FACULTEIT GENEESKUNDE EN GEZONDHEIDSWETENSCHAPPEN

CLINICAL AND RADIOGRAPHIC EVALUATION OF SPONTANEOUS SPACE CLOSURE AFTER EXTRACTION OF FIRST PERMANENT MOLARS IN YOUNG PATIENTS

Eleni Katerina Mouroutsou

Promotor: Prof. Dr. L. Martens

Submitted in partial fulfilment of the requirements for the degree of Master of Science in Advanced Dentistry – Main Subject Pediatric Dentistry and Special Care

Academic year: 2017 – 2018

UNIVERSITEIT GENT

Acknowledgements

I would first like to thank my promoter Professor Dr. Luc Martens. The door to Prof. Marten's office was always open whenever I ran into a trouble spot or had a question about my research or writing. He consistently allowed this paper to be my own work, but steered me in the right direction whenever he thought I needed it.

I would also like to thank the experts who were involved in the research and helped me complete this thesis successfully: Professor Dr. Rita Cauwels, who provided advice and helped me collect some of the patient data. Dr. Jacob Van Acker, for helping me score the radiographs. Dr. Stefanie De Buyser, for all her guidance with the statistical analysis. Professor Dr. Robert Anthonappa, who provided valuable material for my literature review. Without their passionate participation and input, the research could not have been successfully conducted.

Moreover, I would like to thank all the patients and their parents for participating in the study.

I would also like to acknowledge all my colleagues that supported me and helped me through this master program all these years.

Finally, I must express my very profound gratitude to my parents and to my partner for providing me with unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them. Thank you.

Eleni Katerina Mouroutsou

14/05/2018

Eleni Katerina Mouroutsou Prof. Dr. L. Martens

Table of Contents

Abstract

Treatment of compromised first permanent molars in young patients often presents a dilemma for dentists. Severely decayed or hypomineralised first molars with bad long term prognosis may be considered for enforced extractions. Ideally, space closure occurs after mesial migration of the second permanent molar.

Aim: to assess the first permanent molar extraction outcome in young patients and to explore different parameters that, as suggested in the literature, might affect the treatment outcome in the mandible.

Material and methods: A hundred and nine quadrants with extracted first permanent molars from 37 patients were assessed. Study models and dental pantomograms were used to assess remaining diastemas, inclination and rotation of all posterior teeth. The presence or absence of the third permanent molar, the developmental stage and the angulation of the second molar in relation to the first molar were recorded from the pre-extraction radiographs of the patients.

Results: Favorable outcomes occurred in 84% of the maxillary and 32.2% of the mandibular quadrants. The angulation and the developmental stage of the second molar had no significant effect on the extraction outcomes, within this sample.

Conclusion: Enforced extraction of compromised first permanent molars is a beneficial treatment option for young patients. In the maxilla the majority of the cases result in a favorable outcome, while extractions in the mandible present less favorable outcomes and orthodontic intervention might be necessary. Appropriate pre-extraction planning and follow-up are essential for ensuring a positive result.

Abbreviations

IOTN	Index of Orthodontic Treatment Need
IRR	Inter and intra-rater reliability
LM1	Lower first permanent molar
LP1	Lower first premolar
LP2	Lower second premolar
M1	First permanent molar
M2	Second permanent molar
M3	Third permanent molar
UM1	Upper first permanent molar
UP1	Upper first premolar
UP2	Upper second premolar

1 Introduction

Due to its anatomical structure and strategic position in the dental arch, the first permanent molar (M1) is considered one of the most important teeth of the permanent occlusion.

The M1s are the first permanent teeth that develop before birth, usually starting to form approximately during the 17th week of pregnancy. The calcification of the crown normally begins around the time of birth. They are also the first permanent teeth to erupt in the oral cavity at about 6-7 years of age, while the completion of the root formation takes place at about 9-10 years of age.

1.1 First permanent molar and associated caries experience

Dental caries during the past decades was designated as a major oral health issue that dominated most of the fields of dental research. Even though the oral health of children and adolescents nowadays has improved significantly compared to the previous generations, tooth decay is still a common health problem among young children. In 2014 in the UK, it was reported that most hospital admissions of children at the ages 5 to 9, were due to tooth decay (Public Health England 2014). The occlusal surfaces of posterior teeth appear to be the most susceptible areas for caries development in young people. Despite the various preventive measures that are today available, the M1 is likely to develop caries during the first years after eruption. The 2017 Health Report by the Royal College of Pediatrics and Child Health indicates that the extractions of permanent teeth due to decay, amounted at 33% among 15 year old children in 1973, decreasing to 24% in 1983, and to 7% from 1993 forward. (Royal College of Pediatrics and Child Health 2017**).** Although, the percentage of extracted molars due to decay has significantly decreased, until now almost one out of ten adolescents has at least one molar extracted, meaning, that tooth decay in young patients is still a matter of concern. Albadri et al. (2007) published collective data from three hospitals in the UK indicating that the most common reason (89%) for M1 extractions was due to caries.

1.2 First permanent molar and associated developmental defects of enamel

Another oral health problem that increasingly demands the attention of the dental community, is the developmental defects of enamel. The widely used term Molar Incisor Hypomineralisation (MIH) first adopted in 2001 and still used in the latest update of EAPD guidelines in 2015, describes a condition characterized by demarcated opacities of enamel (Weerheijm et al. 2001, Weerheijm 2003, Weerheijm 2015). The M1s are often affected by these qualitative defects of systemic origin and are commonly associated with severe functional and aesthetic problems.

The clinical appearance is characterized by an alteration in the translucency of enamel, visibly seen as well-defined opacities with variable colors, including white, yellow and brown and ranges in between. The prevalence of MIH varies significantly in different studies, including different study populations and using different methods of assessments. In 2017, a collective study including 70 related studies showed the global prevalence of MIH to be 14.2%, and 15.1% among children younger than 10 years old (Zhao et al. 2017). Due to its high incidence globally and to several difficulties presented when managing children and teeth with enamel defects, MIH is characterized as a silent public health problem (Hubbard et al. 2017).

The etiology is still unknown and it is assumed to be multifactorial. In many studies, different prenatal, postnatal, early childhood factors and factors affected by the contemporary lifestyle have been proposed to have an association with MIH. Nevertheless, according to the latest systematic review (Silva et al. 2016) on the etiology of MIH, only childhood illness is likely to be associated with the development of the condition. Interestingly enough, hypomineralised molars have also been found amongst ancient populations (Garot et al. 2017). This finding arguably weakens the hypotheses that connects the incidence of MIH with the contemporary lifestyle factors, although contradictory results have also been reported (Kuhnisch et al. 2016). A twins' study (Texeira et al. 2017) also explored the association between MIH and genetic influence and found greater concordance in the occurrence of MIH in monozygotic twins compared to dizygotic.

Hypomineralised molars are prone to caries and are often subjects of atypical, extensive and repeated restorations (Elhennawy et al. 2016). Children with MIH

present higher caries experience and DMFT scores than unaffected controls (Americano et al. 2016, 2017), and consequently MIH is considered as a risk factor for caries development. (Llena et al. 2017, Kunisch et al. 2017). The vulnerability of MIH-affected teeth could be explained by the lower mineral content (less calcium and phosphate) or the increased porosity of the enamel (Jalevik et al. 2001, Fragell et al. 2010, Neboda et al. 2017).

Management of MIH-affected teeth is also challenging for the dentist and the patient. Due to the variety of clinical appearance and treatment needs of hypomineralised molars, multiple treatment options are available, ranging from reminalization agents, pit and fissure sealants, and conventional composite restorations, full coverage restorations to extraction with or without orthodontic treatment (Lygidakis et al. 2010). Hypomineralised enamel has different structure from normal enamel, affecting its chemical and mechanical properties (Elhennawy et al. 2017). This altered infrastructure complicates the management strategies, mainly the bonding behavior of hypomineralised enamel and increases the retreatment and failure rates (Jalevik and Klingberg 2012**)**. A study conducted in Norway showed a lack of homogeneity between clinicians' management strategies used to treat affected teeth (Kopperud et al. 2017). Adequate anesthesia also presents another obstacle for the dentists when trying to restore hypomineralised molars, most likely due to sub-clinical inflammatory changes of the pulp tissue, caused by penetration of oral bacteria through the porous enamel (Jalevik and Klingberg 2002, Rodd et al. 2007). The same phenomena may also contribute in the occurrence of hypersensitivity that children with hypomineralised molars often suffer from (Fagrell et al. 2008).

Image A

Image B

Figure 1.1 First permanent molar with A) mild and B) severe MIH.

1.3 Treatment of compromised first permanent molars

Due to their high susceptibility to caries and developmental defects of enamel, M1s are prone to extensive decay that may lead to a vicious circle of restorations and questionable prognosis. Treatment of compromised M1s in young patients often presents a challenge for the dentist. Severely decayed or hypomineralised molars with bad long term prognosis may be considered for enforced extractions. Extraction of these teeth is described in the literature as the treatment of choice for certain patients, and subsequent space closure is anticipated after mesial migration of the second permanent molar (M2) (Lygidakis et al. 2010). According to an analysis on the cost-effectiveness of various treatment modalities for severe MIH, enforced extractions were found to be the suggested choice, especially if performed at an ideal age or in the case of numerous affected molars (Elhennawy et al. 2017).

Historically, managing cases involving extractions of M1s has been a clinical dilemma and a matter of debate between orthodontists and dentists for more than a century. It is generally known, that an orthodontist would never elect to extract a first molar instead of a premolar. Also, orthodontic treatment of patients with previously extracted M1s may last longer (Shandler et al. 2000) and often demands advanced and complex techniques, increasing the risk for iatrogenic complications (Jacobs et al. 2011). However, young patients with severally decayed or hypomineralised molars, extensive restorations and/or pulp involvement when their premolars are healthy, should be further evaluated for enforced extractions. Other clinical situations where M1 extractions might be indicated are crowding, reasonably well formed third permanent molars (M3), skeletally divergent malocclusions (dolichofacial vertical pattern) and anterior open bite malocclusion (Ong et al 2010).

1.4 Extraction of first permanent molars

Regardless of the presence of crowding or an underlying skeletal discrepancy, healthy M1s are hardly ever extracted for orthodontic purposes. The position and the mesial-distal dimension of the M1 does not encourage the relief of mild to moderate crowding or the correction of sagittal discrepancies. In general, the extractions of heavily decayed molars are indicated, when they are considered as non-restorable,

meaning, that the margins of the restorations are below the bone level or there is not enough healthy tissue left to support an acceptable restoration. On the other hand, restorable molars with poor long term prognosis are also considered for enforced extractions in young patients. When a patient presents with one or more molars with bad prognosis, different factors that affect the impact of the extractions on the developing dentition should be considered. Ideally, the second permanent molar would migrate mesial and replace the extracted M1. A comprehensive assessment should include clinical (extra-oral, intra-oral) and radiographic control of the following parameters:

- Age of the patient
- Absence of permanent teeth
- Health status of the remaining permanent teeth
- Pattern of facial growth
- Occlusion
- Crowding of the arches

A permanent missing tooth in the same quadrant or multiple permanent teeth missing, multiple permanent teeth with bad prognosis, brachyfacial type of growth, deep bite, arch spacing and Class III malocclusion are generally proposed in the literature as contraindications (Gill et al. 2001). Although, every case should be judged individually.

One more important issue to discuss, regarding M1 extractions, is the cooperation of young patients, when they have to deal with the difficult and stress provoking procedure of an extraction. General anesthesia was the main anesthetic method used for the extraction of M1s in one study (Albadri et al. 2007).

1.5 Orthodontic considerations for the extraction of first permanent molars

The outcome of M1 extractions varies between the two arches and also depends on the degree of crowding and the different growth patterns. In general, extractions of the upper M1s usually result in spontaneous space closure and do not further complicate the developing dentition. The eruption path of the upper M2s,

namely, the more mesial position of the root apex relative to the crown, will enhance the mesial movement of the tooth and will ensure a favorable outcome. More attention is required when the lower molars are scheduled for extraction. Initially, the root apex of the lower M2 is distally positioned in relation to the crown and during eruption the crown tends to tip further towards the mesial (Eichenberger et al. 2015).

The treatment planning for compromised M1s becomes more complicated when one or two molars are considered for extraction and the rest are healthy. Dentists then face the dilemmas of balancing and compensating extractions of healthy molars in order to prevent overeruption and midline asymmetry.

A balancing extraction is the extraction of a healthy contralateral M1 in the same dental arch. Balancing extractions have been proposed to inhibit arch asymmetry. To date, the results of different studies are contradictory (Magere et al. 2005, Jalevic et al. 2007, Caglaroglu et al. 2008). The current guidelines do not recommend routine balancing extractions of a healthy contralateral molar (Cobourne et al. 2014).

A compensating extraction is the extraction of a healthy antagonist molar. Compensating extractions have been proposed to prevent overeruption of the antagonist, which can lead to inhibition of the mesial migration of the erupting M2 and/or cause occlusal interferences. Again, the available studies do not provide strong evidence to answer this question. According to the current data, if a lower M1 needs to be extracted, the compensating extraction of the upper molar is also recommended Conversely, the compensating extraction of a lower M1 when the extraction of the upper M1 is needed, is not advised (Cobourne et al. 2014). Further future research is required for a more evidence-based recommendation on this topic. The dental trial “The SIXES” (Should I eXtract Every Six) was designed to supply such evidence regarding compensating extractions of healthy upper first permanent molars, when the lower molars have to be extracted. It is the first randomized multi-center study on this topic and will provide evidence to support decision making (Innes et al. 2013).

1.6 Extraction timing

To date, there is confusion in the literature and different authors propose different ages as ideal for enforced extractions of the first permanent molars. A summary of different age propositions can be found in Table 1.1.

The first guidelines on the topic were developed by the Royal College of Surgeons of England in 2004. Since then they were revised twice, first in 2009 and then again in 2014. According to the current guidelines, enforced extraction of a M1 at an ideal time is thought to result in spontaneous closure (Cobourne et al. 2014). This ideal time is reported between ages 8-10 and after the eruption of lateral incisors but before the eruption of the second molars and/or premolars. It is clearly mentioned in the guidelines that, traditionally, the development of the second molar is used as a prognostic factor and the 'ideal time' is considered to be the beginning of radiographic calcification of M2 bifurcation. However, according to the latest recommendations, the M2s can variably respond after the extractions of the first molars and favorable results are possible in case of early and late extractions. A systematic review conducted by Eischengmer et al. (2015) failed to deduce any firm conclusions for the maxilla, while the ideal time for the mandible was between 8 and 11.5 years. A subsequent systematic review by Wu et al. (2017), highlighted the lack of high quality research to prove and support an optimal timing.

Table 1.1 Proposed ideal age per study

Author	Ideal age proposition
Gill et all. (2001)	LM1: before M2 eruption, usually at 8-9y
Williams and Gowans (2003)	LM1: 8.5-9y
Lygidakis et al. (2010)	8.5-9y
Ong et al. (2010)	8-9y
Elhennawy et al. (2017)	UM1: 9.5y, LM1: 11y

M1: first permanent molar, M2: second permanent molar

LM1: lower first permanent molar, UM1: upper first permanent molar

2 Review of the literature

2.1 Literature Search

In order to identify all relevant studies investigating the treatment outcome of enforced extractions of first permanent molars in young patients, a comprehensive search was conducted in November 2017. The following electronic databases, namely, PUBMED (MEDLINE), EMBASE (OVID) and Google Scholar were included in the search. Initially, 331 articles were identified and 120 articles had to be excluded after the inclusion of additional filters:

"Human studies"

"Patients <18 years"

"Articles in English"

After this initial elimination, the remaining 211 articles were reviewed and the relevant papers were identified. Literature reviews, case reports and case series with minimum of six cases were also excluded. Studies including patients who received orthodontic treatment after the M1s extractions were excluded as well.

2.2 First permanent molar extraction – Treatment outcome

The first attempt of research to assess space closure after extraction of first molars and identify prognostic factors was undertaken in the 1960s and 1970s. Thilander et al. (1963) found that the best age for extraction would be between 9-11 years (54.2% good/acceptable results) and reported that extractions in the maxilla are more likely to have a favorable outcome in contrast with the mandible. He also evaluated the impact of dental age upon extraction outcome and concluded that the best outcomes are observed if the extractions are done when the lateral incisors have erupted but the second molar and/or premolar have not erupted yet. He also proposed that crowding and presence of third molars appear to have a favorable influence on the results. The combination of crowding and presence of M3 were also confirmed as favorable outcome predictors by Thilander and Skagius (1970). Thunold (1970)

reported that the best results were observed when extractions were performed between 8-10 years of age, in patients with no sagittal discrepancies, while the presence or absence of third molars did not seem to have any influence in the outcome.

Since then, only a few studies evaluated spontaneous space closure after first molar extractions. In the study conducted by Jalevik et al. (2007), 15 out of the 27 children that were examined, had a favorable spontaneous space reduction, as well as a positive development of their permanent dentition without need for any orthodontic treatment. Consequently, it was concluded that favorable outcomes can be achieved when the M1s are extracted before the eruption of the M2s.

Teo et al. (2013) confirmed that favorable outcome is more likely in the upper arch (92.3%) in comparison with the lower arch (61.3%). The authors evaluated the stage of M2 development according to Demirjian (1973) and the post-extraction patient's Angle classification for the first time, and found no significant difference between the parameters tested and the outcome. Interestingly, only 66% of the lower M1s extracted at the 'ideal' developmental stage E resulted in spontaneous space closure. In contrast, 76% of the lower M1s extracted at developmental stage F, which are considered as late extractions, resulted in favorable outcomes, indicating that M2s development stage alone may be an insufficient predictor of favorable spontaneous closure.

Recently, new prognostic factors of spontaneous space closure in the lower arch were proposed and evaluated. Teo et al. (2016) included 66 patients with 127 lower M1s extracted 5years ago. Patients were recalled for clinical examination and the distance, measured with a periodontal probe, between the contact points of each tooth distal to the canine was recorded and graded according to criteria adapted from the Index of Orthodontic Treatment Need (IOTN). In total, 51.2% of the lower M1 extractions resulted in spontaneous space closure. The best results were observed when the following factors were present:

1. Developmental stage of M2: stage D, stage E or stage F (Demirjian 1973)
2. Mesially angulated M2
3. Presence of M3

The overwhelming majority (85%) of the cases fulfilling the above criteria presented complete space closure.

Lastly, a publication by Patel et al. (2017) presented the results of a retrospective cohort study conducted in Eastman dental Hospital in the UK. The

sample included 81 patients with 148 UM1s and 153 LM1s extracted in average 4 years ago. The outcome of the extractions was assessed by means of clinical examination, or study models and/or radiographs in case of patients who were under orthodontic treatment. Equal amount (49 M1s) of early (stage A-D), ideal (stage E) and late (stage F-H) extractions were included in accordance with the Demirjian classification (1973). A favorable outcome was defined as a contact between the second premolar and the second molar with no significant discrepancies on a vertical or transverse dimension. A visible contact was observed in 89.9% of UM2s and 49.9% of the LM2s, which was in accordance with the results of Teo et al. (2013). In the upper arch, dental age played a significant statistical role, but the clinical importance of the statistical difference was questioned by the authors, since the decision making would hardly be influenced by a 0.83% reduction in the success rate for every increasing year of dental age. In contrast, in the lower arch, presence of the M3 and mesial angulation of the M2, found in the pre-extraction pantomograms (DPOs), proved to be statistically and clinically significant ($P<0.01$ and $P<0.05$ respectively), supporting the results of Teo et al. (2016).

A summary of all studies included in this review is presented in Table 2.1 in the next page.

Table 2.1 Studies included in the review and their main results		
Author	**Sample Size (n)**	**Results**
Thilander et al. (1963)	114pt	Space closure: 36% LM1s
Thilander and Skagious (1970)	175 pt 206 LM1s	Space closure: 81.6% UM1s, 34.6% LM1s
Thunold (1970)	55pt 73UM1 92LM1	Best results for LM1 extractions between age 8-10y
Jalevik et al. (2007)	27pt	Space closure:15/22 cases
Teo et al. (2013)	236 M1s 117 UM1s 119 LMI1s	Space closure: 92% UM1s, 61% LM1s Stage E: 66% space closure Stage F: 61% space closure
Teo et al. (2016)	127LM1s	Space closure: 51,2% Stage E: 58% space closure 85% space closure: stage D, E, F + presence M3 + mesial angulation M2
Patel et al. (2017)	148 UM1s 153 LM1s 49 early ext 49 ideal ext 49 late ext	Space closure: 89,9% UM1s, 49% LM1s LM1s: presence of M3+ mesial angulation of M2 statistical significant space closure

M1: first permanent molar, M2: second permanent molar

LM1: lower first permanent molar, UM1: upper first permanent molar

Stages D, E, F according to Demirjian's classification (1973)

2.3 First permanent molar extraction – Outcome on third molar development and eruption

Several studies investigated the impact of extraction of first molars on the development and eruption status of the third permanent molars. Yavuz et al. (2006) examined 165 patients with unilateral M1 extractions and found enhanced development of the third molar on the extraction sites in comparison to the control side. Ay et al. (2006) also reported a better eruption position and more space available for the third mandibular molar in patients that had an extraction of the first mandibular molar compared to the non-extraction cases. These results are in agreement with Bayram et al. (2009) that reported an increase in the eruption space available for the third molar. Lastly, Halicioglu et al. (2014) found an accelerated development of the third molars in the extraction sides.

2.4 First permanent molar extraction – Outcome measurements

During this literature review, the lack of a validated and widely used classification for the outcome after M1 extraction was recognized. This conclusion is also supported from the results of Wu et al. (2017), who reported a big heterogeneity between the studies included. The different methods and classifications used so far for the assessment of treatment outcomes can be found in Table 2.2.

Referring to this table, we can conclude that a wide variety of assessment methods and outcome classifications for first permanent molar extractions have been used among the studies. This fact renders any comparison of results inconclusive. Furthermore, it indicates the need for development of a new global comprehensive index for the classification of treatment outcomes after first permanent molar extraction that correlates with further treatment requirements.

Table 2.2 Methods of assessment and classification of treatment outcome		
Author	**Assessment**	**Classification of treatment outcome**
Jalevik et al. (2007)	DPOs, casts, photographs, bitewings	Spontaneous space reduction, no tilting of teeth that make oral hygiene difficult, no tooth elongation in the opposite jaw, patient satisfaction
Teo et al. (2013)	Clinical examination Ruler between P2-M2	1) Complete space closure between the contact point M2-P2. No angulation, rotation, distal drift 2) 1–5 mm space between contact points of M2-P2 3) 5–10 mm space between contact points of M2-P2 4) > 10 mm space between contact points of M2-P2 5) Presence of angulation, rotation of M2 and/or P2, distal movement of P2
Teo et al. (2016)	Clinical examination Perio probe between M2-P2-P1.	IOTN (worse score per quadrant) 1) Extremely minor malocclusions including contact-point displacements less than 1 mm 2) Contact-point displacement > 1 mm but <2 mm 3) Contact-point displacement >2 mm but <4 mm 4) Severe contact-point displacement > 4 mm
Patel et al. (2017)	Clinical examination or study models, DPO if ortho	Binary outcome (space closed or space present) Space closure: visible contact between M2 and P2 with no significant vertical or transverse discrepancy at the contact

2.5 First permanent molar extraction - Outcome on skeletal development

Traditionally, dental research has focused on the effect of M1 extraction on the development of the posterior region. However, certain parts of the literature focus on the effect of extractions on other structures. The comprehensive analysis of these results is out of scope for this review. Thus, a summary of studies and research focus is given on Table 2.3:

Table 2.3 First permanent molar extraction - Outcome on skeletal development

Author	Conclusion
Cağlaroğlu et al. (2008)	Unilateral M1 extraction: skeletal asymmetry.
Normando and Cavacami (2010)	Bilateral LM1 extraction: lingual tipping of incisors, changes in occlusal plane and face vertical reduction.
Halicioglu et al. (2013)	Unilateral M1 extraction: skeletal asymmetry. Less condylar, ramal, and condylar plus ramal heights.
Halicioglu et al. (2014)	Unilateral M1 extraction: slight difference for condylar-plus-ramal asymmetry index.

2.6 Conclusion

From the review of the literature in this chapter, we conclude that the amount of studies conducted on the topic of enforced M1 extractions is insufficient for producing concrete conclusions on the success of the extraction outcomes and the associations between several prognostic factors and the odds for success. With that in mind, there appears to be a need for further research as well as more universally accepted and used metrics.

3 Aim and Objectives

The literature regarding the first permanent molar extractions in young patients still lacks in high quality studies and strong recommendations for the clinicians. Therefore, this study investigated the following:

The main aim of the study was to assess the spontaneous changes related to the extraction of first permanent molars in young patients. This study focused on remaining diastemas, inclination and rotation of all erupted posterior teeth associated to the extraction space.

The secondary aim was to explore the effect of the developmental stage and the angulation of the lower second permanent molar on the treatment outcome.

The main aim of the present study is further analyzed according to the PICO principles:

*Will the extraction of a first permanent molar **(I)**, in patients under 18 years of age **(P)**, result in spontaneous space closure without any orthodontic intervention **(O)**?*

Population: patients under 18 years of age

Intervention: extraction of one or multiple first permanent molars

Comparison: do not apply

Outcome: spontaneous space closure without any orthodontic treatment

The first null hypothesis is that there will be no complete spontaneous space closure after extraction of first permanent molars in the maxilla and in the mandible. The second null hypothesis is that the different parameters assessed have no influence on favorable treatment outcome after extractions in the mandible.

In order to investigate these aims a retrospective cohort study was designed and the following criteria were assessed:

- Diastemas between each tooth distal to the canine.
- Inclination (tipping) of each tooth distal to the canine.
- Rotation of each tooth distal to the canine.
- Distal drifting of second premolar or first premolar.
- Need for orthodontic advice/treatment because of the M1 extractions.

4 Materials and Methods

4.1 Study design - Patient recruitment

In order to achieve the aforementioned aim, a retrospective cohort study was set. The study was designed and conducted in the Pediatric Dentistry Department of Ghent University Hospital. Since this study involved patient recall and use of patient information, ethical approval was required and granted (Belgian registration number: B6702017319210).

In order to identify the eligible patients for the study, the electronic database EPD was queried for patients younger than 18 years old that had at least one first molar extracted in the past. Initially, 168 patients were identified. Subsequently, patients' records were assessed according to the inclusion and exclusion criteria of Table 4.1 and finally 93 patients were determined as eligible for the study. The reasons for exclusion and the corresponding patient numbers are shown in detail in Table 4.2.

Table 4.1 Study inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Patients younger than 18y who had one or more M1s extracted	Syndromic, medically compromised patients, phobic patients
Extractions occurred at least 24 months before the recall appointment.	Orthodontic treatment in the mean time between extractions and follow-up
ASA I and II	Extraction of other permanent teeth or oligodontia
DPO (denal pantomogram) maximum 6 months before the extractions	NO DPO before the extractions or DPO more than 6 months before extractions

Table 4.2 Excluded patients	
Reasons for exclusion	**Number of patients**
Syndromic, medically compromised patients, phobic patients	12
Orthodontic treatment in the orthodontics department of UZ Ghent immediately after the extractions	14
Oligodontia or extraction of other permanent teeth.	3
No DPO was taken before the extractions or	46
DPO more than 6 months before extractions or	
DPO was taken but could not be found in patients' record or	
DPO of bad quality.	

In the first phase of the study, all the patient's records that were eligible (93), were evaluated by one examiner, and the following characteristics were registered:

- Number of extracted molars per patient
- Type of anesthesia used for the extractions:
  - General anesthesia
  - Local anesthesia
  - Local anesthesia and inhalation sedation with nitrous oxide
- Reason of extraction:
  - MIH
  - Caries
  - Combination of MIH and Caries
  - Orthodontic reasons
- Previous restorations of the M1s:
  - Restoration
  - No restoration

4.2 Data Collection

In the second phase, patients were contacted and invited at the clinic of Pediatric Dentistry of Ghent University Hospital for clinical and radiographic examination. During this session, information about the study was communicated again, both orally and by means of an information letter, and an informed consent form was provided. Patients older than 12 years old that agreed to participate had to sign the informed consent, while for patients younger than 12 years of age, their parents' signature was required.

For the purpose of the study, alginate impressions, a DPO and clinical pictures were taken for further analysis. For patients with an available DPO taken at most two years ago, this image was used for the evaluation. Prophylactic cleaning and oral hygiene instructions were provided to each patient. In case of dental or oral health related problems, patients were informed and advice was given for any further treatment needed. Cast models of the dental arches were constructed from the impressions (Figure 4.1) and the following parameters were assessed regarding the aims of the present study:

- Contact-point displacements using the Index of Orthodontic Treatment Need
- Rotation
- Inclination
- Need for orthodontic treatment

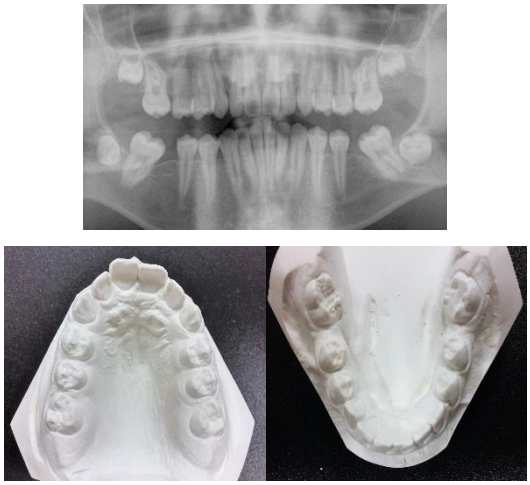

Figure 4.1 Cast models of the dental arches and DPO.

4.3 Assessment of the post-extraction data

When all data were collected, two examiners (LCM, EKM) evaluated the study models and the DPOs. The distance between the contact-point of each tooth distal to the canine was measured in millimeters using a graded periodontal probe**.** The recorded contact-point displacements were further graded according to a scale partly adopted from the Dental Health Component of the Index of Orthodontic Treatment Need (IOTN) (Brook et al. 1989, Teo et al. 2016). For the purpose of this study, only parameters referring to contact-point displacement were included. According to this scale, Grade 1 represents the most favorable outcome and grade 5 the least favorable (Table 4.3). Before the start of the study the two examiners performed several test evaluations on models, in order to calibrate for all the criteria used.

Table 4.3 Grading of extraction outcomes

Grade	Criteria/ Definition
1	Extremely minor malocclusions, including displacements less than 1 mm
2	Displacement of teeth > 1mm but <= 2mm
3	Displacement of teeth >2mm but <=4mm
4	Severe displacements of teeth > 4 mm
5	Impeded eruption of teeth due to displacement

Rotation of all posterior teeth was also assessed and three categories were distinguished, including no rotation, minor rotation and severe rotation. The same categories were used for inclination (no, minor, severe). Examples of the above mentioned categories are given in figures 4.2, 4.3, 4.4, 4.5, 4.6, 4.7. For the assessment of inclination, all post-extraction radiographs of the participants were complementarily used. The presence and the eruption status of the M3 was also evaluated.

For all the above mentioned criteria, namely the IOTN score, rotation and inclination, the two examiners first gave their independent assessments and in case of disagreements, the cases were re-evaluated and a score was given after consensus.

Data from 10 patients were re-assessed from the same two examiners with an interval of two weeks. The inter- and intra-examiner reliability was estimated using the Intraclass Correlation Coefficient (ICC) in SPSS. This method of estimating reliability was selected due to the ordered nature of the data.

For the purpose of the study, cases with no or minor rotation, no or minor inclination and no or minor teeth displacements up to 2 mm (Grade I, II), were determined as showing a favorable space closure. The rest of the cases, showing severe rotation, and/or severe inclination and/or teeth displacements more than 2mm (Grade III, IV, V), were assessed as non-favorable cases, demanding further orthodontic treatment.

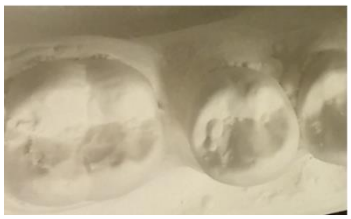

Figure 4.2
No rotation

Figure 4.3
Minor rotation

Figure 4.4
Severe rotation

Figure 4.5
No inclination

Figure 4.6
Minor Inclination

Figure 4.7
Severe Inclination

4.4 Assessment of the pre-extraction data

In the third phase of this study, all the pre-extraction radiographs of the participants were assessed by two examiners (JVA, EKM). All radiographs were re-evaluated after two weeks and inter- and intra-reliability was estimated. The

assessment included the developmental stage of LM2, the angulation of the LM2 germ in relation to LM1 and the presence or absence of M3.

Angulation of the M2 germ was assessed on the pre-extraction radiographs, relative to the first permanent molar using a modification of the method used by Heckmann et al. (2007). A line through the perpendicular axis of the M1 and M2 was drawn and the angle between them was classified. A negative angle indicated a distally angulated M2 (example in Figure 4.8), while a positive angle indicated mesial angulation (example in Figure 4.10). In the case when the two lines formed were parallel or almost parallel to each other within the dimensions of the radiographs, the M2 was considered as up-righted (example in Figure 4.9).

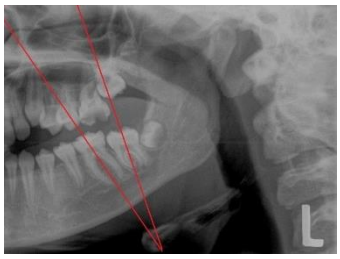

Figure 4.8
Distal angulated M2

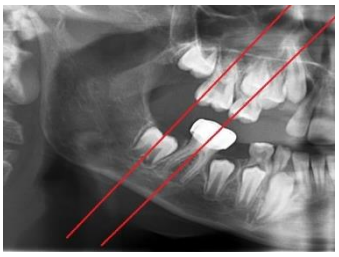

Figure 4.9
Up-righted M2

Figure 4.10
Mesial angulated M2

The observation of a crypt or any initial calcification in the area distal to the second molar was recorded as presence of the M3 (examples in figures 4.12, 4.13). The absence of any such sign was interpreted as absence of the M3 at this developmental stage (example in Figure 4.11).

Figure 4.11
M3 absent

Figure 4.12
M3 present (crypt)

Figure 4.13
M3 present

The 8-stage model of Demirjian (1973) was used to define the developmental stage of M2s. According to the literature, stage E was selected as the "ideal" stage, due to its correspondence to the bifurcation development (Table 4.4).

Table 4.4 Stages of Development for multi-radicular teeth (Demirjian et al. 1973)

Stage		Criteria
A		Cusp tips are mineralized but have not yet coalesced.
B		Mineralized cusp tips are united so the mature coronal morphology is well defined.
C		The crown is about half formed. The pulp chamber is evident and dentinal deposition is occurring.
D		Crown formation is complete to the dentino-enamel junction. The pulp chamber has a trapezoidal form.
E		Formation of the inter-radicular bifurcation has begun. Root length is less than the crown length.
F		Further distinct root formation. Root length is at least as great or twice the crown length. The roots have funnel-shaped endings.
G		Root walls are parallel but apices remain open.
H		The apical ends of the roots are completely closed.

4.5 Statistical Analysis

A complete statistical analysis was performed after data collection with the use of the appropriate tools as described below.

For the first part of this research, descriptive statistics of extraction outcomes with regard to contact point displacement, rotation and inclination of affected teeth were conducted using the software Microsoft Office Excel.

For the second part, potential associations between developmental stages and angulation of the second molar and the extraction outcomes were studied using the software "Statistical Package for the Social Sciences" (SPSS version 25). Data for the lower left and right quadrants were analyzed separately, in order to avoid clustering effects due to multiple measurements within the same patient. In each dataset, binary logistic regression analysis was performed to estimate correlations. Due to the limited sample size, the relationship between the outcomes and each covariate was analyzed separately as well.

Regarding to the reliability testing of the data sets, all variables were considered ordinal (rotation, inclination, IOTN index, developmental stage and angulation) and therefore, the Intraclass Correlation Coefficient (ICC) was used for assessing IRR (inter and intra-rater reliability) (Hallgren et al. 2012). The scale used to judge agreement as proposed by Cicchetti (1994), is indicated in Table 4.5 below:

Table 4.5 Scale used for assessing reliability (Cicchetti 1994)

ICC	IRR
< 0.40	Poor agreement
> 0.40 and < 0.59	Fair agreement
> 0.60 and < 0.74	Good agreement
> 0.75 and < 1.00	Excellent agreement

5 Results

5.1 First permanent molar extraction characteristics

Initially, 93 patients were identified and invited for a follow up appointment. From these eligible patients 32/93 (34.4%) had all four first molars extracted, 4/93 (4.3%) had three molars extracted, 31/93 (33.3%) had two molars extracted and 26/93 (28%) had only one molar extracted. The reasons for extraction were: caries 49/93 (52.7%), MIH 36/93 (38.7%) and combination of MIH and caries 8/93 (8.6%). There were no healthy molars extracted for orthodontic reasons. The main type of anesthesia used was general anesthesia 61/93 (65.6%). Almost half the patients 48/93 (51.6%) had already had restorations on their first molars.

5.2 Participant's characteristics

Forty two patients attended a follow-up appointment and data were collected from 37 patients. Data were not collected from five patients because their M2s had not erupted yet. In four patients only clinical pictures and radiographs were taken.

Out of the 37 participants included, 25 were female and 12 male. The majority of the participants (59.5%) had all four molars extracted. The average age at the time of extractions was 10.7 years old (range 7.8-13.3 years), while the average time between extractions and follow-up was 39 months (range 22-66 months). Twelve out of the 37 patients (32.4%) had their molars extracted between 8-10 years of age, which is the age recommended by the Royal College of Surgeons current guidelines and 24 patients (64.9%) had extractions at a later age. Seven quadrants (3 lower, 4 upper) with extracted M1s had to be excluded from the evaluation (extractions performed less than 24 months before the evaluation, or the pre-extraction DPO dated more than 6 months before the extractions, or the outcome was affected from the presence of a supernumerary tooth). In total, 50 quadrants with extracted M1s were finally evaluated in the maxilla and 59 quadrants in the mandible.

5.3 Reliability

IOTN scores:

Inter-rater reliability testing with ICC (Table 5.1) showed excellent agreement between raters (0.879). Intra-rater reliability testing for the first rater and second rater showed excellent intra-agreement (0.945 and 0.943 respectively):

Table 5.1

IOTN reliability

	Intraclass Correlation	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Inter-Rater	0.879	0.814	0.923	15.992	71	71	.000
Intra-Rater 1	0.945	0.870	0.977	37.000	20	20	.000
Intra-Rater 2	0.943	0.865	0.977	32.619	20	20	.000

Two-way random effects model where both people effects and measures effects are random.

a) The estimator is the same, whether the interaction effect is present or not.

b) Type A intraclass correlation coefficients using an absolute agreement definition.

Rotation and Inclination:

Inter-rater reliability testing with ICC (Table 5.2) showed excellent agreement between raters (0.772 in Rotation and 0.818 in Inclination). Intra-rater reliability testing for the first rater showed excellent intra-agreement (0.797 in Rotation and 0.816 in Inclination). Intra-rater reliability testing for the second rater showed excellent intra-agreement (0.794 in Rotation and 0.901 in Inclination):

Table 5.2

Rotation & Inclination reliability

	Intraclass Correlation	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Inter-Rater							
Rotation	0.772	0.712	0.821	7.892	219	219	.000
Inclination	0.818	0.769	0.857	9.954	219	219	.000
Intra-Rater 1							
Rotation	0.797	0.686	0.872	8.819	62	62	.000
Inclination	0.816	0.717	0.883	9.755	66	66	.000
Intra-Rater 2							
Rotation	0.794	0.677	0.871	9.161	62	62	.000
Inclination	0.901	0.841	0.939	18.924	62	62	.000

Two-way random effects model where both people effects and measures effects are random.

a) The estimator is the same, whether the interaction effect is present or not.

b) Type A intraclass correlation coefficients using an absolute agreement definition.

Developmental Stage and Angulation

Inter-rater reliability testing with ICC (Table 5.3) showed excellent agreement between raters (0.816 in Angulation and 0.851 in Developmental Stage). Intra-rater reliability testing for the first rater showed excellent intra-agreement (0.830 in Angulation and 0.926 in Developmental Stage). Intra-rater reliability testing for the second rater showed excellent intra-agreement (0.784 in Angulation and 0.886 in Developmental Stage).

Table 5.3

Developmental Stage & Angulation reliability

	Intraclass Correlation	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Stage M2	0.851	0.717	0.917	14.714	59	59	.000
Angulation M2	0.816	0.710	0.886	10.165	59	59	.000
Rater 1							
Stage M2	0.926	0.879	0.955	25.722	59	59	.000
Angulation M2	0.830	0.732	0.895	10.830	59	59	.000
Rater 2							
Stage M2	0.886	0.786	0.937	19.408	59	59	.000
Angulation M2	0.784	0.663	0.865	8.162	59	59	.000

Two-way random effects model where both people effects and measures effects are random.

a) The estimator is the same, whether the interaction effect is present or not.

b) Type A intraclass correlation coefficients using an absolute agreement definition.

5.4 First permanent molar - Extraction outcomes

Data were analyzed separately for the maxilla and mandible due to the different outcomes mentioned in the literature. The IOTN scores are shown in Table 5.4. Forty two out of 50 (84%) of the upper quadrants presented a favorable outcome (Grade I, II). In the mandible only 19/59 (32.2%) quadrants showed a spontaneous favorable outcome. Forty out of 59 (67.8%) of the lower quadrants were assessed as Grade III or IV or V according to IOTN index. From these quadrants with an unfavorable outcome, 21/58 (36.2%) of LM2s were severely inclined and 10/58 (17.2%) were severely rotated. The distribution of rotation and inclination for each tooth included is given in Table 5.5 and 5.6 respectively.

Table 5.4	IOTN index scores					
	Grade I	Grade II	Grade III	Grade IV	Grade V	Total
Upper Quadrant	3	39	8	0	0	50
Lower Quadrant	1	18	16	23	1	59

Table 5.5	Rotation					
	UM2	LM2	UP2	LP2	UP1	LP1
No Rotation	14	16	30	23	27	43
Minor Rotation	31	32	16	20	19	13
Severe Rotation	5	10	4	12	4	3
Total	50	58*	50	55**	50	59

** 1 LM2 was not scored because of partial eruption.*

***4 LP2s were not scored due to retained primary molars or partial eruption of premolars.*

Table 5.6	Inclination					
	UM2	LM2	UP2	LP2	UP1	LP1
No Inclination	47	8	50	48	47	49
Minor Inclination	3	29	0	5	3	9
Severe Inclination	0	21	0	2	0	1
Total	50	58*	50	55**	50	59

** 1 LM2 was not scored because of partial eruption.*

***4 LP2s were not scored due to retained primary molars or partial eruption of premolars.*

In the maxilla, 31/50 (62%) of M2s showed minor rotation and 5/50 (10%) severe rotation. Minor rotation was also common among the upper premolars (UP1 - 32%, UP2 - 38%). In contrast, inclination was not a common finding in the upper quadrants with extracted M1s.

In the mandible, minor rotation was found in 32/58 (55.2%) LM2s, 20/55 (36.4%) LP2s and 13/59 (22%) LP1s. Half the LM1s (29/58) presented minor inclination and 21/58 (36.2%) severe inclination. Only 3 lower premolars showed severe inclination.

At review, 47/50 (94%) of the upper quadrants and 54/59 (91.5%) of the lower quadrants showed formation of M3s. Only 7 M3s (2 patients) had erupted at review. The analysis of pre-extraction data revealed that 39/50 (78%) of the upper quadrants and 47/59 (79.7%) of the lower showed some evidence of M3 development.

5.5 Extraction outcomes - Prognostic Factors

Since dental research recently focused to develop new prognostic factors in order to guarantee a favorable outcome after extraction of lower M1s, it was decided to include only the lower quadrants with extracted molars for further analysis.

At the time of M1 extractions, 29/59 (49.1%) LM2s were at developmental stage E. The distribution of lower M2 developmental stages and angulation relative to the M1 is given in Table 5.7 and 5.8 respectively. No M2 classified between stages A-C was found within this data set.

Table 5.7	Stage M2 Development				
	D	E	F	G	H
LM2	1	29	21	6	2

Table 5.8	M2 Angulation		
	D	U	M
LM2	5	28	26

Binary Logistic Regression was employed for the lower left and right quadrants separately, because data from the same patient should not be considered independent. Firstly, the association between M2 developmental stage at the time of extraction and extraction outcome was analyzed. Next, the different M2 angulations relative to M1, were studied for association with the extraction outcome. Due to the fact that patient data were retrospectively assessed, it was impossible to ensure similar amounts of patients in each combination of factors, therefore it was decided to study the potential association of each factor separately as well.

The factors that may influence extraction outcomes, as suggested in the most recent literature, include the presence of M3 and the mesial angulation of M2. In the present study, 91.5% of the participants had their lower M3s present. Because of those patients representing the vast majority of the data set, and in order to have a more homogeneous sample, it was decided to only include patients with presence of M3. Since only 1 LM2 was classified at stage D and 2 LM2s at stage H it was also decided to exclude them from further analysis.

The final data set included 51 lower quadrants. Eighteen quadrants presented favorable outcomes and the rest 33 presented non-favorable outcomes. Interestingly enough, a favorable outcome was found in 11/27 (40.7%) of cases when M2 was at stage E, 5/18 (27.7%) at stage F and 2/6 (33.3%) at stage G. Regarding the M2 angulation in relation to the M1, favorable outcomes were recorded at 10/25 (40%) of M2s with mesial angulation, 5/21 (23.8%) up-righted M2s and 3/5 (60%) of M2s with distal angulation.

Interpreting the results of the Binary Logistic Regression analysis as shown in the following tables (5.9, 5.10, 5.11 and 5.12), we draw the conclusion that no association could be found between any of the factors studied and the odds for a favorable outcome. Due to the limited sample size, this result should be interpreted with caution, and more research and data collection on the subject would yield more concrete conclusions.

Lower Left Quadrant:

Table 5.9	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
37							Lower	Upper
Stage M2	-0.017	0.654	0.001	1	0.979	0.983	0.273	3.544
Constant	-0.549	1.101	0.248	1	0.618	0.578		

Table 5.10	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
37							Lower	Upper
Angulation M2	0.465	0.690	0.454	1	0.500	1.592	0.412	6.151
Constant	-1.258	1.116	1.271	1	0.260	0.284		

Lower Right Quadrant:

Table 5.11	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
47							Lower	Upper
Stage M2	-0.514	0.607	0.719	1	0.396	0.598	0.182	1.963
Constant	0.171	1.012	0.028	1	0.866	1.186		

Table 5.12	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
47							Lower	Upper
Angulation M2	-0.411	0.609	0.456	1	0.500	0.663	0.201	2.187
Constant	-0.094	0.891	0.011	1	0.916	0.910		

5.6 Cases Presentation

Case I

Patient [12] had four M1s extracted at 9.2 years of age. At review, the extraction outcome was considered as favorable.

Image A

Image B

Image C

Image D

Figure 5.1 *A:* Pre-extraction DPO.
B and C: Clinical examination at follow-up.
D: Radiographic examination at follow-up.

Case II

Patient [7] had elements #36 and #46 extracted at 11.8 years of age. At review, the extraction outcome was considered unfavorable (remaining diastemas and severe M2 inclination-tipping).

Image A

Image B

Image C

Figure 5.2 *A*: Pre-extraction DPO.
B and C: Clinical and radiographic examination at follow-up.

Case III

Patient [27] had four M1s extracted at 9.8 years of age. The pre extraction radiographic examination revealed a supernumerary #39 in the region of the first lower right premolars. The supernumerary #39 and the four M1s were removed under general anesthesia. The patient was further followed up in private practice and was invited for participation in the present study 62 months after the extractions. At the recall appointment the patient was 15 years old. Failure of eruption of element #44 was observed during the clinical examination. The radiographic examination revealed two new supernumerary premolars #39, #49. The patient was further referred for a CBCT examination to locate the exact position of the supernumeraries and their relations with the neighboring anatomic structures. Afterwards, the two supernumerary teeth were removed and the patient was referred for orthodontic treatment.

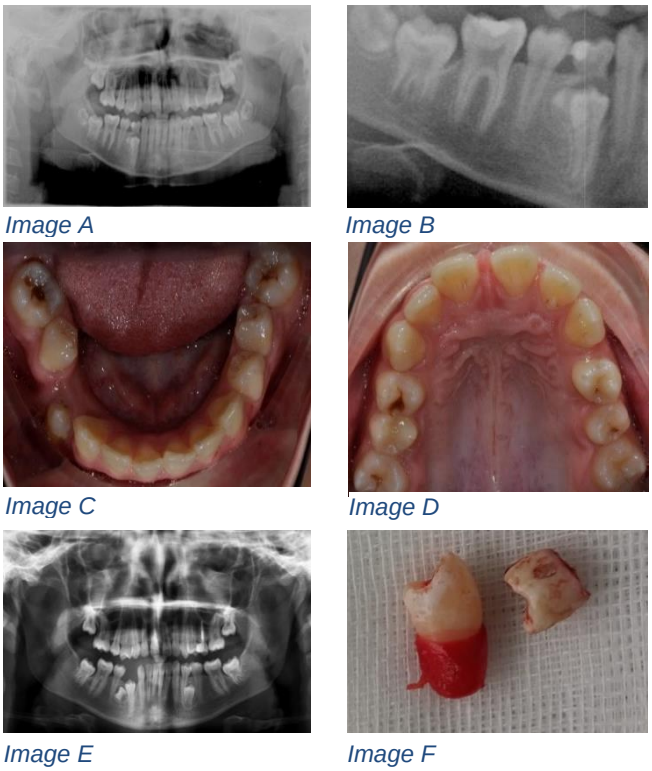

Figure 5.3 *A and B*: Pre-extraction DPO.
C and D: Clinical examination 62 months after the extractions.
E: Radiographic examination at follow-up.
F: Extracted supernumerary #39, #49.

Case IV

Patient [1] had four M1s extracted at 8.9 years of age due to MIH and caries. The pre-extraction radiographic examination revealed agenesis of the upper left lateral incisor (#22). According to the patient's file, four M1s and the element #75 were extracted during general anesthesia. 47 months after the extractions the patient attended a follow-up appointment and the following were observed:

- Impaction of element #13
- Eruption of element #23 distal to the central incisor and mesial to the primary canine #63 which was still in situ
- Distal drift and embedded eruption of element #35
- Retention of element #85
- Dental and skeletal Class III

Elements #53, #63 and #75 were extracted and patient is further referred to the orthodontic department.

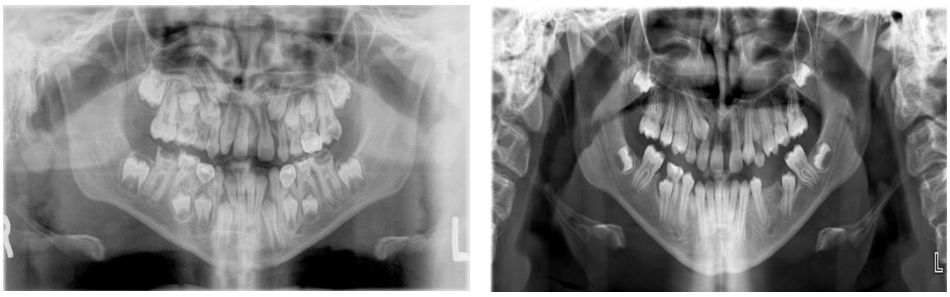

Image A *Image B*

Figure 5.4 *A:* Pre-extraction radiographic examination.
B: Post-extraction radiographic examination. Distal drift and embedded eruption of element #35.

Case V

Patient [33] had element #46 extracted from 10.9 years of age. During the clinical element #11 was diagnosed as macrodont. At the time of extraction the germ of #48 was not present. Two years after the extraction, the patient had no complains, although arrested development of the root of #47 was established along with absence of the third molar. Patient is referred to the orthodontic department.

Image A

Image B

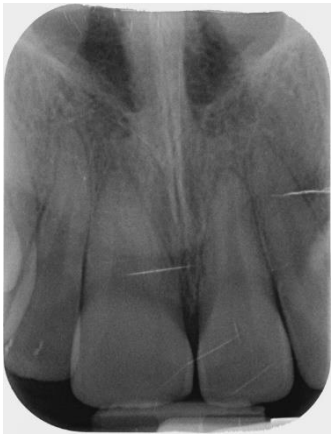

Image C

Image B

Image D

Figure 5.5 *A:* Pre-extraction DPO.
B: Clinical and radiographic examination at follow-up.
C: Radiographic examination of element #11 (macrodont).
D: Arrested development of element #47.

6 Discussion

Pediatric dentists often face, in daily practice, difficulties regarding the management of compromised first permanent molars. Their high susceptibility to caries and developmental defects of enamel, results to a high percentage of young patients with first molars with poor prognosis. The difficulty of making the decision to extract a permanent tooth in young patients and its consequences in the developing dentition makes studies on the topic highly beneficial for pediatric dentists.

6.1 Sample size

Ninety-three patients were identified as eligible for the study but data from thirty-seven were finally analyzed. Small sample size (n=37) is one of the limitations of the present study. The sample in the study of Jalevik et al. (2007) was 27 patients, which is comparable to the present data set. Teo et al. (2013) included 63 patients while Patel et al. (2017) cumulatively assessed data from 81 patients. Both studies took place in central hospitals in the UK where a larger number of patients is seen every day. Even then, a low percentage of attendance was reported by Teo et al. (2013), while in the study by Patel et al. (2017) patients from different sources had to be recruited in order to reach the desired number of patients.

To counteract the limitation of the small sample size, we tried to optimize our inclusion criteria and have a more homogeneous sample. The maximum time between the radiographic examination (DPO) and the extractions was 6 months. In the study of Patel et al (2017) the average time between radiographic examination and extractions was 0.41 years with a range from 0 to 0.85 years, while all the previous studies assessing pre-extraction DPOs (Teo et al. 2013, 2016) did not report the time between the DPO and the extractions. It is expected that the developmental stage of the M2s and the presence of the germ of the M3 could change after a time period of 0.85 years (10 months). Using one of the cases as an example (Figure 6.1), the calcification of the bifurcation of the M2 has begun changing from stage D to stage E only three months after the first DPO. For that reason, a safety net of 6 months was used.

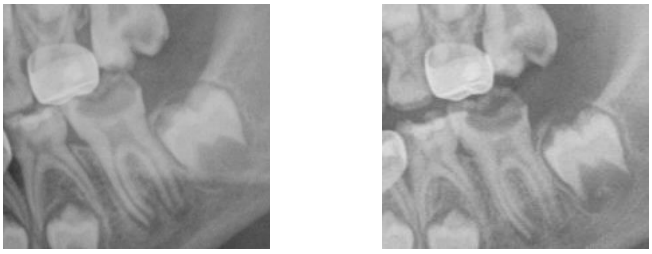

Figure 6.1 Beginning of bifurcation calcification of element #37 three months after the first radiograph.

Furthermore, a minimum follow-up of 24 months after the extractions was selected and the mean time of follow-up was 38 months. Time between extractions and review ranged between 0.9 and 7.5 years in the study of Patel et al. (2017). It can be expected that changes, regarding diastemas, rotation and inclination, can occur after the eruption of a tooth. Thus, the limit of 24 months was used to ensure that the final outcome of the spontaneous changes would be captured. It was also assumed that within this time period all the permanent teeth of the participants would have erupted, although exclusion of participants due to not erupted teeth could not be completely avoided in the present study. From an ethical point of view it was decided not to set a longer time limit for follow-up because some of the participants might need orthodontic treatment. Another advantage of a minimum of 24 months follow-up is the assurance of a more homogeneous sample. In this way the investigators tried to also take into account the spatial aspect between the different follow-up periods between patients. Only the study of Jalevik et al. (2007) had a narrower time of follow-up of 3.8-8.3 years (median 5.7).

6.2 Study design

While some studies (Patel et al. 2017) focus on the remaining diastemas between M2 and P2, the present study tried to perform a more comprehensive assessment of the extraction consequences in the posterior region. The assessment included all the posterior teeth distal to the canine, given the fact that they might be affected from the extractions. According to the present results severe distal drifting of premolars was seen in 3 cases (Figure 6.2, 6.3), and Jalevik et al (2007) also reported

3 such cases. In all cases in both studies a distal inclination of the premolars' tooth germ was already established in the pre-extraction radiographs.

Figure 6.2 Pre - extraction radiograph. Distal inclination of P1.
Post - extraction radiograph. Distal drift and inclination of P1.

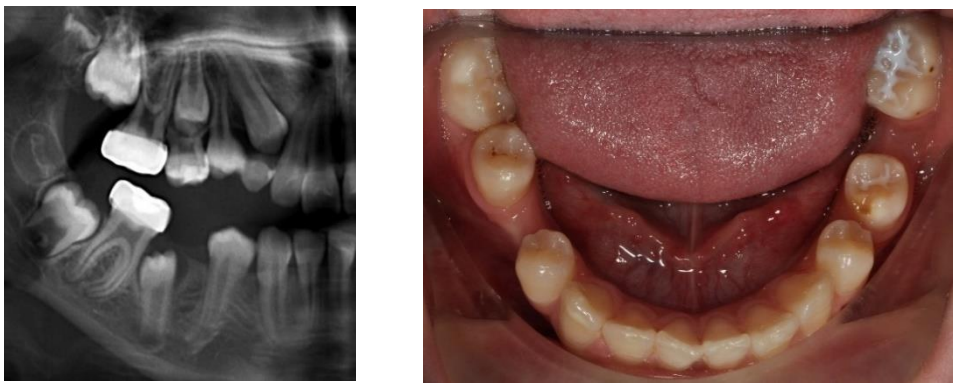

Figure 6.3 Pre - extraction radiograph. Distal inclination of P2.
Post - extraction radiograph. Distal drift of P2.

Moreover, except the remaining diastemas, attention was given in rotation and inclination of the examined teeth. These aspects are crucial for practicing sufficient oral hygiene, the lack of which can hinder the preservation of periodontal health and increase the risk of bone defects. Especially, in the maxilla, where remaining diastemas are uncommon, severe rotations might be overlooked by the clinicians, increasing the risk for periodontal problems. Severe inclination of the lower M2 was a common finding in the present sample, while it was not included as a separate assessment in other studies, rendering their results incomplete. Instead, tooth displacement up to 2mm (Grade I, II) without severe inclination and rotation, was considered as an acceptable outcome in the present study in contrast with other studies where any remaining diastema was considered as failure.

On the other hand, cases with no remaining diastemas but severe rotation and/or inclination were judged as failures in this study (example in Figure 6.4). In the study of Patel et al. (2017), a contact between M2 and P2 without any significant discrepancies in sagittal and transverse way, was considered as successful outcome. Although the authors included severe rotation and inclination in the definition of the successful outcome, there was no clear reporting of the cases that had to be determined as failures due to severe inclination and/or rotation. In our opinion, all three parameters, among others, should be taken into account when assessing the outcome of first molar extractions.

Figure 6.4 Severe rotation of element #47 and severe inclination of element #37.

Given the lack of an objective and widely used classification for the outcome after M1 extraction, in this study we used 2 different methods of assessment. Firstly, we used the grading system adapted from the Index of Orthodontic Treatment Need. This validated index is easy to use and provides an objective and reliable way of assessment. Another advantage of this system is that it estimates malocclusions in all dimensions, taking into account rotation and inclination. Moreover, it associates the different grades of tooth displacement with the need of orthodontic treatment. This index is commonly used in orthodontic studies, (Rolland et al. 2016) but its use for the assessment of treatment outcome after first permanent molar extraction was firstly adopted by Teo et al. (2016). In this study the treatment outcome was assessed by only one examiner during an intra-oral examination. Given the difficulty to use a periodontal probe with different angulations in the mouth cavity and identify differences of 1mm, it was decided for the purposes of this study to use study models for the assessments. Another advantage of study models usage was that two independent examiners were able to assess the study models and inter and intra-

examiner agreement was calculated, increasing the validity and reliability of our results (excellent agreement was observed). Although IOTN takes into account any directional displacements, it was observed during some trial measurements that the exact amount of inclination was difficult to be assessed. Therefore, a separate score for inclination and rotation of the included posterior teeth was given by the two examiners. That way, it was possible to determine the percentage of non-favorable outcomes that was caused by severe rotation, severe inclination or remaining diastemas.

Study models and dental pantomograms were the two main methods of assessment for every patient participating in the present study, in an effort to determine any bodily movement of the affected teeth. The same methods were also included in the study by Jalevik et al. (2007), but only subjective criteria were used. On the other hand, clinical examination was the only method of assessment used by Teo et al. (2013, 2016) and Patel et al. (2017). In the study by Teo et al. (2013) it was argued that there was no clinical justification to expose the patients to further radiation.

In the present study it was decided to include radiographic examination of the patients because useful information regarding the inclination of M2, as well as the presence and the potential for eruption of M3 can be retrieved from this method. For the purpose of this study a DPO was chosen. Exposure to unnecessary radiation that was not justified for the benefit of the patient was avoided, since new radiographs were taken only if there was no available DPO in the last 2 years. DPOs are routinely used in dental practice and have low dose of radiation while providing a reasonably good assessment of the root position and tooth inclination. That said, we should not ignore the distortion that frequently occurs within panoramic radiographs. Moreover, taking study models, dental pantomograms and a lateral cephalograms is the standard diagnostic procedure used in the Orthodontic Department of Ghent University.

All information collected from this study about patients assessed to be in need of orthodontic treatment, was available to be subsequently used for their orthodontic treatment. For patients assessed not to be in need of orthodontic treatment, information could be given for the eruption potential and available space for M3s. Interestingly enough, additional important information (supernumerary teeth, impacted canines, and arrested root development) was discovered for a small amount of patients.

Regarding the index used for the assessment, IOTN index is simple and can be easily used by every pediatric dentist without the need for calibration, although it can be argued that the American Board of Orthodontics (ABO) criteria might be more appropriate for that assessment. This method should be applied by trained and experienced orthodontists, which was not possible within the limitations of this study.

6.3 Findings

In the present study, main reasons for extractions were caries (52.7%) and MIH (38.7%), which is in accordance with the results of Teo et al (2013). In that study, 56% of the extractions were due to caries, while in the study of Albadri et al. (2007) caries (89%) was the main reason for extractions. All these studies attempted to review the reasons of M1 extractions in young patients but the results have to be interpreted with caution due to their retrospective design and the fact that gross caries can mask the diagnosis of MIH. In the current study, general anesthesia was the main type of anesthesia used which is in accordance with the results of previous studies (Albadri et al. 2007).

Regarding the timing of extractions, the participants of the present study had theirs molars extracted on average at the age of 10.7 years. The participants in the study of Jalevik et al. (2007) had the extractions on average at an earlier age (8.2y), while in the studies of Teo et al. (2013), Teo et al. (2016) and Patel et al. (2017) the main age at extractions was 8,9y, 9,2y, and 9,6y respectively.

According to the literature, extractions in the upper arch result in a favorable outcome in the majority of the cases. A high percentage (84%) of favorable space closure in the maxilla was confirmed in the present study, while similar high success rates (92%, 89.9%) were reported in previous studies (Teo et al. 2013, Patel et al. 2017).

In the lower arch, only 32.2% of the quadrants with extracted molars resulted in a favorable outcome, supporting the success rates reported by Thilander and Skagius (1970) and Thilander et al. (1963) (34.6% and 36% respectively). Despite the different criteria used between studies, it is obvious that extractions in the mandible present a lower success rate in comparison with the maxilla. Remarkably, the percentage of favorable outcomes in the present study is significantly lower compared

to more recent studies. (61%, 51.2% and 49%). This might be partly explained by the relatively strict criteria used to assess the outcome in the present study. Another explanation might be that the participants of the present study had their molars extracted on average a year later or more compared to the participants of other studies.

Regarding the developmental stage of M2 as a prognostic factor for a favorable outcome, no significant association could be found, supporting the findings of previous studies (Teo et al. 2013, Teo at al. 2016, Patel et al. 2017). In the present study no significant difference could be found between the varying M2 angulations, which is not in agreement with the results reported by Teo et al. (2016) and Patel et al. (2017). However, a different method for the assessment of M2 angulation was used in the present study and this fact might explain the contradictory results. Moreover, due to the retrospective design of the study, other parameters like the occlusion and skeletal relations before the extractions were unavailable for assessment.

7 Conclusion

When assessing patients presenting with M1s of questionable prognosis, individual criteria on patient and tooth level should be considered. The enforced extraction of compromised molars is a beneficial treatment option for young patients and can result in spontaneous favorable outcomes. Extractions should be preferably planned in collaboration with an orthodontist and every patient should be closely followed up. Even if orthodontic intervention is needed after all, enforced extractions of M1s might still be considered as treatment of choice for some patients, from a clinical and cost-effectiveness point of view.

The outcome of M1 extractions varied between the two arches. The majority of extractions in the maxilla resulted in a favorable outcome while the outcome in the mandible was less predictable. The two parameters that were studied, namely the influence of the LM2 developmental stage and angulation, showed no significant effect on the extraction outcome, within the available sample. Consequently, the first null hypothesis was partly rejected (for the maxilla) and the second null hypothesis was accepted. That said, it should be mentioned that the interpretation of the results must be conducted with caution, due to the limited sample. The influence of new as well as already proposed prognostic factors should be further evaluated in future research on the topic.

8 References

1 Public Health England. Local Authorities Improving Oral Health: Commissioning Better Oral Health for Children and Young People. An Evidence-Informed Toolkit for Local Authorities. London: Public Health England; 2014.

2 Royal College of Pediatrics and Child Health. State of Child Health Report 2017. Available at: http://www.rcpch.ac.uk/ state-of-child-health (accessed March 2017.

3 Albadri S, Zaitoun H, McDonnell ST, Davidson LE. Extraction of first permanent molar teeth: results from three dental hospitals. Br Dent J. 2007;203(7):E14; discussion 408-9.

4 Americano GC, Jacobsen PE, Soviero VM, Haubek D. A systematic review on the association between molar incisor hypomineralization and dental caries. Int J Paediatr Dent. 2017;27(1):11-21.

5 Americano GC, Jorge RC, Moliterno LF, Soviero VM. Relating Molar Incisor Hypomineralization and Caries Experience Using the Decayed, Missing, or Filled Index. Pediatr Dent. 2016;38(5):419-24.

6 Ay S, Agar U, Bicakci AA, Kosger HH. Changes in mandibular third molar angle and position after unilateral mandibular first molar extraction. Am J Orthod Dentofacial Orthop. 2006;129(1):36-41.

7 Bayram M, Ozer M, Arici S. Effects of first molar extraction on third molar angulation and eruption space. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 2009;107(2):e14-20.

8 Brook PH, Shaw WC. The development of an index of orthodontic treatment priority. Eur J Orthod. 1989;11(3):309-20.

9 Caglaroglu M, Kilic N, Erdem A. Effects of early unilateral first molar extraction on skeletal asymmetry. Am J Orthod Dentofacial Orthop. 2008;134(2):270-5.

10 Cicchetti DV. Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. Psychological Assessment. 1994; 6(4):284–290.
11 Cobourne MT, Williams A, Harrison M. National clinical guidelines for the extraction of first permanent molars in children. Br Dent J. 2014;217(11):643-8.
12 Demirjian A, Goldstein H, Tanner JM. A new system of dental age assessment. Human biology. 1973;45(2):211-27.
13 Eichenberger M, Erb J, Zwahlen M, Schatzle M. The timing of extraction of non-restorable first permanent molars: a systematic review. Eur J Paediatr Dent. 2015;16(4):272-8.
14 Elhennawy K, Jost-Brinkmann PG, Manton DJ, Paris S, Schwendicke F. Managing molars with severe molar-incisor hypomineralization: A cost-effectiveness analysis within German healthcare. Journal of dentistry. 2017;63:65-71.
15 Elhennawy K, Manton DJ, Crombie F, Zaslansky P, Radlanski RJ, Jost-Brinkmann PG, et al. Structural, mechanical and chemical evaluation of molar-incisor hypomineralization-affected enamel: A systematic review. Archives of oral biology. 2017;83:272-81.
16 Elhennawy K, Schwendicke F. Managing molar-incisor hypomineralization: A systematic review. Journal of dentistry. 2016;55:16-24.
17 Fagrell TG, Dietz W, Jalevik B, Noren JG. Chemical, mechanical and morphological properties of hypomineralized enamel of permanent first molars. Acta odontologica Scandinavica. 2010;68(4):215-22.
18 Fagrell TG, Lingstrom P, Olsson S, Steiniger F, Noren JG. Bacterial invasion of dentinal tubules beneath apparently intact but hypomineralized enamel in molar teeth with molar incisor hypomineralization. Int J Paediatr Dent. 2008;18(5):333-40.
19 Garot E, Couture-Veschambre C, Manton D, Beauval C, Rouas P. Analytical evidence of enamel hypomineralisation on permanent and primary molars amongst past populations. Sci Rep. 2017;7(1):1712.
20 Gill DS, Lee RT, Tredwin CJ. Treatment planning for the loss of first permanent molars. Dental update. 2001;28(6):304-8.

21 Halicioglu K, Celikoglu M, Buyuk SK, Sekerci AE, Candirli C. Effects of early unilateral mandibular first molar extraction on condylar and ramal vertical asymmetry. European journal of dentistry. 2014;8(2):178-83.

22 Halicioglu K, Celikoglu M, Caglaroglu M, Buyuk SK, Akkas I, Sekerci AE. Effects of early bilateral mandibular first molar extraction on condylar and ramal vertical asymmetry. Clinical oral investigations. 2013;17(6):1557-61.

23 Halicioglu K, Toptas O, Akkas I, Celikoglu M. Permanent first molar extraction in adolescents and young adults and its effect on the development of third molar. Clinical oral investigations. 2014;18(5):1489-94.

24 Hallgren KA. Computing Inter-Rater Reliability for Observational Data: An Overview and Tutorial. Tutorials in quantitative methods for psychology. 2012;8(1):23-34.

25 Heckmann K, Spitzer WJ, Lisson JA. Molar inclination in panoramic x-rays as an indicator for extraction decisions. Journal of orofacial orthopedics = Fortschritte der Kieferorthopadie : Organ/official journal Deutsche Gesellschaft fur Kieferorthopadie. 2007;68(6):491-500.

26 Hubbard MJ, Mangum JE, Perez VA, Nervo GJ, Hall RK. Molar Hypomineralisation: A Call to Arms for Enamel Researchers. Frontiers in physiology. 2017;8:546.

27 Innes N, Borrie F, Bearn D, Evans D, Rauchhaus P, McSwiggan S, et al. Should I eXtract Every Six dental trial (SIXES): study protocol for a randomized controlled trial. Trials. 2013;14:59.

28 Jacobs C, Jacobs-Muller C, Luley C, Erbe C, Wehrbein H. Orthodontic space closure after first molar extraction without skeletal anchorage. Journal of orofacial orthopedics = Fortschritte der Kieferorthopadie: Organ/official journal Deutsche Gesellschaft fur Kieferorthopadie. 2011;72(1):51-60.

29 Jalevik B. Enamel hypomineralization in permanent first molars. A clinical, histo-morphological and biochemical study. Swedish dental journal Supplement. 2001(149):1-86.

30 Jalevik B, Klingberg G. Treatment outcomes and dental anxiety in 18-year-olds with MIH, comparisons with healthy controls - a longitudinal study. Int J Paediatr Dent. 2012;22(2):85-91.

31 Jalevik B, Klingberg GA. Dental treatment, dental fear and behavior management problems in children with severe enamel hypomineralization of their permanent first molars. Int J Paediatr Dent. 2002;12(1):24-32.

32 Jalevik B, Moller M. Evaluation of spontaneous space closure and development of permanent dentition after extraction of hypomineralized permanent first molars. Int J Paediatr Dent. 2007;17(5):328-35.

33 Kopperud SE, Pedersen CG, Espelid I. Treatment decisions on Molar-Incisor Hypomineralization (MIH) by Norwegian dentists - a questionnaire study. BMC oral health. 2016;17(1):3.

34 Kuhnisch J, Kabary L, Malyk Y, Rothmaier K, Metz I, Hickel R, et al. Relationship between caries experience and demarcated hypomineralised lesions (including MIH) in the permanent dentition of 15-year-olds. Clinical oral investigations. 2017.

35 Kuhnisch J, Lauenstein A, Pitchika V, McGlynn G, Staskiewicz A, Hickel R, et al. Was molar incisor hypomineralisation (MIH) present in archaeological case series? Clinical oral investigations. 2016;20(9):2387-93.

36 Llena C, Calabuig E. Risk factors associated with new caries lesions in permanent first molars in children: a 5-year historical cohort follow-up study. Clinical oral investigations. 2018;22(3):1579-86.

37 Lygidakis NA. Treatment modalities in children with teeth affected by molar-incisor enamel hypomineralisation (MIH): A systematic review. Eur Arch Paediatr Dent. 2010;11(2):65-74.

38 Lygidakis NA, Wong F, Jalevik B, Vierrou AM, Alaluusua S, Espelid I. Best Clinical Practice Guidance for clinicians dealing with children presenting with Molar-Incisor-Hypomineralisation (MIH): An EAPD Policy Document. Eur Arch Paediatr Dent. 2010;11(2):75-81.

39 Mejare I, Bergman E, Grindefjord M. Hypomineralized molars and incisors of unknown origin: treatment outcome at age 18 years. Int J Paediatr Dent. 2005;15(1):20-8.

40 Neboda C, Anthonappa RP, King NM. Tooth mineral density of different types of hypomineralised molars: a micro-CT analysis. Eur Arch Paediatr Dent. 2017;18(6):377-83.

41 Normando AD, Maia FA, Ursi WJ, Simone JL. Dentoalveolar changes after unilateral extractions of mandibular first molars and their influence on third

molar development and position. World journal of orthodontics. 2010;11(1):55-60.

42 Ong DC, Bleakley JE. Compromised first permanent molars: an orthodontic perspective. Australian dental journal. 2010;55(1):2-14; quiz 105.

43 Patel S, Ashley P, Noar J. Radiographic prognostic factors determining spontaneous space closure after loss of the permanent first molar. Am J Orthod Dentofacial Orthop. 2017;151(4):718-26.

44 Rodd HD, Boissonade FM, Day PF. Pulpal status of hypomineralized permanent molars. Pediatr Dent. 2007;29(6):514-20.

45 Rolland SL, Treasure E, Burden DJ, Fuller E, Vernazza CR. The orthodontic condition of children in England, Wales and Northern Ireland 2013. Br Dent J. 2016;221(7):415-9.

46 Sandler PJ, Atkinson R, Murray AM. For four sixes. Am J Orthod Dentofacial Orthop. 2000;117(4):418-34.

47 Silva MJ, Scurrah KJ, Craig JM, Manton DJ, Kilpatrick N. Etiology of molar incisor hypomineralization - A systematic review. Community Dent Oral Epidemiol. 2016;44(4):342-53.

48 Teixeira R, Andrade NS, Queiroz LCC, Mendes FM, Moura MS, Moura L, et al. Exploring the association between genetic and environmental factors and molar incisor hypomineralization: evidence from a twin study. Int J Paediatr Dent. 2018;28(2):198-206.

49 Teo TK, Ashley PF, Derrick D. Lower first permanent molars: developing better predictors of spontaneous space closure. Eur J Orthod. 2016;38(1):90-5.

50 Teo TK, Ashley PF, Parekh S, Noar J. The evaluation of spontaneous space closure after the extraction of first permanent molars. Eur Arch Paediatr Dent. 2013;14(4):207-12.

51 Thilander B, Skagius S. Orthodontic sequelae of extraction of permanent first molars. A longitudinal study. Rep Congr Eur Orthod Soc. 1970:429-42.

52 Thilander B, Jakobsson SO, Skagius S. Orthodontic sequelae of extraction of permanent first molars. Scand Dent J 1963;71:380-412.

53 Thunold K. Early loss of the first molars 25 years after. Rep Congr Eur Orthod Soc. 1970:349-65.

54 Weerheijm K. The European Academy of Paediatric Dentistry and Molar Incisor Hypomineralisation. Eur Arch Paediatr Dent. 2015;16(3):233-4.

55 Weerheijm KL. Molar incisor hypomineralisation (MIH). Eur J Paediatr Dent. 2003;4(3):114-20.

56 Weerheijm KL, Jalevik B, Alaluusua S. Molar-incisor hypomineralisation. Caries research. 2001;35(5):390-1.

57 Williams JK, Gowans AJ. Hypomineralised first permanent molars and the orthodontist. Eur J Paediatr Dent. 2003;4(3):129-32.

58 Wu M, Chen L, Bawole E, Anthonappa RP, King NM. Is there sufficient evidence to support an optimum time for the extraction of first permanent molars? Eur Arch Paediatr Dent. 2017.

59 Yavuz I, Baydas B, Ikbal A, Dagsuyu IM, Ceylan I. Effects of early loss of permanent first molars on the development of third molars. Am J Orthod Dentofacial Orthop. 2006;130(5):634-8.

60 Zhao D, Dong B, Yu D, Ren Q, Sun Y. The prevalence of molar incisor hypomineralization: evidence from 70 studies. Int J Paediatr Dent. 2018;28(2):170-9.

9 Appendices

Appendix 1: Information letter and Inform Consent

Informatiebrief voor ouders van kinderen van 8 tot 12 jaar die deelnemen aan de studie

EVALUATION OF THE ERUPTION PATTERN AND SPACE CLOSURE OF THE PERMANENT SECOND MOLAR AFTER EXTRACTION OF HYPOMINERALISED PERMANENT FIRST MOLARS.

Evaluatie van het eruptiepatroon en sluiten van de open ruimte van de definitieve 2de molaar na extractie van de gehypomineraliseerde 6-jaarsmolaar.

Doel van de studie

Bij sommige kinderen is het glazuur van de definitieve 1ste molaren (‘kiezen’), die rond de leeftijd van 6 jaar zijn doorgebroken, minder goed ontwikkeld. Vaak noemt men deze tanden, ‘kaastanden’ of gebruikt men de term glazuurhypomineralisatie. Deze tanden vertonen een mat en vaak wit-gelig aspect, waarbij defecten kunnen voorkomen in vlekken of over heel de tand. Door een fout in de samenstelling van het glazuur zijn deze tanden gevoeliger voor koude en warmte prikkels zal er zich sneller cariës (‘gaatjes’) ontwikkelen omwille van de porositeit van de tanden. Soms zijn deze molaren (‘kiezen’) zo ernstig aangetast dat we deze dienen te extraheren/verwijderen. Zo dan de 2de molaar (kies) bij doorbraak door verplaatsing de open ruimte innemen. Met dit onderzoek willen wij nagaan hoe de verplaatsing van deze 2de molaar gebeurt na extractie van de kaastand.

Beschrijving van de studie

Opdat wij ons een duidelijk beeld kunnen vormen van de ontwikkeling en verplaatsing van de 2de molaar na extractie van kaasmolaren, dienen wij deze zone te evalueren. Alle patiënten, die wensen deel te nemen aan deze studie, worden uitgenodigd in de Polikliniek Tandheelkunde van het UZ Gent voor evaluatie van beide tanden naast de extractieruimte. Het betreft een kort bezoek bij de tandarts, waarbij hij/zij de tanden naast de extractieruimte evalueert, gevolgd door radiologische opname van het gebit, het nemen van klinische foto's alsook gebitsafdrukken en opmeten van waarden betreffende de gezondheid van het tandvlees en bot. Dit onderzoek zal 1 zittijd van 30 min. in beslag nemen. (20 tot 30 deelnemers)

Alle gegevens zullen grondig geanalyseerd worden teneinde een exacte conclusie te bekomen betreffende de verplaatsing van de 2de molaar en sluiten van de extractieruimte.

Verwachtingen ten aanzien van de deelnemer

De deelname aan deze studie vindt plaats op vrijwillige basis.

U kan weigeren om deel te nemen aan de studie, en u kunt zich op elk ogenblik terugtrekken uit de studie zonder dat u hiervoor een reden moet opgeven en zonder dat dit een invloed zal hebben op die van het kind en uw verdere relatie en/of behandeling met de behandelende tandarts/onderzoeker.

Procedures

Onderstaande tandheelkundige testen worden meerdere keren afgenomen en dit in de volgorde zoals ze hier beschreven staan:

- *Mondonderzoek:*

  Dit vindt plaats bij de tandarts

- *Radiografische opname*

  Hierbij zullen de tanden in beeld worden gebracht. Hiervoor zal 1 orthopantomogram (= overzichtsfoto van het gebit van links naar rechts) genomen worden.

- *Gebitsmodellen*

Een afdruk van de boven- en onderkaak zal genomen worden.

- *Klinische foto's:*

  De tanden worden meermaals met fotografie in beeld gebracht.

Risico's en nadelen

Er worden geen risico's verwacht bij deelname aan het onderzoek. Bovendien zijn er geen nadelen bij deelname aan dit onderzoek behalve dat u een keer met uw kind naar de polikliniek moet komen. Natuurlijk zullen we deze afspraken combineren met de gewoonlijke 6-maandelijkse controle.

U hebt het recht op elk ogenblik vragen te stellen over de mogelijke en/of gekende risico's, nadelen van deze studie. Als er in het verloop van de studie gegevens aan het licht komen, die een invloed zouden kunnen hebben op uw bereidheid om te blijven deelnemen aan deze studie, zult u daarvan op de hoogte worden gebracht.

Deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan dit ziekenhuis en wordt uitgevoerd volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki opgesteld ter bescherming van mensen deelnemend aan klinische studies. Deze goedkeuring was in geen geval de aanzet om te beslissen om deel te nemen aan deze studie.

Vertrouwelijkheid

De verzamelde informatie van uw kind zal zeker vertrouwelijk behandeld worden. Tijdens en na de studie zullen wij de identiteit en onderzoeksgegevens onder goed beveiligde omstandigheden beschermen.
In overeenstemming met de Belgische wet van 8 december 1992 en de Belgische wet van 22 augustus 2002, zal de persoonlijke levenssfeer van uw kind worden gerespecteerd en zal u en uw kind toegang krijgen tot de verzamelde gegevens. Elk onjuist gegeven kan op uw verzoek of van uw kind verbeterd worden.
Vertegenwoordigers van de opdrachtgever, auditoren, de Commissie voor Medische Ethiek en de bevoegde overheden hebben rechtstreeks toegang tot uw medische dossiers om de procedures van de studie en/of de gegevens te controleren, zonder de vertrouwelijkheid te schenden. Dit kan enkel binnen de grenzen die door de betreffende wetten zijn toegestaan.

Door het toestemmingsformulier, na voorafgaande uitleg, te ondertekenen stemmen u en uw kind in met deze toegang.
Als u en uw kind akkoord gaat om aan deze studie deel te nemen, zullen de persoonlijke en klinische gegevens van uw kind tijdens deze studie worden verzameld.
Verslagen waarin uw kind wordt geïdentificeerd, zullen niet openlijk beschikbaar zijn. Als de resultaten van de studie worden gepubliceerd, zal de identiteit van uw kind vertrouwelijke informatie blijven.

Letsels ten gevolge van deelname aan de studie

De onderzoeker voorziet in een vergoeding en/of medische behandeling in het geval van schade en/of letsel tengevolge van deelname aan de studie. Voor dit doeleinde is een verzekering afgesloten met foutloze aansprakelijkheid conform de wet inzake experimenten op de menselijke persoon van 7 mei 2004. Op dat ogenblik kunnen uw gegevens doorgegeven worden aan de verzekeraar.

Deelname

Deelname aan deze studie is kostenloos en er zijn geen vergoedingen voorzien. Mocht u naar aanleiding van wat u gelezen hebt in deze informatiebrief toestemmen met deelname van uw kind, dan vragen wij U het bijgevoegde toestemmingsformulier in te vullen en te ondertekenen.

Contactpersonen

Als u aanvullende informatie wenst over de studie of over uw rechten en plichten, kunt u in de loop van de studie op elk ogenblik contact opnemen met de onderzoekers.

Prof. Dr. L. Martens
+ 32 (0)9 332 40 08
luc.martens@ugent.be

Tandarts E. Mouroutsou
+ 32 (0)460 97 10 06
helen.mouroutsou@ugent.be

Toestemmingsformulier

Ik, _____ heb het document "Informatiebrief voor de ouders van kinderen van 8 tot 12 jaar die deelnemen aan de studie" pagina 1 tot en met 4 gelezen en er een kopij van gekregen. Ik stem in met de inhoud van het document en stem ook in dat mijn zoon/dochter deelneemt aan de studie.

Ik heb een kopij gekregen van dit ondertekende en gedateerde formulier voor "Toestemmingsformulier". Ik heb uitleg gekregen over de aard, het doel, de duur, en de te voorziene effecten van de studie en over wat men van mij verwacht. Ik heb uitleg gekregen over de mogelijke risico's en voordelen van de studie. Men heeft me de gelegenheid en voldoende tijd gegeven om vragen te stellen over de studie, en ik heb op al mijn vragen een bevredigend antwoord gekregen, ook op medische vragen.

Ik stem ermee in om volledig samen te werken met de toeziende onderzoeker/arts.

Men heeft mij ingelicht over het bestaan van een verzekeringspolis in geval er letsel zou ontstaan dat aan de studieprocedures is toe te schrijven.

Ik ben me ervan bewust dat deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan het UZ Gent en dat deze studie zal uitgevoerd worden volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki, opgesteld ter bescherming van mensen deelnemend aan experimenten. Deze goedkeuring was in geen geval de aanzet om te beslissen om deel te nemen aan deze studie.

Ik mag mijn kind op elk ogenblik uit de studie terugtrekken zonder een reden voor deze beslissing op te geven en zonder dat dit op enigerlei wijze een invloed zal hebben op mijn verdere relatie met de onderzoeker/arts.

Men heeft mij ingelicht dat zowel persoonlijke gegevens als gegevens aangaande de gezondheid van mijn kind worden verwerkt en bewaard gedurende minstens 20 jaar.

Ik stem hiermee in en ben op de hoogte dat ik recht heb op toegang en verbetering van deze gegevens. Aangezien deze gegevens verwerkt worden in het kader van medisch-wetenschappelijke doeleinden, begrijp ik dat de toegang tot mijn gegevens kan uitgesteld worden tot na beëindiging van het onderzoek. Indien ik toegang wil tot mijn gegevens, zal ik mij richten tot de toeziende onderzoeker/arts, die verantwoordelijk is voor de verwerking.

Ik begrijp dat auditors, vertegenwoordigers van de opdrachtgever, de Commissie voor Medische Ethiek of bevoegde overheden, de gegevens van mijn kind mogelijk willen inspecteren om de verzamelde informatie te controleren. Door dit document te ondertekenen, geef ik toestemming voor deze controle. Bovendien ben ik op de hoogte dat bepaalde gegevens doorgegeven worden aan de opdrachtgever. Ik geef hiervoor mijn toestemming, zelfs indien dit betekent dat mijn gegevens doorgegeven worden aan een land buiten de Europese Unie. Ten alle tijden zal mijn privacy gerespecteerd worden.

Ik verleen de onderzoekers mijn toestemming om:

(kruis aan welke items van toepassing zijn)

- ☐ Eventueel het medisch dossier van mijn kind, aanwezig hier in het UZ Gent, te raadplegen
- ☐ Resultaten van eerder afgenomen tandheelkundige testen schriftelijk op te vragen in de medische instelling waar ze werden afgenomen.
- ☐ voor deelname van mijn dochter/zoon aan de studie

Naam van de instemmende ouders:

_____

Datum:

_____

_____

Handtekening:

LUIK BESTEMD VOOR DE ONDERZOEKER:

Ik bevestig dat ik de aard, het doel, en de te voorziene effecten van de studie heb uitgelegd aan de bovenvermelde vrijwillige ouder van het deelnemende kind.

De vrijwillige ouder stemde toe om zijn/haar zoon/dochter te laten deelnemen door zijn/haar persoonlijk gedateerde handtekening te plaatsen.

Naam van de persoon die voorafgaande uitleg heeft gegeven:

_____

Datum:

_____

_____

Handtekening:

Informatiebrief voor deelnemers aan de studie tussen 12 en 18 jaar oud

EVALUATION OF THE ERUPTION PATTERN AND SPACE CLOSURE OF THE PERMANENT SECOND MOLAR AFTER EXTRACTION OF HYPOMINERALISED PERMANENT FIRST MOLARS.

Evaluatie van het eruptiepatroon en sluiten van de open ruimte van de definitieve 2de molaar na extractie van de gehypomineraliseerde 6-jaarsmolaar.

Doel van de studie

Bij sommige personen is het glazuur van de definitieve 1ste kiezen, die rond de leeftijd van 6 jaar zijn doorgebroken, minder goed ontwikkeld. Vaak noemt men deze tanden, 'kaastanden' of gebruikt men de term glazuurhypomineralisatie. Deze tanden vertonen vaak een mat, wit-gelig aspect. Door een fout in de samenstelling van het glazuur, zijn deze tanden gevoeliger voor koude en warmte prikkels en kunnen er zich sneller 'gaatjes' ontwikkelen. Soms zijn deze kiezen zo ernstig aangetast dat we deze dienen te verwijderen. Zo kan de 2de kies bij doorbraak door verplaatsing de open extractieruimte innemen. Met dit onderzoek willen wij nagaan hoe de verplaatsing van deze 2de kies gebeurt na het verwijderen van de kaastand.

Beschrijving van de studie

Omdat wij ons een duidelijk beeld kunnen vormen van de ontwikkeling en verplaatsing van de 2de kies na extractie van kaastanden, dienen wij deze zone te bekijken. Alle patiënten, die wensen deel te nemen aan deze studie, worden uitgenodigd in de Polikliniek Tandheelkunde van het UZ Gent. Het betreft een kort bezoek bij de tandarts, waarbij hij/zij de tanden naast de open ruimte evalueert, gevolgd door radiografische opname van het gebit, het nemen van klinische foto's alsook gebitsafdrukken en opmeten van waarden betreffende de gezondheid van het tandvlees en bot. Dit onderzoek zal 1 zittijd van 30 min. in beslag nemen (20 tot 30 deelnemers).

Alle gegevens zullen grondig geanalyseerd worden teneinde een goed besluit te bekomen betreffende de verplaatsing van de 2de kies.

Verwachtingen ten aanzien van de deelnemer

De deelname aan deze studie vindt plaats op vrijwillige basis.

U kan weigeren om deel te nemen aan de studie, en u kunt zich op elk ogenblik terugtrekken uit de studie zonder dat u hiervoor een reden moet opgeven en zonder dat dit een invloed zal hebben op uw verdere relatie en/of behandeling met de behandelende tandarts/onderzoeker.

Procedures

Onderstaande tandheelkundige testen worden meerdere keren afgenomen en dit in de volgorde zoals ze hier beschreven staan:

- *Mondonderzoek:*

  Dit vindt plaats bij de tandarts.

- *Radiografische opname*

  Hierbij zullen de tanden in beeld worden gebracht. Hiervoor zal 1 orthopantomogram (= overzichtsfoto van het gebit van links naar rechts) genomen worden.

- *Gebitsmodellen*

  Een afdruk van de boven-en onderkaak zal genomen worden.

- *Klinische foto's:*

  De tanden worden met fotografie in beeld gebracht.

Risico's en nadelen

Er worden geen risico's verwacht bij deelname aan het onderzoek. Bovendien zijn er geen nadelen bij deelname aan dit onderzoek behalve dat u 1 keer naar de polikliniek moet komen. Natuurlijk zullen we deze afspraken combineren met de gewoonlijke 6-maandelijkse controle.

U hebt het recht op elk ogenblik vragen te stellen over de mogelijke en/of gekende risico's, nadelen van deze studie. Als er in het verloop van de studie gegevens aan het licht komen, die een invloed zouden kunnen hebben op uw bereidheid om te blijven deelnemen aan deze studie, zult u daarvan op de hoogte worden gebracht.

Deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan dit ziekenhuis en wordt uitgevoerd volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki opgesteld ter

bescherming van mensen deelnemend aan klinische studies. Deze goedkeuring was in geen geval de aanzet om te beslissen om deel te nemen aan deze studie.

Vertrouwelijkheid

De verzamelde informatie zal zeker vertrouwelijk behandeld worden. Tijdens en na de studie zullen wij uw identiteit en onderzoeksgegevens onder goed beveiligde omstandigheden beschermen.
In overeenstemming met de Belgische wet van 8 december 1992 en de Belgische wet van 22 augustus 2002, zal uw persoonlijke levenssfeer worden gerespecteerd en zal u toegang krijgen tot de verzamelde gegevens. Elk onjuist gegeven kan op uw verzoek verbeterd worden.
Vertegenwoordigers van de opdrachtgever, auditoren, de Commissie voor Medische Ethiek en de bevoegde overheden hebben rechtstreeks toegang tot uw medische dossiers om de procedures van de studie en/of de gegevens te controleren, zonder de vertrouwelijkheid te schenden. Dit kan enkel binnen de grenzen die door de betreffende wetten zijn toegestaan. Door het toestemmingsformulier, na voorafgaande uitleg, te ondertekenen stemt u in met deze toegang.
Als u akkoord gaat om aan deze studie deel te nemen, zullen uw persoonlijke en klinische gegevens tijdens deze studie worden verzameld.
Verslagen waarin u wordt geïdentificeerd, zullen niet openlijk beschikbaar zijn. Als de resultaten van de studie worden gepubliceerd, zal uw identiteit vertrouwelijke informatie blijven.

Letsels ten gevolge van deelname aan de studie

De onderzoeker voorziet in een vergoeding en/of medische behandeling in het geval van schade en/of letsel tengevolge van deelname aan de studie. Voor dit doeleinde is een verzekering afgesloten met foutloze aansprakelijkheid conform de wet inzake experimenten op de menselijke persoon van 7 mei 2004. Op dat ogenblik kunnen uw gegevens doorgegeven worden aan de verzekeraar.

Deelname

Deelname aan deze studie is kostenloos en niet voorzien van een vergoeding. Mocht u naar aanleiding van wat u gelezen hebt in deze informatiebrief toestemmen met deelname, dan vragen wij U het bijgevoegde toestemmingsformulier in te vullen en te ondertekenen.

Contactpersonen

Als u aanvullende informatie wenst over de studie of over uw rechten en plichten, kunt u in de loop van de studie op elk ogenblik contact opnemen met de onderzoekers.

Prof. Dr. L. Martens
+ 32 (0)9 332 40 08
luc.martens@ugent.be

Tandarts E. Mouroutsou
+ 32 (0)460 97 10 06
helen.mouroutsou@ugent.be

Toestemmingsformulier

Ik, _____ heb het document "Informatiebrief deelnemers aan de studie tussen 12 en 18 jaar oud" van pagina 1 tot en met 4 gelezen en er een kopij van gekregen. Ik stem in met de inhoud van het document en neem deel aan de studie.

Ik heb een kopij gekregen van dit ondertekende en gedateerde formulier voor "Toestemmingsformulier". Ik heb uitleg gekregen over de aard, het doel, de duur, en de te voorziene effecten van de studie en over wat men van mij verwacht. Ik heb uitleg gekregen over de mogelijke risico's en voordelen van de studie. Men heeft me de gelegenheid en voldoende tijd gegeven om vragen te stellen over de studie, en ik heb op al mijn vragen een bevredigend antwoord gekregen, ook op medische vragen.

Ik stem ermee in om volledig samen te werken met de toeziende onderzoeker/arts.

Men heeft mij ingelicht over het bestaan van een verzekeringspolis in geval er letsel zou ontstaan dat aan de studieprocedures is toe te schrijven.

Ik ben me ervan bewust dat deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan het UZ Gent en dat deze studie zal

uitgevoerd worden volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki, opgesteld ter bescherming van mensen deelnemend aan experimenten. Deze goedkeuring was in geen geval de aanzet om te beslissen om deel te nemen aan deze studie.

Ik mag mij op elk ogenblik uit de studie terugtrekken zonder een reden voor deze beslissing op te geven en zonder dat dit op enigerlei wijze een invloed zal hebben op mijn verdere relatie met de onderzoeker/arts.

Men heeft mij ingelicht dat zowel persoonlijke gegevens als gegevens aangaande de gezondheid worden verwerkt en bewaard gedurende minstens 20 jaar. Ik stem hiermee in en ben op de hoogte dat ik recht heb op toegang en verbetering van deze gegevens. Aangezien deze gegevens verwerkt worden in het kader van medisch-wetenschappelijke doeleinden, begrijp ik dat de toegang tot mijn gegevens kan uitgesteld worden tot na beëindiging van het onderzoek. Indien ik toegang wil tot mijn gegevens, zal ik mij richten tot de toeziende onderzoeker/arts, die verantwoordelijk is voor de verwerking.

Ik begrijp dat auditors, vertegenwoordigers van de opdrachtgever, de Commissie voor Medische Ethiek of bevoegde overheden, mijn gegevens mogelijk willen inspecteren om de verzamelde informatie te controleren. Door dit document te ondertekenen, geef ik toestemming voor deze controle. Bovendien ben ik op de hoogte dat bepaalde gegevens doorgegeven worden aan de opdrachtgever. Ik geef hiervoor mijn toestemming, zelfs indien dit betekent dat mijn gegevens doorgegeven worden aan een land buiten de Europese Unie. Ten alle tijden zal mijn privacy gerespecteerd worden.

Ik verleen de onderzoekers mijn toestemming om:

(kruis aan welke items van toepassing zijn)

- ☐ Eventueel mijn medisch dossier, aanwezig hier in het UZ Gent, te raadplegen
- ☐ Resultaten van eerder afgenomen tandheelkundige testen schriftelijk op te vragen in de medische instelling waar ze werden afgenomen.
- ☐ voor deelname aan de studie.

Naam: _____

Datum:_____
_____

Handtekening:

Appendix 2: Ethical Committee Approval

Universitair Ziekenhuis Gent

UNIVERSITEIT GENT

Afz: Commissie voor Medische Ethiek

Tand-, mond- en kaakziekten
Polikliniekgebouw 8 - gelijkvloers
Prof. dr. Luc MARTENS
ALHIER

COMMISSIE VOOR MEDISCHE ETHIEK
Voorzitter:
Prof. Dr. D. Matthys
Secretaris:
Prof. Dr. J. Decruyenaere

CONTACT	TELEFOON	FAX	E-MAIL
Secretariaat	+32 (0)9 332 56 13 +32 (0)9 332 59 25	+32 (0)9 332 49 62	ethisch.comite@ugent.be
UW KENMERK	**ONS KENMERK**	**DATUM**	**KOPIE**
	2017/0375	27-mrt-17	Zie "CC"

BETREFT

Advies voor monocentrische studie met als titel:
Evaluation of the eruption pattern and space closure of the permanent second molar after extraction of hypomineralised permanent first molars
-Scriptie Eleni Katerina Mouroutsou

Belgisch Registratienummer: B670201731921

* Diverse, (Alle goedgekeurde documenten cfr. Project 2012/106)
* Adviesaanvraagformulier dd. 14/03/2017, (document E)
* Begeleidende brief

Advies werd gevraagd door:
Prof. dr. L. MARTENS ; Hoofdonderzoeker

BOVENVERMELDE DOCUMENTEN WERDEN DOOR HET ETHISCH COMITÉ BEOORDEELD.
ER WERD EEN POSITIEF ADVIES GEGEVEN OVER DIT PROTOCOL OP 24/03/2017. INDIEN DE STUDIE NIET WORDT OPGESTART VOOR 24/03/2018, VERVALT HET ADVIES EN MOET HET PROJECT TERUG INGEDIEND WORDEN.
Vooraleer het onderzoek te starten dient contact te worden genomen met Bimetra Clinics (09/332 05 00).

THE ABOVE MENTIONED DOCUMENTS HAVE BEEN REVIEWED BY THE ETHICS COMMITTEE.
A POSITIVE ADVICE WAS GIVEN FOR THIS PROTOCOL ON 24/03/2017. IN CASE THIS STUDY IS NOT STARTED BY 24/03/2018, THIS ADVICE WILL BE NO LONGER VALID AND THE PROJECT MUST BE RESUBMITTED.
Before initiating the study, please contact Bimetra Clinics (09/332 05 00).

DIT ADVIES WORDT OPGENOMEN IN HET VERSLAG VAN DE VERGADERING VAN HET ETHISCH COMITE VAN 18/04/2017
THIS ADVICE WILL APPEAR IN THE PROCEEDINGS OF THE MEETING OF THE ETHICS COMMITTEE OF 18/04/2017

* *Het Ethisch Comité werkt volgens 'ICH Good Clinical Practice' - regels*
* *Het Ethisch Comité bekomtoont dat een gunstig advies niet betekent dat het Comité de verantwoordelijkheid voor het onderzoek op zich neemt. Bovendien dient U er over te waken dat Uw mening als betrokken onderzoeker wordt weergegeven in publicaties, rapporten voor de overheid enz., die het resultaat zijn van dit onderzoek.*
* *In het kader van 'Good Clinical Practice' moet de mogelijkheid bestaan dat het farmaceutisch bedrijf en de autoriteiten inzage krijgen van de originele data. In dit verband dienen de onderzoekers erover te waken dat dit gebeurt zonder schending van de privacy van de proefpersonen.*
* *Het Ethisch Comité benadrukt dat het de promotor is die garant dient te staan voor de conformiteit van de anderstalige informatie- en toestemmingsformulieren met de nederlandstalige documenten.*
* *Geen enkele onderzoeker betrokken bij deze studie is lid van het Ethisch Comité.*
* *Alle leden van het Ethisch Comité hebben dit project beoordeeld. (De ledenlijst is bijgevoegd)*

* *The Ethics Committee is organized and operates according to the 'ICH Good Clinical Practice' rules.*
* *The Ethics Committee stresses that approval of a study does not mean that the Committee accepts responsibility for it. Moreover, please keep in mind that your opinion as investigator is presented in the publications, reports to the government, etc., that are a result of this research.*
* *In the framework of 'Good Clinical Practice', the pharmaceutical company and the authorities have the right to inspect the original data. The investigators have to assure that the privacy of the subjects is respected.*
* *The Ethics Committee stresses that it is the responsibility of the promotor to guarantee the conformity of the non-dutch informed consent forms with the dutch documents.*
* *None of the investigators involved in this study is a member of the Ethics Committee.*
* *All members of the Ethics Committee have reviewed this project. (The list of the members is enclosed)*

Namens het Ethisch Comité / On behalf of the Ethics Committee

Prof. dr. D. MATTHYS
Voorzitter / Chairman

CC: De heer T. VERSCHOORE - UZ Gent - Bimetra Clinics
FAGG - Research & Development; Victor Hortaplein 40, postbus 40 1060 Brussel

Universitair Ziekenhuis Gent
De Pintelaan 185,B- 9000 Gent
www.uzgent.be

Ann Haenebalcke
09/332 22 66

Appendix 3: Evaluation forms

EVALUATION FORM		
PATIENT NAME:	PATIENT NUMBER:	
DATE OF BIRTH:	AGE:	SEX:
EXTRACTED M1s:		
AGE DURING EXTRACTIONS:		
DATE OF EVALUATION:	TIME BTW EXTRACTION-EVALUATION:	

	CLINICAL EVALUATION M2/P2 /P1				
	CRITERIA				
1	Distance between contact points in mm	17-15	27-25	37-35	47-45
		15-14	25-24	35-34	45-44
		14-13	24-23	34-33	44-43
2	Rotation M2 No-Minor-Severe	17	27	37	47
3	Rotation P2 No-Minor-Severe	15	25	35	45
4	Rotation P1 No-Minor-Severe	14	24	34	44
5	Inclination M2 No-Minor-Severe	17	27	37	47
6	Inclination P2 No-Minor-Severe	15	25	35	45
7	Inclination P1 No-Minor-Severe	14	24	34	44
8	Ortho treatment need IOTN	Q1	Q2	Q3	Q4

	RADIOGRAPHIC EVALUATION BEFORE EXTRACTION OF M1s				
	CRITERIA				
1	Developmental Stage M2	37		47	
	A-B-C-D-E-F-G-H				
2	Inclination M2 relative to M1	37/36		47/46	
	D-U-M				
3	Presence germ M3	18	28	38	48
	YES-NO				