outcome

- Cut-off points for angles and/or linear measurements to predict when interceptive extraction is beneficial versus unnecessary.

STATISTICAL ANALYSIS

Sample size calculation

The sample size calculation for papers III-IV was based on the alpha significance level of 0.05 and a beta of 0.10 to achieve 90 % power to detect a difference of 5 degrees (SD 6.38) over time in the sagittal and mesioangular angles measured in the CBCT images, between the extraction and the control group. The calculation indicated that a total of 60 patients with unilateral PDC were needed, i.e. 30 patients in each group. Since the inclusion criteria were both unilateral and bilateral PDC, the more bilateral PDC that were included the fewer patients were needed. To compensate for possible dropouts during the study, a total of 70 patients were enrolled.

- *Descriptive statistics* were calculated and presented as mean values and standard deviation (paper I-IV).
- *Dahlbergs formula* (1940): $s = \sqrt{\sum d^2/2n}$, where d=difference between duplicate determinations and n = number of determinations, was used for the random error in paper I.
- *Paired sample t-test* was used to calculate the systematic error in paper I, for the parametric data in paper II, and to compare the baseline variables and changes in time within the groups in papers III- IV.
- *Independent t-test* was used in papers III-IV to compare the baseline variables and changes in time between the groups and to test the significant differences in linear and angular variables between successful versus non-successful outcome in paper III- IV and to test the significance between canines erupting between T1 and T2 and after T2.
- *Fisher's exact test* was used in paper II for proportions and in paper III to calculate differences in categorical data as well as the main outcome, i.e. eruption

or non-eruption in the EG versus the CG. In addition, *Fisher's exact test* and *McNemar's test* was used in order to test whether the canines in the bilateral group would be considered as independent observations or dependent paired observations.

- *Two-way ANOVA* and *post hoc test* was used in paper II to analyse the patient reported changes over time.

- *Pearson's correlation coefficient (r)* was used in paper II to present correlations between the variables of: DAS, previous dental experiences, pain and discomfort during injection, extraction at the first evening post-extraction and one week post-extraction. $r > 0.8$ was considered a good correlation.

- *Multiple stepwise regression analysis* and *logistic regression analysis* were used in paper IV to detect possible predictors influencing the eruption of the PDC by calculating the odds ratio (OR).

- *Receiver-operating characteristic (ROC) curve analysis* was used in paper IV of the CG with erupted canines and of the EG with non-erupted canines to detect cut-off points for successful versus unsuccessful outcome. The discriminatory ability of the test will be greater as the ROC curve climbs towards the upper left hand corner of the graph, i.e. there is a larger area under the curve (AUC). A rough guideline for interpretation of the AUC is: 0.50 to 0.75 = fair, 0.75 to 0.92 = good, 0.92 to 0.97 = very good, 0.97 to 1.00 = excellent.

A p-value of <5% ($P < 0.05$) was considered statistically significant.

Statistical analyses were performed using versions 15.0 and 18.0 of the SPSS software package (SPSS Inc., Chicago, IL, USA) in papers I-II and SAS, version 9.3 for Windows (SAS Institute Inc., Cary, North Carolina, USA) in papers III-IV.

ETHICAL APPROVAL

Studies I-IV were all pre-approved by the research ethics committee of Sahlgrenska Academy at the University of Gothenburg, Sweden (Dnr 578-08) and by the radiation protection committee, Sahlgrenska Academy at the University of Gothenburg, Sweden. Children and parents received verbal and written information and were asked to sign the informed consent form before entering the trial. A signed informed consent form was provided by an adult with parental responsibilities and rights in accordance with the Declaration of Helsinki.

RESULTS

PAPER I

Reliability of the radiographic procedure

The mean differences for the double intra-examiner measurements were below 0.01 degrees for angular measurements and below 0.13 mm for linear measurements. Inter-examiner mean differences were also low and statistically insignificant but somewhat higher than the intra-examiner measurements: the angular measurements were below 0.53 degrees and linear measurements below 0.27 mm (Table 3).

Table 3. Mean and standard deviations differences, p-values and confidence intervals of the inter-examiner and intra-examiner measurements.

	Inter-examiner						Intra-examiner		
	Observer 1			Observer 2			Mean±SD	P	CI
	Mean±SD	P	CI	Mean±SD	P	CI			
Angular measurements (°)									
Mesioangular angle	-0.32±0.82	0.16	-0.77±0.13	0.35±0.47	0.09	-0.05±0.76	-0.01±0.27	0.94	-0.26±0.24
Sagittal angle	0.35±0.41	0.15	-0.75±0.12	0.53±0.55	0.10	-0.12±0.19	0.01±0.47	0.96	-0.33±0.35
Linear measurements (mm)									
Vertical position	-0.14±0.39	0.18	-0.35 ±0.06	-0.05±0.33	0.58	-0.23±0.13	-0.01±0.09	0.98	-0.13±0.13
Canine cusp tip-dental arch plane	0.25±0.33	0.09	-0.03±0.33	-0.27±0.29	0.39	-0.23±0.09	0.13±0.18	0.98	-0.13±0.13
Canine root apex-dental arch	-0.27±0.37	0.48	-0.28±0.13	-0.23±0.56	0.39	-0.45±0.18	0.11±0.13	0.60	-0.10±0.17
Canine cusp tip-midline	-0.02±0.37	0.84	-0.22±0.18	-0.12±0.25	0.08	-0.25±0.01	-0.01±0.13	0.87	-0.16±0.14

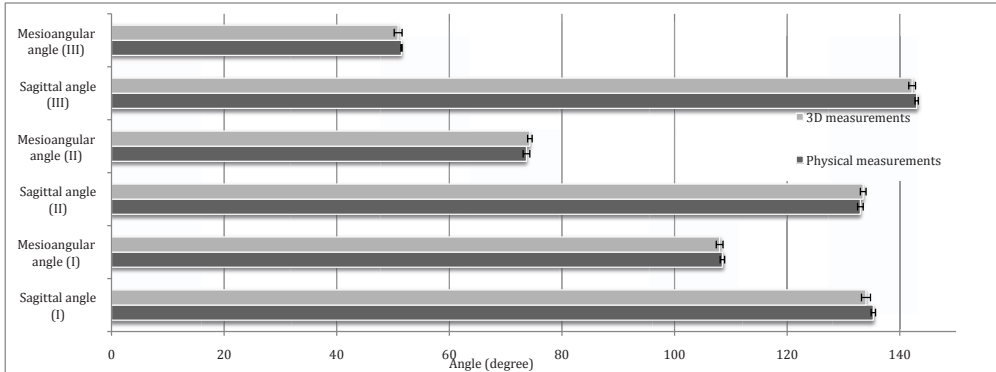
SD, Standard deviation; **P-value** < 0.05 are considered significant; CI, Confidence interval.

Validity of the radiographic procedure

Mean differences between angular measurements made on CBCT images compared with the physical dry skull measurements were 0.51 ± 0.39 degree for the sagittal angle and 0.22 ± 0.19 for the mesioangular angle (Figure 22). No

statistical differences were found between the physical and 3D measurements for both angles.

Figure 22. Comparison of physical and 3D measurements of the sagittal and mesioangular angles with mean values and standard deviation, measured on three occasions (I, II, III).



PAPER II

Reported pain & discomfort

The overall reported pain and discomfort on the different occasions, during extraction, the first evening post-extraction and 1 week post-extraction were low and no gender differences regarding reported pain (Figure 23) and discomfort (Figure 24) were found. However, when the interventions were compared to each other, the results revealed that both girls and boys experienced injection as most painful. Among girls, the first evening post-extraction was more painful than during the extraction at 1 week post-extraction.

Significantly more discomfort during the injection than 1 week post-extraction was reported among both girls and boys. Girls reported more discomfort during the extraction and during the first evening than 1 week post-extraction. In general, although not found to be significant, girls answered more often in detail what they had experienced as unpleasant during the different interventions. Creaking sounds and wiggling the tooth was the main complaints in both genders.

A strong positive relationship was seen between previous dental experiences, DAS and the present intervention.

Figure 23. Reported mean intensity of *pain* and standard deviation for boys and girls on the different occasions. Significance is indicated by * ($P<0.05$), ** ($P<0.01$).

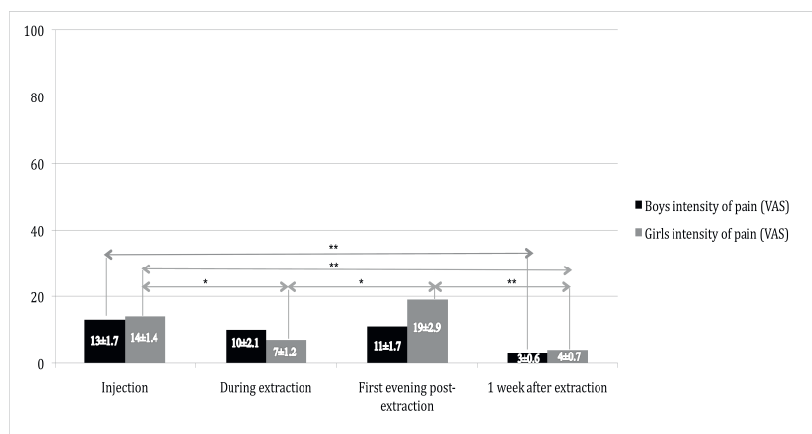
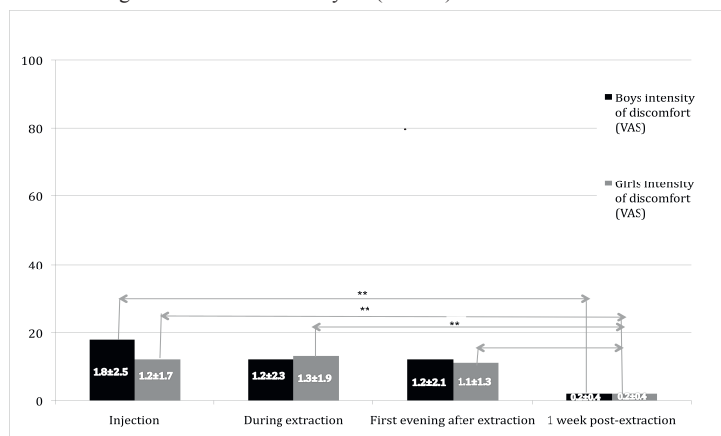


Figure 24. Reported mean intensity of *discomfort* and standard deviation for boys and girls on the different occasions. Significance is indicated by ** ($P<0.01$).



Use of analgesics

There were no significant differences for intake of painkillers among the genders. Analgesics mainly acetaminophen (paracetamol), ibuprofen and aspirin were only used on the first evening post-extraction by 35% of the boys and 50% of the girls. Both girls and boys had more pain during the first evening than 1 week post-extraction, and boys who had more pain the first evening used significantly more

painkillers, while girls who took medication reported more pain 1 week post-extraction than the ones who did not take analgesics.

Patients' acceptance of treatment

Full acceptance was rated for injection in 89 % and for extraction in 85 % of the children. Indifferent acceptance of injection was observed among 11% of the children and 15 % for the extraction. A higher value on the VAS scale for *experience of overall dental treatment* and *previous tooth extraction* was noted for children who had indifferent acceptance of injection. Gender differences were not found between DAS and acceptance of injection or DAS and extraction.

Limitations in activities and jaw impairment

The extraction of the deciduous canine did not cause disturbed sleep, jaw impairment or the necessity that the children had to stay home from school. However, a strong correlation was found for the item *to laugh* and *resistance when chewing* during the first evening. Only two children refrained from spare time activities, taekwondo and horse riding, the same day as the extraction was performed.

Influence of previous dental experience on the present extraction

A strong positive relationship was found between several baseline measures (DAS and questions about previous dental treatment experience) and the present extraction.

Comparison between the study and the reference group

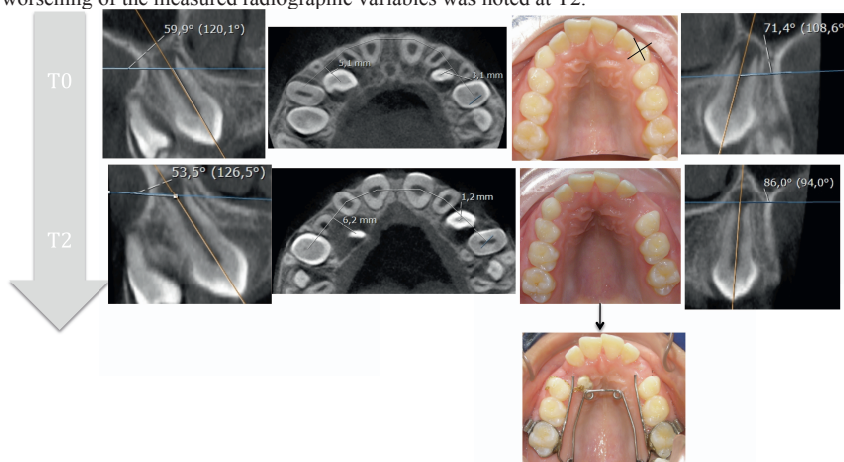
Significant differences between the study and the reference group or between the genders about earlier treatment experiences was not found. When the two groups were merged, it was found that boys reported significantly higher levels of pain during injection than girls.

PAPER III

Primary outcome

The prevalence of an erupted PDC on the extracted site was 69% compared to 39% on the untreated control site ($p=0.001$). Figure 25 shows a clinical example of these results.

Figure 25 . Patient (Age: 11 years, 2 months) with a similar grade of displacement of both maxillary canines at baseline (T0). The left canine indicated with X was randomized for extraction. At the 12-month control (T2) on the *extracted site*: the permanent canine had improvement of angular and linear measurements on the CBCT images. The canine was therefore followed up clinically and with x-rays until it erupted, which occurred at 20 months. The right permanent canine at the *control site* was surgically exposed, followed by orthodontic treatment since worsening of the measured radiographic variables was noted at T2.



Secondary outcome

Significantly more beneficial changes of the canine position were observed over time in the EG compared to the CG for 3 of 6 variables between T0 and T1 and for all variables except for the sagittal angle between T1 and T2 (Table 4).

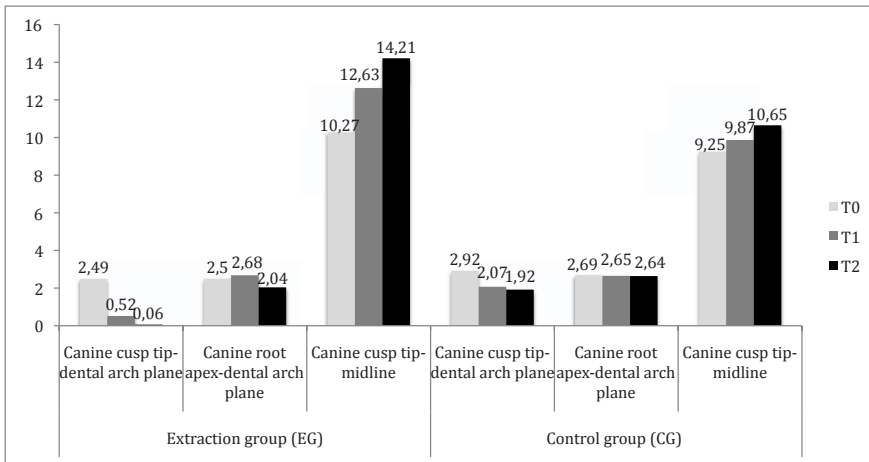
In the EG, the canine cusp tip moved significantly closer to the dental arch plane and more away from the midline between T0 and T1 than T1 and T2, while the canine root apex came closer to the dental arch plane between T1 and T2 than between T0 and T1 (Figure 26). More positional changes of the canine cusp tip and root apex to the dental arch plane in the EG than the CG between T1 and T2 than between T0 and T1 were observed.

Table 4. Positional changes over time of the permanent canine at T1-T0 (6- month control - baseline) and T2-T1 (12-month control - 6 month control) within and between the EG and the CG.

Variable	T1-T0 (patients, n=67)					T2-T1 (patients, n=67)						
	EG ^a (n=45 PDC)		CG ^b (n=44 PDC)		Differences Mean (95% CI) ^c EG-CG	P- value ^c EG-CG	EG ^a (n=45 PDC)		CG ^b (n=44 PDC)		Differences Mean (95% CI) ^c EG-CG	P- value ^d EG- CG
	Mean±SD ^c	P- value ^d	Mean±SD ^c	P- value ^d			Mean±SD ^c	P- value ^d	Mean±SD ^c	P- value ^d		
Mesioangular angle(°)	-3.4±5.8	***	-0.8±5.8	NS	-2.6 (-5.1, -0.10)	*	-3.3±6.4	***	-0.5±5.9	NS	-2.8 (-5.4, -0.2)	*
Sagittal angle (°)	1.9±5.9	*	1.2±7.3	NS	0.7 (-2.1, 3.6)	NS	2.5±5.3	***	1.7±8.6	NS	1.7(-1.2, 4.7)	NS
Vertical position (mm)	2.7±1.5	***	1.7±1.6	***	0.9 (0.3, 1.6)	**	3.2±1.8	***	1.9±1.9	***	1.2 (0.5, 2.0)	**
Canine cusp tip-dental arch plane(mm)	-1.9±1.5	***	-0.9±1.7	**	-0.3 (-1.2, 0.6)	NS	-0.5±2.4	NS	-0.1±1.9	NS	-1.1 (-1.8, -0.4)	***
Canine root apex- dental arch plane(mm)	0.2±1.9	NS	-0.1±1.3	NS	0.2 (-0.4, 0.8)	NS	-0.6±1.1	***	-0.0±1.4	NS	0.8 (0.2, 1.4)	**
Canine cusp tip-midline (mm)	2.3±1.5	****	0.6±1.9	*	1.7 (0.9, 2.5)	***	1.6±1.6	***	0.7±1.3	***	-0.62 (-1.1, -0.1)	**

^a EG: extraction group. ^bCG: control group. ^c SD: standard deviation. ^d p-value: * (P<0.05), ** (P<0.01), *** (P<0.001). ^e CI: confidence interval.

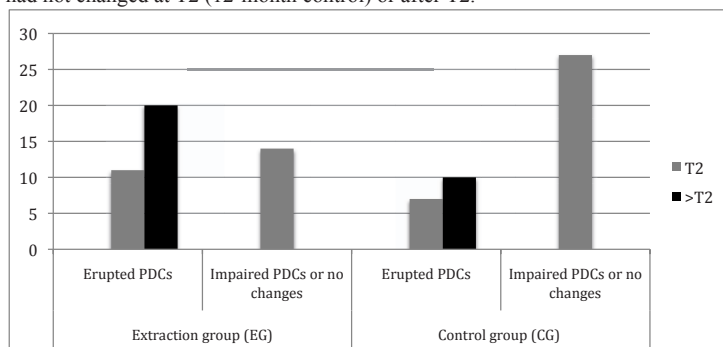
Figure 26. Mean values for the measured variables between the extracted group (EG) and the control group (CG) at baseline (T0), the 6-month control (T1) and the 12-month control (T2).



The mean eruption time was significantly shorter in the EG than in the CG. However, a significant difference was not seen for the mean eruption time between younger and older patients. Surgical exposure and orthodontic treatment were necessary in 31% of the PDCs in the EG and 61% of the PDCs in the CG since

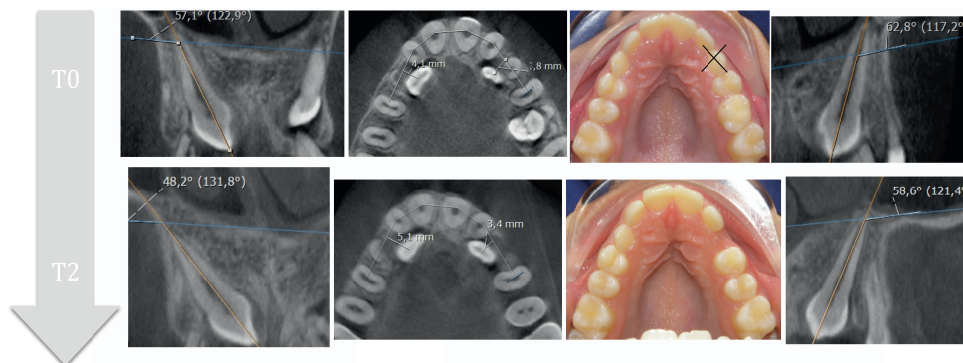
these canines had impaired or no changes of their position at T2 (Figure 27). The remaining PDCs that were followed up after T2 in the EG and the CG all erupted. Five out of 10 deciduous canines in the CG that were followed up after T2 were not mobile and were extracted, while the mobile ones were left to spontaneously exfoliate. Figure 28 shows an example of a patient from papers III-IV with bilateral PDC that had surgical exposure on both the extracted and the control site.

Figure 27. Number of PDCs in the extracted (EG) and the control group (CG) that had erupted, were impaired or had not changed at T2 (12-month control) or after T2.



Note that 5 deciduous canines in the control group that were not mobile (n=5) were extracted at T2.

Figure 28. Patient (12 years, 1 month) with a more severe displacement of the right permanent canine than the left canine at baseline (T0). The left deciduous canine indicated with X was randomized for extraction. At the 12-month control (T2), the canine on both the *extracted site* and the *control site* had surgical exposure followed by orthodontic treatment since the angular and linear measurements on the CBCT images had become worse.



Although not significantly the amount of root resorption of grade 2 of adjacent teeth increased from T0 to T2 and more teeth were resorbed in the CG than in the EG at T1 ($p= 0.4218$) and at T2 ($p= 0.2123$). The adjacent teeth that had root resorption were all lateral incisors.

PAPER IV

Primary outcome

In the “erupted” group, regardless of whether the deciduous canine was extracted, the mesioangular angle and the distance canine cusp tip-dental arch plane was smaller while the distance of canine cusp tip-midline was larger (Table 5), demonstrating that a PDC with a more favourable position at baseline would have erupted even if the deciduous canine was not extracted. In addition, patients were significantly younger in the “erupted” group. On the other hand, PDC that had erupted in the CG had less deviating angles and distances mentioned above from the “ideal” position compared to the EG. This indicates that PDCs, even with a more deviating baseline position, may erupt if the deciduous canine is extracted.

No significant differences for the angular and linear measurements between the EG and the CG were seen regarding the non-erupted PDCs.

Table 5. Baseline means (T0) with mean and standard deviation (SD) for the erupted and non-erupted canines in the extraction group (EG) and the control group (CG) and p-values between the EG and the CG as well as between the erupted and non-erupted PDC. P < 0.05 is considered statistically significant.

Variables at T0	Erupted (n= 40 patients,48 PDC)			Non-erupted (n= 27 patients,41 PDC)			
	EG (n= 31) Mean ±SD	CG (n= 17) Mean ± SD	P-value EG-CG	EG (n= 14) Mean ± SD	CG (n= 27) Mean ± SD	P-value EG-CG	P-value Erupted vs Non-erupted
Mesioangular angle(°)	105.5±2.1	100.7±5.9	0.027	115.4±6.8	112.8 ±9.1	0.409	0.000
Sagittal angle (°)	99.4±8.1	104.9±7.9	0.625	93.5±10.1	98.2±12.7	0.538	0.364
Vertical position (mm)	15.2±2.4	14.3±2.2	0.178	16.6±4.0	15.6 ±2.3	0.502	0.168
Canine cusp tip- dental arch plane (mm)	2.9±1.2	2.0±1.7	0.051	4.1±1.7	3.7±0.7	0.707	0.000
Canine root apex- dental arch plane (mm)	2.4±1.2	2.5±1.4	0.130	2.9±1.8	2.3±1.9	0.599	0.324
Canine cusp tip-midline (mm)	10.5±2.2	12.9±1.7	0.048	6.5±2.6	7.7±1.8	0.311	0.000
Age, years	11.0±0.9	10.7±0.99	0.676	12.0±1.0	11.9±1.0	0.112	0.000

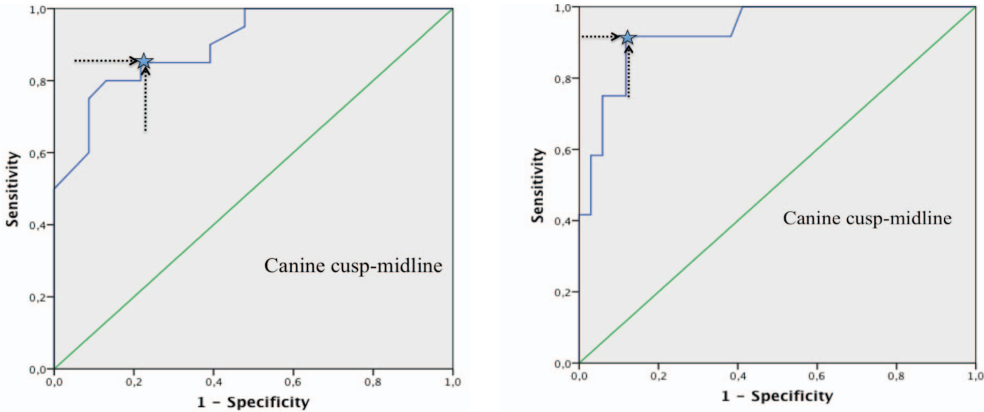
Age did not have an effect on the time to the canine eruption. However, higher values of the vertical position variable i.e. closer to the occlusal plane, in combination with extraction of the deciduous canine resulted in earlier eruption of the PDCs. The multiple stepwise regression analysis revealed that the vertical position, the canine root apex-dental arch plane and extraction of the deciduous canine altogether explained 24.1% ($p=0.026$, $R^2= 0.240$) of the variance in the time to eruption. The variable that most affected the main outcome was extraction of the deciduous canine followed by the age of the patient. The logistic regression disclosed that the probability of spontaneous eruption of the PDC in the EG was 18 times of that in the CG. In addition, every unit of change in millimetres of the canine cusp tip-midline and every unit of change in degrees of the mesioangular angle increased the odds ratio for successful outcome by 2.995 and 1.187, respectively.

Secondary outcome

Cut-off points of “easy” and “severe” cases of PDCs

The area under the ROC curve (AUC) was highest for the variable *canine cusp-midline* for both “easy” (erupted PDCs in the CG) and “severe” (non-erupted PDCs in the EG) cases of PDC (Figure 29). Thus canine cusp-midline has a very good discriminatory power and is therefore of value as a diagnostic test in determining whether a PDC will erupt spontaneously or not. An initial distance of the canine cusp tip-midline of 11 mm was crucial for spontaneous eruption without prior extraction of the deciduous canine and a value of 6 mm indicates that the canine will not erupt in spite of extraction of the deciduous canine.

Figure 29. ROC curve analysis with optimum cut-off point (marked with a star) of the variable: *canine cusp tip-midline* for spontaneous eruption of the PDC without prior interceptive extraction of the deciduous canine to the left (11 mm; sensitivity, 0.850; specificity, 0.739) and for PDCs needing surgical exposure despite interceptive extraction of the deciduous canine to the right (6 mm; sensitivity, 0.917; specificity, 0.853). Sensitivity indicates the percentage of PDCs in the CG and in the EG not erupting spontaneously in that the radiographic predictors identified as needing other intervention. Specificity is the percentage of PDCs in the CG and the EG erupting spontaneously in that the radiographical predictors identified as not needing any intervention. The diagonal line shows what could be expected from simple guessing i.e. pure chance.



The variable *canine cusp tip-dental arch plane* also had a high AUC for “easy” (0.893) and “severe” (0.890) PDCs, indicating a good validity of the test. An initial distance of 2.5 mm was crucial for spontaneous eruption without prior extraction of the deciduous canine (sensitivity, 0.950; specificity, 0.783; $p=0.000$) and 5 mm for not erupting spontaneously (sensitivity, 0.875; specificity, 0.818; $p=0.000$). The optimum cut-off point for the initial *mesioangular angle* was found to be 103° (sensitivity, 0.800; specificity, 0.739; $p=0.003$, AUC, 0.770) as being essential for spontaneous eruption of the PDC and 116° (sensitivity, 0.864; specificity, 0.750; $p=0.052$, AUC, 0.883) for not erupting spontaneously. The age of the patient had a rather low AUC for both “easy” (AUC, 0.676; sensitivity, 0.700; specificity, 0.608; $p=0.049$) and “severe” (AUC, 0.719; sensitivity, 0.719; specificity, 0.641; $p=0.038$) cases of PDC, indicating only a fair validity of the test. Figures 30-31 show two clinical cases that exemplify the cut-off points, and Figure 32 illustrates a summary of the cut-off points.

Figure 30. Bilateral PDCs (girl, 12.7 years of age) with more severe displacement on the right side at baseline (T0). The right deciduous canine as randomized for extraction (indicated with X). At the 12-month control (T2), a worsening of the canine position was seen on the control side and more and or less no changes of the canine on the right side. Both canines were surgically exposed. Retrospectively, extraction of the deciduous canine on the left side would be more beneficial according to the cut-off points.

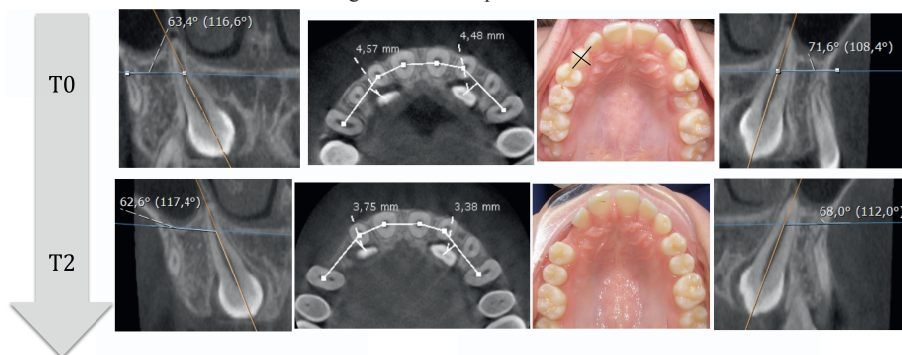


Figure 31. Bilateral PDCs (boy, 12.3 years of age) with a similar grade of displacement on both sides at baseline (T0). Extraction was done of the right deciduous canine (indicated as X) and the permanent canine was under eruption at T2. On the control side, an improvement of the canine position was seen on the radiographic measurements at the 12-months control (T2) and was therefore followed up and the canine emerged through the gingiva after 24 months. Retrospectively, interceptive extraction of the deciduous canines in this case was unnecessary since the cut-off points show that both permanent canines would have erupted anyway.

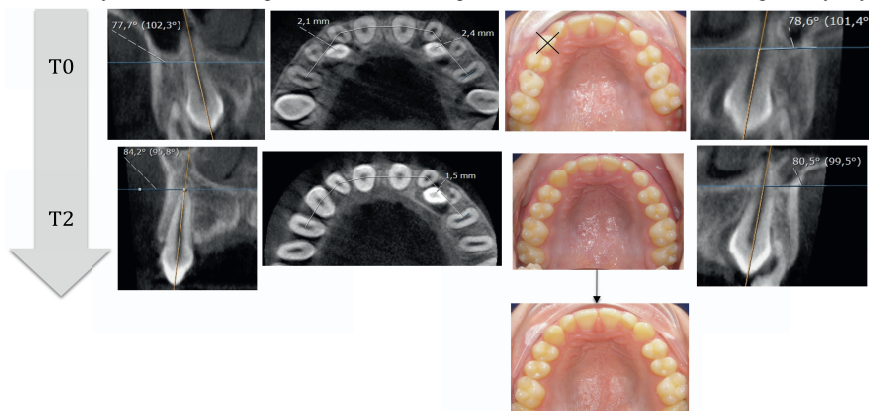
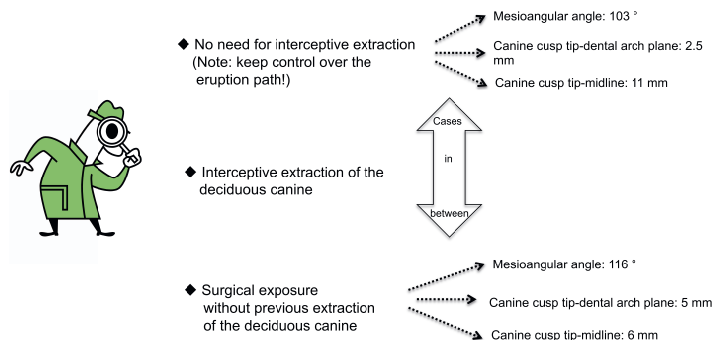


Figure 32. Cut-off points for the variables: canine cusp tip-midline, canine cusp tip-dental arch plane and mesioangular angle, as to when interceptive extraction is beneficial and when it is not.



DISCUSSION

Interceptive extraction of the deciduous canine was recommended to facilitate the eruption of the PDCs as early as in 1936 (Buchner, 1936). An early interceptive treatment is beneficial since PDCs that become impacted will cause great inconvenience for the patients, will lengthen and complicate the orthodontic treatment (Becker et al., 2003; Stewart et al., 2001), increase the treatment cost (Bazargani et al., 2013) and increase the risk of resorbing the adjacent teeth (Ericson and Kurol, 1987; Rimes et al., 1997; Saldarriaga et al., 2003). However, the scientific evidence on interceptive treatment of PDCs is limited according to two newly published systematic reviews (Naoumova et al., 2011; Parkin et al., 2012). Even though several clinical studies (Baccetti et al., 2011; Bonetti et al., 2011; Smailienė et al., 2011; Bazargani et al., 2014) have been published after the publication of the systematic reviews, still the evidence for interceptive treatment of PDCs is limited and there are still no interceptive studies evaluating the effect and positional changes of PDCs after extraction of the deciduous canine on 3D images. Therefore the aims of this thesis were to develop a method to measure the PDC on CBCT images, to evaluate the effect that interceptive extraction of a deciduous canine might have on patients with PDC and to describe the patient's experience of the tooth extraction. The most important finding in this thesis was to increase the evidence concerning the interceptive measure of extracting deciduous canines in patients with PDC as it was shown that spontaneous eruption of the permanent canine occurred significantly more often when the deciduous canine was extracted. Furthermore, by using the cut-off points as a guideline for successful outcome versus non-successful outcome, unnecessary extractions might be avoided and in severe cases exposure can be performed without delay. The newly developed method to measure linear and angular measurements of PDC on CBCT showed a high reproducibility and validity. The

post-extraction pain and discomfort experienced by the children was low. However, 42% used analgesics the first evening after extraction. It is therefore important for clinicians to prescribe appropriate analgesics and recommendation doses pre-and post-extraction.

Strengths and limitations

One of the strengths of this thesis is that three different research designs were used: methodological study (paper I), qualitative study (paper II) and RCT study (papers III-IV). By choosing an RCT design, we aimed for the highest level of evidence since bias and confounding factors can be avoided. A sample size calculation was done in advance to detect the differences in the eruption path of the PDC after interceptive extraction of the deciduous canine as compared to a control group. The well-described and controlled randomization procedure with allocation concealment resulted in equally distributed subjects between the groups and results from these studies might therefore be generalized to other Caucasian patients with PDC aged 10-13 years and in the case that the exclusion criteria are met. The reason for withdrawal before the treatment start were known and explained, as were the dropouts after the treatment start, which were none. The intention-to-treat (ITT) approach was used, i.e. data on unsuccessful cases were included in the final analysis. The radiographic method to measure and analyse the position of the PDC was assessed for intra-and inter-examiner error as well as for the validity, and the two examiners that carried out all the measurements underwent a calibration of the technique. This method was reliable and had high validity. The CBCT images were taken on the same day as the clinical examination and the extraction of the deciduous canine in the EG, resulting in precise control intervals for all subjects. Whenever the permanent canine was seen clinically, the patients did not undergo additional radiographic examinations. By using this design, the number of CBCT images taken and the radiation dose the patients received were minimized.

A limitation was that 15 patients were not followed up by CBCT and imputation values were instead used. Therefore the changes between T1 and T2 should be interpreted with some caution, since imputation values always can give uncertainty in the results. Another limitation of this thesis was that blinded measurements were only done on the baseline images, since the extracted canine was visible at the 6- and 12-month controls and it was not possible to block out the deciduous canine space on CBCT images. However, the main aim of paper III was to assess whether the permanent canine will spontaneously erupt after extracting the deciduous canine. An alternative would have been an assessor who had no knowledge of the study, but this was not possible since the method to measure the canine on CBCT images was developed with the oral radiologist. Even though the CBCT images contain higher radiation than the conventional radiographs, an additional strength of this thesis was that the CBCT images that had already been taken could be used for future studies to evaluate the cause and the sequelae of canine impaction.

Strict cut-off points were used in this thesis to maximize the sensitivity and specificity. The limitation of the ROC curve analysis is that the cut-off points may differ in different studies depending on how strict the authors have been in deciding on where to place the cut-off. To counter this limitation and to be able to get a true understanding of the diagnostic test's utility, pooling results of several studies examining the same test is needed in order to generate average specificity, sensitivity and ROC. In addition to evaluating the treatment effect of interceptive extraction of the deciduous canine, the children's perception should also be assessed. A questionnaire was thus distributed to explore the pain and discomfort caused by the interceptive extraction.

Subjects

Patients in this thesis were consecutively recruited from 15 different public dental clinics in Gothenburg and represent patients from a wide urban area. The group

could thus be considered a good representation of patients with PDC. The PDCs included were diagnosed twice since both the general practitioner and the consulting orthodontist examined the patients before the randomization, which might have resulted in a more accurate diagnosis of the canines. Patients were included by their chronological age, i.e. 10-13 years of age as the majority of permanent canines erupts during these time period. And clinical recommendations are easier to follow using the chronological age of the patient. No restriction was place to whether the canine was unilaterally or bilaterally displaced in order to be able to include all palatal displacements. The number of patients having bilateral displacement in our sample was 32 %, which is higher than the 10% reported in previous studies (Nordenram and Strömberg, 1966; Becker et al., 1981; Ericson and Kuroi, 1988; Peck et al., 1994). The explanation to this is, however, unclear. Patients with craniofacial syndromes, cleft lip and/or palate, odontomas and cysts were excluded since the primary aim of this thesis was to evaluate PDC in an average population. Patients with crowding exceeding 2 mm in the maxilla were also excluded, as we believe that only extraction of the deciduous canine is not sufficient. Resorption of adjacent teeth with grades 3 and 4 was also excluded either at the start or during the trial for ethical reasons.

Measurement reliability and validity on CBCT images (paper I)

Since CBCT has lately become very popular among orthodontists, and is more often used for diagnosis and treatment planning, it is very important to have methodological studies to evaluate their reliability and the validity before applying the method clinically. The aim of paper I was hence to evaluate the reliability and the validity in measuring the position of the PDCs using a coordinate system in 3D images obtained with the 3D Accuitomo FPD. When a specific radiographic examination is chosen, it is always important to consider the risks and costs (Ludlow et al., 2009). In papers I and III-IV, we used volumes of 60x60 mm to

keep the radiation dose as low as possible. Each volume gave an effective dose of 0.025mSV, which can be compared to one week of cosmic background radiation. However, it should be kept in mind that, even though the amounts of radiation doses are the same, the DNA damage is higher in a short time of exposure. Therefore, the ALARA (As Low As Reasonable Achievable) principle must be followed and considered when a clinician chooses to make a radiographic examination. Volumes of 40x40 mm would have given lower radiation doses but, since the posterior part of the reference line is not visible, 60x60 mm images were used. In all previous studies (Kurok and Ericson, 1988; Power and Short, 1993; Leonardi et al., 2004; Baccetti et al., 2008; Baccetti et al., 2009; Armi et al., 2010; Baccetti et al., 2011; Bonetti et al., 2010; Bonetti et al., 2011, Smailienė et al., 2011; Bazargani et al., 2013) evaluating the effect of extracting the deciduous canine on patients with PDCs, the occlusal plane has been used as a reference line. In papers I and III-IV we decided not to use the occlusal plane, as it is unstable in patients in the mixed dentition. Neither is the reference line: spina nasalis anterior-spina nasalis posterior stable as the maxilla moves down and forward in these growing patients. However, we judged it to be more reliable than the occlusal plane and we considered that the growth changes in the maxilla are of minor importance during the short follow-up time of 12 months. The most precise method would have been to use a stable line achieved by radiopaque bone markers in the jaw, for example by inserting two mini-crews during the observation period. This method was not considered for ethical reasons. Moreover, the above-mentioned interceptive studies used only 2D images: panoramic radiographs. Using panoramic radiographs increases the risk of misinterpretation since the diagnostic accuracy and the validity for localizing the impacted canine and adjacent structures can be underestimated because of deficiencies such as blurred images, distortion projection errors and complex maxillofacial structures that overlap on 2D images (Ericson and Kurok, 1987, 1988; Peene et al., 1990; Elefteriadis and Athanasiou, 1996; Stewart et al., 2001). The literature is limited in terms of studies comparing

linear and angular measurements of impacted canines made on 2D and 3D images and to our knowledge there are only two studies on CBCT (Walker et al., 2005; Liu et al., 2008) that have used linear and angular measurements and the occlusal plane as a reference line mimicking the method used by Ericson and Kurol (1988) to localize the maxillary impacted canines. A comparison of the canine angulation: canine angulation-lateral incisor, canine angulation-midline, canine angulation-occlusal plane on panoramic radiographs according to Ericson and Kurol (1988) and CBCT images according to Walker et al. (2005), has been recently assessed (Alqerban et al., 2011). A highly significant difference was found between 2D and 3D images in canine angulation-occlusal plane and to the midline. Compared with the CBCT images, the panoramic radiographs were less reliable and resulted in lower measurement accuracy and less agreement between the observers. Moreover a significant difference was also seen for the canine location and for detection of root resorption on adjacent teeth between 2D and 3D images. The authors thus concluded that CBCT images are more accurate for the different diagnostic tasks regarding canine impaction than panoramic radiographs.

Several factors can influence the measurement accuracy such as: the precision of the calliper, which software that is used, the size, material and the resolutions of the images (Gribel et al., 2011). In paper I, a calliper offering measurements to the nearest 0.01 mm was used for the direct measurements, and the CBCT images had a higher resolution capability, with a 0.5 mm slice thickness, which was greater than in previous studies (Richardson, 1981; Rakosi, 1982; Ongkosuwito et al., 2002; Chen et al., 2004; Liu et al., 2008). In addition, we used validated i-Dixel software for the measurements (Lund et al., 2009; 2010). A more precise inter- and intra-examiner error could have been achieved in paper I by including more observers than the two calibrated examiners.

Unplanned patient movement of the head is possible in a clinical situation, although the present study did not investigate the effect of changing the head

position in the CBCT machine on the accuracy of the obtained measurements since several recent studies have been published in this field. In the study by Hassan et al. (2009), the skulls were scanned in ideal and a 15-degree tilted position, while, in the study by Berco et al. (2009), the ideally positioned skulls were compared with skulls tilted at 45 degrees. Both studies showed that there were no statistically significant differences between the measurements and that small variations in the patients' head position did not influence the measurement accuracy. In the same context, El-Beialy et al. (2011) investigated 5 different skull positions in addition to the centered position dictated by the manufacturer. The authors concluded that the accuracy and reliability of the CBCT measurements are not affected by changing the skull orientation. Upper lip or chin rest, which can be used to ensure stabilization, should not be considered as an absolute requirement during CBCT imaging, especially as these head positioning devices may cause obliteration and distortion of the patient's facial soft tissues.

The validity of linear measurements has been assessed in many studies of objects such as, cube, acrylic block or Plexiglas plates with metal balls compared to radiographic images or direct measurements on dry skulls, compared to CBCT images. The common finding is that measurements made on CBCT images are highly accurate and reproducible (Marmulla et al., 2005; Pinsky et al., 2006; Kumar et al., 2007, Lagravère et al., 2008; Stratemann et al., 2008; Hassan et al., 2009, Lund et al., 2009; 2010). Another finding is that artificial measurements have higher accuracy and precision than measurements made in patients: This can be explained by that anatomical structures being more difficult to define (Lund et al., 2009; 2010). Studies that assess the validity of angular measurements are still limited, however. Therefore, in paper I, the validity of the angular measurements were evaluated only on dry skulls. Dry skulls are commonly used to validate new craniofacial imaging modalities and direct measurements are used as the gold standard for purposes of comparison (Lascalea et al., 2004; Hassan et al., 2009;

Berco et al., 2009). The validation in paper I was done by measuring specific distances and using mathematical formula to calculate the angles. An alternative would have been to measure angles directly on the dry skull. Some earlier studies have compared measurements obtained from several skulls (Hilgers et al., 2005; Hassan et al., 2009) whereas we focused on repeated measurements taken on the same skull. With the use of many skulls to draw a mean for a specific measurement, a higher variability of the mean could have been achieved than from repeated measurements on one dry skull, since the latter method is more sensitive to the smallest differences.

The *in vivo* results from paper I showed that the overall CBCT measurements had high accuracy and reproducibility with less than 1 measuring unit (mm or degree) of difference, which is the magnitude of clinical significance for radiographic measurements mentioned in the literature (Richardson, 1981; Rakosi, 1982). No statistically significant differences for the intra- and inter-examiner measurements were seen, indicating a low risk of systematic errors. The inter-examiner error was higher, however, which is in accordance with previous studies (Ongkosuwito et al., 2002; Nagasaka et al., 2003; Chen et al., 2004). We can thereby reject our hypothesis that inter- and intra-examiner reliability and validity of the measured angles of the PDC on CBCT are low. Although statistically insignificant, a somewhat higher measuring error was observed for the variables of canine cusp tip-dental arch and canine apex-dental arch in both intra and inter-examiner measurements. The reason for this can be explained by the geometrical principle illustrated by Nagasaka and co-workers (2003): “the closer two landmarks are, the greater the linear measurement error tends to be”. Another explanation can be that the measured images contained a greater variation of canine apex development or position of the canine cusp tip since CBCTs from 20 patients at three different developmental occasions were measured instead of measuring 60 images on one occasion.

Patient experience of extracting the deciduous canine (paper II)

The effect of interceptive treatment of PDCs has received considerable attention in the literature (Ericson and Kuroi, 1988; Power and Short, 1993; Baccetti et al., 2008; 2009; 2011; Sigler et al., 2011; Armi et al., 2011; Bonetti et al., 2010; 2011). Nevertheless, the Cochrane systematic review (Parkin et al., 2012) or the later search was not able to find any study on patient satisfaction and pain experience during extraction of the deciduous canine in patients with PDC. Therefore, to our knowledge, paper II in this thesis is the first published study on the perception of pain and discomfort after deciduous canine extraction as an interceptive treatment in children with PDC.

Before extracting the deciduous canine, patients responded to the dental anxiety scale (DAS), which has a high internal reliability and test-retest reliability (Newton and Buck, 2000). Although we decided to use DAS, the Dental Subscale of the Children's Fear Survey Schedule (CFSS-DS) could have been a better choice, as it is a more detailed and well-known questionnaire measuring dental fear in children (Cuthbert and Melamed, 1982), than DAS that is more used for adolescent and older patients. Furthermore, the reliability and the validity of CFSS-DS have been evaluated in several studies (Aartman et al., 1998; Alvesalo et al., 1993; ten Berge et al., 1998) and normative data for Swedish children have been established (Klingberg et al., 1994), which would have made it easy to make comparisons with our results. The post-extraction questionnaires used in paper II were earlier tested for reliability and validity by Feldmann et al. (2007).

To evaluate in more detail, the pain and discomfort the children experienced during extracting a deciduous canine, an optimal study design would be to call the patients by phone every day for one week, as in the study by Bergius et al. (2002). That study design would make it possible to ask more precisely the time when analgesics were taken, whether the child had pain at that particular moment or if

the analgesics were taken in order to prevent possible pain from occurring. Another alternative study design could have been to interview the patients and parents 1 week post-extraction.

The mean pain and discomfort levels at the different occasions measured in paper II, i.e. injection, extraction, first evening post-extraction and 1 week post-extraction, were all low. Thus we can accept the first part of the hypothesis, that extraction of the deciduous canine does not cause high levels of pain and discomfort. There are several plausible explanations for these low values: the children might have taken analgesics just before the effect of the local anaesthetics had declined and they started to feel strong pain, the uncomplicated extraction of the deciduous canine with one root, the positive expectation of not having surgical exposure of the impacted canine and the participation in a research project. In general, more girls than boys reported pain and discomfort when the different interventions were compared to each other, which is in agreement with earlier studies (Acs et al., 1986; Liddel and Locker, 2000; Chambers et al., 2000). Injection was rated as more painful than extraction, which is in line with other studies showing that injection is the highest ranked dental pain among children (Barrett, 1997; Krekmanova et al., 2009). Unfortunately, there was no question in the questionnaire as to whether the patient had taken analgesics before the extraction, which would have been useful for a better understanding of the rating of the injection. To minimize the experience of pain during injection, application of topical anaesthetics prior to injection can be used (Barrett, 1997), as was done in paper II. A good injection technique and a psychological approach such as the “tell-show-do” method are other steps that the operator can take to minimize the pain. Use of the computer controlled anaesthetic delivery system The Wand® has been shown to offer less pain than the traditional syringe injection (Sumer et al., 2006) and can therefore be an alternative for use by the dentist. Only one dentist performed all the injections and the extractions in the present study, which could

have affected the results, since this operator might have been extra careful and caring and had more time to explain and show the patients on the different occasions. Conclusions on the influence of the operator can thus not be drawn.

To rule out differences in pain sensitivity and experience of previous treatment, a reference group was included. The pre-extraction DAS was compared between the study and the reference group, showing mean values that parallel the population mean. Both groups had a low experience of previous dental procedures and rated similar responses to pain. Thus we can reject the second part of the hypothesis, that DAS is higher in patients with PDC. The limited experience of dental treatment in Sweden can be expected, as 60% of 12- year-old children are caries free because of the prophylactic programs in the public dental service (Socialstyrelsen, 2010). The results of the study reported in paper II can therefore not be generalized, since children with several fillings, previous extractions and caries would most probably have answered differently. It is known that children who have experienced pain in an early invasive treatment may later experience pain negatively by reacting more strongly and earlier to pain compared to children without early painful experiences (Taddio et al., 1997; Berggren and Meynert, 1984; Skaret et al., 1998).

The reference group was also included in this trial to evaluate whether children with PDC had more previous dental treatment experience. As the probability of having other dental abnormalities is higher in children with PDC (Jacoby, 1983; Peck et al., 1996; Pirinen et al., 1996; Becker, 2007), this could if so have caused more dental anxiety and/or increased pain reporting in the present extraction. The results showed no differences between the groups, indicating that either potential additional dental abnormalities had not been diagnosed or treated yet or that the included patients had no other dental abnormalities.

A strong positive correlation was seen between baseline measures (DAS and previous dental treatment experience) and the present extraction. Berggren and Meynert, (1984), and Skaret et al. (1998), also found a strong relationship between

dental anxiety and poor collaboration and satisfaction with the dentist. Furthermore, the operator in paper II rated indifferent acceptance for injection in children who reported higher values on the VAS scale for previous tooth extraction experiences. This is in line with earlier studies, indicating that fear reduces the threshold of pain and triggers the pain experience, especially if pain is referred to earlier experience (Locker et al., 1996; Skaret et al., 1998).

A recent study done in Sweden reported that dentists tend to underuse local analgesia, analgesics and sedatives for pain management during dental treatment of children and adolescents (Wondimu and Dahllöf, 2005). To identify the need and the time when analgesics were consumed in this study, children and parents were recommended to use non-prescription analgesics at their own discretion. The results showed that, despite the low pain and discomfort levels, 42% of the children used painkillers the first evening. Girls required more analgesics than boys, and the greatest need for analgesics was after the extraction, which agrees with previous studies (Acs et al., 1986; Logan et al., 2004). These results, and the fact that the injection was assessed as more painful than the extraction, indicate that routine use of pre-and post-extraction medication should be prescribed to reduce pain in children. A lower percentage (20%) of analgesic intake was reported by Sjögren et al. (2010), who also studied deciduous canine extraction, but of younger children (7-9 years of age), which can be explained by parents being hesitant to give younger children medicine. Arribas and Muzyka (2003), showed that after an invasive treatment in the oral cavity, the peak in post-operative pain occurs after 24 hours and that pain decreased within 73 hours. The authors therefore concluded that, following tooth extraction or other invasive dental treatments, analgesics should be recommended for 2-3 days postoperatively. In the present study, the children used analgesics only on the first day postoperatively, which can be explained by the uncomplicated deciduous tooth extraction. . The use of analgesics may differ on the grounds of whether it was a permanent tooth or a

tooth with several roots. On the other hand, studies have shown that the use of analgesics does not differ with age, even though older children report pain more frequently than younger ones in conjunction with extraction. This finding can be interpreted such that the use of analgesics is an early learned response and that reporting pain is a late learned response (Acs et al., 1986; Tate and Acs, 2002).

Interceptive treatment of PDC (papers III-IV)

When designing the study method in papers III-IV, we tried to fulfil all the important criteria needed for a study to be classified as having high value of evidence, recommended by the Cochrane systematic review that assessed the effect of interceptive deciduous canine extraction in patients with PDC (Parkin et al., 2009). To our knowledge studies III-IV are the first papers published where positional changes of the PDC after extraction of the deciduous canine were assessed 3 dimensionally. Using this method, it was also possible to predict cut-off points of the measurement variables obtained from the 3D images. In addition, all PDCs regardless of their severity, were included in papers III-IV, applying Clark's rule on two intraoral radiographs and using the clinical criteria of absence of palpation of buccal canine bulge or canine bulge palpable palatally. The reason for using this method is that it is widely used in the clinical setting by the general practitioners. Some previous studies have defined the inclusion of the PDCs with radiographic criteria in more detail as: "alpha angle greater than or equal to 15 degrees" (Baccetti et al., 2010; 2011), "canine within sectors 2-5 according to the method by Ericson and Kurol "(1988) and "exceeding the long axis of the lateral incisors" (Bazargani et al., 2014) or "inclination of the canine to a vertical line passing through the midline exceeding 25 degrees and overlapping of the canine crown with the lateral incisor" (Bonetti et al., 2010; 2011). By not strictly defining the appearance of the canine on radiographs, we had the possibility in paper IV to determine cut-off points for the "easy" PDCs, i.e. cases where interceptive

extraction is not necessary. This was done using receiver operating characteristic (ROC) analysis, which is the best method for determining the validity of a diagnostic measure (Swets, 1988). The ROC curve was originally developed for use in radar signal detection theory to separate information from noise (Griner et al., 1981). In the 1970s, it was introduced in clinical laboratory medicine and diagnostic radiology and became widely used in medical decision making theory (Hanley, 1989). The ROC curve is a plot of the true positive rate (sensitivity) and false positive rate (1-specificity) of a test. Curves that occupy a larger percentage of the entire area of the graph, also called area under the curve (AUC), i.e. is closer to the upper left corner of the graph, have a higher sensitivity and lower false-positive rates at all cut-off points and are considered a better test (Metz, 1978). Sensitivity is referred in paper IV to as the percentage of PDCs in the CG and in the EG, not erupting spontaneously in that the radiographic predictors identified them as needing other intervention. Specificity is the percentage of PDCs in the CG and the EG erupting spontaneously in that the radiographical predictors identified them as not needing any intervention.

The findings in paper III show that extraction of the deciduous canine is an effective interceptive treatment. The majority of the PDCs would spontaneously correct following extraction; significantly more positional changes over time were noted in the EG, and the mean eruption time was shorter in the EG than in the CG. By this means, we can reject the first two hypotheses that there are no differences between the EG and the CG regarding the success rate of spontaneous eruption of the PDC and the change in eruption pattern. Our success rates are similar to most previous studies (Power and Short, 1993; Baccetti et al., 2008; Baccetti et al., 2011; Bazargani et al., 2014). However, some studies present higher rates (Ericson and Kuroi, 1988; Bonetti et al., 2010; 2011) or lower rates (Smailienė et al., 2011). The reasons for the higher success rates might be: inclusion of both erupted canines and those with improvement of canine eruption path (Ericson and Kuroi,

1988) or inclusion of centrally placed canines together with the PDCs (Bonetto et al., 2010) and non-randomized control group (Bonetti et al., 2011). The lower success rate can be due to the inclusion of older patients. The different definitions of a successful outcome either as “fully erupted canines, thus permitting bracket positioning for final arch alignment when needed” (Baccetti et al., 2008; Bonetti et al., 2010; Baccetti et al., 2011; Bonetti et al., 2011; Smailienė et al., 2011) or as “above the gingival margin in an aesthetically acceptable location in the dental arch” (Bazargani et al., 2014) may also play a role for the different prevalence rates reported. In our opinion, the goal of interceptive treatment is emergence of the permanent canine through the gingiva, not the final position.

Furthermore, paper III is the only study that used the intention-to-treat (ITT) approach, which might also have affected the results. An additional difference that might have affected the success rate is that patients in papers III-IV had individual treatment plans after one year as compared to the above mentioned studies that had longer follow-ups, since we considered it unethical not to carry out an intervention, especially as data from paper III show a tendency of more resorbed adjacent teeth in the CG at T2 than at T0 and as more canines had erupted in the EG during the first 12 months. Also, with increased age and the more mesial the cusps of the PDCs are, the duration of the orthodontic treatment of impacted canines increases (Becker and Chaushu, 2003; Zuccati et al., 2006) as does the risk of developing ankylosis (Azaz and Shteyer, 1978).

As mentioned before, the mean eruption time was significantly shorter in the EG than in the CG. In addition, canines closer to the occlusal plane in the EG, i.e. with a shorter distance of the canine root apex-dental arch plane, erupted earlier. Age did not affect the eruption time. As the majority of the canines erupted after 12 months, we suggest that canines with an improved position at T2 should be clinically and, if necessary, radiographically followed up, preferably with 2D images. The systematic use of CBCT images in papers III-IV was designed for research purposes and a routine use of CBCT to detect PDC or to evaluate the

effect of deciduous canine extraction on daily bases is not recommended due to the higher radiation doses.

In Sweden, children 9 to 11 years are strictly monitored by the general dentist to find PDCs at an early age, according to the recommendations in the study by Ericson and Kurol (1988). This is a possible explanation for the greater number of patients between 10 and 11 years than 12-13 years in papers III-IV. The younger patients had a significantly more successful eruption of the canine; interceptive treatment should therefore be performed around the age of 10-11. We can thus reject our final hypothesis in paper IV, that there are no age differences between the successful and unsuccessful groups. Older patients, i.e. older than 15-16 years of age would most probably have a slower eruption due to the closed apices and poorer prognosis. Age is only a fair predictor of the outcome according to the ROC analysis made in paper IV. It is therefore not possible to determine a specific cut-off point for age. Furthermore, as there is a poor correlation between dental and chronological age, it is important to consider the overall stage of dental development of the child. In patients with PDCs, the dental development is, according to several studies, delayed, whereas those with buccally displaced canines had a more normal dental development as compared to a control group (Zilberman et al., 1990; Becker and Chaushu, 2000; Rozylo-Kalinowska et al., 2011; Naser et al., 2011).

We decided, for ethical reasons, not to take CBCT on canines that were erupted at T2. Instead imputation values of normally positioned canines from the unilateral group were used in these cases. An alternative would have been to consider these patients as drop-outs but, this would have biased the results since those teeth that had erupted between T1 and T2 are probably in the “best” position. A comparison of imputation values of normally positioned canines and the erupted canines from the bilateral group showed no significant differences in the angular and positional changes.

Using 3D images in this thesis made it possible not only to diagnose more accurately the canine position and its 3 dimensional movement, but also to detect small root resorptions of adjacent teeth caused by the PDCs. In paper III, the frequency of root resorptions was 23.5 %, and there were no significant differences between the two groups. Thus we can accept our final hypothesis, that there are no differences between the EG and the CG regarding the number of root resorptions of adjacent teeth. Our finding on the frequency of root resorption is not in accordance with previous studies, which have reported figures of around 50% (Ericson & Kuroi, 2000; Walker et al., 2005; Bjerklin & Ericson 2006; Liu et al., 2008). The main reason for this difference might be that paper III was a prospective randomized study while above mentioned were retrospective studies including selected patients with available CT images. Another factor is the age of the patient; the peak frequency of root resorption is, according to Ericson& Kuroi (2000), between 11 and 12 years of age, whereas the majority of the patients in paper III were 10-11 years of age.

The results reported in paper IV showed that the permanent canine erupted significantly more often in younger patients with a smaller mesioangular angle, shorter distance of the canine cusp tip-dental arch plane and greater distance of the canine cusp tip-midline. We can therefore reject the first hypothesis in paper IV, that there is no difference in the initial angulation and position of the PDC regarding the success rate and the time it takes for the canine to erupt.

Cut-off points of the above mentioned 4 variables were determined as to when the canine will spontaneously emerge. If it could be forecasted whether a patient would benefit from interceptive extraction or not, one could avoid interceptive extraction in the “easy cases” while the PDC in the “severe” cases could be surgical exposed immediately. Double treatment might be avoided, i.e. wait for an unsure spontaneous eruption that might lead to a more severely displacement and cause resorption of the adjacent teeth during the observation time. Although

not the same method used, the alpha angle (Ericson and Kurol, 1988; Power and Short, 1993; Baccetti et al., 2008; Bonetti et al., 2010; Baccetti et al., 2011; Bonetti et al., 2011; Smailienė et al., 2011; Bazargani et al., 2014) can be roughly compared with the mesioangular angle in paper IV, which has been associated with successfulness in facilitating canine eruption. Angles of 20 degrees (Smailienė *et al.*, 2011) or more than 31 degrees (Power & Short, 1993) have been reported as a critical angle for reduced change of spontaneous eruption. The cut-off point for the mesioangular angle at baseline for canines that will need surgical exposure despite of interceptive extraction of the deciduous canine was 116 degrees. In contrast, there are studies that report that the alpha angle is not associated with a successful outcome (Baccetti et al., 2007, Zuccati et al., 2006). Canine cusp-midline had the best value of the area under the curve (AUC), meaning the highest validity of the test. This was also seen by Power & Short (1993), who found, that sector measurement is the single most important factor to assess the outcome.

Cut-off point for the “depth” of impaction i.e. canine cusp tip-dental arch plane revealed that cases with a distance of 2.5 mm, interceptive extraction is not needed since the permanent canine will spontaneously erupt without any intervention. Cases with canine cusp tip-midline of 6 mm will not benefit by interceptive extraction and should be surgically exposed. When cut-off points are changed, the specificity and sensitivity will systematically change in opposite directions, but it would be reasonable to suspect that a spontaneous eruption after interceptive extraction of the deciduous canine will not occur in cases positioned worse than the cut-off points. On the contrary, one might expect spontaneous eruption without prior extraction of the deciduous canine in cases positioned more favourably than the cut-off points indicate. In these cases it is important to keep control over the eruption path and intervene with extraction if the x-rays indicate that the canine position impairs during eruption. Cases “in between” could be clinically interpreted as that interceptive extraction is beneficial. As some PDCs present different radiographical variables both below and above the cut-off points for

successful and unsuccessful outcome, looking at the AUC is recommended, since the test with the best performance has the largest AUC (Metz, 1978). According to the result, this would be the canine cusp tip-midline, followed by the canine cusp tip-dental arch plane and the mesioangular angle.

Clinical considerations and recommendations

Early diagnosis of PDCs and extraction of the deciduous canine as an interceptive approach are recommended. Permanent canines with an improved position at the 12-month control should be followed up with a clinical and if necessary, a radiographic examination, as spontaneous eruption after 12 months is still possible. By using the cut-off points as a guideline as to when to extract the deciduous canine or not to extract it, some surgical interventions and unnecessary extractions of the deciduous canine might be avoided. However, new prospective studies are needed in order to obtain an average value of the cut-off points found in this thesis. For everyday diagnostics and follow-up of uneventful cases of unerupted permanent canines, conventional 2D periapical radiographs are quite sufficient and are recommended. Three dimensional CBCT examinations should only be used in more complex cases when root resorption is suspected and/or surgical exposure is needed and the anatomy is obscure and difficult to assess. When 3D images are used, the method described in paper I for assessing the position of the displaced canine can be used since it is a reliable and a valid method.

The questionnaire the children received in this thesis indicated that the mean pain and discomfort levels at the different occasions were low. Despite that, 42 % of the children used painkillers the first evening, demonstrating that routine use of pre- and post-extraction medication should be prescribed to reduce pain in children.

FUTURE PERSPECTIVES

An early and easy interceptive treatment is preferable, both from a health economic perspective and also to reduce the risk of root resorption of the adjacent teeth and to avoid later comprehensive treatments. Therefore, the costs and the risks with PDC are of importance and should be evaluated in future studies.

Other future research is to compare CBCT images with the available intraoral radiographs and panoramic radiographs in the patients who participated in papers III-IV in order to form a thumb of rule for when and in which cases interceptive treatment will be successful. A work on a joint classification system and definition of PDC would facilitate future research in this field and make comparison between studies easier.

It would be of interest to follow up, how much children remember of the extraction and whether it had affected their dental anxiety.

CONCLUSIONS

- CBCT images were accurate and precise for measuring linear and angular measurements and can be used to assess the exact position of PDCs.
- The validity of the mesioangular and sagittal angles measured on CBCT images was high.
- The overall reported pain and discomfort during and after the extraction were low. The injection was experienced as more painful than the extraction. Despite of the reported low pain, 42% of the children took analgesics the first evening; therefore, a simple recommendation including appropriate analgesics and recommendation doses pre- and post-extraction should be given.
- Extraction of the deciduous canine was an effective interceptive treatment in patients with PDCs; 69% of the permanent canines erupt spontaneously after deciduous canine extraction compared to 39% in the control group.
- Significantly more positional changes and shorter mean eruption times were achieved following deciduous canine extraction.
- A slight resorption of lateral incisors was seen in both the extraction and the control group.
- Canine cusp tip-midline, canine cusp tip-dental arch plane and mesioangular angle might be useful for distinguishing when an interceptive extraction of the deciduous canine is beneficial or when exposure of the PDC should be implemented without previous interceptive treatment.

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APPENDIX

Questionnaire T1: Dental Anxiety scale and previous dental experiences.

Dental Anxiety Scale (DAS)

1. If you had to go to the dentist tomorrow for a check-up, how would you feel about it?
 - a. I would look forward to it as a reasonably enjoyable experience.
 - b. I wouldn't care one way or the other.
 - c. I would be a little uneasy about it.
 - d. I would be afraid that it would be unpleasant and painful.
 - e. I would be very frightened of what the dentist would do.

2. When you are waiting in the dentist's office for your turn in the chair, how do you feel?
 - a. Relaxed.
 - b. A little uneasy.
 - c. Tense.
 - d. Anxious.
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick.

3. When you are in the dentist's chair waiting while the dentist gets the drill ready to begin working on your teeth, how do you feel?
 - a. Relaxed.
 - b. A little uneasy.
 - c. Tense.
 - d. Anxious.
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick.

4. Imagine you are in the dentist's chair to have your teeth cleaned. While you are waiting and the dentist or hygienist is getting out the instruments which will be used to scrape your teeth around the gums, how do you feel?
 - a. Relaxed.
 - b. A little uneasy.
 - c. Tense.
 - d. Anxious.
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick.

Previous dental experiences

End-phrases/Alternatives

- | | |
|---|-----------------------------------|
| 1. How do you experience dental treatment in overall? | VAS (Not at all-Worst imaginable) |
| 2. Have you previously experienced dental injection? | Yes/No/ Don't remember |
| 3. If yes, was it painful? | Yes/No/ Don't remember |
| 4. If painful, how much? | VAS (Not at all-Worst imaginable) |
| 5. Have you previously experienced tooth drilling? | Yes/No/ Don't remember |
| 6. If yes, was it painful? | Yes/No/ Don't remember |
| 7. If painful, how much? | VAS (Not at all-Worst imaginable) |
| 8. Have you previously experienced tooth restoration? | Yes/No/ Don't remember |
| 9. If yes, was it painful? | Yes/No/ Don't remember |
| 10. If painful, how much? | VAS (Not at all-Worst imaginable) |
| 11. Have you previously experienced tooth extraction? | Yes/No/ Don't remember |
| 12. If yes, was it painful? | Yes/No/ Don't remember |
| 13. If painful, how much? | VAS (Not at all-Worst imaginable) |

Questionnaire **T2**: Assessment of pain, discomfort and analgesic consumption assessed the first evening after the extraction.

<i>Pain and discomfort</i>	<i>End-phrases/Alternatives</i>
1. Did you have pain during the injection of the anesthetic?	VAS (Not at all-Worst imaginable)
2. Did you have pain during extraction?	VAS (Not at all-Worst imaginable)
3. Did you have discomfort during the injection of the anesthetic?	VAS (Not at all-Worst imaginable)
4. Did you have discomfort during extraction?	VAS (Not at all-Worst imaginable)
5. Did you experience any part of the surgery/extraction as particularly unpleasant?	Yes/No
6. If yes, which part did you experience as particularly unpleasant?	Open-ended
7. Do you have pain from the extraction site right now?	VAS (Not at all-Worst imaginable)
8. Do you have discomfort from the extraction site right now?	VAS (Not at all-Worst imaginable)
<i>Analgesic consumption</i>	<i>End-phrases/Alternatives</i>
9. Have you taken analgesics for pain?	Yes/No
10. If yes, what kind of analgesics did you use?	Open-ended

Questionnaire **T3**: Assessment of pain, discomfort, analgesic consumption and daily activities assessed one week after the extraction.

<i>Pain and discomfort</i>	<i>End-phrases/Alternatives</i>			
1. Do you have pain from the extraction site right now?	VAS (Not at all-Worst imaginable)			
2. Do you have discomfort from the extraction site right now?	VAS (Not at all-Worst imaginable)			
<i>Analgesic consumption</i>	<i>End-phrases/Alternatives</i>			
3. Have you taken analgesics for pain during the last week?	Yes/No			
4. If yes, how many days did you take analgesic?	Number of days			
5. Was it a non-prescription drug?	Yes/No			
6. If yes, what kind of analgesic did you use?	Open-ended			
7. Was it a prescription drug?	Yes/No			
8. If yes, what kind of analgesic did you use?	Open-Ended			
<i>Daily activities</i>	<i>End-phrases/Alternatives</i>			
9. Did you stay at home from school the last week because of the pain from the extraction site?	Yes/No			
10. If yes, how many days did you stay home from school?	Number of days			
11. Did you refrain from leisure activities the last week because of pain from the extraction site?	Yes/No			
12. If yes, what activities did you refrain from?	Open-ended			
13. Has your sleep been disturbed in the last week because of pain from the extraction sites?	Yes/No			
<i>Functional jaw impairment</i>	<i>End-phrases/Alternatives</i>			
14. If you had difficulties after the extraction, how much has it influenced?				
	No difficulties Some difficulties Very difficult Extremely difficult			
1. Your leisure	🍏	🍏	🍏	🍏
2. Your speech	🍏	🍏	🍏	🍏
3. To take a big bite	🍏	🍏	🍏	🍏
4. To chew hard food	🍏	🍏	🍏	🍏
5. To chew soft food	🍏	🍏	🍏	🍏
6. School work	🍏	🍏	🍏	🍏
7. To drink	🍏	🍏	🍏	🍏
8. To laugh	🍏	🍏	🍏	🍏
9. Resistance when chewing	🍏	🍏	🍏	🍏
10. To yawn	🍏	🍏	🍏	🍏