Tooth crown dimensions and cusp number in hypodontia: assessed by a new three-dimensional technique

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List of Abbreviations

Complex Adaptive System	(CAS)
Mesio-distal	(MD)
Bucco-lingual	(BL)
Crown height	(CH)
Intra-class correlation coefficient	(ICC)
Technical error of measurements	(TEM)
Probable Mutations Effect	(PME)
Orthopantomogram	(OPG)
Polyvinyl siloxane	(PVS)
Linear mixed effect	(LME)
Ordinal logistic generalized estimating equations	(GEE)

Abstract

Title: Tooth crown dimensions and cusp number in hypodontia: assessed by a new three-dimensional technique

Background: Development of the dentition is a valuable model for studying craniofacial and general development. It is a Complex Adaptive System (CAS) in which the outcome of interactions between genetic, epigenetic and environmental factors, at the molecular, cellular and tissue levels leads to a phenotype with variation in tooth number, size, shape and mineralization. These variations are important as they underpin evolutionary change.

This study is part of a major international collaborative project investigating hypodontia: a variation of tooth number. The project aims to investigate the development of hypodontia from genotype to phenotype in the same group of patients. The phenotype of hypodontia is more extensive than agenesis. The present study investigates part of the phenotype of hypodontia, the relationship of congenitally absent teeth and the crown size and shape of the formed teeth.

Aim: Compare the crown dimensions and cusp numbers in patients with mild or moderate hypodontia to matched controls with normal numbers of teeth.

Materials and Methods: The sample consisted of 69 patients, 36 females and 33 males, with between 1 and 5 congenitally missing teeth and a set of matched controls. From imaging the dental study casts 3D digital models were produced. Linear measurements were made of the mesio-distal (MD), bucco-lingual (BL) and crown height (CH) dimensions. In addition, the cusp numbers of premolar and molar teeth were counted. Statistical methods used included linear mixed effect models and generalized estimating equations. The new method was validated against traditional 2D calipers, the measuring tool software was tested for repeatability, and for the intra and inter-operator reliability.

Results: Intra-class correlation coefficient (ICC) and technical error of measurements (TEM) were used to determine reliability. ICC values were above 0.75 in almost all analyses, and the TEM was negligible, which is indicative of high agreement.

The crown dimensions of the hypodontia group were statistically significantly ($p<0.05$) smaller than the control group in the majority of all three dimensions (MD, BL and CH). There were fewer cusps present on the occlusal surfaces of the first premolar and first molar teeth in the hypodontia patients than in the control group. Interestingly, patients with hypodontia of one upper lateral incisor who retained the antimeric incisor, had significantly reduced crown dimensions when compared to the remaining hypodontia group.

Conclusion: The findings of this study confirm that the phenotype of hypodontia includes reduction in all three tooth crown dimensions and in cusp numbers of existing teeth as well as agenesis. The results support the concept that dental development is a Complex Adaptive System whose outcomes are a range of variations of number, size and shape of teeth. These variations are compatible with evolutionary changes and the suggestion of recent reductions in the human dentition.

Thesis Declaration

Name: Sadaf Sassani

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Discipline: The School of Dentistry

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1. Introduction

Hypodontia, also referred to as congenitally missing teeth or dental agenesis, is the most common human dental variation (Brook 1974). The aetiology of hypodontia is still not fully understood, reflecting the complexity of general dental development and how it is still enigmatic to researchers (Brook & O'Donnell 2011). Approaching dental development, hypodontia included, as a Complex Adaptive System which accounts for genetic, epigenetic, and environmental factors, as well as considering field theories, thresholds, limitations, sexual dimorphisms, evolutionary forces, has been the most robust and inclusive solution in recent literature (Brook, Koh & Toh 2016; Brook 2009; Brook & O'Donnell 2011; Brook et al. 2014(a); Koh et al. 2016; Townsend et al. 2012). It was through the lens of a Complex Adaptive System that this study was carried out.

Comparing the size and morphology of teeth between individuals can provide valuable insights in understanding the relationships between the phenotype and the genetic, epigenetic and environmental factors (Brook 1984; Brook et al. 2009(a); Garn, Lewis & Kerewsky 1965; Townsend, Alvesalo & Brook 2008; Townsend et al. 2012; Townsend et al. 2009(a); Townsend et al. 2009(b); Townsend et al. 2005). Multiple studies have been conducted to understand this relationship further (Brook, Koh & Toh 2016; Brook et al. 2014(a); Brook et al. 2014(b); Taduran et al. 2016; Townsend et al. 2012; Townsend et al. 2009). The literature demonstrates that there are vast interconnections between multiple variables which are involved in producing the phenotype (Brook et al. 2014(b); Taduran et al. 2016; Townsend et al. 2009(a); Yong et al. 2014). Though it has been the trend in recent years for many studies to focus on the genotype, in order to sufficiently understand the breadth of interaction between these variables a detailed understanding of the hypodontia phenotype is required.

The literature published on the decreasing size of the human dentition also raises queries in relation to hypodontia (Brace 1967, 1976; Brace & Mahler 1971; Brace, Rosenberg & Hunt 1987). The spectrum of tooth size and number has hypodontia and microdontia on one end, with supernumeraries and macrodontia on the other (Brook, Koh & Toh 2016). With the pressures of natural selection, it would be expected to see a normal distribution of this spectrum in the population. However, natural selection has been strongly relaxed in modern times. The trend described in the literature suggests a greater prevalence of reduced tooth size, lesser complexity and lower tooth number (Flores-Mir 2006).

The vast majority of hypodontia studies, when concerned with the phenotype, have solely relied upon caliper measurements to measure the remaining dentition. Brook et al. (1998, 2005) has often used a 2D measurement system which has been extensively validated and often considered the gold standard for odontometrics. However, Townsend et al. (2009(a)) recognized the necessity for evolving technology in the field and have

encouraged further research with 3D technologies. Al-Shahrani (2012) performed the first 3D geometric morphometric analysis upon a hypodontia cohort and since then many studies have outlined the benefits of 3D odontmetrics over traditional calipers. Subsequently, this study of the hypodontia phenotype was solely undertaken in 3D and validated extensively.

This thesis addressed topics in the recent literature related to dental development and hypodontia. This is a cross-sectional study measuring the dental phenotype of hypodontia patients compared to controls that were matched for age, biological sex and ethnicity. The novel 3D methodology used in this study was validated and statistical analyses of the results were performed using linear mixed effects models. The significance of the results produced and future directions were then discussed.

2. Literature Review

2.1 Biological Development

2.1.1 Biological Complex Systems

A complex biological system has been defined as 'one whose properties are not fully explained by an understanding of its component parts' (Gallagher & Appenzeller 1999). Furthermore, it is becoming increasingly apparent in the literature that the health sciences are no longer subscribing to the reductionist method of thinking, e.g. where one gene codes for one syndrome (Gallagher & Appenzeller 1999). The over-simplification of complex biological systems often fails to account for multiple significant factors such as epigenetics, the environment and degrees of genetic expression. Studying individual components of a complex system provides limited information; particularly in biological systems where these components often do not interact in a linear and straight-forward manner (Beardsley 2010; Mitchell 2009). The multitude of exceptions to the rule within biological compared to non-living systems means predicting the behaviors of complex biological systems is substantially more difficult (Beardsley 2010); this translates to challenges in biological research from the sheer quantity and intricacy of data as well as all the interacting variables (Mitchell 2009; Weng, Bhalla & Iyengar 1999). Gallagher & Appenzeller proposed that the computing power was emerging in order to tackle these complex biological systems (Gallagher & Appenzeller 1999) and though biology is awkward compared to physics it is not beyond the grasp of research scientists. Goldenfeld & Kadanoff (1999) explained that there are 'no general laws for complexity'; however, one might find key insights in one complex biological system that can then be applied to another. Kennedy & Ford (2011) offered a potential solution to understand the complexity of biological systems: using complex models with multicriteria analysis - this allows for a multitude of applicable intermediary calculations as well as integration of critical components.

2.1.2 Evolution and variation in outcomes

Life, noticeably, has an abundance of diversity and this can largely be attributed to the basic mechanisms of evolution, namely: mutation and natural selection. Mutations are common and unavoidable even amongst species with small and concise genetic information (McCutcheon & Moran 2012). Most mutations are deleterious or neutral in effect with only a small percentage being beneficial (Loewe & Hill 2010). If a mutation is too deleterious it is likely to remove an organism from the population before it would have the opportunity for any reproduction, or significantly curtail its reproductive capacity. Advantageous mutations will allow an organism to thrive and pass on its genetic information to its progeny more readily. The organism's environment

can often determine whether a mutation is to be considered deleterious, neutral or advantageous. Therefore, the abundance of variation in a species reflects the abundance of mutations that have occurred and deemed acceptable through the process of natural selection.

The genetic information of an organism only reflects one aspect of an organism's phenotype or behavior, with epigenetics and environmental factors also playing a significant role (Hall & Hallgrimsson 2011). *Homo sapiens* shares 99% of the genetic information with chimps (Prufer et al. 2012) and the remaining 1% difference is crucial but does not adequately explain the significant differences between humans and chimps (King & Wilson 1975). King and Wilson (1975) published their seminal paper in 1975 describing regulatory mechanisms for gene expression with subsequent research has supporting this (Bird et al. 2007; Bush & Lahn 2008; Capra et al. 2013; Pollard et al. 2006; Prabhakar et al. 2006) and what was previously thought to be 'junk' or 'non-coding' DNA we now understand contain 'gene switches' which can turn gene transcription off and on as well as enhance the quantity of transcription that takes place. Environmental factors such as climate, food quantity and quality, and pathogen exposure can all play a role in controlling these gene switches (Hall & Hallgrimsson 2011).

2.2 Dental Development

2.2.1 As a Complex Adaptive System

The development of the dentition has been described as a Complex Adaptive System (CAS). It exhibits self-adaptation, self-organization, multitasking, bottom-up emergence, tipping points, critical phases and robustness (Brook & O'Donnell 2011; Brook et al. 2014(b)). The lower-order interactions on the molecular level between the genetic, epigenetic and environmental factors produce the array of dental phenotypes in different species, within a species and within the same family (Brook, Koh & Toh 2016; Brook 2009; Brook & O'Donnell 2011; Brook et al. 2014(b)). Diversity increases the performance of a CAS, allowing for multiple responses to both external stimuli and internal changes (Brook et al. 2014(b)). This diversity also allows for a higher probability of a major change in the phenotypic outcome due to the increased likelihood of passing biological thresholds (Brook et al. 2014(b)).

Dental development demonstrates spatiotemporal, multidimensional, multilevel and multifactorial properties which are characteristic of a CAS (Brook et al. 2014(b)). The spatiotemporal property is expressed in the formation of four distinct tooth types within their morphogenetic fields which then have a staggered eruption pattern (Brook 2009). The development of the dentition occurs in three spatial dimensions (x, y, z) and the

fourth dimension of time - this reflects its multidimensional property (Brook 2009). The multilevel property is exhibited in the molecular and cellular interactions that occur; this produces macroscopic and phenotypic outcomes (Brook 2009).

Approaching dental development as a CAS can yield valuable research and clinical outcomes (Brook, AH & O'Donnell 2011). Evident in Brook, Koh & Toh's (2016) study on the Romano-Briton population from 200-400AD; considering this sample from the perspective of a CAS clearly demonstrated how the population's dental phenotype was a reflection of consistent environmental insults. The patterning of the dentition in the Romano-Britons was not unlike modern Britons but still displayed a higher frequency of dental anomalies, smaller crowns and roots, and greater enamel defects (Brook, Koh & Toh 2016). Brook (1984) illustrated this in the unifying aetiological model (Figure 1). Brook's model has been modified to demonstrate the status of the Romano-Briton's dentition: a normal distribution where males have a greater propensity towards megadontia and supernumeraries and the females a greater propensity towards microdontia and hypodontia. The Romano-Britons, for both males and females, were skewed more towards microdontia and hypodontia compared to modern Britons.

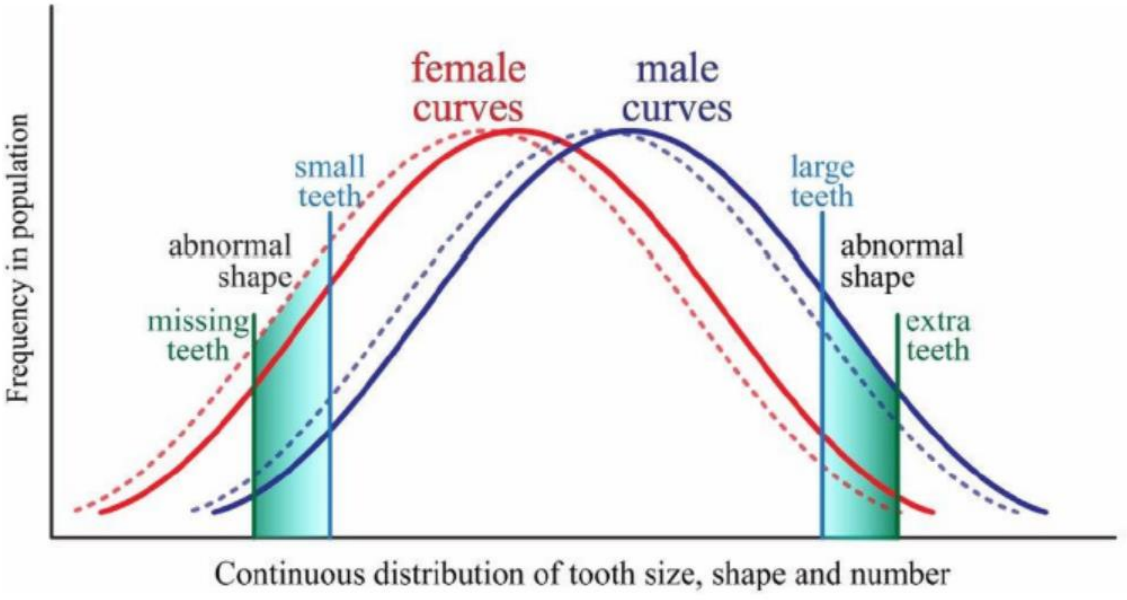


Figure 1: The unifying aetiological model (Brook 1984) illustrating the Romano-Briton's sample in the dotted line, while the solid line represents the modern Britons.

2.2.2 As a paradigm for general development

The development of the dentition is a very stable evolutionary trait and this is evident in the highly conserved epithelial and mesenchymal genes necessary for tooth development (Smith et al. 2015). Tooth germ originates

from this very epithelial and mesenchymal tissue through a series of extensive signaling pathways (Bei 2009; Brook et al. 2014(b)). Teeth require extremely specialized and highly differentiated cells such as ameloblasts and odontoblasts to produce enamel and dentine. Interestingly, this illustrates how dental development is an extremely stable evolutionary trait while also being extremely sensitive to even minute changes at the genetic level, epigenetic level or environmental level. This can alter molecular signaling pathways and highly differentiated cell function subsequently altering the dental phenotype. The multilayered dental developmental process (Brook et al. 2014(a)) illustrates this (Figure 2). Since dental development occurs progressively from 6 weeks in utero up to 20 years of age, this allows for a unique insight into an individual's, a population's, and our species' general development when contextualizing their genetic, epigenetic and environmental factors. The additional bonus of the dentition is its stability from an archaeological perspective so research can be conducted effectively on otherwise well decomposed specimens from key historical periods.

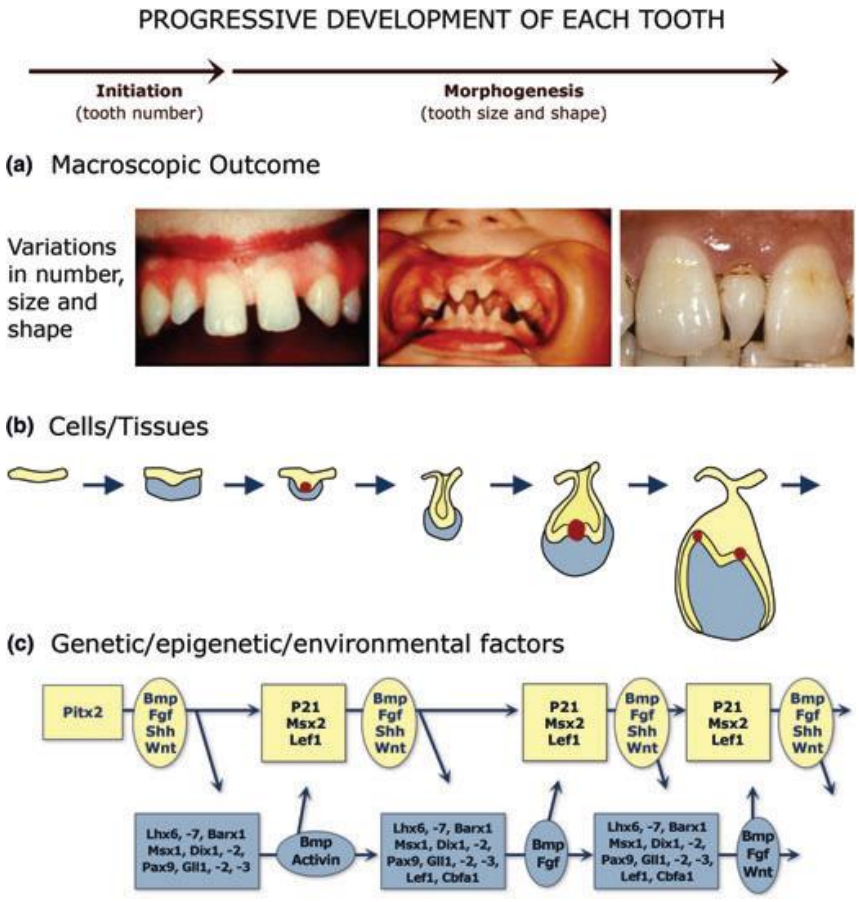


Figure 2: The multilayered developmental process (Brook et al. 2014(a))

2.2.3 In human evolution

When comparing the dentition of *Homo sapiens* to our nearest living relative the chimpanzee or the bonobo the immediate recognizable difference is the smaller dimensions of the canines and incisors while the molars have remained similar in size. To understand how this difference occurred we look to *Ardipithecus ramidus* which existed approximately 4.4 million years ago, it was approximately 1.2 metres tall, omnivorous but primarily ate fruits, and is one of our earliest hominin ancestors (Clark & Henneberg 2017). Prior to Ardipithecus, hominids would fight for access to females and so required significant canine and incisor display, this is supported by the anterior dentition being sexually dimorphic and males possessing a greater canine projection (Emes, Aybar & Yalcin 2011; Plavcan 2001). Ardipithecus, however, began collaborative parenting; the females were rendered relatively helpless by the demands of pregnancy, nursing and care of infants so they traded exclusive sexual access with males for food and enhanced paternal confidence in their offspring (Turner, Machalek & Maryanski 2015). The coupling of Ardipithecus lead to a relaxation of selective pressure on large canine size. The reduction in size of the remaining anterior dentition is thought to be the result of changes in our diet (Emes, Aybar & Yalcin 2011). Clark and Henneberg (2017) suggest, however, that the reduction in the remaining anterior dentition was a product of speech and communication being highly advantageous in a collaborative parenting setting. Structural reduction of the anterior dentition as well as shortening of the anterior maxilla had to occur to allow for adequate speech and vowel production. Furthermore, advances in speech and communication lead to greater reproductive success (Clark & Henneberg 2017).

The greater reproductive success produced larger body sizes and required greater caloric intake. The archaic hominins and the archaic megadont hominins approximately 1.5 to 2.6 million years ago still possessed smaller and less incumbent anterior dentition but developed larger posterior dentition to support a more robust diet including more meat (Haile-Selassie 2001; Lucas, Constantino & Wood 2008; Wood & Stack 1980). The orodental structures of the hominins were not carnivorous so construction of extra-oral processing tools, including sharpened stone tools assisted in meat consumption. The earliest record of fire for food processing is approximately 1.8 to 1.9 million years ago and this corresponds to the flourishing of *Homo erectus* who had a further reduction in tooth size as well as the appearance of the shovel shaped incisors we see in modern humans (Attwell, Kovarovic & Kendal 2015). Since that time further developments in extra-oral food processing and cooking lessened selective pressure on tooth size and tooth number. This trend has been continuing to this day.

2.3 Hypodontia

2.3.1 Terminology and classification

A variety of terms have been used to describe the primary failure of a tooth to form, including, dental or teeth aplasia, tooth or dental agenesis (Cobourne 2007), and reduction in tooth number. The term congenitally missing teeth has also been used, however this may be considered ambiguous as dental development is completed post-natally (Al-Ani et al. 2017; Nieminen 2009; Parkin et al. 2009) Hypodontia is the developmental absence of less than six teeth, excluding the third molars, in the primary or secondary dentition (AlShahrani, Togoo & AlQarni 2013; Nunn et al. 2003). The term 'oligodontia' is usually referencing six or more absent teeth, while 'anodontia' is the absence of the entire dentition (Nunn et al. 2003). The more severe presentations of tooth agenesis are often associated with systemic disorders and are infrequently occurring within populations (Dhanrajani 2002; Werther & Rothenberger 1939). Hypodontia, however, is one of the most prevalent human dental variations (Brook 1974; Hobkirk & Brook 1980; Pemberton, Das & Patel 2005; Vastardis 2000).

Hypodontia can be further classified on whether it occurs in conjunction with a syndrome, syndromic hypodontia, or in isolation, isolated hypodontia (Arte et al. 2001; Tan, van Wijk & Prahl-Andersen 2011). Hypodontia has been associated with over a hundred various syndromes (Winter & Baraitser 2001), it is particularly common in those with facial clefts, ectodermal dysplasia, and Down syndrome (Haque & Alam 2015; Mestrovic, Rajic & Papic 1998; Prager, Finke & Miethke 2006; Satokata & Maas 1994; Suri, Thompson & Atenafu 2011; Suzuki et al. 2017)

2.3.2 Prevalence in the primary and secondary dentition

The prevalence of hypodontia in the primary dentition is considerably low and uncommon in the general population, particularly when compared to the secondary dentition. Depending on the population between 0.1% and 2.4% of primary tooth agenesis has been reported (Brook 1974; Larmour et al. 2005; Wu, Wong & Hagg 2007). Patients with primary tooth agenesis will subsequently have agenesis of the permanent successor is almost always guaranteed (Arte et al. 2001; Bailleul-Forestier et al. 2008; Olmsted 2011). Nieminen (2009) reported that 50%-90% of deciduous tooth agenesis concerns maxillary lateral and mandibular central incisors. Salama and Abdel-Megid (1994) studying the Saudi Arabian population determined the maxillary and mandibular lateral incisors were the most frequently missing. The majority of hypodontia cases in the deciduous dentition are mild (1-2 teeth missing) and unilateral; there have been no reports of a significant difference in prevalence for either sex (Arte et al. 2001).

The prevalence of hypodontia in the permanent dentition appears to vary depending on the population, participant age, the research methods, and diagnostic criteria used (Larmour et al. 2005; Wu, Wong & Hagg 2007). A large-scale meta-analysis conducted by Polder investigated the prevalence of non-syndromic hypodontia in the permanent dentition and found a range of 2.2%-10.1% when excluding third molars (Polder et al. 2004). Australian Europeans had the highest prevalence at 6.3% and 5.5% respectively, followed by North Americans of European Ancestry at 3.9%. The prevalence rate amongst British children in 1974 was 3.5-6.5% while excluding third molars (Brook 1974). Similarly, other reviews have demonstrated a prevalence of 4.0-4.5% in the United Kingdom, 2.6% in Saudi Arabia and 11.3% in Ireland (Larmour et al. 2005; Shimizu & Maeda 2009). The African American population's prevalence of hypodontia was reported at 7.7% (Jorgenson 1980), the Indian population at 4.19% (Gupta et al. 2011), and up to 30% in the Japanese (Sofaer, J. A. 1975). Interestingly, the reports of dental agenesis have been increasing in recent times amongst the people of European descent, whether this translates to other populations or is due to better screening and reporting is not clear (Mattheeuws, Dermaut & Martens 2004).

2.3.3 Sexual dimorphism

There appears to be a consensus in the literature that females are more affected by dental agenesis than males (Bergstrom 1977; Brook 1974; Harris, Evans & Smith 2011; Larmour et al. 2005; Muller et al. 1970; Polder et al. 2004; Silva Meza 2003; Vastardis 2000). Authors have reported different degrees of male to female ratio in hypodontia: Brook (1974) reported a male to female ratio of 1:1.5, Polder et al. (2004) supported this finding with a ratio of 1:1.4. Similarly, Larmour et al. (2005) reported a male to female ratio of 2:3. Amongst European American children the females had a greater prevalence at 63% of their cohort (Harris, Evans & Smith 2011). Outliers amongst the data include tooth agenesis reported more so in males specifically for the maxillary right central incisor (Sisman, Uysal & Gelgor 2007).

2.3.4 Location of missing teeth

The third molar has the highest prevalence of agenesis; estimated globally at 22.63%in a meta-analysis (Carter & Worthington 2015) and similarly at 20% amongst the Australian population in a previous report (Lynham 1990). Excluding third molars, the majority of patients affected by dental agenesis present with only one or two missing teeth. The missing teeth in order of prevalence are: the mandibular second premolars, maxillary lateral incisors, maxillary second premolars and mandibular incisors (Polder et al. 2004; Symons, Stritzel & Stamation 1993).

It is unclear whether hypodontia has a predilection for the maxillary or mandibular arch. Some reports have noted dental agenesis predominantly in the maxilla (Amini, Rakhshan & Babaei 2012; Celikoglu et al. 2010; Fekonja, A. 2005; Sisman, Uysal & Gelgor 2007), while other investigators have had greater frequencies apparent in the mandible (Backman & Wahlin 2001; Chung, Han & Kim 2008; Kim 2011). It should be noted that these variations could be unique to these studies' samples of orthodontic patients or specific ethnic groups. No significant association between dental agenesis and the left or right side has been reported.

2.3.5 Dental features associated with hypodontia

The reported dental characteristics associated with hypodontia are microdontia, peg shaped lateral incisors, delayed eruption, retained deciduous dentition, ectopic eruptions, impactions, taurodontism, transpositions and rotations (Baccetti 1998; Backman & Wahlin 2001; Brook 2009; Brook et al. 2009(b); Brook et al. 2009(c); Chung, Han & Kim 2008; Peck, Peck & Kataja 1996; Schalk-van der Weide, Steen & Bosman 1993; Schalk van der Weide, Prahl-Andersen & Bosman 1993; Wu, Wong & Hagg 2007). It appears the most commonly reported feature in patients with hypodontia, and even in their relations, is microdontia (reduced tooth size) and simplified morphology (McKeown et al. 2002). Clinical presentation of the maxillary lateral incisor as peg shaped and its antimeric incisor not present at all has been well documented (Brook 1974; Gupta et al. 2011; Schalk-van der Weide & Bosman 1996; Schalk-van der Weide, Steen & Bosman 1992). As previously mentioned, Brook (1984) has proposed that the size and shape of the microdont teeth exist at one end of a phenotypic continuum; extension of that continuum results in dental agenesis.

2.3.6 Skeletal pattern

Various studies report different skeletal associations with hypodontia. Readily apparent would be the association between hypodontia and cleft lip and palate (Ajami, Pakshir & Samady 2017; Bartzela et al. 2013; Haque & Alam 2015; Mikulewicz et al. 2014; Shapira, Lubit & Kuftinec 2000; Suzuki et al. 2017). Severe cases of syndromic hypodontia associated with hypohidrotic ectodermal dysplasia have resulted in patients with a retrognathic maxilla, reduced mandibular plane angle and facial height, and a flat or concave facial profile (Bondarets & McDonald 2000). Several studies have associated various forms of hypodontia with a restricted anterior maxilla and Class III malocclusion (Acharya et al. 2010; Chung, Han & Kim 2008; Chung et al. 2000; Ogaard & Krogstad 1995; Woodworth, Sinclair & Alexander 1985). The general consensus amongst authors is the greater severity of tooth agenesis is related to greater severity of skeletal changes.

2.3.7 Significance for human dental development and evolution

For millennia when significantly deleterious mutations occurred in an individual they would often result in an inability to thrive, reach sexual maturity or be capable of reproduction. Technological advances have offered a

multitude of benefits, particularly in the field of medicine where there is effective management and treatment of conditions derived from genetic mutations. The rhythm of deleterious mutations being removed from the population through natural selection has now significantly relaxed. The result of this relaxed selective pressure means modern humans are accumulating mutations at a significant rate with each generation (Lynch 2016; Ruhli & Henneberg 2013). In relation to the dentition there is also the added effect of the modern Western diet: which is extremely soft and carbohydrate rich discouraging any selective pressure for a large and structurally complex dentition or surrounding hard tissues (Rose & Roblee 2009). Contrast this with observations of indigenous populations, Polynesian societies and the native Australians, up until very recently were still using their dentition in a robust and functional way for a fibrous and carnivorous diet. As to be expected, the dentition of these indigenous populations is significantly larger and structurally more complex (Smith, Brown & Wood 1981). The aforementioned statement ties in with Brace's Probable Mutation Effect: when an organ or complex becomes non-essential it will eventually be structurally reduced simply by accumulated mutations in the population (Brace 1964). The next sequence of events for the dentition of modern humans has thought to be a decrease of size and structure of the teeth and increasing agenesis of the least stable teeth. This is apparent now in the well documented loss of third molars (Garn, Lewis & Kerewsky 1963; Garn, Lewis & Vicinus 1962).

2.4 Aetiology of hypodontia

Brook et al. (2014(a)) considers hypodontia a phenotypic outcome of general dental development and characterizes this as a Complex Adaptive System. It is nuanced and multifactorial and there is not a complete understanding of the exact genetic and subsequent molecular pathways that result in the primary failure of a tooth germ. It is clear there is a strong genetic component, as well as epigenetic and environmental factors (see section 2.4.1). Multiple aetiological models have been suggested to explain the pattern and phenotypic appearance of dental agenesis (Brook 1984; Butler 1939; Osborn 1978; Sofaer et al. 1971; Townsend et al. 2009(a)) (see section 2.4.2).

2.4.1 Genetic factors

The literature, particularly in the form of twin studies, strongly suggests the underpinning of hypodontia has a genetic basis (Arte et al. 2001; Cobourne 2007; Townsend et al. 2009(b);Vastardis 2000). As early as 1956 hypodontia was associated with strong genetic controls. Grahnen's (1956) Swedish familial study demonstrated an autosomal dominant pattern. The biological plausibility of this has not only been substantiated but is logical given the tight genetic control of general dental development (Brook 1974, 1984; Brook et al. 2009(a); Dempsey & Townsend 2001; Hughes et al. 2000; McKeown et al. 2002; Townsend 978, 1980; Townsend et al. 2012; Townsend et al. 2009(b)). Key genes have been identified in hypodontia patients exerting influence over their relative's dentition (Arte et al. 2001; Bailleul-Forestier et al. 2008; Cobourne 2007; Grahnen 1956;

Vastardis 2000). The regulatory homeobox genes, MSX1, PAX9, AXIN2, have been heavily implicated (Bergendal et al. 2011; Callahan et al. 2009; Das et al. 2002; Satokata & Maas 1994) due to their roles in regulating and mediating the epithelial and mesenchymal interaction during dental development (Arte et al. 2001; Cobourne 2007). MSX1 (muscle segment homeobox 1) is expressed in the tooth germ around areas of condensed ectomesenchymal tissue (MacKenzie, Ferguson & Sharpe 1992) and has been heavily implicated in the loss of second premolars, third molars, and more recently lower central incisors (Shimizu & Maeda 2009). PAX9 (paired box gene 9) expresses transcription factor in the mesenchyme during dental development and has been documented in families with non-syndromic severe hypodontia (Brook et al. 2009(a)), hypodontia in molars (Mostowska, Biedziak & Jagodzinski 2006; Thesleff 2000), and more recently associated with maxillary lateral incisor agenesis (Alves-Ferreira et al. 2014). AXIN2 (axis inhibition protein 2) is associated with control of cell growth, regulation and proliferation. Mutations of this gene have been connected with various forms of hypodontia (Callahan et al. 2009; Cobourne 2007; Mostowska, Biedziak & Jagodzinski 2006) and associated syndromes (Nieminen 2009).

2.4.2 Epigenetic factors

A phenotype is the product from a complex interaction between genetics factors, environmental factors, and epigenetic factors (Brook 2009). The study of epigenetics relates to the heritable changes of gene expression that do not alter the base sequence of DNA. Although epigenetics controls were described as far back as 1942 there has been a renewed interest in the field and now epigenetics are considered the missing piece of the phenotypic puzzle. Though epigenetics is a well-established component of the medical literature, as recently as 2014 Williams et al. characterized epigenetics in relation to dental research as ‘in its infancy’. Williams et al. further described the relationship between DNA methylation and its role in inactivation of amelogenin, this directly affected the process of amelogenesis and produced a range of phenotypic outcomes in enamel development. Epigenetics has also been implicated in relation to hypodontia. Townsend et al. (2005) postulated that the predisposition towards hypodontia or supernumeraries between monozygotic twin pairs was due to epigenetic events that occurred during odontogenesis.

2.4.3 Environmental factors

Though there is a strong genetic component several studies have proposed associations between environmental factors and hypodontia. The origin of dental tissue is in neural crest cells that become highly differentiated and tightly controlled under specific molecular pathways (Bei 2009). In such an environment there is sensitivity for environmental insult to have a significant effect on the phenotype.

Initial insult to the developing tooth germ in the form of infection has been implicated (Gullikson 1975). This has been substantiated with changes to the dental phenotype associated with congenital forms of syphilis (Ioannou et al. 2016). Exposure to toxins in the form of maternal smoking and alcohol consumption has been implicated in hypodontia as well as cleft lip and palate (Brook 2009; Graber 1978; Vastardis 2000). The developing dentition is susceptible to insult from chemotherapy and radiotherapy, with one report suggesting the effects of radiotherapy are significantly more severe (Nasman, Forsberg & Dahllof 1997; Parkin et al. 2009). Recently, a study involving Romano-Britons reported a recent synergistic effect of environmental influences on hypodontia and dental development including: excess lead ingestion, poor nutrition and recurrent infections (Brook, Koh & Toh 2016)

2.4.4 Aetiological models

Multiple models have been suggested to explain the morphological development of teeth. The most prominent evolutionary model is Butler's field theory (Butler 1939), originally constructed for mammalian dentition. The theory states that teeth grow and differentiate in various morphogenetic fields and the key tooth of that field is the most stable while the teeth more distal from the key tooth are more variable phenotypically and unstable (Butler 1939). Butler's theory was later modified by Dahlberg for the human dentition to include fields for each tooth class: incisors, canines, premolars and molars (Dahlberg 1945, 1951).

The concept of compensatory tooth size interaction was put forward by Sofaer et al. (1971) stating that when there is absence of a tooth or extreme reduction in its size then the remaining teeth (of the same morphological class on the affected side) will compensate in size. Osborn proposed the odontogenic clone concept: from a single cell mass (clone) all teeth within that particular class formed. For example, a molar clone would induce the formation of all molars (Brook et al. 1998; Osborn 1978). Kjaer et al. (1994) theorized that the most unstable tooth in each class was closely related to where the innervation developed and ended, this model accounted for the mandibular central incisors having greater instability than the mandibular lateral incisors.

Townsend et al. (2009(a)) proposed that the field theories and complexities surrounding dental development should be viewed as complimentary and not competing. Brook's unifying aetiological model (Figure 1) characterizes tooth size (microdontia and megadontia) and number (hypodontia and supernumeraries) as part of a spectrum of related dental phenotypes that are influenced by single genes, polygenes, epigenetic, and environmental factors (Brook et al. 2014(b)). The emphasis in this model is that dental development is not binary or linear: it is a Complex Adaptive System.

2.5 Clinical implications and management

Hypodontia can have significant aesthetic, functional, and financial implications for affected patients (Nunn et al. 2003). The number and location of missing teeth will significantly affect possible treatment outcomes. Missing teeth in the anterior segment from childhood to adolescence could precipitate aesthetic and psychosocial concerns. Patients affected with hypodontia have commonly expressed concerns regarding the spacing between teeth, the location of the missing teeth and their aesthetics (Hobkirk, Goodman & Jones 1994).

Early identification by the clinician is necessary for planning of future interdisciplinary treatment (Carter et al. 2003). The clinician may become aware of dental agenesis when normal eruption patterns are not adhered to, then confirm suspicions with a radiograph. Pursuant to these findings an appropriate interdisciplinary approach would be designed. Currently there is no consensus in the literature to suggest that one particular protocol should be adhered to in treating hypodontia: each patient should have a tailored treatment. An international conference on the management of severe hypodontia suggested the ideal interdisciplinary team would include the general dentist, dental nurses, orthodontists, pediatric dentists, prosthodontists, oral and maxillofacial surgeons, laboratory technicians, clinical psychologist, clinical geneticist, dermatologists, speech and language therapists (Hobkirk et al. 2006). The need for all these disciplines to work cohesively is apparent when considering all the implications of hypodontia (previously mentioned in Sections 2.3.5 and 2.3.6). Concerns regarding space maintenance, Bolton's discrepancies, orthognathic concerns and skeletal changes, ectopic eruptions, the number, quality and position of the remaining dentition. Patient considerations such as their age, motivation, financial concerns, and psychosocial concerns should also be taken into account. Though a multidisciplinary approach is arduous, time consuming and financially costly many authors still emphasized its importance when considering optimal treatment outcomes (Al-Ani et al. 2017; Hobkirk & Brook 1980; Hobkirk et al. 2006; Nunn et al. 2003; Valle et al. 2011; Wu, Wong & Hagg 2007).

2.6 Odontometrics

Odontometrics is the acquisition and study of dental measurements. According to Kieser (1990) the first odontometric study was conducted in 1874. Since then the field has found multiple applications, particularly in the area of comparative odontometry where it has allowed a further understanding of dental development and the genetic, epigenetic and environmental factors underpinning it. Odontometry has been used in forensic dentistry for identification purposes, physical anthropology, archaeology, and clinical dentistry (Kieser 1990).

The acquisition of dental measurements, including the roots and dental arches, has also undergone extensive changes in the last twenty years. Methods have included hand-held calipers, standardized radiographs, computer tomography, photography, laser scanning, 3D modelling and printing, and geometric morphometrics (Al

Shahrani 2012; Brook et al. 2005; El-Zanaty et al. 2010; Hunter & Priest 1960; Lahdesmaki & Alvesalo 2004; Smith et al. 2009).

Sliding digital calipers with sharp beaks that can fit inter-proximally have been extensively used in dental measurements (Hunter & Priest 1960; Jensen et al. 1957). Calipers allow for measurement directly on the patient intra-orally or on dental study models. Both approaches have different advantages and limitations. Measuring directly on the patient can produce very accurate results, though it can be difficult to obtain a measurement posteriorly or in areas with crowding (Hunter & Priest 1960). Odontometrics from dental models allows measurements that are independent of the patient, easy to visualise and access, and keeps records of the dentition at various stages (Jensen et al. 1957). Improper impression and casting technique could distort the model leading to inaccurate measurements (Brook et al. 2005). Concerns may arise from repeated measurements on the same models with sharp caliper beaks.

Brook et al. (2005) pioneered the use of standardized photography in odontometric studies to produce 2D image analysis systems. Subsequently, technologies were developed that could study measurements of area, perimeter, volume, crown subdivisions, and crown to root ratios (Harris & Smith 2008). Another advantage of this methodology is that accurate measurements of areas with crowding and imbrications are more accessible as opposed to traditional calipers (Brook et al. 2005).

3D dental scanners use specifically calibrated lasers to form an accurate representation of the dentition. The scanning occurs in various planes of the dentition, and many modern scanners have a standardized scan routine for dental models, an algorithm is applied to combine these images together in the form of a 3D mesh composed of thousands of triangles. The 3D image analysis has been extensively validated and several reports suggest greater accuracy compared to traditional calipers (Bell, Ayoub & Siebert 2003; El-Zanaty et al. 2010). A 3D image analysis allows for the measurements aforementioned with 2D analyses, but also measurements of curvatures (Smith et al. 2009) and extensive geometric morphometric analyses concerned with shape (Al Shahrani 2012).

3. Aims of this research

The aim of this research is to determine if there is a significant difference in crown dimensions and cusp numbers of patients with mild to moderate hypodontia when compared to a sample of unaffected matched controls.

The main hypothesis of this study is that patients with hypodontia will have smaller crown dimensions and fewer cusp numbers than the unaffected controls.

Specific objectives of this research are as follows:

- To construct a sample of hypodontia patients from The University of Otago, School of Dentistry, Faculty of Orthodontics, paired with matched controls for age, sex, and ethnicity
- To scan the models of the collected sample in a standardized 3D protocol
- To establish a 3D linear measurement protocol and have it validated against calipers, and for intra and inter-operator error
- To determine if there is a difference in mesio-distal, bucco-lingual, and crown height dimensions between the hypodontia and the control group
- To determine if there is a difference in cusp number between the hypodontia and the control group

4. Materials and methods

4.1 Study design

This is a retrospective cross-sectional case controlled study designed to determine if there is a significant difference in the linear crown dimensions and cusp number of patients with mild to moderate hypodontia and a matched control group. The 3D technique used to acquire data necessary for the comparison was validated for intra and inter-operator reliability. Values produced were analyzed using a linear mixed effects model to determine significance, if any, of differences between groups compared.

4.2 The sample

4.2.1 Inclusion and exclusion criteria

The sample of this study comprises 36 female and 33 male orthodontic patients from The University of Otago with mild to moderate hypodontia (1-5 missing teeth) in their permanent dentition. The hypodontia group was screened by The Orthodontic Faculty and their status confirmed via an orthopantomogram (OPG) that was pre-existing and of good quality to determine the types of agenesis. A corresponding group of 36 female and 32 male patients without missing teeth who were matched for sex, age, and ethnicity acted as the control group. Age range of the sample was between 10.1 and 19.3 years. Consent to participate and self-identified ethnicity was obtained in a written form. Each participant's name was removed and replaced by a unique code.

This study focuses on non-syndromic presentations of hypodontia, participants were excluded if their hypodontia was associated with related syndromic conditions such as cleft lip and/or palate, or if it exceeded 5 missing teeth. Participants were also excluded if there were any missing teeth due to previous trauma or extraction and this information was readily available in their dental history and radiographs.

A tooth within the arch was excluded from linear measurements if it met the following criteria:

- A retained deciduous tooth
- Insufficiently erupted to obtain appropriate measurement
- Angulation or crowding prevented accurate measurement
- Restoration, trauma, erosion or wear present

The sample size was influenced by Brook (Brook et al. 2002), suggesting a comparison of two groups of 20 will provide an 80% power to determine a significant size difference of 0.90 millimeters for linear measurements.

4.3 Study models and scanning protocol

The patient's study models were duplicated using polyvinyl siloxane (PVS) impression material at The University of Otago. The impressions were poured in die stone and trimmed. The models were then scanned using an Amann Girrbach Ceramill Map 400 to provide a 3D digital model in a STL file format.

Figure 3: The Amann Girrbach Ceramill Map 400 scanner: it provides a 3D scan in STL file format with less than a 20-micron resolution.

The following scanning protocol was used:

1. A folder with the patient's 'LF' Code (e.g. LF336) was created in the designated Dropbox.

2. Within the newly created folder two more subsequent folders assigned 'Upper' for the maxillary model and 'Lower' for the mandibular model scanned. The scans were saved in STL file format in the appropriate folder.

3. The scanner was calibrated to the same standardized and default setting for all scans. Detail was maximized as much as possible, particularly in interproximal areas, and gaps or ‘gray zones’ in the scans were minimized.

4. Once the scan of a patient was complete it was marked off the spread sheet. The patients were placed into one of the following groups 5:
   a. Extras
   b. Male Controls
   c. Male Experimental Group
   d. Female Controls
   e. Female Experimental Group

5. In some instances, there was two sets of upper and lower models for the same patient. In this case the patient was highlighted in yellow on the spreadsheet. When these models were scanned two new separate folders with the appropriate LF code and the relevant date were created. For example, ‘LF228 14/08/12’ would be one folder with the upper and lower scan in it, ‘LF 228 30/04/14’ would be a separate folder.

4.4 Linear measurements and landmark definition

Linear measurements were performed in MeshLab software. This is an open access software which is frequently used for manipulation of data dense 3D images and meshes.

4.4.1 Mesio-distal (MD) landmark identification and linear measurement

The mesio-distal (MD) crown dimension: defined as the maximum distance between the mesial and distal surfaces of the tooth crown. In instances of insufficient proximal contacts, crowding, rotations or with absent teeth, the measurement was taken from where the tooth contact should occur where this is possible to discern (Brook et al. 1998; Brook et al. 2005). The central and lateral incisors MD dimensions were assessed from the buccal and labial view, and if this were not possible then from the palatal view, while the MD dimensions of the canines, premolars and molars were assessed from the occlusal view.

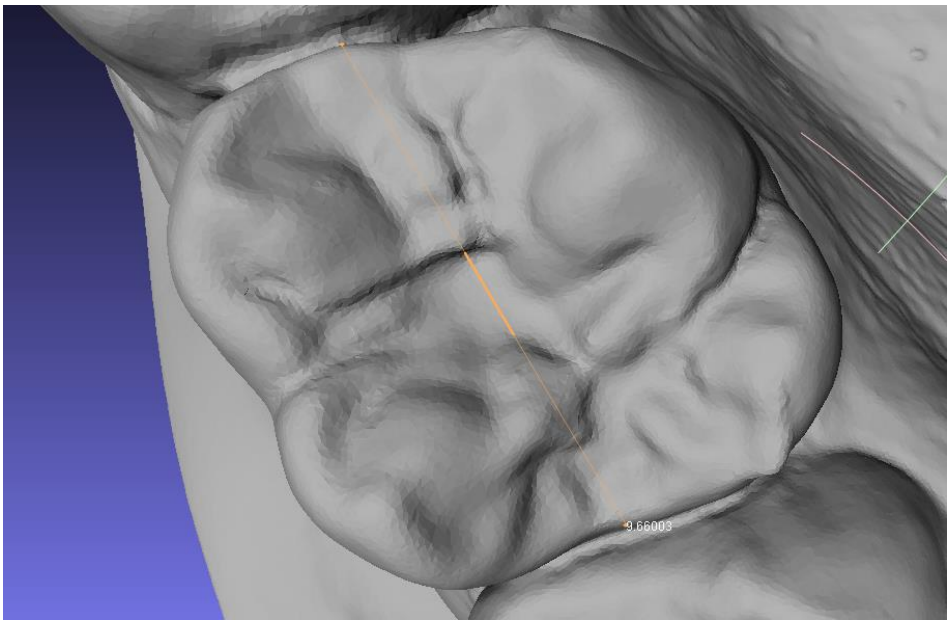


Figure 4: Mesio-distal (MD) crown dimension of the right maxillary first molar from the occlusal view

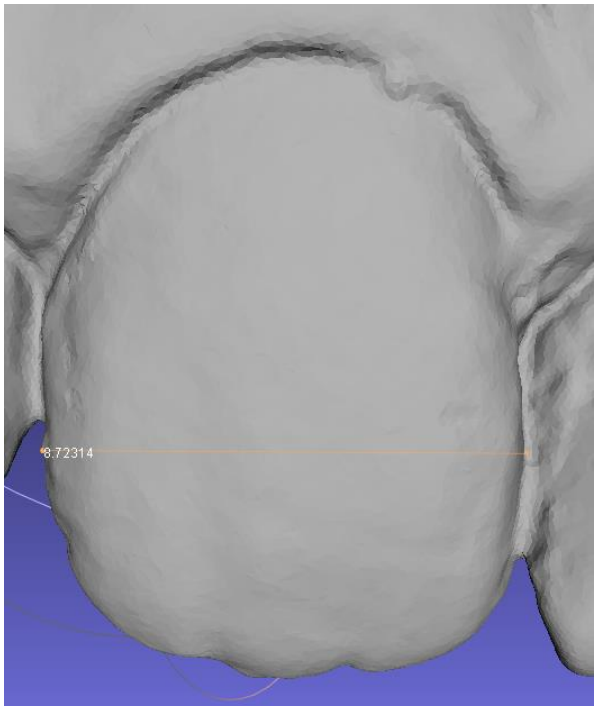


Figure 5: Mesio-distal (MD) crown dimension of the right maxillary central incisor from the buccal view

4.4.2 Bucco-lingual landmark identification and linear measurement

The bucco-lingual (BL) crown dimension: defined as the greatest distance between the most buccal and most lingual points of the crown. It is perpendicular to and bisects the line defining the MD dimension (Brook et al. 1998; Brook et al. 2005). The bucco-lingual dimension was assessed from the occlusal view

using the most cervical point of the buccal surface and the most cervical point of the lingual surface, the buccal and lingual groove will act as landmarks for molars (Ribeiro 2012).

4.4.3 Crown height landmark identification and linear measurement

The crown height (CH) is defined as the distance between the highest point on the occlusal surface and the gingival level of the crown, perpendicular to MD at its midpoint (Brook et al. 1998; Brook et al. 2005). The crown height can be affected by the position of the gingival margin in relation to the tooth, by the labio-lingual or bucco-lingual inclination of the tooth, by tooth wear or damage, and when the tooth is not fully erupted (Ribeiro 2012). The incisor CH was determined by measuring the maximum distance between the middle point in the incisal portion of the tooth crown and the middle point in the cervical line of the tooth crown in a buccal view (Ribeiro 2012). The canine and premolar CH was determined by measuring the distance from the buccal cusp tip and the cervical line of the crown in a buccal view. The molar CH was determined by measuring the vertical distance between the mesio-buccal cusp tip and the cervical line of the tooth in the buccal view (Ribeiro 2012).

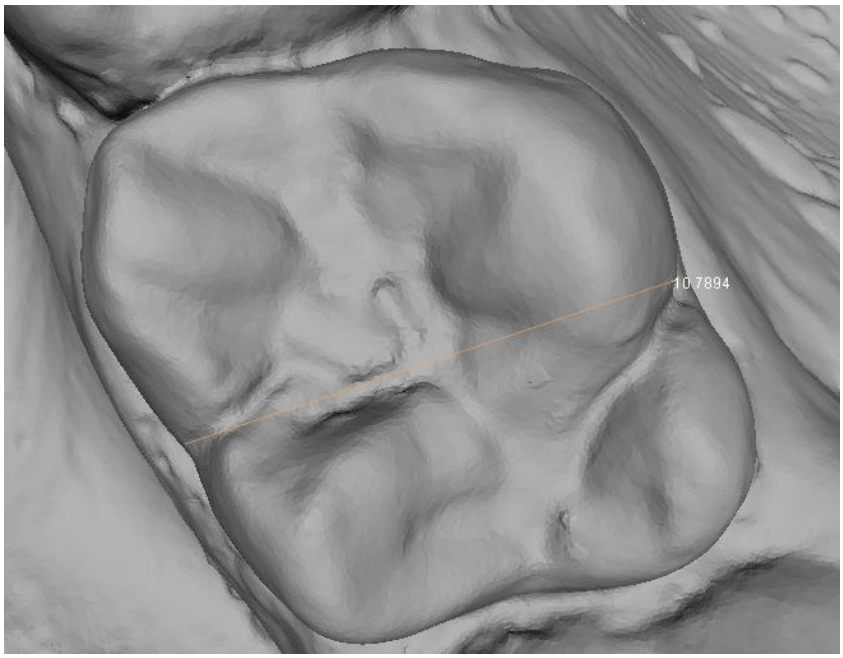


Figure 6: Bucco-lingual (BL) crown dimension of the right maxillary first molar from the occlusal view, please note that the dimension is actually measured from the gingival margin, though it is not visible in this view.

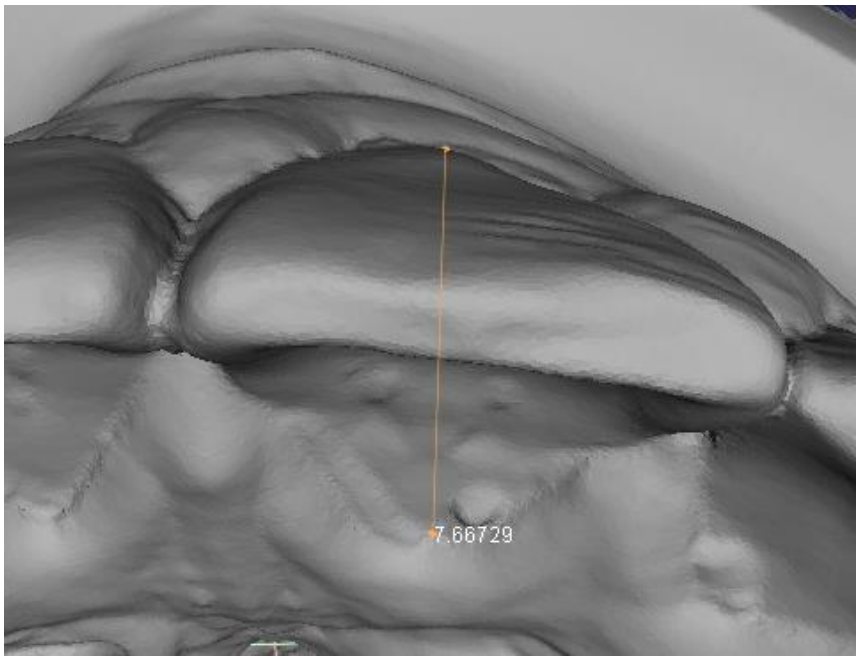


Figure 7: Bucco-lingual (BL) crown dimension of the left maxillary central incisor from the occlusal view

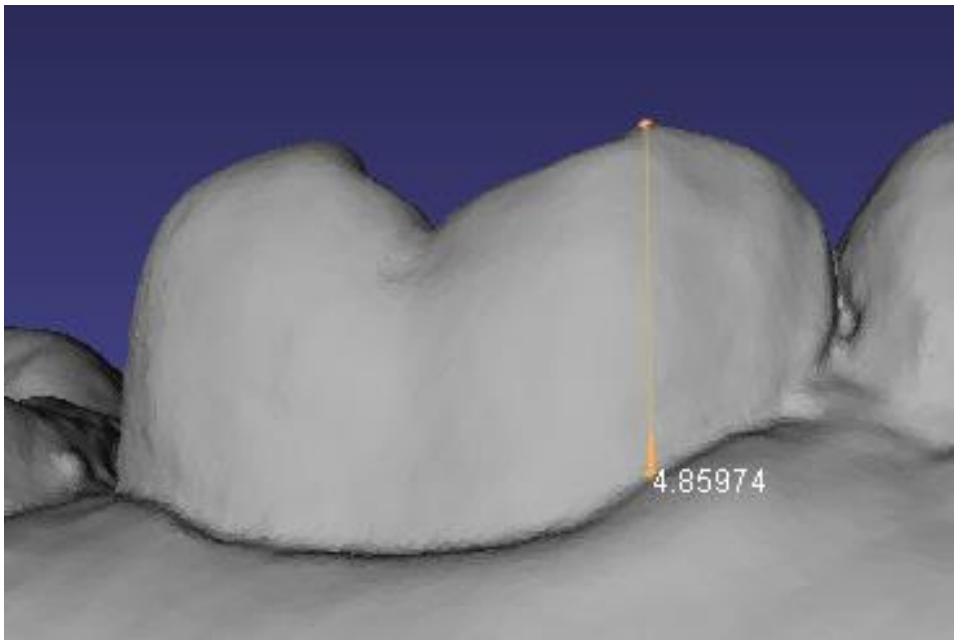


Figure 8: Crown-height (CH) of the left maxillary first molar from the buccal view

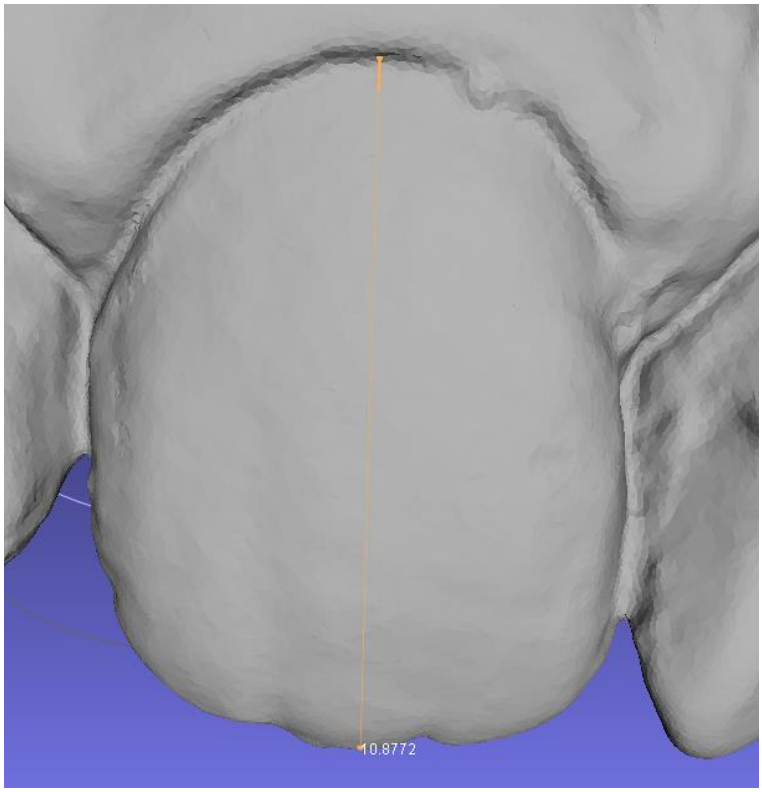


Figure 9: Crown-height (CH) of the right maxillary central incisor from the buccal view

4.5 Evaluating cusps

The method used to count and evaluate the cusps present was based upon the method used by Kerekes-Ma´the´ et al. (2015). All cusps were counted on the digital scans of casts for fully erupted premolars and molars. Well-established rating scales were applied in determining the number of cusps present on these teeth. For example, the lower second premolar may have 2 or 3 cusps with the third cusp represented as a disto-lingual cusp. The upper first permanent molar may vary in the number of cusps on the occlusal surface and may have an additional cusp, the cusp of Carabelli on the palatal surface adjacent to the mesio-palatal cusp.

There can be considerable variation in determining the robustness of the third cusp on the lower second premolar. A rating scale described by Scott et al. (2018) has been utilised in determining the number of cusps as per figure 10 below. In this study only presence or absence of this cusp was scored, presence being grades 3, 4, and 5.

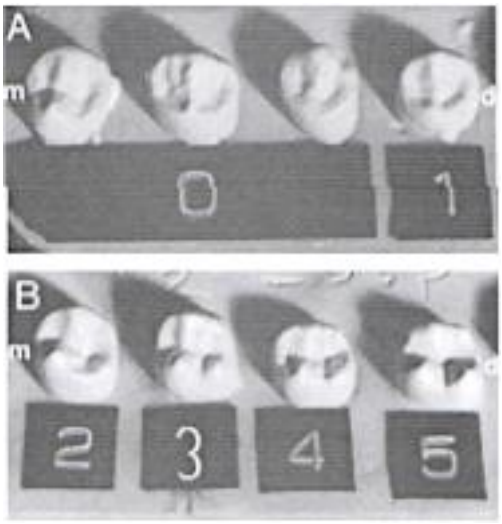


Figure 10: Diagram representing the variation in lingual cusp number on the lower second premolar (Scott GR, 2018).

In the upper first permanent molar, Carabelli cusps were evaluated based on Dahlberg's (1963) scale (figure 11). Scores 0 to 4 were marked as absent and scores 5, 6 and 7 were counted as cusps present. These cusps were robust enough to be considered as their own cusp and these classifications are defined in the following way:

- Form 5: a small tubercle
- Form 6: a broad cusp outline or moderate tubercle
- Form 7: a large tubercle with free apex in contact with the lingual groove

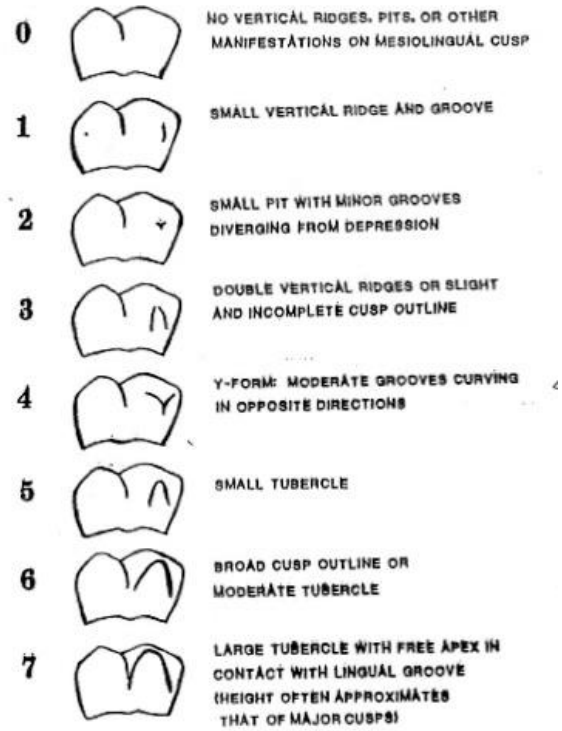


Figure 11: Eight grade classification employed for scoring the degree of expression of Carabelli's trait based on Dahlberg's 1963 classification (Scott GR, 1980).

4.5.1 Cusp Terminology

Comparisons between the paleontological terms and clinical terms for cusps are discussed due to the evolutionary discussion in the literature review.

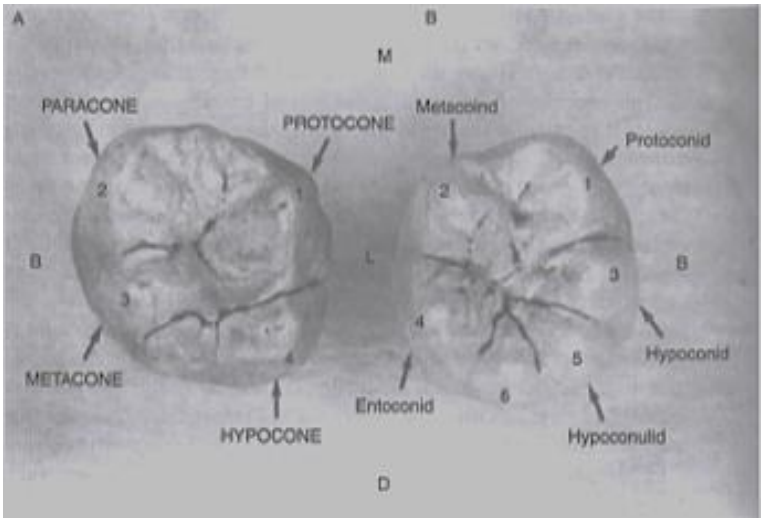


Figure 12: Paleontological terms for cusps on upper (A) and lower (B) permanent molars.

The relationship of these paleontological terms to those used clinically is given below in table 1: -

	Paleontological terms	**Clinical Terms**
Upper molar	Paracone	Mesio-buccal
	Protocone	Mesio-lingual
	Metacone	Disto-buccal
	Hypocone	Disto-lingual
Lower molar	Metaconid	Mesio-lingual
	Entoconid	Disto-lingual
	Hypoconulid	Distal
	Hypoconid	Disto-buccal
	Protoconid	Mesio-buccal

All data are described using the clinical terminology and the paleontological relevance will be considered in the discussion. A missing or extra cusp was also recorded based against a most frequent number of cusps for each tooth type.

When comparing the hypodontia and control groups it was decided to compare these based on combining the left-hand side (LHS) and right-hand side (RHS) teeth as listed below:

RHS tooth	LHS tooth	Combined tooth term (Tooth ID)	Most frequent Cusp Number
14	24	U4	2
15	25	U5	2
16	26	U6	4
17	27	U7	4
34	44	L4	2
35	45	L5	3
36	46	L6	5
37	47	L7	4

5. Errors of measurement and technique validation

Measuring any object to its true size will have its own unique challenges and possibility for error. Odontometrics is no different in this regard, the operator's experience will often equate to greater accuracy and repeated measurements will obtain the measurement as close to the tooth's true size as possible (Hunter & Priest 1960). Ribeiro (2012) has described three factors that affect the fidelity of these measurements and can also be sources of error:

1. Landmark identification: this is completely operator dependent and differences can occur between operators
2. The precision of the measuring equipment
3. How the operator uses that equipment, their skill and knowledge with that equipment

The errors that arise in odontometrics can be classified as systematic or random (Houston 1983; Hunter & Priest 1960; Jensen et al. 1957). Sources of systematic errors in this methodology could have been introduced during the impression stage and the casting stage of the dental models. Distortion can occur in the casts; alginate impressions can lose water through syneresis and shrink prior to being poured if not stored in an appropriate environment. This source of systematic error was minimized as much as possible by using an experienced dental laboratory with the same dental technician and the same materials at the same ratio for the entirety of this process. Another source of systematic error would be potentially in the MeshLab software used in this study. Sources of random error could have occurred from the operator's skill in imaging techniques, measuring techniques and landmark identification.

The method used in this study was validated from three aspects and the degree of error determined:

1. Validation of the 3D measurement technique against traditional caliper measurements (section 5.1)
2. Repeatability of the 3D software used in this study: MeshLab (section 5.2)
3. Intra and inter-operator reliability using the 3D software and technique (section 5.3)

5.1 3D technique compared to calipers

This study used a new point to point linear measurement technique and it was prudent to validate it against hand calipers that have been used consistently and reliably in odontometric studies (Kieser 1990).

5.1.1 Method re errors

Models from the pool of controls, given the code E1-E10, were used. The teeth selected for measurement were the upper second premolar on the right side (15), and the lower second premolar on the left side (35). Readily identifiable points were established as the basis for validation, this was the inter-cuspal distance (Figure 10). Some lower premolars have additional cusp tips, in this instance the distance from the distal cusp tip was measured. The same operator took the measurements in 3D with MeshLab software and also performed caliper measurements with digital Vernier calipers.

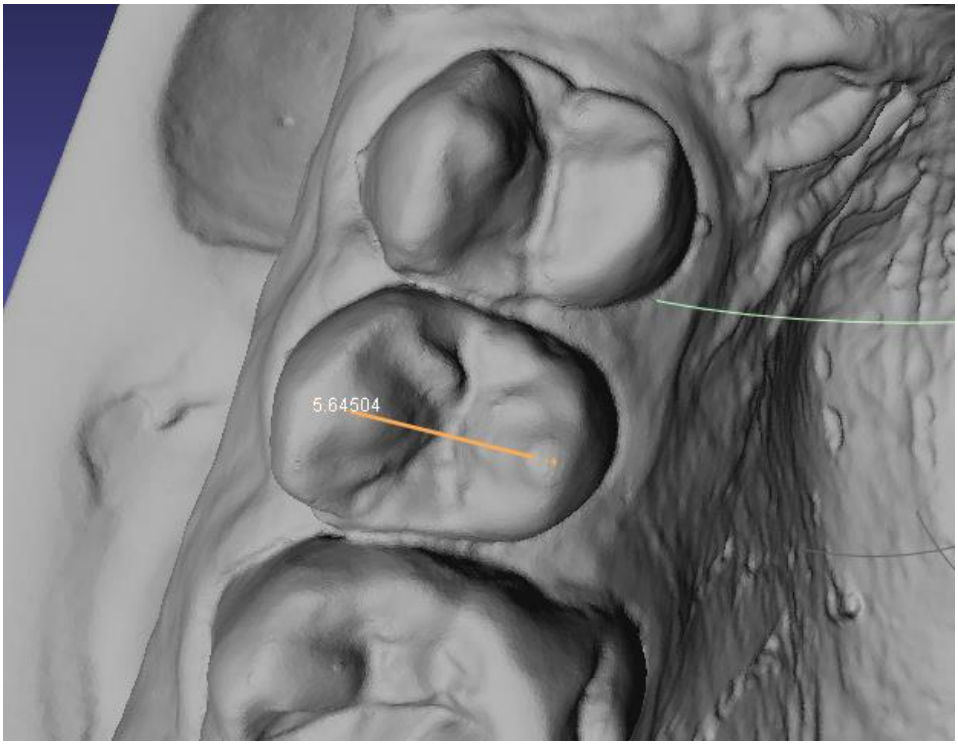


Figure 13: Premolar inter-cuspal distance measurement from the occlusal view

5.1.2 Results re errors

The results are displayed in Table 1. Using SPSS software an intra-class correlation coefficient model (ICC), specifically a two-way random effect with absolute agreement, was applied to the values produced by the first and second operator to assess their reliability. Values produced for an ICC range from 0 to -1, where 1 is a perfect correlation. ICC values above 0.75 are considered to indicate good reliability (Cicchetti 1994; Harris &

Smith 2008). The ICC was 0.871. The technical error of measurement (TEM) was calculated at 0.186mm, this indicates there was not a statistically significant difference between the repeated measurements.

5.1.3 Discussion re errors

Digital models may be more reliable than hand calipers because of the ability to zoom in and rotate the models in multiple planes (Stevens et al. 2006). The evidence from the literature suggests that measurements taken on 3D digital models are more reliable than traditional caliper hand measurements (Bell, Ayoub & Siebert 2003; El-Zanaty et al. 2010). The results produced in this analysis support this as there was a small TEM value and an ICC above 0.75.

Table 2: Inter-cuspal measurements of teeth 15 and 35 for hand calipers and 3D MeshLab

Model and Tooth Number	Caliper	MeshLab	Differential
E1 (15)	5.66	5.67	-0.01
E2 (15)	5.60	5.76	-0.16
E3 (15)	5.60	5.52	0.08
E5 (15)	6.41	6.26	0.15
E7 (15)	5.73	5.04	0.69
E8 (15)	6.28	6.26	0.02
E9 (15)	5.86	5.71	0.15
E1 (35)	5.49	5.92	-0.43
E2 (35)	4.44	4.52	-0.08
E3 (35)	6.01	5.89	0.12
E5 (35)	5.37	5.52	-0.15
E6 (35)	3.38	3.79	-0.41
E7 (35)	5.14	4.87	0.27
E8 (35)	5.26	5.33	-0.07
E9 (35)	4.92	4.79	0.13
		Mean:	**0.02**

5.2 Repeatability of 3D software

To further validate the method used in this study, the measuring tool (in this case MeshLab software) needed to demonstrate repeatability between uses.

5.2.1 Method

The same method used in section 5.1.1 was repeated with the exception of no caliper measurements, and the MeshLab measurements were taken twice. The same operator took the measurements in 3D with MeshLab software and the two data sets were compared.

5.2.2 Results

The ICC and TEM values were calculated as they were in section 5.1.2. ICC was 0.937 and TEM was 0.135mm.

Table 3: Inter-cuspal measurements of teeth 15 and 35 for 3D MeshLab comparison

Model and Tooth Number	MeshLab 1	MeshLab 2	Differential
E1 (15)	5.73	5.67	0.05
E2 (15)	5.57	5.76	-0.19
E3 (15)	5.62	5.52	0.09
E5 (15)	6.13	6.26	-0.13
E7 (15)	5.35	5.04	0.31
E8 (15)	6.20	6.26	-0.05
E9 (15)	5.72	5.71	0.02
E1 (35)	6.09	5.92	0.17
E2 (35)	4.54	4.52	0.02
E3 (35)	6.03	5.89	0.14
E5 (35)	5.48	5.52	-0.04
E6 (35)	3.27	3.79	-0.52
E7 (35)	5.08	4.87	0.21
E8 (35)	5.22	5.33	-0.10
E9 (35)	4.85	4.79	0.07
		Mean	**.003**

5.2.3 Discussion

As the ICC was 0.937 which indicative of a high degree of reliability and the TEM was 0.135mm which would be a negligible difference between measurements. It is acceptable to conclude the measurement software (MeshLab) demonstrates high repeatability between uses.

5.3 Intra and inter-operator reliability

Performing intra and inter-operator reliability measurements fulfilled three main objectives:

1. It re-established the reliability of the MeshLab software used (see section 5.2)
2. It established reliability of the main operator when performing linear measurements
3. It established reliability between operators of similar skill level when performing linear measurements

5.3.1 Method

The intra-operator error was determined by having the first operator take ten initial inter-cuspal measurements, from the upper and lower second premolar. The first operator then took the same measurements from the same teeth eight weeks later and the differentials between the two sets of measurements were calculated.
The inter-operator error was determined by having a second operator take the same ten inter-cuspal measurements from the upper and lower second premolar, the differentials between the first and second operator were then calculated.

5.3.2 Results

The results are presented in the following Tables (1-4) and have been rounded up to three significant figures. Tables 1 and 2 are the values the first operator measured on two separate occasions with the differentials (intra-operator), followed by the mean of the differentials: which were 0.20mm and 0.32mm for the upper and lower second premolar respectively. Table 3 and 4 are the values the first operator and the second operator measured followed by the difference between them (inter-operator): the average for this was 0.09mm and 0.58mm for the upper and lower second premolar respectively. The ICC for the first operator's intra-operator reliability was 0.818 for the upper second premolar and 0.852 for the lower second premolar. The ICC for the first operator's and the second operator's inter-operator reliability was 0.955 for the upper second premolar and 0.685 for the lower second premolar.

5.3.3 Discussion

All the values for intra and inter-operator reliability, except for the lower second premolar, were above the threshold and it suggests there is evidence of reliability. The reasons for the lower second premolar having decreased reliability likely stems from its morphology; it can have one or two lingual cusp tips and this could be open to interpretation by the operator. Some degree of variability between operators will always exist when operators choose anatomical points because of their interpretation of where that anatomical landmark is. Variability also exists between operators measuring with traditional calipers and plaster models where the points have been marked for them to measure, simply due to the slight variation in the manual positioning of the calipers (Bell, Ayoub & Siebert 2003). Previous studies have demonstrated that, while there is inter-operator error when measuring on a 3D model, this is still less than traditional plaster models and calipers (Bell, Ayoub & Siebert 2003; Moreira et al. 2014; Stevens et al. 2006).

Table 4: First operator intra-operator error differentials for the upper second premolar (mm)

First operator measurements of the upper second premolar	First operator measurements of the upper second premolar eight weeks later	Differentials
5.49	5.73	0.235
5.77	5.57	0.207
5.89	5.62	0.273
6.27	6.13	0.142
5.49	5.35	0.133
6.40	6.20	0.199
5.50	5.72	0.224
		Mean: 0.202

Table 5: First operator intra-operator error differentials for the lower second premolar (mm)

First operator measurements of the lower second premolar	First operator measurements of the upper second premolar eight weeks later	Differentials
5.96	6.09	0.129
4.09	4.53	0.447
5.88	6.03	0.149
5.29	5.48	0.189
4.31	3.27	1.04
5.18	5.08	0.103
5.46	5.22	0.233
5.10	4.85	0.242
		Mean: 0.317

Table 6: First and second operator inter-operator error for the upper second premolar (mm)

First operator upper second premolar measurements	Second operator upper second premolar measurements	Differentials
5.49	5.54	0.047
5.77	5.71	0.064
5.89	6.09	0.199
6.27	6.34	0.071
5.49	5.48	0.006
6.40	6.23	0.169
5.50	5.58	0.083
		Mean: 0.091

Table 7: First and second operator inter-operator error for the lower second premolar (mm)

First operator lower second premolar measurements	Second operator lower second premolar measurements	Differentials
5.96	5.63	0.334
4.09	3.77	0.319
5.88	5.38	0.500
5.29	5.13	0.162
4.31	3.33	0.985
5.18	3.97	1.210
5.46	5.21	0.243
5.10	4.20	0.902
		Mean: 0.582

5.4 Cusp error analysis

Similar to the above measurement, in order to successfully record the number of cusps on each posterior tooth and accurately determine if the cusp was fully developed with particular attention to the lower second premolar and the cusp of Carabelli in the upper first molar. Intra and inter-operator error testing was required for this.

5.4.1 Method

Before this analysis a pilot study was completed to ensure the correct method was applied in count the number of cusps, the outcomes of this were then discarded. A total of ten sets of casts were used across all 4 groups in the study and tested for intra and inter-operator error.

5.4.2 Results

To test the intra-rater reliability for two repeated (cusp total per tooth) recordings by the same operator and to test the inter-rater reliability for (cusp total per tooth) across two different operators, simple Kappa scores were calculated. A kappa coefficient is a statistic which measures inter-rater or intra-rater agreement for categorical items. It is generally thought to be a more robust measure than simple percent agreement calculation, as the kappa coefficient takes into account the possibility of the agreement occurring by chance

As previously described, Cicchetti (1994) gives the following often quoted guidelines for interpretation for kappa or ICC inter-rater agreement measures:

- Less than 0.40—poor.
- Between 0.40 and 0.59—fair.

- Between 0.60 and 0.74—good.
- Between 0.75 and 1.00—excellent.

Table 1 below gives simple Kappa coefficients and 95% confidence intervals for each comparison. The variable 'Extra cusps' was not included as there were either none or 1 value for each Operator. The term Operator (1) and Operator 1(2) refers to the first and second time the recordings for intra-operator error were taken.

Table 8: Intra-operator and inter-operator error testing for cusp analysis.

Variable	Comparison operator	Reference operator	Simple Kappa	95% CI	Interpretation
Number of cusps	Operator 2	Operator 1	0.85	0.75, 0.96	Excellent
Number of cusps	Operator 1 (1)	Operator 1 (2)	1.00	1.00, 1.00	Excellent
Missing cusp	Operator 2	Operator 1	1.00	1.00, 1.00	Excellent
Missing cusp	Operator 1 (1)	Operator 1 (2)	1.00	1.00, 1.00	Excellent
Carabelli present	Operator 2	Operator 1	0.85	0.56, 1.00	Excellent
Carabelli present	Operator 1 (1)	Operator 1 (2)	1.00	1.00, 1.00	Excellent

5.4.3 Discussion

There is excellent intra-operator and inter-operator reliability across Operator 1(1) and Operator 1(2) and across Operator 1 versus Operator 2 for all the cusp variables tested. This validates the method utilised in counting the cusps on each tooth

6. Results of linear mixed effects analysis of crown dimensions and cusp number

6.1 Introduction

The following chapter illustrates the linear mixed effects (LME) analyses performed on the data, linear measurements and cusp numbers, described in Chapter 4. The software used was SAS 9.4 (SAS Institute Inc., Cary, NC, USA). The LME models used were appropriate given the degree of matching between the hypodontia and the control group (sex, age, ethnicity) and allowed for controlling, if necessary, for confounding variables such as Polynesian ethnicity. The analyses related to cusp numbers were ordinal logistic generalized estimating equations (GEE). This model was deemed appropriate because it accommodates readily binary variables such as the existence of a cusp. It became evident that there was no significant difference in linear size between the left and right-side dentition, so the data from both sides were combined. The three dimensions measured, MD, BL, CH were added together to form the module. The module provided a cumulative value of the entire tooth size for comparative purposes. The most consistent statistical significance was demonstrable in all models related to MD dimension, followed by BL, and CH was the most inconsistent outcome. The consistency of significant relationships demonstrable with the module value varied based on the cumulative relationships of the MD, BL and CH dimensions.

Table 9: MD dimension means of the hypodontia and control group for both female and male.

Female			Male		
	Mean	Significance		Mean	Significance
Hypodontia	7.68	P=0.0011	Hypodontia	7.85	P=0.0016
Control	7.97		Control	8.16	

6.2 LME Models 1-4: The hypodontia group compared to the control group, controlling for sex interaction, and adjusting for age, ethnicity and tooth identification (combining pairs of teeth).

***Appendix LME models 1-4**

Models 1-4 (appendix) were LME models of MD, BL, CH and module outcomes versus the hypodontia group, the control group and controlling for sex interaction. There was not a statistically significant interaction for the linear dimensions (MD, BL, CH) and the module value between the groups and sex (module interaction P value = 0.5944). This was likely due to insufficient power to demonstrate this. However, there were some interesting significant post hoc comparisons for each model:

6.2.1 Model 1 (MD dimension and sex) post hoc comparisons

Comparing female controls to the female hypodontia group, the female controls were on average larger by 0.29mm in the MD dimension than the controls (p = 0.0011). The male controls were 0.31mm on average larger than the males in the hypodontia group (p= 0.0016). The male control group were 0.20mm on average larger than the female control group (p=0.0337), which is to be expected due to the sexual dimorphism between males and females. Males of the hypodontia group were on average 0.17mm larger in the MD dimensions than the females hypodontia group, however this interaction was not statistically significant (p=0.068). The subsequent models, models 2-4, produced similar results to Model 1.

6.2.2 Model 2 (BL dimension and sex) post hoc comparisons

Comparing the female control group to the female hypodontia group for BL dimension, the female controls on average were 0.29mm larger (p = 0.0076). The male control group were 0.37mm on average larger than the male hypodontia group (p= 0.0019). The male controls were 0.22mm on average larger than the female controls (p=0.0445). The male hypodontia group were 0.14mm larger on average than the female hypodontia group, but not to a statistically significant degree (p=0.23).

Table 10: BL dimension means of the hypodontia and control group for both female and male.

Female			Male		
	Mean	Significance		Mean	Significance
Hypodontia	22.72	P=0.006	Hypodontia	23.25	P=0.001
Control	23.57		Control	24.34	

6.2.3 Model 3 (CH dimension and sex) post hoc comparisons

Comparing the female control group to the female hypodontia group for the CH dimensions, the females control group on average were 0.31mm larger with borderline statistical significance (p=0.058). The male control group was 0.41mm on average larger than the male hypodontia group (p=0.021). The male control group was on average 0.31mm larger than the female control group, with borderline statistical significance (p=0.061). The male hypodontia group was 0.20mm larger than the female hypodontia group, though this was not to a statistically significant degree.

Table 11: CH dimension means of the hypodontia and control group for both female and male.

Female			Male		
	Mean	Significance		Mean	Significance
Hypodontia	6.68	P=0.058	Hypodontia	6.89	P=0.021
Control	6.99		Control	7.30	

6.2.4 Model 4 (module value and sex) post hoc comparisons

Comparing the female control group to the female hypodontia group, on average the female control group was 0.85mm larger for module value (p=0.006). The male control group was 1.09mm larger on average than the male hypodontia group (p=0.001). The male control group was 0.77mm larger on average than the female control group (p=0.0143). The male hypodontia group was 0.53mm larger on average than the female hypodontia group, not to a statistically significant degree.

Table 12: Module value means of the hypodontia and control group for both female and male.

Female			Male		
	Mean	Significance		Mean	Significance
Hypodontia	8.34	P=0.0076	Hypodontia	8.48	P=0.0019
Control	8.63		Control	8.85	

6.3 LME Models 5-8: The hypodontia group compared to the control group, controlling for tooth identification (combined), and adjusting for age, ethnicity and controlling for clustering on patient identification.

***Appendix LME models 5-8**

These LME models were applied to determine if there was any statistically significant difference between the hypodontia group and the control group for specific tooth identification numbers. Tooth identification (ID) numbers were the combined values of two antimeric teeth, it was determined appropriate to combine the data for each tooth class (e.g. 11 and 21 coded as U1) as there was no significant difference between their values.

6.3.1 Model 5 (MD dimension and tooth ID)

There was a statistically significant interaction between the hypodontia group and the control group for the tooth ID's in the MD dimension (p=0.008). All of the control group's tooth ID's for the MD dimensions were on average greater than the hypodontia group's and all of these interactions were statistically significant ($p<0.05$).

6.3.2 Model 6 (BL dimension and tooth ID)

There was a statistically significant interaction between the hypodontia group and the control group for the tooth ID's in the BL dimension ($p<0.0001$). All of the control group's tooth ID's for the BL dimensions were on average greater than the hypodontia group's. However, the interactions involving L2, L6 and L7 were borderline for statistical significance: at $p=0.055$, $p=0.078$, $p= 0.074$ respectively.

6.3.3 Model 7 (CH dimension and tooth ID)

There was not a statistically significant interaction between the hypodontia group and the control group for the tooth ID's in the CH dimension, it showed a tendency towards significance at $p=0.067$. All of the control group's tooth ID's for the CH dimensions were on average greater than the hypodontia group's, many of these interactions were statistically significant or trending towards it.

6.3.4 Model 8 (module value and tooth ID)

There was a borderline statistically significant interaction between the hypodontia group and the control group for the tooth ID's in the module value, it showed a tendency towards significance at $p=0.059$. All of the control group's tooth ID's for the module value were on average greater than the hypodontia group's; all of these interactions were statistically significant ($p<0.05$).

6.4 LME Models 9-12: Comparison within the hypodontia group only: linear dimensions and module value versus the missing tooth and tooth number (combined) interaction, adjusting for age, sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient).

***Appendix models 9-12**

This series of LME models compared hypodontia patients with agenesis of one tooth of a particular class against the remaining cohort of hypodontia patients tooth class dimensions. For example: hypodontia patients with agenesis of a single upper lateral incisor had their remaining upper lateral incisor compared to the rest of the hypodontia cohort's upper lateral incisors.

6.4.1 Model 9 (MD dimension comparison based on tooth class)

There was a statistically significant interaction between having tooth agenesis and combined tooth number for MD dimension, adjusting for age, Polynesian ethnicity and sex, and controlling for clustering on Patient ID ($p=0.0022$). However, this interaction is only present due to the interaction of the upper lateral incisor compared

to the rest of the hypodontia cohort ($p<0.0001$). The remaining classes of teeth, lower central incisors, lower lateral incisors and lower second premolars demonstrated no significant interaction. On average, the remaining lateral incisors in the hypodontia group were 1.39mm larger in the MD dimension compared to hypodontia patients with only one lateral incisor.

6.4.2 Model 10 (BL dimension comparison based on tooth class)

There was not a statistically significant interaction between having tooth agenesis and combined tooth number for BL dimension, adjusting for age, Polynesian ethnicity and sex, and controlling for clustering on Patient ID ($p=0.20$). However, the interaction of the upper lateral incisor compared to the rest of the hypodontia cohort demonstrates a tendency this way ($p=0.070$). The remaining class of teeth, lower central incisors, lower lateral incisors and lower second premolars demonstrated no significant interaction. On average, the remaining lateral incisors in the hypodontia group were 0.86mm larger in the BL dimension compared to hypodontia patients with only one lateral incisor.

6.4.3 Model 11 (CH dimension comparison based on tooth class)

There was a statistically significant interaction between having tooth agenesis and combined tooth number for CH dimension, adjusting for age, Polynesian ethnicity and sex, and controlling for clustering on Patient ID ($p=0.037$). However, this interaction is only present due to the interaction of the upper lateral incisor compared to the rest of the hypodontia cohort ($p<0.008$). The remaining class of teeth, lower central incisors, lower lateral incisors and lower second premolars demonstrated no significant interaction. On average, the remaining lateral incisors in the hypodontia group were 1.30mm larger in the CH dimension compared to hypodontia patients with only one lateral incisor.

6.4.4 Model 12 (module value comparison based on tooth class)

There was a statistically significant interaction between having tooth agenesis and combined tooth number for module value, adjusting for age, Polynesian ethnicity and sex, and controlling for clustering on Patient ID ($p<0.0001$). However, this interaction is only present due to the interaction of the upper lateral incisor compared to the rest of the hypodontia cohort ($p<0.0001$). The remaining class of teeth, lower central incisors, lower lateral incisors and lower second premolars demonstrated no significant interaction. On average, the remaining lateral incisors in the hypodontia group were 5.90mm larger for module value compared to hypodontia patients with only one lateral incisor.

6.5 LME models 13-16: Comparison of the Polynesian group's linear tooth dimensions and module value against non-Polynesian, adjusting for age, tooth ID, sex and controlling for clustering on Patient ID.

***Appendix models 13-16**

The series of models 13-16 are comparing the linear tooth dimensions (MD, BL, CH,) and module value. The general trend was smaller linear dimensions in the non-Polynesian group than the Polynesian group, except for the CH dimension which, as previously mentioned, demonstrated the most variability. On average the Polynesian module value was larger for both the hypodontia and control groups; though this was not to a statistically significant degree. The Polynesian control group was on average 0.12mm larger in module value compared to the non-Polynesian control group, while the Polynesian hypodontia group was on average 0.26mm larger in module value compared to the non-Polynesian hypodontia group.

6.6 Cusp analysis results

Analysis was conducted to determine the number of cusps present on each tooth type comparing hypodontia to control groups. Further analysis was conducted to determine the number of missing and extra cusps present and which cusp was missing on each tooth ID. The final cusp analysis was carried out to compare the presence of Carabelli's cusp on U6 tooth type ID between hypodontia and control groups. While there was often no statistically significant difference in these tests, each tooth type showed the pattern of less cusps in the hypodontia group.

6.6.1 Contingency tables comparing number of cusps by group (control and hypodontia) for the whole dentition (U4-U7 and L4-L7 only) and then by combined tooth ID

For all the 8 combined tooth IDs, there is a statistically significant association between number of cusps and group, with the hypodontia group having less cusps (Chi Square Test P value=0.03).

Table 13: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
2	361	335	696
	51.87	48.13	
	41.64	42.89	
3	116	71	187
	62.03	37.97	
	13.38	9.09	

Table 13: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
4	232 49.47 26.76	237 50.53 30.35	469
5	158 53.38 18.22	138 46.62 17.67	296
Total	867	781	1648

Frequency Unaffected = 2

Chi-Square P value=0.03

For the individual tooth type IDs, not including U4, U5 and L4, there is a statistically significant association between number of cusps and group, again with the hypodontia group having less cusps (Chi Square Test P value=0.02).

Table 14: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
2	2 33.33 0.39	4 66.67 0.89	6
3	116 62.03 22.83	71 37.97 15.78	187
4	232 49.47 45.67	237 50.53 52.67	469
5	158 53.38 31.10	138 46.62 30.67	296
Total	508	450	958

Frequency Unaffected = 2

Chi-Square P value=0.02

The following tables represent results for individual tooth ID.

Combined_tooth_ID=L4

Table 15: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
2	126 51.43 100.00	119 48.57 100.00	245
Total	126	119	245

Combined_tooth_ID=L5

Table 16: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
2	2 33.33 2.00	4 66.67 7.69	6
3	98 67.12 98.00	48 32.88 92.31	146
Total	100	52	152

Frequency Unaffected = 1

Fisher's Exact Test P value=0.18

Combined_tooth_ID=L6

Table 17: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
4	17 38.64 12.69	27 61.36 19.57	44
5	117 51.32 87.31	111 48.68 80.43	228

Table 17: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
Total	134	138	272

Chi Square P value=0.12

Combined_tooth_ID=L7

Table 18: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
4	71 52.21 97.26	65 47.79 98.48	136
5	2 66.67 2.74	1 33.33 1.52	3
Total	73	66	139

Frequency Unaffected = 1

Fisher's Exact Test P value=1.0000

Combined_tooth_ID=U4

Table 18: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
2	125 50.81 100.00	121 49.19 100.00	246
Total	125	121	246

Combined_tooth_ID=U5

Table 19: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
2	108 54.27 100.00	91 45.73 100.00	199
Total	108	91	199

Combined_tooth_ID=U6

Table 20: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
3	0 0.00 0.00	3 100.00 2.17	3
4	95 46.57 70.90	109 53.43 78.99	204
5	39 60.00 29.10	26 40.00 18.84	65

Table 20: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
Total	134	138	272

Fisher's Exact Test P value=0.03

Combined_tooth_ID=U7

Table 21: Number_Cusps by Group

Number_Cusps	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
3	18 47.37 26.87	20 52.63 35.71	38
4	49 57.65 73.13	36 42.35 64.29	85
Total	67	56	123

Chi Square P value=0.29

6.6.2 Contingency tables comparing differences in missing cusps between the hypodontia and control groups for the whole dentition (U4-7 and L4-7 only) and then by combined tooth ID

Contingency table of type of missing cusps by Group and contingency table of type of missing cusps by Group was performed for each combined tooth ID and P values calculated.

For combined tooth IDs with significant data, there is no statistically significant association between number of cusps and Group (Chi Square Test P value=0.27). For the type of missing cusps versus Group for each combined tooth ID, there was missing data for most of the teeth. For the tooth type U7, there was no statistically significant association for the type of missing cusps between the control and hypodontia group (Fisher's Exact Test P value=0.22).

Table 22: Missing_Cusp by Group

Missing_Cusp	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
DB	18 42.86 50.00	24 57.14 51.06	42
DL	2 100.00 5.56	0 0.00 0.00	2
DP	16 41.03 44.44	23 58.97 48.94	39
Total	36	47	83

Frequency Unaffected = 2125

Fisher's Exact Test P value=0.33

6.6.3 Contingency tables comparing differences in extra cusps between the hypodontia and control groups for the whole dentition (U4-7 and L4-7 only) and then by combined tooth ID

Extra cusps were only seen in L7 and there is no statistically significant association between number of extra cusps between the control and hypodontia group (Fisher's Exact Test P value=0.62).

Table 23: Extra_Cusp on L7 by Group

Extra_Cusp	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
DB	2 66.67 100.00	1 33.33 100.00	3
Total	2	1	3

Frequency Unaffected = 2205

6.6.4 Contingency tables for difference in cusp of Carabelli presence between the hypodontia and control groups for U6 only

A contingency table of Carabelli's cusp presence or absence was performed and P value calculated. For U6 combined tooth IDs only, there is a statistically significant association in Carabelli presence between the control

and hypodontia groups (Chi Square P value=0.03). 29% of the control group have a Carabelli present and 18% of the hypodontia group have a Carabelli present.

Table 24: Carabelli_present by Group

Carabelli_present	*Group*		
Frequency *Row Pct* *Col Pct*	*control*	*hypodontia*	*Total*
0	97	115	212
	45.75	54.25	
	71.32	82.14	
1	39	25	64
	60.94	39.06	
	28.68	17.86	
Total	136	140	276

Chi Square P value=0.03

7. Discussion

7.1 Reliability of the results

The 3D digital linear measurement used in this study was an advanced approach, many modern odontometric studies still use calipers for their dental measurements (Fekonja, Anita 2013; Gungor & Turkkahraman 2013; Shireen & Ara 2016; Sravya et al. 2016). Questions may arise regarding the reliability of this approach, specifically in terms of validity and reproducibility (Houston 1983). The method used was validated against conventional calipers and produced ICC and TEM values above the threshold of acceptable reliability. Similarly, the measuring tool (MeshLab) was demonstrated to be repeatable and reliable. Previously stated in Chapter 5 the intra and inter-operator reliability was determined with ICC and the results showed strong evidence for reliability, with the exception of the lower second premolar which can have significantly varied morphology. A limitation of determining reliability was the selection of cusp tips for linear measurements. These are well circumscribed points that would be easily identifiable and have limited room for interpretation. Maximum points defined in the protocol for the MD, BL and CH dimensions are not as well circumscribed morphologically and open to greater interpretation.

The same operator performed all measurements and was blinded to the models belonging to the hypodontia or control group. However, hypodontia has a clinically recognizable appearance and dental patterning which could have been identifiable to the operator who is a dentist. This leaves open the potential for unintended bias in the measurements.

Patients or their parents reported self-identified ethnicity and this assisted in controlling for the Polynesian dentition which is larger than the Europeans (Hanihara & Ishida 2005). An important consideration when considering the majority of the sample identified as New Zealand European and uncontrolled Polynesian dentition could skew the data. The results demonstrated the Polynesian participants had on average larger dental dimensions although it did not reach the statistically significant level. Concerns regarding self-identified ethnicity in biomedical research have been raised previously (Mersha & Abebe 2015). The potential for participants to under or over-report belonging to an ethnic group when, from a genetic standpoint, they may not have the specific genetic endowment expected of their identified group. Potential future solutions for this have been screening for ethnicity or ancestry using genomic markers (Mersha & Abebe 2015), though this may raise ethical and financial concerns.

Identification of the hypodontia sample occurred from screening OPGs and two cases in our sample were identified with mandibular lateral incisor agenesis. However, the ability to differentiate between mandibular central incisors or lateral incisors radiographically or clinically can be extremely difficult as they have very similar crown and root morphology. The more common pattern of hypodontia in the mandibular anterior region is agenesis of the central incisor, while the lateral incisor is more stable (Dahlberg 1945, 1951). With respect to the clinicians who screened these patients this study has maintained the assertion of mandibular central incisor agenesis.

7.2 Comparison with previous studies

The trend in hypodontia studies is not to include third molars. This is due to the difficulty in studying third molars in concert with the rest of the dentition, as well as the increased variability and instability. It has, however, been demonstrated that third molar hypodontia is associated with smaller remaining crown size (Garn, Lewis & Kerewsky 1963). It would not have been feasible to account for third molar agenesis in this study as the age of the radiographs would not provide visualization of all of the third molar crypts in order to know which members of the control group to preclude.

In this study the MD dimension was considered the most stable compared to the BL and CH measurements. Though these values are still likely concordant with each other, it may be that the MD dimension is least dependent upon the gingival margin. Once the mesial and distal margin of the tooth has erupted even slightly then the MD dimension is fixed, while BL and CH dimensions are still dependent on the degree of eruption. The assessment of complete eruption is operator dependent and variation would likely exist between operators. Another explanation for the discrepancy between these values is that the ability to accurately measure the BL dimension would diminish in comparison to the MD dimension due to its smaller size. The only way to know with certainty the CH and BL dimensions would be if the tooth was extracted and then measured. The results from this study support this notion as consistent statistical significance was most apparent in the MD dimensions analyzed.

The three dimensions measured, MD, BL, CH were added together to form a fourth variable: module. The module value has not been used in previous hypodontia studies. The module provided a cumulative value of the entire tooth: this was particularly useful when comparing specific tooth classes between groups, sex and ethnicities. The module also allowed control of any outlier measurements: one outlier measurement of three measurements observed could not grossly exaggerate the module value.

In many odontometric studies consideration is given to the natural wear of the dentition occlusally and inter-proximally. Wear was not a consideration in this case due to the young age of the sample and their soft carbohydrate based Western diet, the likelihood of any significant wear or erosion was minimal.

Linear mixed effect models were used as the primary statistical model. In terms of odontometric measurement this has been applied once previously to a deer sample (Pérez-Barbería, Carranza & Sánchez-Prieto 2015). This is the first human odontometric study to use LME models. The sample in this study warranted the use of LMEs as there were multiple confounders for tooth measurement such as Polynesian ethnicity and sex. The advantage of LMEs is that they allow for significant flexibility when determining sources of variability in the model and incorporating patient specific characteristics (Linear Mixed Effects Models 2006).

The results demonstrate a consistency with previous hypodontia studies demonstrating statistically significant reduced crown and cusp size in a hypodontia cohort compared to their controls (Al Shahrani 2012; Baum & Cohen 1971; Brook 1984; Brook et al. 2009(c); Garn & Lewis 1970; Kerekes-Ma´the´ et al. 2015; McKeown et al. 2002; Ooshima et al. 1996; Rune & Sarnas 1974), though there are slight variations in our results. Al Shahrani (2012) used 3D technology while studying hypodontia, specifically employing 3D geometric morphometric techniques, this study differs by using 3D techniques to obtain linear measurements. It is thought that the current study is the first to use LME models and to use statistical modelling to control for the confounding variable of ethnicity.

Kerekes-Ma´the´et al. (2015) observed reduced cusp numbers in hypodontia patients and the present results support their findings since they demonstrate a trend of reduced number of cusps in hypodontia patients. This reduction presented more commonly in teeth which usually have a variation in cusp number, so that the maxillary first and second molars and mandibular second premolar were the teeth more frequently having fewer cusp numbers.

An additional trend is noticed in the present study where there were a statistically significantly lower number of cusps of Carabelli in the hypodontia group compared with controls.

In interpreting results from the present study it is important to bear in mind that both hypodontia and control groups were collected from the orthodontic unit at the University of Otago. All patients in this study had to meet the criteria for referral for public orthodontic treatment and so often presented with a malocclusion or crowding. A large amount of cusp data in both hypodontia and control groups was listed as not recordable (NR) for the following reasons:-

- Teeth were unerupted or impacted due to a lack of space in the arch.
- Teeth were absent due to hypodontia.

- The impression did not accurately record U7 and L7 which may have not been required for the orthodontic treatment.
- The teeth were only partially erupted or unerupted (especially U7 or L7). This was dependant on the age of the subjects when records were taken.
- Crowns or restorations were present obliterating the original cuspal anatomy, this did not occur often.
- Teeth were extracted due to caries.

In order to mitigate the above issues, the analysis was conducted excluding all NR teeth. Teeth U4, U5 and L4 did not show any variation in anatomy and analysis of these was also excluded when comparing hypodontia and control groups.

The overall effect is reduced due to cusps being marked purely as present or absent. With the future application of shape analysis on this data set a greater effect in difference may be identified.

Missing cusps presented most often on specific teeth and were most frequently the disto-lingual (entoconid) cusp on L5, the disto-buccal (hypoconid) cusp on L6 and the disto-palatal (hypocone) cusp on U7.

7.3 Importance of the results

Townsend et al. (2009(a)) have suggested pushing technology forward in odontometric measurements. Despite the evidence that 3D models and measurements have multiple advantages over traditional caliper measurements many modern studies use calipers. Similarly, Harris & Smith (2009) urged rigorous error testing and critical analysis of measurement protocols in dental studies, yet few studies have pursued validation of their protocol with repeat measurements. It was with intention that the protocol pursued in this study supports the need in odontometrics for new methodologies that are also rigorously validated.

Previous studies have well established there is significant sexual dimorphism in the size of the dentition. This study supported those findings amongst the control group. However, amongst the hypodontia group the dimorphism was not as significantly pronounced - suggesting that males affected by hypodontia are more heavily expressed phenotypically than females. This assertion supports Brook's (1984) aetiological model whereby males have a significantly higher threshold to cross before they present with hypodontia when considering their position in the phenotypic spectrum.

Previously discussed were the ramifications of continued structural reductions in relation to anatomical size and complexity. Several studies have described the reductions in number, size and complexity of the dentition and surrounding structures, even amongst those who are related to hypodontia patients (Bailit & Friedlaender 1966; Cobourne 2007; Garn & Lewis 1962; Garn Lewis & Kerewsky 1963; Kerekes-Ma´the´ et al. 2015; McKeown et al. 2002). The results of this study demonstrate that these structural reductions in the dentition are still occurring. The Probable Mutations Effect would be the likely explanation for this (Brace 1963, 1964, 1967; Brace & Mahler 1971; Brace, Rosenberg & Hunt 1987). The mutations responsible for hypodontia, for example PAX9 (Brook et al. 2009(a)), would appear and maintain themselves in a modern population because there are no selective pressures to remove them from the gene pool. Natural selection for smaller dentition and the subsequent benefits, such as accommodation of third molars, less pronounced malocclusion and generalized crowding, has also been proposed for the trend in the reduction of the human dentition (Calcagno & Gibson 1988). It would be biologically plausible that with sufficient selection for smaller dentition enough mutations expressed synergistically would produce smaller dentition, but also push the threshold required for the least stable teeth to not form at all. Regardless if the mechanism is PME, natural selection, or a combination of the two, the phenotypic outcome is the same in the population: reduction in dentition and removal of the least stable teeth in the arch.

The results confirmed previous studies demonstrating the reduced size and simplified morphology of the dentition in hypodontia patients. Noticeably, participants with hypodontia of one upper lateral incisor who retained the antimeric incisor, had significantly reduced dimensions when compared to the remaining hypodontia group. One possible explanation is that as the upper lateral incisor is forming, approximately at 10-11 months (Schour & Massler 1941), the molecular and environmental influences that would cause agenesis of one lateral incisor also significantly affects the size of the antimeric lateral. This explanation supports the idea that dental development is complex and nuanced (Brook, Koh & Toh 2016; Brook 2009; Brook et al. 2014(a); Brook et al. 2014(b); Townsend et al. 2009(a)), phenotypic outcome is not binary but exists within a spectrum of variation.

With the expansion of genomic sequencing there has been a shift in the literature to publishing genomic data without accompanying detailed phenotypic findings. However, it is increasingly evident that to effectively understand the complexities of biological systems, disease, and variation in a species an approach from a holistic perspective has distinct benefits. Specifically, an increased appreciation of multiple interacting variables (Brook et al. 2014(a); Taduran et al. 2016; Townsend et al. 2012; Townsend et al. 2009(a); Yong et al. 2014). There must be recognition of the genetic factors, epigenetic factors, environmental factors, and their multiple interactions resulting in variable phenotypic outcomes. Therefore, the results from this study reflect an

important shift in research dynamics that will, hopefully, encourage future analyses to consider data as one element of a complex stomatognathic system.

7.4 Future directions and research

Furthering this research would involve:

- A larger hypodontia sample, complete with a significant number of mild, moderate and severe hypodontia cases
- The new technique validated in this study extended to provide other parameters such as areas and perimeters of occlusal and buccal surfaces, as well as crown volume
- Future data analysis on this sample comprising a matched pair-analysis, as well as synthesis with other phenotypic data such as the arch dimensions, root morphology and length, and chronological dating.
- Genotype-phenotype analysis once detailed phenotypic data have been acquired

8. Conclusion

The hypodontia group will had smaller crown dimensions and fewer cusp numbers than the controls group. Therefore, the null hypothesis that stipulated there would be no difference in crown dimensions or cusp number between the hypodontia group and the control group can be rejected.

Each of the original aims outlined have been fulfilled:

- To screen and collect a new sample of hypodontia patients from The University of Otago, School of Dentistry, Faculty of Orthodontics, paired with matched controls for age, sex, and ethnicity - **FULFILLED**
- To scan the models of the collected sample in a standardized 3D protocol - **FULFILLED**
- To establish a 3D linear measurement protocol and have it validated against calipers, and for intra and inter-operator error - **FULFILLED**
- To determine if there is a difference in mesio-distal, bucco-lingual, and crown height dimensions between the hypodontia and the control group - **FULFILLED**
- To determine if there is a difference in cusp number between the hypodontia and the control group – **FULFILLED**

9. Ethical approval

Ethical approval was granted by the Human Research Ethics Committee of The University of Adelaide; this work was deemed to be of negligible risk.

10. Publications and presentations

10.1 Publications

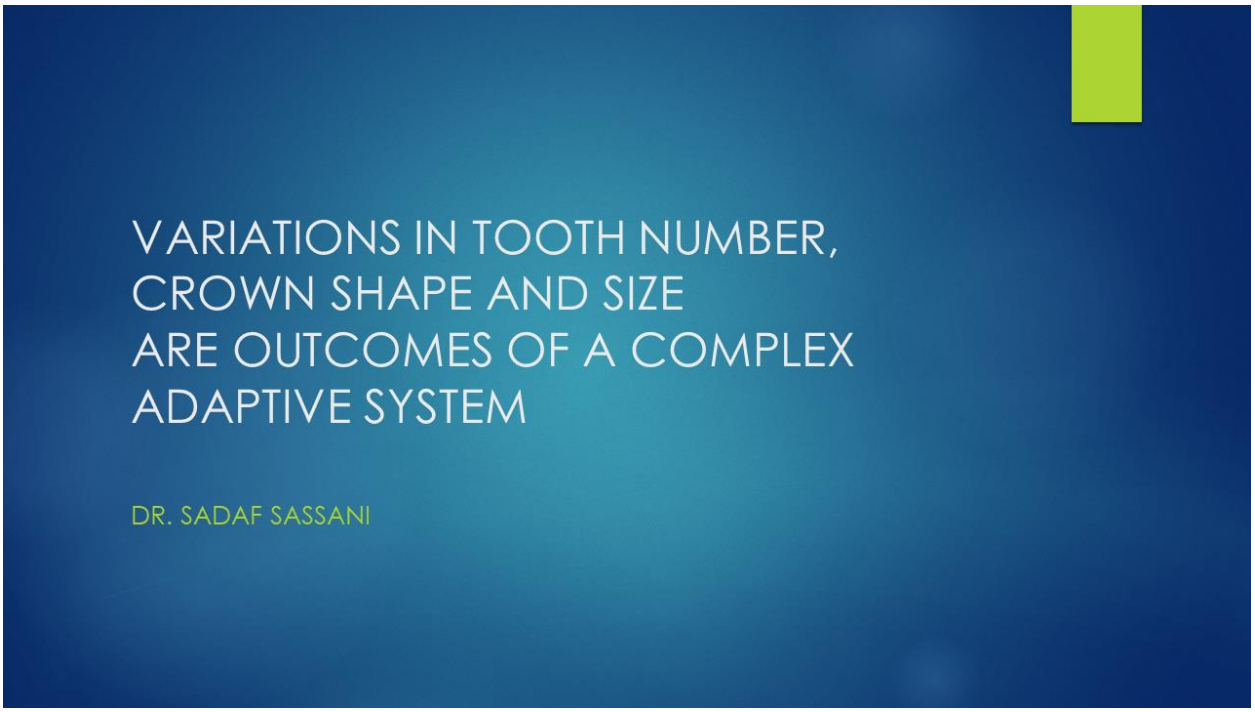
Sadaf Sassani, Dilan Patel, Mauro Farella, Maciej Henneberg, Sarbin Ranjitkar, Robin Yong, Stephen Swindells and Alan H. Brook. International Journal of Design & Nature and Ecodynamics 2017, *Variation in tooth crown size and shape are outcomes of the complex adaptive system associated with the number variation of hypodontia.*

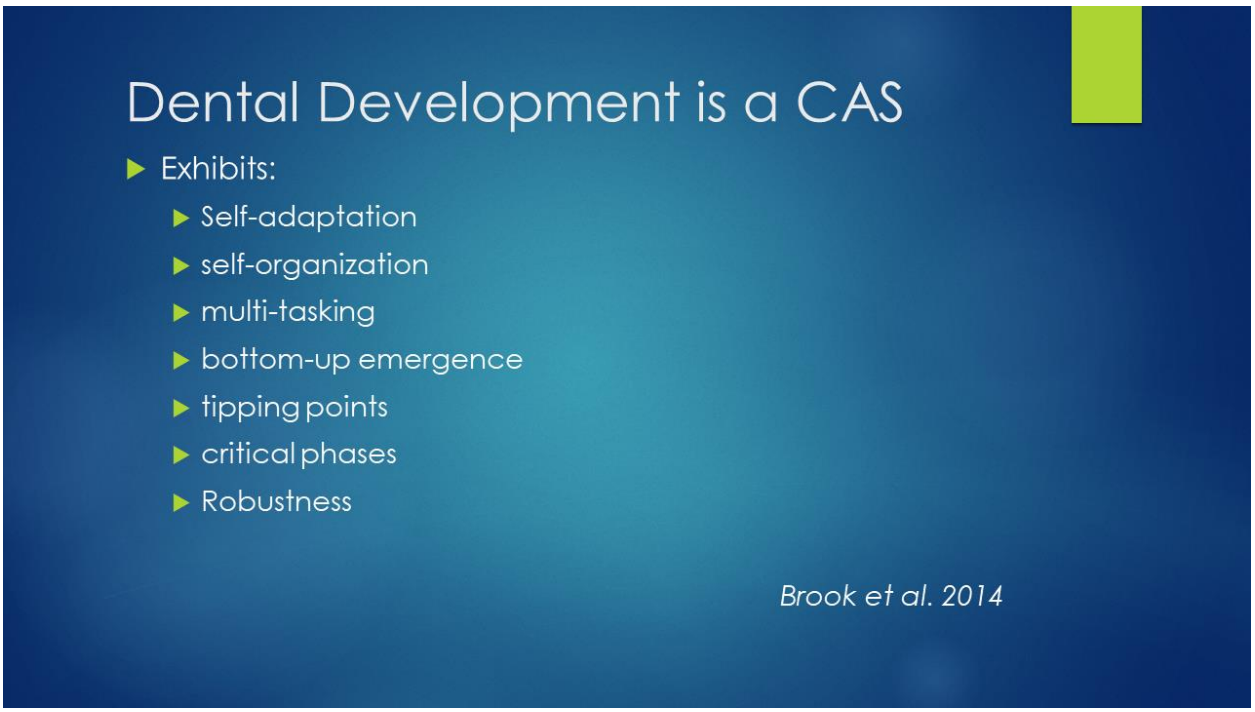
Dilan Patel, Sadaf Sassani, Mauro Farella, Sarbin Ranjitkar, Robin Yong, Stephen Swindells, and Alan H. Brook. International Journal of Design & Nature and Ecodynamics 2017, *Variation in dental arch morphology are outcomes of the complex adaptive system associated with the developmental variation of hypodontia.*

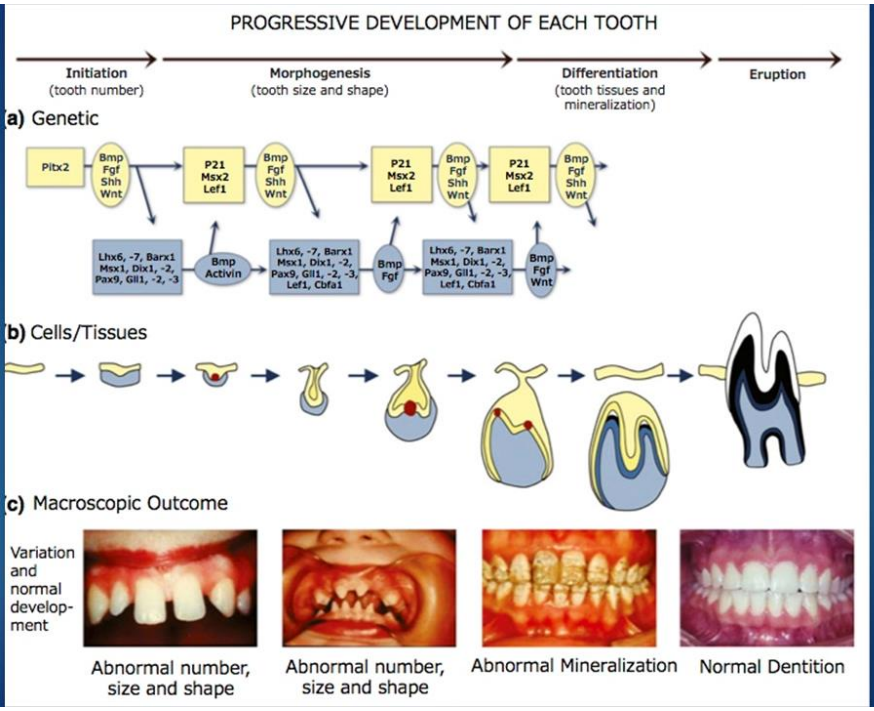
Leo Chen, Helen Liversidge, Ke Chen, Mauro Farella, Sadaf Sassani, Dilan Patel, Azza Al-Ani and Alan H. Brook. International Journal of Design & Nature and Ecodynamics 2017, *Delay in dental development and variations in root morphology are outcomes of the complex adaptive system associated with the numerical variation of hypodontia.*

10.2 Presentations

Complex Systems 2017 at the Balmar Lawn Hotel in New Forest, UK on the 25th of May.

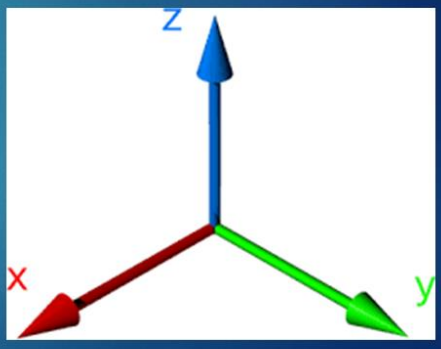






Dental Development is a CAS

- Molecular and cellular interactions produces macroscopic and phenotypic outcomes
- Spatiotemporal properties
- Development in three spatial dimensions: X, Y, Z



Dental development as a model for general development

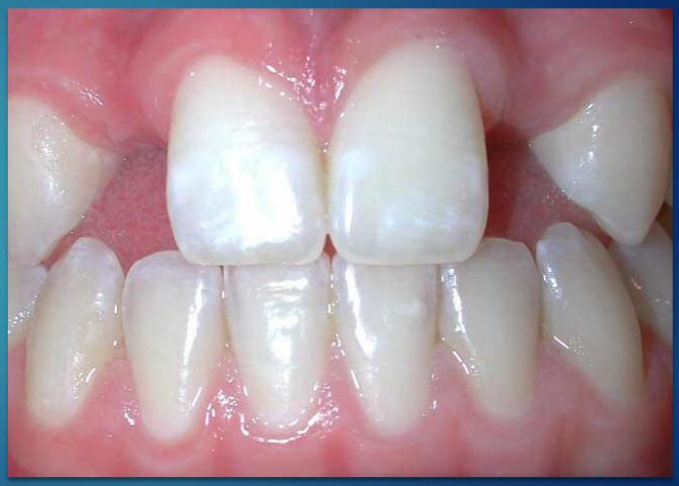
- Exploration in roles of genetic, epigenetic and environmental influences on the phenotype
- Accessibility: extensive dental records are possible and robust (archaeologically)

Hypodontia: Tooth size and shape

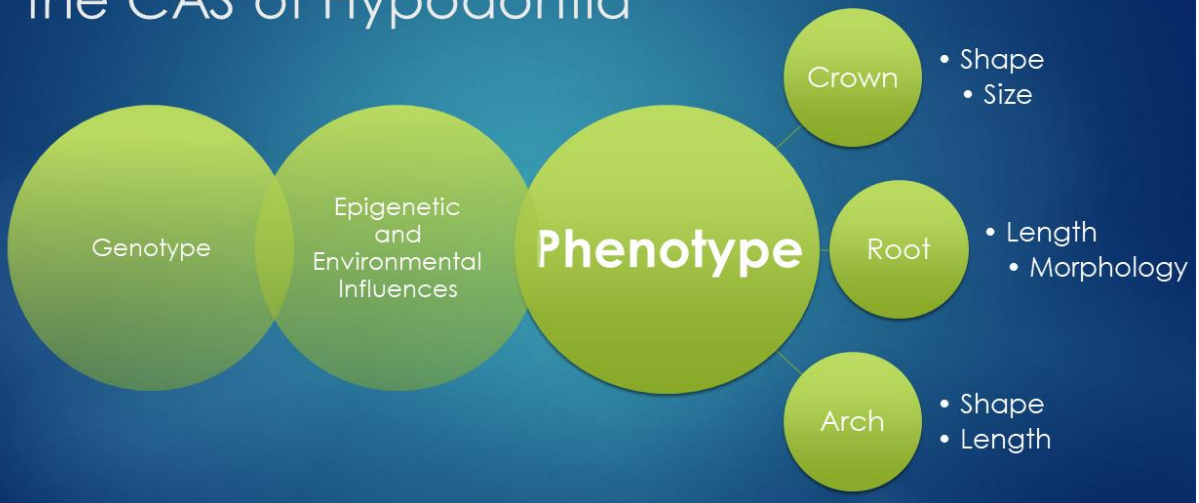
- The congenital absence of teeth: missing teeth
- The most prevalent human dental variation
- More frequently occurring in the adult dentition
- Female to male frequency is 3:2
- Ethnicity
- Remaining teeth: reduced size and less complex morphology

Clinical appearance:

- Hypodontia of the lateral incisors



International collaborative study on the CAS of Hypodontia



Aim:

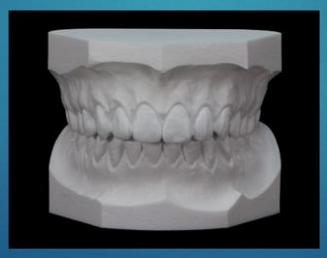
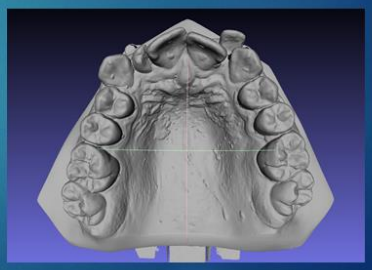
Is there a difference in crown size?

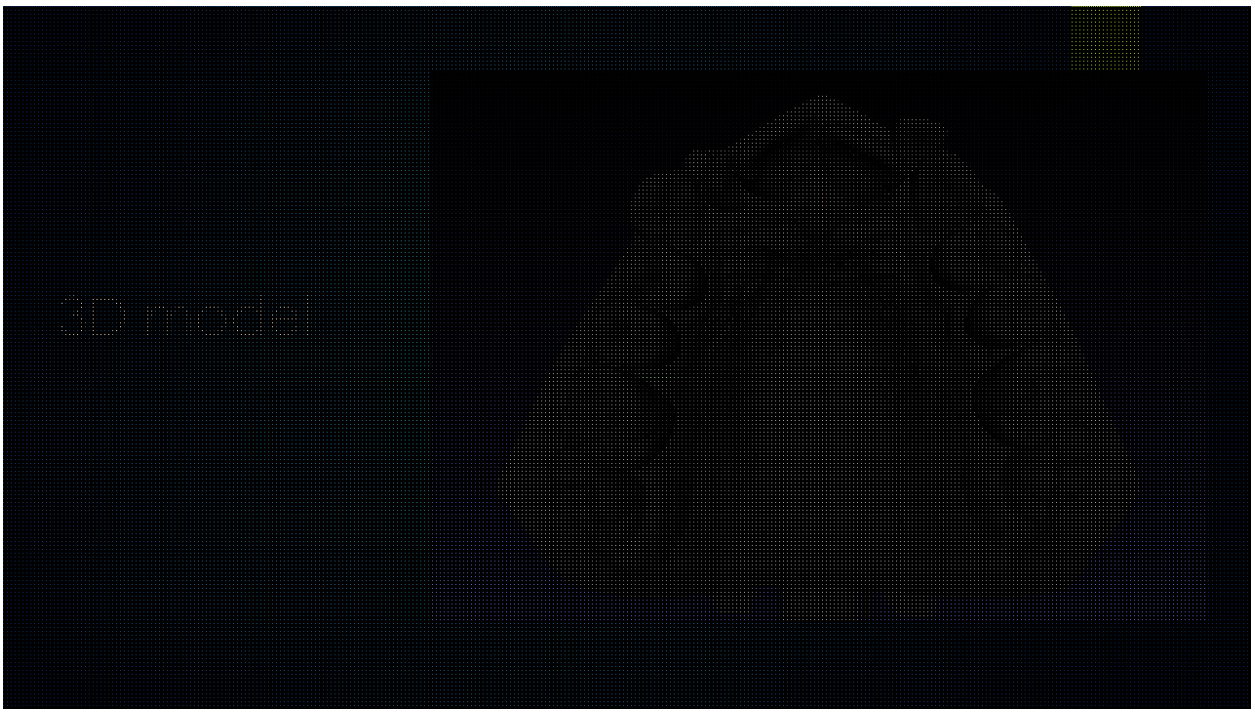
Hypodontia vs. matched control group

Methods

1. Study sample
   - 60 hypodontia patients and 60 controls
   - 30 males and 30 females in each group

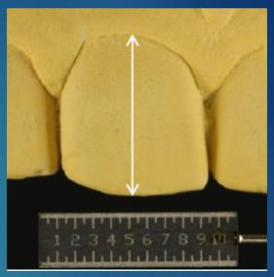
2. Study models
   - Dental impressions → stone casts → 3D scans/models

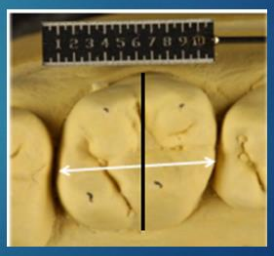






Measurements

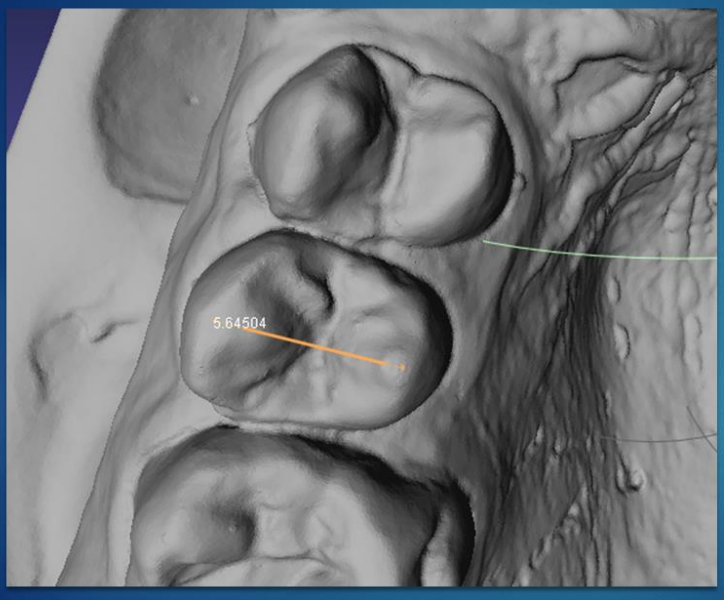
- Linear Measurements: point to point
  - Crown height
  - Mesio-distal
  - Bucco-lingual
- Perimeter
  - Occlusal (biting surface)
  - Insert image from dilan
- Surface area





Pilot study: Intra and inter-operator error

- Novel 3D measurements
- Intra and inter-operator error
- Intraclass correlation coefficient model (ICC)
- Intercuspal measurements



inter-cuspal measurement

Results:

Table 1: First operator intra-operator error differentials for the upper second premolar (mm).

First operator measurements of the upper second premolar	First operator measurements of the upper second premolar eight weeks later	Differentials
5.49	5.73	0.24
5.77	5.57	0.21
5.89	5.60	0.27
n/a	n/a	n/a
6.27	6.13	0.14
n/a	n/a	n/a
5.49	5.35	0.13
6.40	6.20	0.20
5.50	5.72	0.22
n/a	n/a	n/a
		Mean: 0.20

Results:

Table 4: First and second operator inter-operator error for the lower second premolar (mm).

First operator lower second premolar measurements	Second operator lower second premolar measurements	Differentials
5.96	5.63	0.33
4.09	3.77	0.32
5.88	5.38	0.50
n/a	n/a	n/a
5.29	5.13	0.16
4.31	3.33	0.98
5.18	3.97	1.21
5.46	5.21	0.24
5.10	4.20	0.90
n/a	n/a	n/a
		Mean: 0.58

Results

- Values for ICC range from 0 to 1
- Intra-operator reliability:
  - 0.82 (upper second premolar)
  - 0.85 (lower second premolar)
- Inter-operator reliability:
  - 0.96 (upper second premolar)
  - 0.69 (lower second premolar)

Discussion

- ICC values above .75: indicate good levels of reliability
- Obtained for all measures: except the lower second premolar
  - Why?
  - The lower second premolar has two cusps → operator interpretation

Conclusions:

- 3D models are more practical than traditional caliper measurements
- Potentially more reliable than traditional measurements
- 3D images allows almost infinite storage of models
  - Undisturbed, high quality, accurate resolution

Discussion project to date. Future?

- Initial study has provided the foundation for continued research
- Indication of reliability between dental operators
- Custom software for 3D analysis


Thank you.
Any questions?

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12. Appendix

Model 1: Linear mixed-effects model of MD Dimension versus Hypodontia/Control and sex interaction, adjusting forage, tooth_ID (combined) and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	MD_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2641
Number of Observations Not Used	1195

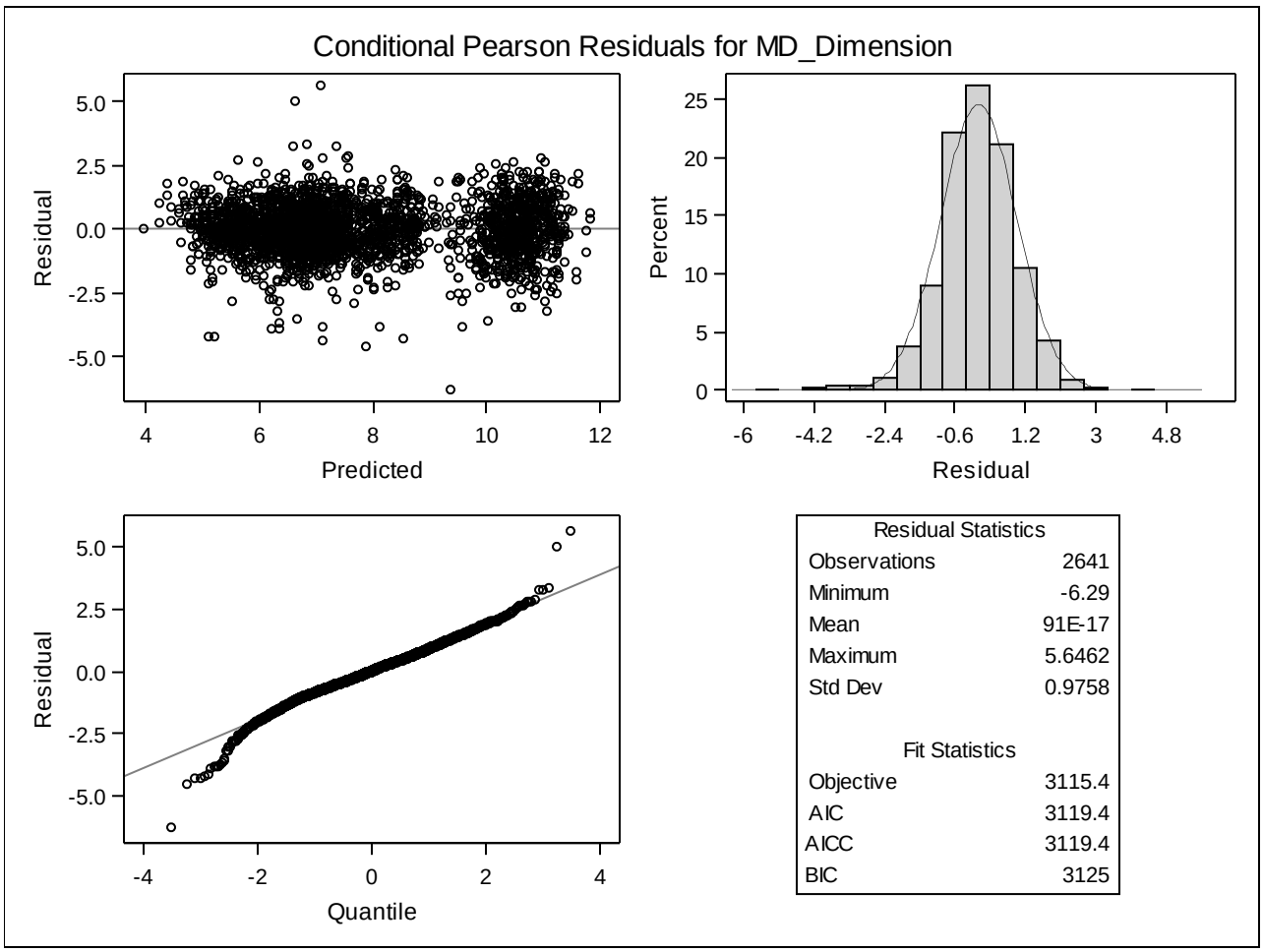
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.1215
Residual		0.1623

Fit Statistics	
-2 Res Log Likelihood	3115.4
AIC (Smaller is Better)	3119.4
AICC (Smaller is Better)	3119.4
BIC (Smaller is Better)	3125.0

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2506	20.17	<.0001
Sex	1	2506	7.69	0.0056
Sex*Group	1	2506	0.02	0.8764
Age_days	1	2506	2.19	0.1393
Tooth_IDc	13	2506	4024.63	<.0001
Ethnicity_Polynesian	1	2506	1.74	0.1868



Outcome MD dimension: Marginal means

Effect	*Sex*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Sex*Group	F	control	7.9660	0.08654	7.7963	8.1357
Sex*Group	F	hypodontia	7.6750	0.07905	7.5200	7.8300
Sex*Group	M	control	8.1611	0.08763	7.9892	8.3329
Sex*Group	M	hypodontia	7.8496	0.08400	7.6849	8.0143

Outcome MD dimension: Differences of marginal means: control versus hypodontia

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	F	hypodontia	0.2910	0.08920	0.1160	0.4659	0.0011
Sex*Group	M	control	M	hypodontia	0.3115	0.09862	0.1181	0.5048	0.0016

Outcome MD dimension: Differences of marginal means: Right teeth versus left teeth

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	M	control	-0.1951	0.09184	-0.3752	-0.01501	0.0337
Sex*Group	F	hypodontia	M	hypodontia	-0.1746	0.09557	-0.3620	0.01280	0.0678

Model 2. Linear mixed-effects model of BL Dimension versus Hypodontia/Control and Sex interaction, adjusting forage, tooth_ID (combined) and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	BL_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2605
Number of Observations Not Used	1231

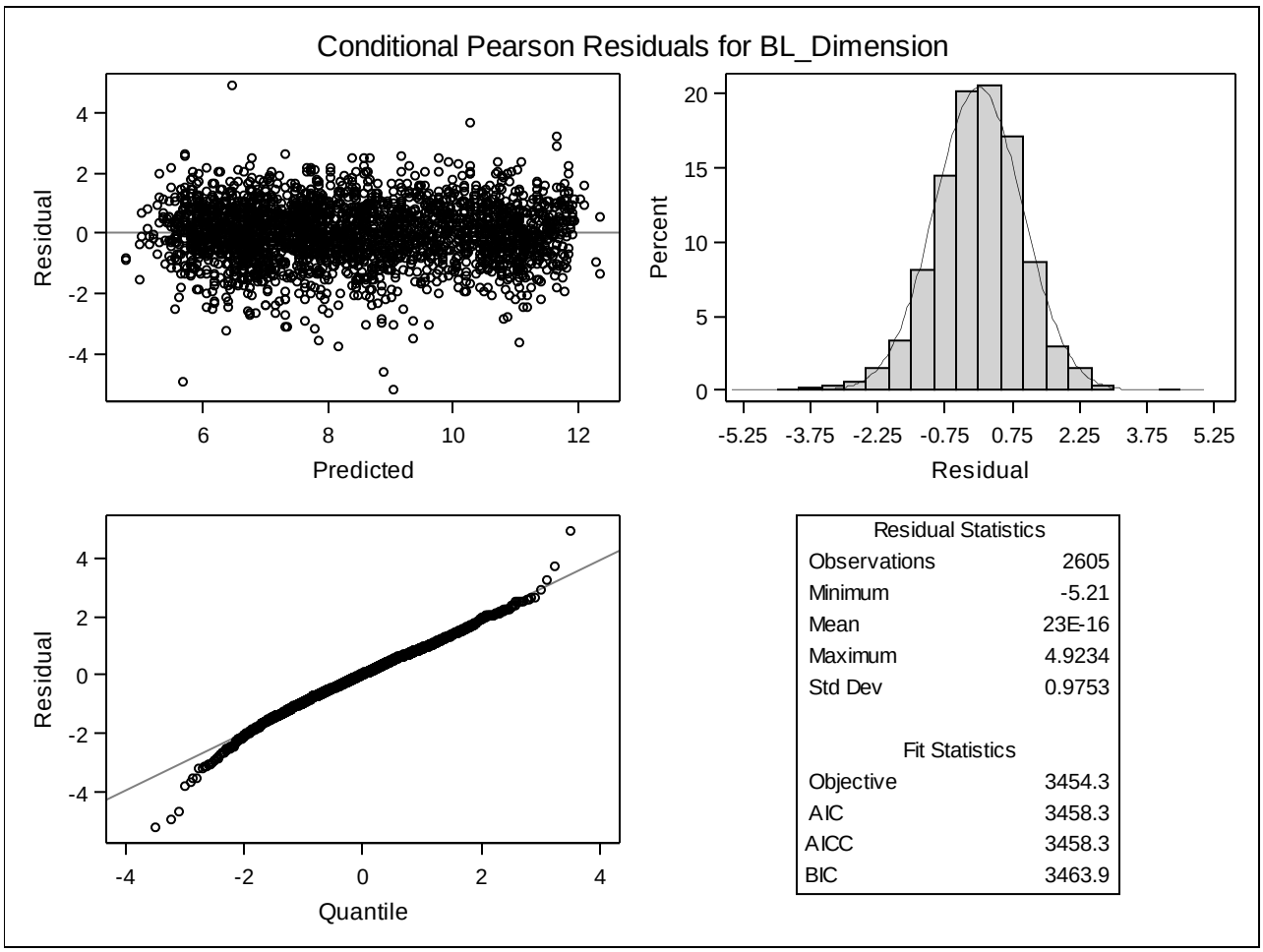
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.1756
Residual		0.1860

Fit Statistics	
-2 Res Log Likelihood	3454.3
AIC (Smaller is Better)	3458.3
AICC (Smaller is Better)	3458.3
BIC (Smaller is Better)	3463.9

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2470	16.53	<.0001
Sex	1	2470	5.08	0.0243
Sex*Group	1	2470	0.27	0.6010
Age_days	1	2470	4.75	0.0294
Tooth_IDc	13	2470	3326.20	<.0001
Ethnicity_Polynesian	1	2470	0.43	0.5130



Outcome BL dimension: Marginal means

Effect	*Sex*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Sex*Group	F	control	8.6294	0.1035	8.4264	8.8323
Sex*Group	F	hypodontia	8.3445	0.09443	8.1593	8.5296
Sex*Group	M	control	8.8501	0.1049	8.6445	9.0557
Sex*Group	M	hypodontia	8.4828	0.1005	8.2856	8.6799

Outcome BL dimension: Differences of marginal means: control versus hypodontia

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	F	hypodontia	0.2849	0.1066	0.07577	0.4940	0.0076
Sex*Group	M	control	M	hypodontia	0.3673	0.1179	0.1361	0.5985	0.0019

Outcome BL dimension: Differences of marginal means: Right teeth versus left teeth

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	M	control	-0.2207	0.1098	-0.4360	-0.00546	0.0445
Sex*Group	F	hypodontia	M	hypodontia	-0.1383	0.1142	-0.3624	0.08572	0.2261

Model 3. Linear mixed-effects model of CH Dimension versus Hypodontia/Control and Sex interaction, adjusting forage, tooth_ID (combined) and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	CH_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2624
Number of Observations Not Used	1212

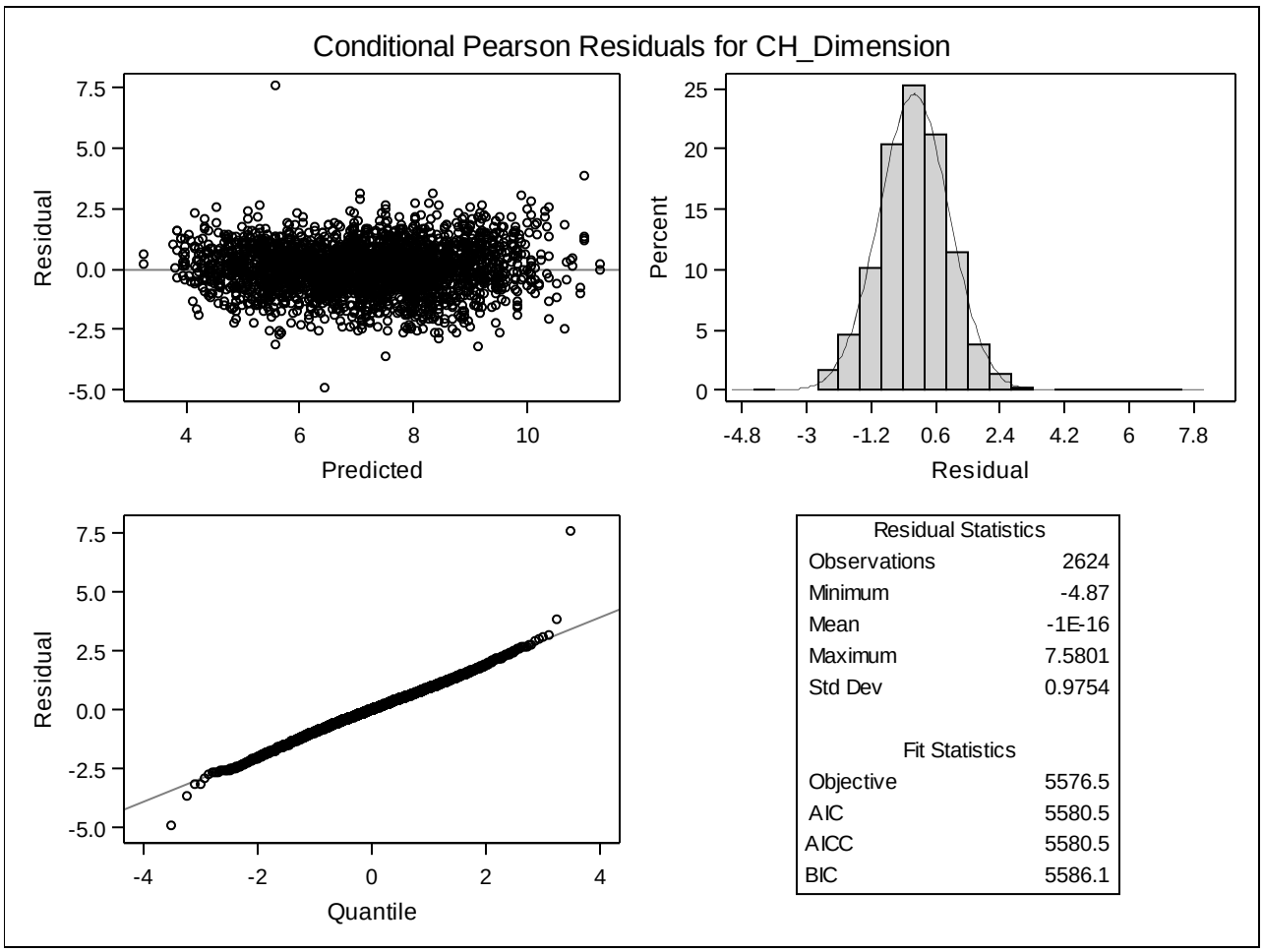
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.3983
Residual		0.4161

Fit Statistics	
-2 Res Log Likelihood	5576.5
AIC (Smaller is Better)	5580.5
AICC (Smaller is Better)	5580.5
BIC (Smaller is Better)	5586.1

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2489	8.77	0.0031
Sex	1	2489	4.59	0.0323
Sex*Group	1	2489	0.20	0.6519
Age_days	1	2489	31.42	<.0001
Tooth_IDc	13	2489	796.03	<.0001
Ethnicity_Polynesian	1	2489	0.00	0.9829



Outcome CH dimension: Marginal means

Effect	*Sex*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Sex*Group	F	control	6.9866	0.1558	6.6811	7.2922
Sex*Group	F	hypodontia	6.6827	0.1421	6.4040	6.9614
Sex*Group	M	control	7.2970	0.1578	6.9875	7.6065
Sex*Group	M	hypodontia	6.8861	0.1513	6.5894	7.1827

Outcome CH dimension: Differences of marginal means: control versus hypodontia

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	F	hypodontia	0.3040	0.1605	-0.01080	0.6187	0.0584
Sex*Group	M	control	M	hypodontia	0.4110	0.1774	0.06306	0.7589	0.0206

Outcome CH dimension: Differences of marginal means: Right teeth versus left teeth

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	M	control	-0.3104	0.1653	-0.6346	0.01376	0.0605
Sex*Group	F	hypodontia	M	hypodontia	-0.2034	0.1719	-0.5405	0.1337	0.2368

Model 4. Linear mixed-effects model of Modules versus Hypodontia/Control and Sex interaction, adjusting forage, tooth_ID (combined) and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	Modules
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2510
Number of Observations Not Used	1326

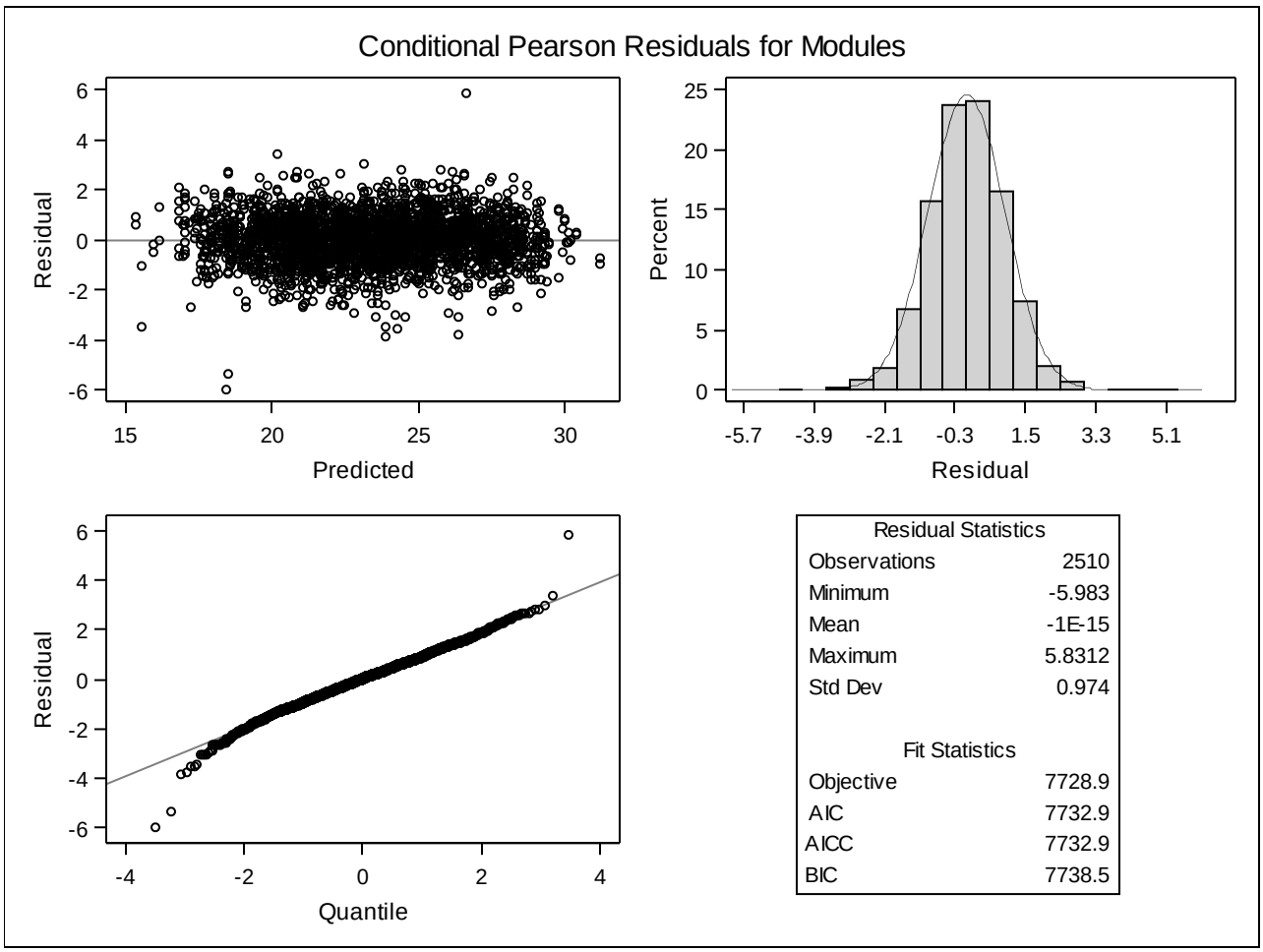
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	1.4726
Residual		1.0654

Fit Statistics	
-2 Res Log Likelihood	7728.9
AIC (Smaller is Better)	7732.9
AICC (Smaller is Better)	7732.9
BIC (Smaller is Better)	7738.5

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2375	17.69	<.0001
Sex	1	2375	8.14	0.0044
Sex*Group	1	2375	0.28	0.5944
Age_days	1	2375	16.17	<.0001
Tooth_IDc	13	2375	1316.44	<.0001
Ethnicity_Polynesian	1	2375	0.28	0.6000



Outcome Modules: Marginal means

Effect	*Sex*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Sex*Group	F	control	23.5675	0.2977	22.9837	24.1514
Sex*Group	F	hypodontia	22.7184	0.2714	22.1862	23.2506
Sex*Group	M	control	24.3419	0.3016	23.7505	24.9333
Sex*Group	M	hypodontia	23.2514	0.2891	22.6845	23.8184

Outcome Modules: Differences of marginal means: control versus hypodontia

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	F	hypodontia	0.8492	0.3066	0.2479	1.4505	0.0057
Sex*Group	M	control	M	hypodontia	1.0904	0.3390	0.4257	1.7552	0.0013

Outcome Modules: Differences of marginal means: Right teeth versus left teeth

Effect	*Sex*	*Group*	*_Sex*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Sex*Group	F	control	M	control	-0.7743	0.3158	-1.3937	-0.1550	0.0143
Sex*Group	F	hypodontia	M	hypodontia	-0.5331	0.3283	-1.1769	0.1108	0.1046

Model 5. Linear mixed-effects model of MD Dimension versus Hypodontia/Control and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	MD_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	50
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2641
Number of Observations Not Used	1195

Convergence criteria met.

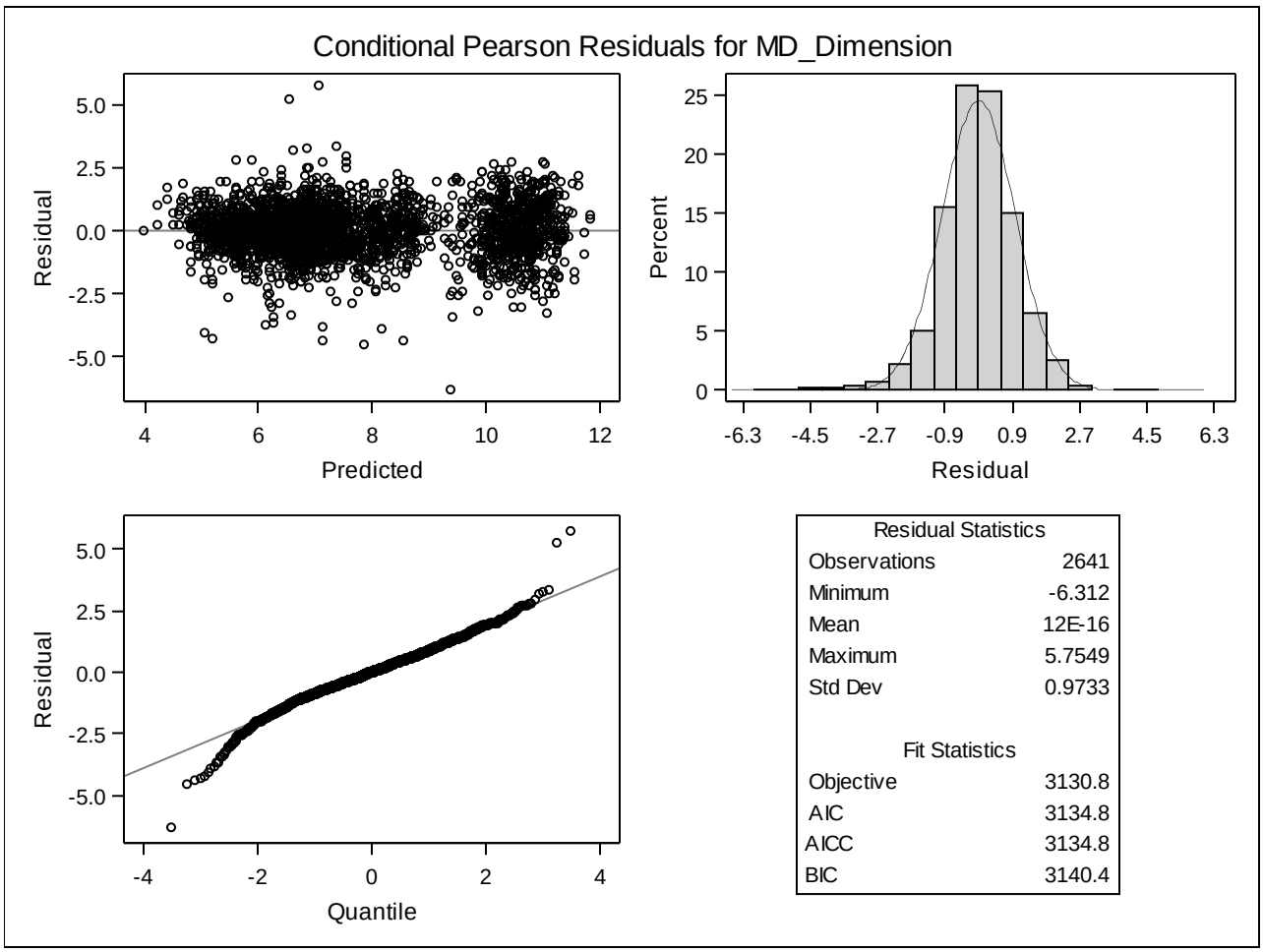
Covariance Parameter Estimates

Cov Parm	*Subject*	*Estimate*
Intercept	Patient_ID	0.1206
Residual		0.1613

Fit Statistics	
-2 Res Log Likelihood	3130.8
AIC (Smaller is Better)	3134.8
AICC (Smaller is Better)	3134.8
BIC (Smaller is Better)	3140.4

Type 3 Tests of Fixed Effects

Effect	*Num DF*	*Den DF*	*F Value*	*Pr > F*
Group	1	2494	23.61	<.0001
Tooth_IDc	13	2494	4012.14	<.0001
*Tooth_IDc*Group*	13	2494	2.20	0.0078
Age_days	1	2494	2.16	0.1420
Sex	1	2494	7.92	0.0049
Ethnicity_Polynesian	1	2494	1.79	0.1814



Outcome MD dimension: Marginal means

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	L1	control	5.5088	0.08122	5.3495	5.6681
Tooth_IDc*Group	L1	hypodontia	5.2315	0.07492	5.0846	5.3784
Tooth_IDc*Group	L2	control	5.9685	0.08148	5.8087	6.1282
Tooth_IDc*Group	L2	hypodontia	5.7585	0.07489	5.6117	5.9054
Tooth_IDc*Group	L3	control	6.9148	0.08211	6.7537	7.0758
Tooth_IDc*Group	L3	hypodontia	6.6698	0.07570	6.5214	6.8182
Tooth_IDc*Group	L4	control	7.2576	0.08199	7.0968	7.4184
Tooth_IDc*Group	L4	hypodontia	6.9689	0.07694	6.8180	7.1197
Tooth_IDc*Group	L5	control	7.3680	0.08390	7.2034	7.5325
Tooth_IDc*Group	L5	hypodontia	6.9629	0.09123	6.7839	7.1418
Tooth_IDc*Group	L6	control	11.0874	0.08148	10.9276	11.2472
Tooth_IDc*Group	L6	hypodontia	10.7978	0.07510	10.6505	10.9450
Tooth_IDc*Group	L7	control	10.8756	0.09428	10.6907	11.0605
Tooth_IDc*Group	L7	hypodontia	10.2583	0.09392	10.0742	10.4425

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	U1	control	8.6073	0.08122	8.4481	8.7666
Tooth_IDc*Group	U1	hypodontia	8.3713	0.07456	8.2251	8.5175
Tooth_IDc*Group	U2	control	6.7181	0.08156	6.5582	6.8780
Tooth_IDc*Group	U2	hypodontia	6.3071	0.08046	6.1493	6.4648
Tooth_IDc*Group	U3	control	7.9229	0.08476	7.7567	8.0891
Tooth_IDc*Group	U3	hypodontia	7.5753	0.07919	7.4201	7.7306
Tooth_IDc*Group	U4	control	7.0825	0.08211	6.9215	7.2436
Tooth_IDc*Group	U4	hypodontia	6.7175	0.07720	6.5661	6.8689
Tooth_IDc*Group	U5	control	6.7901	0.08397	6.6254	6.9548
Tooth_IDc*Group	U5	hypodontia	6.5920	0.08290	6.4295	6.7546
Tooth_IDc*Group	U6	control	10.6436	0.08142	10.4840	10.8033
Tooth_IDc*Group	U6	hypodontia	10.3733	0.07484	10.2266	10.5201
Tooth_IDc*Group	U7	control	10.2694	0.09242	10.0881	10.4506
Tooth_IDc*Group	U7	hypodontia	9.8825	0.09161	9.7029	10.0622

Outcome MD dimension: Differences of marginal means: control versus hypodontia

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L1	hypodontia	0.2773	0.08305	0.1144	0.4401	0.0009
Tooth_IDc*Group	L2	control	L2	hypodontia	0.2099	0.08334	0.04652	0.3734	0.0118
Tooth_IDc*Group	L3	control	L3	hypodontia	0.2449	0.08450	0.07924	0.4107	0.0038
Tooth_IDc*Group	L4	control	L4	hypodontia	0.2887	0.08561	0.1208	0.4566	0.0008
Tooth_IDc*Group	L5	control	L5	hypodontia	0.4051	0.1009	0.2072	0.6030	<.0001
Tooth_IDc*Group	L6	control	L6	hypodontia	0.2896	0.08339	0.1261	0.4531	0.0005
Tooth_IDc*Group	L7	control	L7	hypodontia	0.6172	0.1116	0.3985	0.8360	<.0001
Tooth_IDc*Group	U1	control	U1	hypodontia	0.2361	0.08274	0.07382	0.3983	0.0044
Tooth_IDc*Group	U2	control	U2	hypodontia	0.4110	0.08814	0.2382	0.5839	<.0001
Tooth_IDc*Group	U3	control	U3	hypodontia	0.3476	0.09016	0.1708	0.5244	0.0001
Tooth_IDc*Group	U4	control	U4	hypodontia	0.3650	0.08593	0.1965	0.5335	<.0001
Tooth_IDc*Group	U5	control	U5	hypodontia	0.1981	0.09307	0.01559	0.3806	0.0334
Tooth_IDc*Group	U6	control	U6	hypodontia	0.2703	0.08307	0.1074	0.4332	0.0012
Tooth_IDc*Group	U7	control	U7	hypodontia	0.3868	0.1079	0.1752	0.5985	0.0003

Outcome MD dimension: Differences of marginal means: tooth comparisons

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L2	control	-0.4596	0.05103	-0.5597	-0.3596	<.0001
Tooth_IDc*Group	L1	control	L3	control	-1.4059	0.05207	-1.5080	-1.3038	<.0001
Tooth_IDc*Group	L1	control	L4	control	-1.7488	0.05196	-1.8506	-1.6469	<.0001
Tooth_IDc*Group	L1	control	L5	control	-1.8591	0.05495	-1.9669	-1.7514	<.0001
Tooth_IDc*Group	L1	control	L6	control	-5.5786	0.05103	-5.6786	-5.4785	<.0001
Tooth_IDc*Group	L1	control	L7	control	-5.3668	0.06973	-5.5035	-5.2300	<.0001
Tooth_IDc*Group	L1	control	U1	control	-3.0985	0.05060	-3.1977	-2.9993	<.0001
Tooth_IDc*Group	L1	control	U2	control	-1.2093	0.05116	-1.3096	-1.1090	<.0001
Tooth_IDc*Group	L1	control	U3	control	-2.4141	0.05604	-2.5240	-2.3042	<.0001
Tooth_IDc*Group	L1	control	U4	control	-1.5737	0.05207	-1.6758	-1.4716	<.0001
Tooth_IDc*Group	L1	control	U5	control	-1.2813	0.05494	-1.3890	-1.1735	<.0001
Tooth_IDc*Group	L1	control	U6	control	-5.1348	0.05093	-5.2347	-5.0349	<.0001
Tooth_IDc*Group	L1	control	U7	control	-4.7606	0.06721	-4.8924	-4.6288	<.0001
Tooth_IDc*Group	L1	hypodontia	L2	hypodontia	-0.5270	0.05397	-0.6328	-0.4212	<.0001
Tooth_IDc*Group	L1	hypodontia	L3	hypodontia	-1.4383	0.05488	-1.5459	-1.3307	<.0001
Tooth_IDc*Group	L1	hypodontia	L4	hypodontia	-1.7373	0.05669	-1.8485	-1.6262	<.0001
Tooth_IDc*Group	L1	hypodontia	L5	hypodontia	-1.7313	0.07578	-1.8799	-1.5827	<.0001
Tooth_IDc*Group	L1	hypodontia	L6	hypodontia	-5.5662	0.05411	-5.6723	-5.4601	<.0001
Tooth_IDc*Group	L1	hypodontia	L7	hypodontia	-5.0268	0.07851	-5.1808	-4.8729	<.0001
Tooth_IDc*Group	L1	hypodontia	U1	hypodontia	-3.1398	0.05346	-3.2446	-3.0349	<.0001
Tooth_IDc*Group	L1	hypodontia	U2	hypodontia	-1.0755	0.06111	-1.1954	-0.9557	<.0001
Tooth_IDc*Group	L1	hypodontia	U3	hypodontia	-2.3438	0.05972	-2.4609	-2.2267	<.0001
Tooth_IDc*Group	L1	hypodontia	U4	hypodontia	-1.4860	0.05702	-1.5978	-1.3742	<.0001
Tooth_IDc*Group	L1	hypodontia	U5	hypodontia	-1.3605	0.06490	-1.4877	-1.2332	<.0001
Tooth_IDc*Group	L1	hypodontia	U6	hypodontia	-5.1418	0.05373	-5.2472	-5.0365	<.0001
Tooth_IDc*Group	L1	hypodontia	U7	hypodontia	-4.6510	0.07560	-4.7993	-4.5028	<.0001
Tooth_IDc*Group	L2	control	L3	control	-0.9463	0.05246	-1.0492	-0.8434	<.0001
Tooth_IDc*Group	L2	control	L4	control	-1.2891	0.05236	-1.3918	-1.1864	<.0001
Tooth_IDc*Group	L2	control	L5	control	-1.3995	0.05531	-1.5080	-1.2910	<.0001
Tooth_IDc*Group	L2	control	L6	control	-5.1189	0.05145	-5.2198	-5.0180	<.0001
Tooth_IDc*Group	L2	control	L7	control	-4.9071	0.07001	-5.0444	-4.7698	<.0001
Tooth_IDc*Group	L2	control	U1	control	-2.6389	0.05103	-2.7390	-2.5388	<.0001
Tooth_IDc*Group	L2	control	U2	control	-0.7496	0.05157	-0.8508	-0.6485	<.0001
Tooth_IDc*Group	L2	control	U3	control	-1.9545	0.05640	-2.0650	-1.8439	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L2	control	U4	control	-1.1141	0.05246	-1.2170	-1.0112	<.0001
Tooth_IDc*Group	L2	control	U5	control	-0.8216	0.05533	-0.9301	-0.7131	<.0001
Tooth_IDc*Group	L2	control	U6	control	-4.6752	0.05136	-4.7759	-4.5744	<.0001
Tooth_IDc*Group	L2	control	U7	control	-4.3009	0.06750	-4.4333	-4.1686	<.0001
Tooth_IDc*Group	L2	hypodontia	L3	hypodontia	-0.9113	0.05488	-1.0189	-0.8037	<.0001
Tooth_IDc*Group	L2	hypodontia	L4	hypodontia	-1.2104	0.05668	-1.3215	-1.0992	<.0001
Tooth_IDc*Group	L2	hypodontia	L5	hypodontia	-1.2043	0.07564	-1.3527	-1.0560	<.0001
Tooth_IDc*Group	L2	hypodontia	L6	hypodontia	-5.0392	0.05414	-5.1454	-4.9331	<.0001
Tooth_IDc*Group	L2	hypodontia	L7	hypodontia	-4.4998	0.07847	-4.6537	-4.3460	<.0001
Tooth_IDc*Group	L2	hypodontia	U1	hypodontia	-2.6128	0.05349	-2.7177	-2.5079	<.0001
Tooth_IDc*Group	L2	hypodontia	U2	hypodontia	-0.5486	0.06116	-0.6685	-0.4286	<.0001
Tooth_IDc*Group	L2	hypodontia	U3	hypodontia	-1.8168	0.05971	-1.9339	-1.6997	<.0001
Tooth_IDc*Group	L2	hypodontia	U4	hypodontia	-0.9590	0.05706	-1.0709	-0.8471	<.0001
Tooth_IDc*Group	L2	hypodontia	U5	hypodontia	-0.8335	0.06487	-0.9607	-0.7063	<.0001
Tooth_IDc*Group	L2	hypodontia	U6	hypodontia	-4.6148	0.05376	-4.7202	-4.5094	<.0001
Tooth_IDc*Group	L2	hypodontia	U7	hypodontia	-4.1240	0.07556	-4.2722	-3.9758	<.0001
Tooth_IDc*Group	L3	control	L4	control	-0.3428	0.05310	-0.4469	-0.2387	<.0001
Tooth_IDc*Group	L3	control	L5	control	-0.4532	0.05600	-0.5630	-0.3434	<.0001
Tooth_IDc*Group	L3	control	L6	control	-4.1726	0.05246	-4.2755	-4.0698	<.0001
Tooth_IDc*Group	L3	control	L7	control	-3.9608	0.07053	-4.0991	-3.8225	<.0001
Tooth_IDc*Group	L3	control	U1	control	-1.6926	0.05207	-1.7947	-1.5905	<.0001
Tooth_IDc*Group	L3	control	U2	control	0.1967	0.05259	0.09354	0.2998	0.0002
Tooth_IDc*Group	L3	control	U3	control	-1.0082	0.05705	-1.1200	-0.8963	<.0001
Tooth_IDc*Group	L3	control	U4	control	-0.1678	0.05321	-0.2721	-0.06344	0.0016
Tooth_IDc*Group	L3	control	U5	control	0.1247	0.05601	0.01482	0.2345	0.0261
Tooth_IDc*Group	L3	control	U6	control	-3.7289	0.05240	-3.8316	-3.6261	<.0001
Tooth_IDc*Group	L3	control	U7	control	-3.3546	0.06808	-3.4881	-3.2211	<.0001
Tooth_IDc*Group	L3	hypodontia	L4	hypodontia	-0.2991	0.05721	-0.4112	-0.1869	<.0001
Tooth_IDc*Group	L3	hypodontia	L5	hypodontia	-0.2930	0.07610	-0.4423	-0.1438	0.0001
Tooth_IDc*Group	L3	hypodontia	L6	hypodontia	-4.1280	0.05504	-4.2359	-4.0200	<.0001
Tooth_IDc*Group	L3	hypodontia	L7	hypodontia	-3.5885	0.07897	-3.7434	-3.4337	<.0001
Tooth_IDc*Group	L3	hypodontia	U1	hypodontia	-1.7015	0.05439	-1.8081	-1.5948	<.0001
Tooth_IDc*Group	L3	hypodontia	U2	hypodontia	0.3627	0.06192	0.2413	0.4842	<.0001
Tooth_IDc*Group	L3	hypodontia	U3	hypodontia	-0.9055	0.06017	-1.0235	-0.7875	<.0001
Tooth_IDc*Group	L3	hypodontia	U4	hypodontia	-0.04773	0.05758	-0.1606	0.06517	0.4072
Tooth_IDc*Group	L3	hypodontia	U5	hypodontia	0.07779	0.06534	-0.05034	0.2059	0.2339

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L3	hypodontia	U6	hypodontia	-3.7035	0.05454	-3.8105	-3.5966	<.0001
Tooth_IDc*Group	L3	hypodontia	U7	hypodontia	-3.2127	0.07591	-3.3616	-3.0639	<.0001
Tooth_IDc*Group	L4	control	L5	control	-0.1104	0.05590	-0.2200	-0.00077	0.0484
Tooth_IDc*Group	L4	control	L6	control	-3.8298	0.05236	-3.9325	-3.7272	<.0001
Tooth_IDc*Group	L4	control	L7	control	-3.6180	0.07047	-3.7562	-3.4798	<.0001
Tooth_IDc*Group	L4	control	U1	control	-1.3498	0.05196	-1.4517	-1.2479	<.0001
Tooth_IDc*Group	L4	control	U2	control	0.5395	0.05248	0.4366	0.6424	<.0001
Tooth_IDc*Group	L4	control	U3	control	-0.6653	0.05696	-0.7770	-0.5537	<.0001
Tooth_IDc*Group	L4	control	U4	control	0.1750	0.05311	0.07089	0.2792	0.0010
Tooth_IDc*Group	L4	control	U5	control	0.4675	0.05590	0.3579	0.5771	<.0001
Tooth_IDc*Group	L4	control	U6	control	-3.3860	0.05229	-3.4886	-3.2835	<.0001
Tooth_IDc*Group	L4	control	U7	control	-3.0118	0.06801	-3.1452	-2.8785	<.0001
Tooth_IDc*Group	L4	hypodontia	L5	hypodontia	0.006021	0.07702	-0.1450	0.1571	0.9377
Tooth_IDc*Group	L4	hypodontia	L6	hypodontia	-3.8289	0.05684	-3.9404	-3.7174	<.0001
Tooth_IDc*Group	L4	hypodontia	L7	hypodontia	-3.2895	0.08009	-3.4465	-3.1324	<.0001
Tooth_IDc*Group	L4	hypodontia	U1	hypodontia	-1.4024	0.05620	-1.5126	-1.2922	<.0001
Tooth_IDc*Group	L4	hypodontia	U2	hypodontia	0.6618	0.06362	0.5370	0.7866	<.0001
Tooth_IDc*Group	L4	hypodontia	U3	hypodontia	-0.6065	0.06170	-0.7275	-0.4855	<.0001
Tooth_IDc*Group	L4	hypodontia	U4	hypodontia	0.2513	0.05912	0.1354	0.3673	<.0001
Tooth_IDc*Group	L4	hypodontia	U5	hypodontia	0.3769	0.06664	0.2462	0.5075	<.0001
Tooth_IDc*Group	L4	hypodontia	U6	hypodontia	-3.4045	0.05632	-3.5149	-3.2940	<.0001
Tooth_IDc*Group	L4	hypodontia	U7	hypodontia	-2.9137	0.07727	-3.0652	-2.7621	<.0001
Tooth_IDc*Group	L5	control	L6	control	-3.7194	0.05531	-3.8279	-3.6110	<.0001
Tooth_IDc*Group	L5	control	L7	control	-3.5076	0.07245	-3.6497	-3.3655	<.0001
Tooth_IDc*Group	L5	control	U1	control	-1.2394	0.05495	-1.3471	-1.1316	<.0001
Tooth_IDc*Group	L5	control	U2	control	0.6499	0.05542	0.5412	0.7585	<.0001
Tooth_IDc*Group	L5	control	U3	control	-0.5550	0.05966	-0.6719	-0.4380	<.0001
Tooth_IDc*Group	L5	control	U4	control	0.2854	0.05600	0.1756	0.3952	<.0001
Tooth_IDc*Group	L5	control	U5	control	0.5779	0.05844	0.4633	0.6924	<.0001
Tooth_IDc*Group	L5	control	U6	control	-3.2757	0.05527	-3.3840	-3.1673	<.0001
Tooth_IDc*Group	L5	control	U7	control	-2.9014	0.06999	-3.0387	-2.7642	<.0001
Tooth_IDc*Group	L5	hypodontia	L6	hypodontia	-3.8349	0.07578	-3.9835	-3.6863	<.0001
Tooth_IDc*Group	L5	hypodontia	L7	hypodontia	-3.2955	0.09382	-3.4795	-3.1115	<.0001
Tooth_IDc*Group	L5	hypodontia	U1	hypodontia	-1.4084	0.07530	-1.5561	-1.2608	<.0001
Tooth_IDc*Group	L5	hypodontia	U2	hypodontia	0.6558	0.08146	0.4961	0.8155	<.0001
Tooth_IDc*Group	L5	hypodontia	U3	hypodontia	-0.6125	0.07956	-0.7685	-0.4565	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L5	hypodontia	U4	hypodontia	0.2453	0.07740	0.09354	0.3971	0.0015
Tooth_IDc*Group	L5	hypodontia	U5	hypodontia	0.3708	0.08290	0.2083	0.5334	<.0001
Tooth_IDc*Group	L5	hypodontia	U6	hypodontia	-3.4105	0.07537	-3.5583	-3.2627	<.0001
Tooth_IDc*Group	L5	hypodontia	U7	hypodontia	-2.9197	0.09140	-3.0989	-2.7405	<.0001
Tooth_IDc*Group	L6	control	L7	control	0.2118	0.07002	0.07452	0.3491	0.0025
Tooth_IDc*Group	L6	control	U1	control	2.4800	0.05103	2.3800	2.5801	<.0001
Tooth_IDc*Group	L6	control	U2	control	4.3693	0.05157	4.2682	4.4704	<.0001
Tooth_IDc*Group	L6	control	U3	control	3.1645	0.05642	3.0538	3.2751	<.0001
Tooth_IDc*Group	L6	control	U4	control	4.0048	0.05246	3.9020	4.1077	<.0001
Tooth_IDc*Group	L6	control	U5	control	4.2973	0.05530	4.1888	4.4057	<.0001
Tooth_IDc*Group	L6	control	U6	control	0.4438	0.05136	0.3431	0.5445	<.0001
Tooth_IDc*Group	L6	control	U7	control	0.8180	0.06749	0.6857	0.9503	<.0001
Tooth_IDc*Group	L6	hypodontia	L7	hypodontia	0.5394	0.07858	0.3853	0.6935	<.0001
Tooth_IDc*Group	L6	hypodontia	U1	hypodontia	2.4265	0.05362	2.3213	2.5316	<.0001
Tooth_IDc*Group	L6	hypodontia	U2	hypodontia	4.4907	0.06126	4.3706	4.6108	<.0001
Tooth_IDc*Group	L6	hypodontia	U3	hypodontia	3.2224	0.05991	3.1050	3.3399	<.0001
Tooth_IDc*Group	L6	hypodontia	U4	hypodontia	4.0802	0.05720	3.9681	4.1924	<.0001
Tooth_IDc*Group	L6	hypodontia	U5	hypodontia	4.2057	0.06508	4.0781	4.3334	<.0001
Tooth_IDc*Group	L6	hypodontia	U6	hypodontia	0.4244	0.05388	0.3188	0.5301	<.0001
Tooth_IDc*Group	L6	hypodontia	U7	hypodontia	0.9152	0.07564	0.7669	1.0635	<.0001
Tooth_IDc*Group	L7	control	U1	control	2.2682	0.06973	2.1315	2.4050	<.0001
Tooth_IDc*Group	L7	control	U2	control	4.1575	0.07009	4.0200	4.2949	<.0001
Tooth_IDc*Group	L7	control	U3	control	2.9527	0.07321	2.8091	3.0962	<.0001
Tooth_IDc*Group	L7	control	U4	control	3.7930	0.07053	3.6547	3.9313	<.0001
Tooth_IDc*Group	L7	control	U5	control	4.0855	0.07246	3.9434	4.2276	<.0001
Tooth_IDc*Group	L7	control	U6	control	0.2320	0.06994	0.09482	0.3691	0.0009
Tooth_IDc*Group	L7	control	U7	control	0.6062	0.08154	0.4463	0.7661	<.0001
Tooth_IDc*Group	L7	hypodontia	U1	hypodontia	1.8871	0.07813	1.7339	2.0403	<.0001
Tooth_IDc*Group	L7	hypodontia	U2	hypodontia	3.9513	0.08346	3.7876	4.1149	<.0001
Tooth_IDc*Group	L7	hypodontia	U3	hypodontia	2.6830	0.08210	2.5220	2.8440	<.0001
Tooth_IDc*Group	L7	hypodontia	U4	hypodontia	3.5408	0.08033	3.3833	3.6983	<.0001
Tooth_IDc*Group	L7	hypodontia	U5	hypodontia	3.6663	0.08558	3.4985	3.8341	<.0001
Tooth_IDc*Group	L7	hypodontia	U6	hypodontia	-0.1150	0.07819	-0.2683	0.03834	0.1415
Tooth_IDc*Group	L7	hypodontia	U7	hypodontia	0.3758	0.09355	0.1924	0.5592	<.0001
Tooth_IDc*Group	U1	control	U2	control	1.8892	0.05116	1.7889	1.9896	<.0001
Tooth_IDc*Group	U1	control	U3	control	0.6844	0.05604	0.5745	0.7943	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	U1	control	U4	control	1.5248	0.05207	1.4227	1.6269	<.0001
Tooth_IDc*Group	U1	control	U5	control	1.8172	0.05494	1.7095	1.9250	<.0001
Tooth_IDc*Group	U1	control	U6	control	-2.0363	0.05093	-2.1361	-1.9364	<.0001
Tooth_IDc*Group	U1	control	U7	control	-1.6620	0.06721	-1.7938	-1.5302	<.0001
Tooth_IDc*Group	U1	hypodontia	U2	hypodontia	2.0642	0.06069	1.9452	2.1832	<.0001
Tooth_IDc*Group	U1	hypodontia	U3	hypodontia	0.7959	0.05927	0.6797	0.9122	<.0001
Tooth_IDc*Group	U1	hypodontia	U4	hypodontia	1.6537	0.05656	1.5428	1.7646	<.0001
Tooth_IDc*Group	U1	hypodontia	U5	hypodontia	1.7793	0.06448	1.6528	1.9057	<.0001
Tooth_IDc*Group	U1	hypodontia	U6	hypodontia	-2.0021	0.05323	-2.1064	-1.8977	<.0001
Tooth_IDc*Group	U1	hypodontia	U7	hypodontia	-1.5113	0.07522	-1.6587	-1.3638	<.0001
Tooth_IDc*Group	U2	control	U3	control	-1.2048	0.05646	-1.3155	-1.0941	<.0001
Tooth_IDc*Group	U2	control	U4	control	-0.3644	0.05259	-0.4676	-0.2613	<.0001
Tooth_IDc*Group	U2	control	U5	control	-0.07200	0.05543	-0.1807	0.03668	0.1940
Tooth_IDc*Group	U2	control	U6	control	-3.9255	0.05148	-4.0265	-3.8246	<.0001
Tooth_IDc*Group	U2	control	U7	control	-3.5513	0.06756	-3.6838	-3.4188	<.0001
Tooth_IDc*Group	U2	hypodontia	U3	hypodontia	-1.2683	0.06623	-1.3981	-1.1384	<.0001
Tooth_IDc*Group	U2	hypodontia	U4	hypodontia	-0.4105	0.06381	-0.5356	-0.2853	<.0001
Tooth_IDc*Group	U2	hypodontia	U5	hypodontia	-0.2849	0.07125	-0.4247	-0.1452	<.0001
Tooth_IDc*Group	U2	hypodontia	U6	hypodontia	-4.0663	0.06089	-4.1857	-3.9469	<.0001
Tooth_IDc*Group	U2	hypodontia	U7	hypodontia	-3.5755	0.08094	-3.7342	-3.4167	<.0001
Tooth_IDc*Group	U3	control	U4	control	0.8404	0.05708	0.7284	0.9523	<.0001
Tooth_IDc*Group	U3	control	U5	control	1.1328	0.05968	1.0158	1.2499	<.0001
Tooth_IDc*Group	U3	control	U6	control	-2.7207	0.05636	-2.8312	-2.6102	<.0001
Tooth_IDc*Group	U3	control	U7	control	-2.3465	0.07074	-2.4852	-2.2077	<.0001
Tooth_IDc*Group	U3	hypodontia	U4	hypodontia	0.8578	0.06194	0.7363	0.9793	<.0001
Tooth_IDc*Group	U3	hypodontia	U5	hypodontia	0.9833	0.06913	0.8478	1.1189	<.0001
Tooth_IDc*Group	U3	hypodontia	U6	hypodontia	-2.7980	0.05938	-2.9144	-2.6816	<.0001
Tooth_IDc*Group	U3	hypodontia	U7	hypodontia	-2.3072	0.07924	-2.4626	-2.1518	<.0001
Tooth_IDc*Group	U4	control	U5	control	0.2924	0.05598	0.1827	0.4022	<.0001
Tooth_IDc*Group	U4	control	U6	control	-3.5611	0.05240	-3.6638	-3.4583	<.0001
Tooth_IDc*Group	U4	control	U7	control	-3.1868	0.06807	-3.3203	-3.0533	<.0001
Tooth_IDc*Group	U4	hypodontia	U5	hypodontia	0.1255	0.06684	-0.00554	0.2566	0.0605
Tooth_IDc*Group	U4	hypodontia	U6	hypodontia	-3.6558	0.05668	-3.7669	-3.5447	<.0001
Tooth_IDc*Group	U4	hypodontia	U7	hypodontia	-3.1650	0.07733	-3.3166	-3.0134	<.0001
Tooth_IDc*Group	U5	control	U6	control	-3.8535	0.05526	-3.9619	-3.7452	<.0001
Tooth_IDc*Group	U5	control	U7	control	-3.4793	0.07005	-3.6166	-3.3419	<.0001

Effect	Tooth_IDc	Group	_Tooth_IDc	_Group	Estimate	StdErr	Lower	Upper	Probt
Tooth_IDc*Group	U5	hypodontia	U6	hypodontia	-3.7813	0.06458	-3.9080	-3.6547	<.0001
Tooth_IDc*Group	U5	hypodontia	U7	hypodontia	-3.2905	0.08310	-3.4535	-3.1276	<.0001
Tooth_IDc*Group	U6	control	U7	control	0.3742	0.06742	0.2420	0.5064	<.0001
Tooth_IDc*Group	U6	hypodontia	U7	hypodontia	0.4908	0.07528	0.3432	0.6384	<.0001

Model 6. Linear mixed-effects model of BL Dimension versus Hypodontia/Control and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	BL_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	Levels	Values
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	50
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2605
Number of Observations Not Used	1231

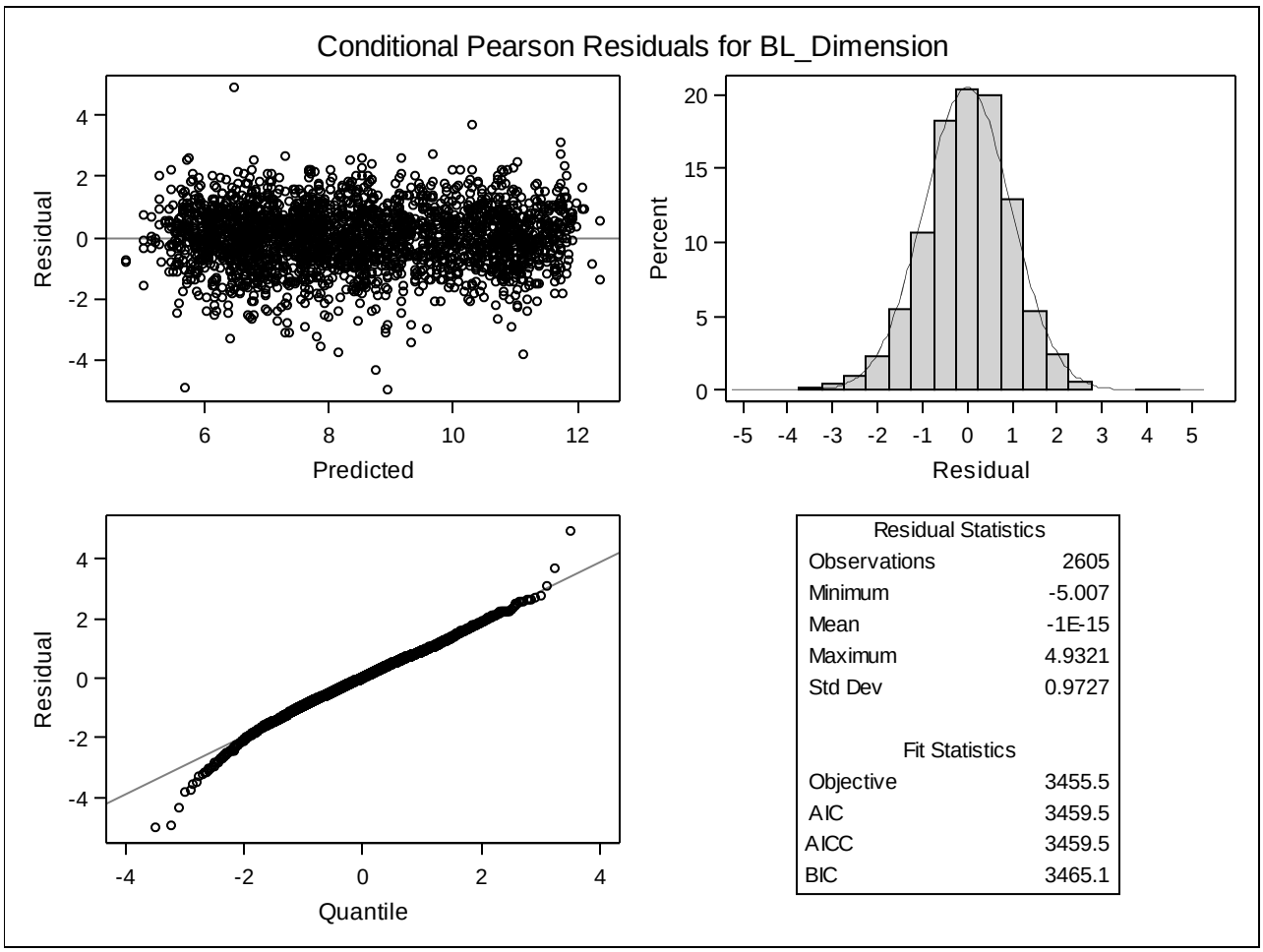
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.1752
Residual		0.1838

Fit Statistics	
-2 Res Log Likelihood	3455.5
AIC (Smaller is Better)	3459.5
AICC (Smaller is Better)	3459.5
BIC (Smaller is Better)	3465.1

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2457	16.27	<.0001
Tooth_IDc	13	2457	3302.50	<.0001
Tooth_IDc*Group	13	2457	3.20	<.0001
Age_days	1	2457	4.80	0.0286
Sex	1	2457	5.11	0.0239
Ethnicity_Polynesian	1	2457	0.46	0.4990



Outcome BL dimension: Marginal means

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	L1	control	6.2256	0.09595	6.0375	6.4138
Tooth_IDc*Group	L1	hypodontia	5.8857	0.08812	5.7129	6.0585
Tooth_IDc*Group	L2	control	6.5008	0.09615	6.3122	6.6893
Tooth_IDc*Group	L2	hypodontia	6.3141	0.08878	6.1400	6.4882
Tooth_IDc*Group	L3	control	7.5114	0.09780	7.3196	7.7031
Tooth_IDc*Group	L3	hypodontia	7.1825	0.08907	7.0078	7.3571
Tooth_IDc*Group	L4	control	8.1531	0.09660	7.9637	8.3425
Tooth_IDc*Group	L4	hypodontia	7.8831	0.08950	7.7076	8.0587
Tooth_IDc*Group	L5	control	8.7432	0.09834	8.5503	8.9360
Tooth_IDc*Group	L5	hypodontia	8.4962	0.1032	8.2938	8.6986
Tooth_IDc*Group	L6	control	10.7633	0.09587	10.5753	10.9513
Tooth_IDc*Group	L6	hypodontia	10.5938	0.08779	10.4217	10.7660
Tooth_IDc*Group	L7	control	10.5800	0.1048	10.3744	10.7855

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	L7	hypodontia	10.1973	0.1013	9.9986	10.3959
Tooth_IDc*Group	U1	control	7.4151	0.09575	7.2273	7.6028
Tooth_IDc*Group	U1	hypodontia	7.0361	0.08777	6.8640	7.2082
Tooth_IDc*Group	U2	control	6.4430	0.09595	6.2548	6.6311
Tooth_IDc*Group	U2	hypodontia	6.1611	0.09440	5.9760	6.3463
Tooth_IDc*Group	U3	control	8.2286	0.09961	8.0333	8.4239
Tooth_IDc*Group	U3	hypodontia	7.9301	0.09274	7.7483	8.1120
Tooth_IDc*Group	U4	control	9.4616	0.09664	9.2721	9.6511
Tooth_IDc*Group	U4	hypodontia	8.8848	0.08971	8.7088	9.0607
Tooth_IDc*Group	U5	control	9.5830	0.09830	9.3902	9.7757
Tooth_IDc*Group	U5	hypodontia	9.0916	0.09523	8.9048	9.2783
Tooth_IDc*Group	U6	control	11.4293	0.09575	11.2415	11.6171
Tooth_IDc*Group	U6	hypodontia	11.0771	0.08722	10.9060	11.2481
Tooth_IDc*Group	U7	control	11.3150	0.1040	11.1110	11.5189
Tooth_IDc*Group	U7	hypodontia	11.1042	0.1036	10.9011	11.3073

Outcome BL dimension: Differences of marginal means: control versus hypodontia

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L1	hypodontia	0.3399	0.09650	0.1507	0.5291	0.0004
Tooth_IDc*Group	L2	control	L2	hypodontia	0.1867	0.09741	-0.00430	0.3777	0.0554
Tooth_IDc*Group	L3	control	L3	hypodontia	0.3289	0.09903	0.1347	0.5231	0.0009
Tooth_IDc*Group	L4	control	L4	hypodontia	0.2699	0.09840	0.07698	0.4629	0.0061
Tooth_IDc*Group	L5	control	L5	hypodontia	0.2470	0.1133	0.02491	0.4691	0.0293
Tooth_IDc*Group	L6	control	L6	hypodontia	0.1695	0.09606	-0.01888	0.3579	0.0778
Tooth_IDc*Group	L7	control	L7	hypodontia	0.3827	0.1168	0.1537	0.6117	0.0011
Tooth_IDc*Group	U1	control	U1	hypodontia	0.3790	0.09596	0.1908	0.5672	<.0001
Tooth_IDc*Group	U2	control	U2	hypodontia	0.2818	0.1020	0.08172	0.4819	0.0058
Tooth_IDc*Group	U3	control	U3	hypodontia	0.2985	0.1042	0.09421	0.5028	0.0042
Tooth_IDc*Group	U4	control	U4	hypodontia	0.5768	0.09861	0.3834	0.7702	<.0001
Tooth_IDc*Group	U5	control	U5	hypodontia	0.4914	0.1055	0.2845	0.6983	<.0001
Tooth_IDc*Group	U6	control	U6	hypodontia	0.3523	0.09546	0.1651	0.5394	0.0002
Tooth_IDc*Group	U7	control	U7	hypodontia	0.2108	0.1180	-0.02053	0.4421	0.0741

Outcome BL dimension: Differences of marginal means: tooth comparisons

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L2	control	-0.2752	0.05551	-0.3840	-0.1663	<.0001
Tooth_IDc*Group	L1	control	L3	control	-1.2858	0.05829	-1.4001	-1.1715	<.0001
Tooth_IDc*Group	L1	control	L4	control	-1.9275	0.05648	-2.0382	-1.8167	<.0001
Tooth_IDc*Group	L1	control	L5	control	-2.5176	0.05945	-2.6341	-2.4010	<.0001
Tooth_IDc*Group	L1	control	L6	control	-4.5377	0.05506	-4.6457	-4.4297	<.0001
Tooth_IDc*Group	L1	control	L7	control	-4.3544	0.06950	-4.4906	-4.2181	<.0001
Tooth_IDc*Group	L1	control	U1	control	-1.1895	0.05481	-1.2970	-1.0820	<.0001
Tooth_IDc*Group	L1	control	U2	control	-0.2174	0.05519	-0.3256	-0.1091	<.0001
Tooth_IDc*Group	L1	control	U3	control	-2.0030	0.06125	-2.1231	-1.8829	<.0001
Tooth_IDc*Group	L1	control	U4	control	-3.2360	0.05643	-3.3466	-3.1253	<.0001
Tooth_IDc*Group	L1	control	U5	control	-3.3573	0.05924	-3.4735	-3.2412	<.0001
Tooth_IDc*Group	L1	control	U6	control	-5.2037	0.05483	-5.3112	-5.0962	<.0001
Tooth_IDc*Group	L1	control	U7	control	-5.0894	0.06827	-5.2232	-4.9555	<.0001
Tooth_IDc*Group	L1	hypodontia	L2	hypodontia	-0.4284	0.06013	-0.5463	-0.3105	<.0001
Tooth_IDc*Group	L1	hypodontia	L3	hypodontia	-1.2968	0.06030	-1.4150	-1.1785	<.0001
Tooth_IDc*Group	L1	hypodontia	L4	hypodontia	-1.9974	0.06113	-2.1173	-1.8776	<.0001
Tooth_IDc*Group	L1	hypodontia	L5	hypodontia	-2.6105	0.08066	-2.7687	-2.4523	<.0001
Tooth_IDc*Group	L1	hypodontia	L6	hypodontia	-4.7081	0.05852	-4.8229	-4.5934	<.0001
Tooth_IDc*Group	L1	hypodontia	L7	hypodontia	-4.3116	0.07776	-4.4641	-4.1591	<.0001
Tooth_IDc*Group	L1	hypodontia	U1	hypodontia	-1.1504	0.05856	-1.2652	-1.0356	<.0001
Tooth_IDc*Group	L1	hypodontia	U2	hypodontia	-0.2754	0.06779	-0.4084	-0.1425	<.0001
Tooth_IDc*Group	L1	hypodontia	U3	hypodontia	-2.0444	0.06582	-2.1735	-1.9154	<.0001
Tooth_IDc*Group	L1	hypodontia	U4	hypodontia	-2.9991	0.06140	-3.1195	-2.8787	<.0001
Tooth_IDc*Group	L1	hypodontia	U5	hypodontia	-3.2059	0.06964	-3.3425	-3.0693	<.0001
Tooth_IDc*Group	L1	hypodontia	U6	hypodontia	-5.1914	0.05771	-5.3045	-5.0782	<.0001
Tooth_IDc*Group	L1	hypodontia	U7	hypodontia	-5.2185	0.08057	-5.3765	-5.0605	<.0001
Tooth_IDc*Group	L2	control	L3	control	-1.0106	0.05856	-1.1254	-0.8958	<.0001
Tooth_IDc*Group	L2	control	L4	control	-1.6523	0.05677	-1.7636	-1.5410	<.0001
Tooth_IDc*Group	L2	control	L5	control	-2.2424	0.05973	-2.3595	-2.1253	<.0001
Tooth_IDc*Group	L2	control	L6	control	-4.2625	0.05543	-4.3712	-4.1538	<.0001
Tooth_IDc*Group	L2	control	L7	control	-4.0792	0.06971	-4.2159	-3.9425	<.0001
Tooth_IDc*Group	L2	control	U1	control	-0.9143	0.05519	-1.0225	-0.8061	<.0001
Tooth_IDc*Group	L2	control	U2	control	0.05782	0.05556	-0.05113	0.1668	0.2982
Tooth_IDc*Group	L2	control	U3	control	-1.7278	0.06150	-1.8484	-1.6072	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L2	control	U4	control	-2.9608	0.05671	-3.0720	-2.8496	<.0001
Tooth_IDc*Group	L2	control	U5	control	-3.0822	0.05952	-3.1989	-2.9655	<.0001
Tooth_IDc*Group	L2	control	U6	control	-4.9285	0.05520	-5.0368	-4.8203	<.0001
Tooth_IDc*Group	L2	control	U7	control	-4.8142	0.06855	-4.9486	-4.6798	<.0001
Tooth_IDc*Group	L2	hypodontia	L3	hypodontia	-0.8684	0.06133	-0.9887	-0.7482	<.0001
Tooth_IDc*Group	L2	hypodontia	L4	hypodontia	-1.5691	0.06216	-1.6910	-1.4472	<.0001
Tooth_IDc*Group	L2	hypodontia	L5	hypodontia	-2.1821	0.08132	-2.3416	-2.0226	<.0001
Tooth_IDc*Group	L2	hypodontia	L6	hypodontia	-4.2798	0.05965	-4.3967	-4.1628	<.0001
Tooth_IDc*Group	L2	hypodontia	L7	hypodontia	-3.8832	0.07841	-4.0370	-3.7295	<.0001
Tooth_IDc*Group	L2	hypodontia	U1	hypodontia	-0.7220	0.05961	-0.8389	-0.6051	<.0001
Tooth_IDc*Group	L2	hypodontia	U2	hypodontia	0.1529	0.06888	0.01786	0.2880	0.0265
Tooth_IDc*Group	L2	hypodontia	U3	hypodontia	-1.6161	0.06672	-1.7469	-1.4852	<.0001
Tooth_IDc*Group	L2	hypodontia	U4	hypodontia	-2.5707	0.06244	-2.6931	-2.4482	<.0001
Tooth_IDc*Group	L2	hypodontia	U5	hypodontia	-2.7775	0.07041	-2.9156	-2.6394	<.0001
Tooth_IDc*Group	L2	hypodontia	U6	hypodontia	-4.7630	0.05885	-4.8784	-4.6476	<.0001
Tooth_IDc*Group	L2	hypodontia	U7	hypodontia	-4.7901	0.08121	-4.9494	-4.6309	<.0001
Tooth_IDc*Group	L3	control	L4	control	-0.6417	0.05912	-0.7577	-0.5258	<.0001
Tooth_IDc*Group	L3	control	L5	control	-1.2318	0.06190	-1.3532	-1.1104	<.0001
Tooth_IDc*Group	L3	control	L6	control	-3.2520	0.05812	-3.3659	-3.1380	<.0001
Tooth_IDc*Group	L3	control	L7	control	-3.0686	0.07149	-3.2088	-2.9284	<.0001
Tooth_IDc*Group	L3	control	U1	control	0.09628	0.05795	-0.01735	0.2099	0.0967
Tooth_IDc*Group	L3	control	U2	control	1.0684	0.05830	0.9541	1.1827	<.0001
Tooth_IDc*Group	L3	control	U3	control	-0.7173	0.06360	-0.8420	-0.5925	<.0001
Tooth_IDc*Group	L3	control	U4	control	-1.9502	0.05914	-2.0662	-1.8342	<.0001
Tooth_IDc*Group	L3	control	U5	control	-2.0716	0.06167	-2.1925	-1.9507	<.0001
Tooth_IDc*Group	L3	control	U6	control	-3.9179	0.05796	-4.0316	-3.8043	<.0001
Tooth_IDc*Group	L3	control	U7	control	-3.8036	0.07032	-3.9415	-3.6657	<.0001
Tooth_IDc*Group	L3	hypodontia	L4	hypodontia	-0.7007	0.06181	-0.8219	-0.5795	<.0001
Tooth_IDc*Group	L3	hypodontia	L5	hypodontia	-1.3137	0.08115	-1.4728	-1.1546	<.0001
Tooth_IDc*Group	L3	hypodontia	L6	hypodontia	-3.4113	0.05980	-3.5286	-3.2941	<.0001
Tooth_IDc*Group	L3	hypodontia	L7	hypodontia	-3.0148	0.07827	-3.1683	-2.8613	<.0001
Tooth_IDc*Group	L3	hypodontia	U1	hypodontia	0.1464	0.05970	0.02931	0.2635	0.0143
Tooth_IDc*Group	L3	hypodontia	U2	hypodontia	1.0213	0.06870	0.8866	1.1560	<.0001
Tooth_IDc*Group	L3	hypodontia	U3	hypodontia	-0.7476	0.06632	-0.8777	-0.6176	<.0001
Tooth_IDc*Group	L3	hypodontia	U4	hypodontia	-1.7023	0.06212	-1.8241	-1.5805	<.0001
Tooth_IDc*Group	L3	hypodontia	U5	hypodontia	-1.9091	0.07008	-2.0465	-1.7717	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L3	hypodontia	U6	hypodontia	-3.8946	0.05898	-4.0102	-3.7789	<.0001
Tooth_IDc*Group	L3	hypodontia	U7	hypodontia	-3.9217	0.08087	-4.0803	-3.7631	<.0001
Tooth_IDc*Group	L4	control	L5	control	-0.5901	0.06023	-0.7082	-0.4720	<.0001
Tooth_IDc*Group	L4	control	L6	control	-2.6102	0.05629	-2.7206	-2.4998	<.0001
Tooth_IDc*Group	L4	control	L7	control	-2.4269	0.07017	-2.5645	-2.2893	<.0001
Tooth_IDc*Group	L4	control	U1	control	0.7380	0.05613	0.6279	0.8481	<.0001
Tooth_IDc*Group	L4	control	U2	control	1.7101	0.05649	1.5993	1.8209	<.0001
Tooth_IDc*Group	L4	control	U3	control	-0.07553	0.06210	-0.1973	0.04624	0.2240
Tooth_IDc*Group	L4	control	U4	control	-1.3085	0.05737	-1.4210	-1.1960	<.0001
Tooth_IDc*Group	L4	control	U5	control	-1.4299	0.06001	-1.5475	-1.3122	<.0001
Tooth_IDc*Group	L4	control	U6	control	-3.2762	0.05614	-3.3863	-3.1661	<.0001
Tooth_IDc*Group	L4	control	U7	control	-3.1619	0.06898	-3.2971	-3.0266	<.0001
Tooth_IDc*Group	L4	hypodontia	L5	hypodontia	-0.6130	0.08145	-0.7727	-0.4533	<.0001
Tooth_IDc*Group	L4	hypodontia	L6	hypodontia	-2.7107	0.06054	-2.8294	-2.5920	<.0001
Tooth_IDc*Group	L4	hypodontia	L7	hypodontia	-2.3141	0.07884	-2.4687	-2.1595	<.0001
Tooth_IDc*Group	L4	hypodontia	U1	hypodontia	0.8471	0.06044	0.7285	0.9656	<.0001
Tooth_IDc*Group	L4	hypodontia	U2	hypodontia	1.7220	0.06951	1.5857	1.8583	<.0001
Tooth_IDc*Group	L4	hypodontia	U3	hypodontia	-0.04698	0.06703	-0.1784	0.08447	0.4835
Tooth_IDc*Group	L4	hypodontia	U4	hypodontia	-1.0016	0.06274	-1.1246	-0.8786	<.0001
Tooth_IDc*Group	L4	hypodontia	U5	hypodontia	-1.2084	0.07068	-1.3471	-1.0698	<.0001
Tooth_IDc*Group	L4	hypodontia	U6	hypodontia	-3.1939	0.05972	-3.3110	-3.0768	<.0001
Tooth_IDc*Group	L4	hypodontia	U7	hypodontia	-3.2210	0.08165	-3.3811	-3.0609	<.0001
Tooth_IDc*Group	L5	control	L6	control	-2.0202	0.05926	-2.1364	-1.9040	<.0001
Tooth_IDc*Group	L5	control	L7	control	-1.8368	0.07222	-1.9784	-1.6952	<.0001
Tooth_IDc*Group	L5	control	U1	control	1.3281	0.05909	1.2122	1.4440	<.0001
Tooth_IDc*Group	L5	control	U2	control	2.3002	0.05942	2.1837	2.4167	<.0001
Tooth_IDc*Group	L5	control	U3	control	0.5145	0.06475	0.3876	0.6415	<.0001
Tooth_IDc*Group	L5	control	U4	control	-0.7184	0.06026	-0.8366	-0.6002	<.0001
Tooth_IDc*Group	L5	control	U5	control	-0.8398	0.06257	-0.9625	-0.7171	<.0001
Tooth_IDc*Group	L5	control	U6	control	-2.6861	0.05911	-2.8020	-2.5702	<.0001
Tooth_IDc*Group	L5	control	U7	control	-2.5718	0.07109	-2.7112	-2.4324	<.0001
Tooth_IDc*Group	L5	hypodontia	L6	hypodontia	-2.0977	0.08026	-2.2551	-1.9403	<.0001
Tooth_IDc*Group	L5	hypodontia	L7	hypodontia	-1.7011	0.09380	-1.8850	-1.5172	<.0001
Tooth_IDc*Group	L5	hypodontia	U1	hypodontia	1.4601	0.08022	1.3028	1.6174	<.0001
Tooth_IDc*Group	L5	hypodontia	U2	hypodontia	2.3350	0.08768	2.1631	2.5070	<.0001
Tooth_IDc*Group	L5	hypodontia	U3	hypodontia	0.5660	0.08525	0.3989	0.7332	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L5	hypodontia	U4	hypodontia	-0.3886	0.08179	-0.5490	-0.2282	<.0001
Tooth_IDc*Group	L5	hypodontia	U5	hypodontia	-0.5954	0.08759	-0.7672	-0.4237	<.0001
Tooth_IDc*Group	L5	hypodontia	U6	hypodontia	-2.5809	0.07960	-2.7370	-2.4248	<.0001
Tooth_IDc*Group	L5	hypodontia	U7	hypodontia	-2.6080	0.09643	-2.7971	-2.4189	<.0001
Tooth_IDc*Group	L6	control	L7	control	0.1834	0.06934	0.04740	0.3193	0.0082
Tooth_IDc*Group	L6	control	U1	control	3.3482	0.05471	3.2410	3.4555	<.0001
Tooth_IDc*Group	L6	control	U2	control	4.3204	0.05507	4.2124	4.4284	<.0001
Tooth_IDc*Group	L6	control	U3	control	2.5347	0.06115	2.4148	2.6546	<.0001
Tooth_IDc*Group	L6	control	U4	control	1.3018	0.05629	1.1914	1.4121	<.0001
Tooth_IDc*Group	L6	control	U5	control	1.1804	0.05906	1.0645	1.2962	<.0001
Tooth_IDc*Group	L6	control	U6	control	-0.6660	0.05472	-0.7733	-0.5587	<.0001
Tooth_IDc*Group	L6	control	U7	control	-0.5516	0.06816	-0.6853	-0.4180	<.0001
Tooth_IDc*Group	L6	hypodontia	L7	hypodontia	0.3966	0.07726	0.2451	0.5481	<.0001
Tooth_IDc*Group	L6	hypodontia	U1	hypodontia	3.5577	0.05797	3.4441	3.6714	<.0001
Tooth_IDc*Group	L6	hypodontia	U2	hypodontia	4.4327	0.06734	4.3006	4.5647	<.0001
Tooth_IDc*Group	L6	hypodontia	U3	hypodontia	2.6637	0.06532	2.5356	2.7918	<.0001
Tooth_IDc*Group	L6	hypodontia	U4	hypodontia	1.7091	0.06089	1.5897	1.8285	<.0001
Tooth_IDc*Group	L6	hypodontia	U5	hypodontia	1.5022	0.06918	1.3666	1.6379	<.0001
Tooth_IDc*Group	L6	hypodontia	U6	hypodontia	-0.4832	0.05712	-0.5952	-0.3712	<.0001
Tooth_IDc*Group	L6	hypodontia	U7	hypodontia	-0.5104	0.08004	-0.6673	-0.3534	<.0001
Tooth_IDc*Group	L7	control	U1	control	3.1649	0.06915	3.0293	3.3005	<.0001
Tooth_IDc*Group	L7	control	U2	control	4.1370	0.06943	4.0008	4.2731	<.0001
Tooth_IDc*Group	L7	control	U3	control	2.3513	0.07384	2.2065	2.4961	<.0001
Tooth_IDc*Group	L7	control	U4	control	1.1184	0.07012	0.9809	1.2559	<.0001
Tooth_IDc*Group	L7	control	U5	control	0.9970	0.07213	0.8556	1.1385	<.0001
Tooth_IDc*Group	L7	control	U6	control	-0.8493	0.06916	-0.9850	-0.7137	<.0001
Tooth_IDc*Group	L7	control	U7	control	-0.7350	0.07934	-0.8906	-0.5794	<.0001
Tooth_IDc*Group	L7	hypodontia	U1	hypodontia	3.1612	0.07723	3.0097	3.3126	<.0001
Tooth_IDc*Group	L7	hypodontia	U2	hypodontia	4.0361	0.08433	3.8708	4.2015	<.0001
Tooth_IDc*Group	L7	hypodontia	U3	hypodontia	2.2671	0.08215	2.1061	2.4282	<.0001
Tooth_IDc*Group	L7	hypodontia	U4	hypodontia	1.3125	0.07900	1.1576	1.4674	<.0001
Tooth_IDc*Group	L7	hypodontia	U5	hypodontia	1.1057	0.08503	0.9389	1.2724	<.0001
Tooth_IDc*Group	L7	hypodontia	U6	hypodontia	-0.8798	0.07663	-1.0300	-0.7295	<.0001
Tooth_IDc*Group	L7	hypodontia	U7	hypodontia	-0.9069	0.09370	-1.0907	-0.7232	<.0001
Tooth_IDc*Group	U1	control	U2	control	0.9721	0.05481	0.8646	1.0796	<.0001
Tooth_IDc*Group	U1	control	U3	control	-0.8135	0.06093	-0.9330	-0.6941	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	U1	control	U4	control	-2.0465	0.05608	-2.1564	-1.9365	<.0001
Tooth_IDc*Group	U1	control	U5	control	-2.1679	0.05888	-2.2833	-2.0524	<.0001
Tooth_IDc*Group	U1	control	U6	control	-4.0142	0.05448	-4.1211	-3.9074	<.0001
Tooth_IDc*Group	U1	control	U7	control	-3.8999	0.06797	-4.0332	-3.7666	<.0001
Tooth_IDc*Group	U1	hypodontia	U2	hypodontia	0.8749	0.06726	0.7430	1.0068	<.0001
Tooth_IDc*Group	U1	hypodontia	U3	hypodontia	-0.8940	0.06520	-1.0219	-0.7662	<.0001
Tooth_IDc*Group	U1	hypodontia	U4	hypodontia	-1.8487	0.06077	-1.9678	-1.7295	<.0001
Tooth_IDc*Group	U1	hypodontia	U5	hypodontia	-2.0555	0.06908	-2.1910	-1.9200	<.0001
Tooth_IDc*Group	U1	hypodontia	U6	hypodontia	-4.0410	0.05715	-4.1530	-3.9289	<.0001
Tooth_IDc*Group	U1	hypodontia	U7	hypodontia	-4.0681	0.08002	-4.2250	-3.9112	<.0001
Tooth_IDc*Group	U2	control	U3	control	-1.7857	0.06119	-1.9056	-1.6657	<.0001
Tooth_IDc*Group	U2	control	U4	control	-3.0186	0.05646	-3.1293	-2.9079	<.0001
Tooth_IDc*Group	U2	control	U5	control	-3.1400	0.05924	-3.2562	-3.0238	<.0001
Tooth_IDc*Group	U2	control	U6	control	-4.9863	0.05485	-5.0939	-4.8788	<.0001
Tooth_IDc*Group	U2	control	U7	control	-4.8720	0.06828	-5.0059	-4.7381	<.0001
Tooth_IDc*Group	U2	hypodontia	U3	hypodontia	-1.7690	0.07345	-1.9130	-1.6249	<.0001
Tooth_IDc*Group	U2	hypodontia	U4	hypodontia	-2.7236	0.06968	-2.8602	-2.5870	<.0001
Tooth_IDc*Group	U2	hypodontia	U5	hypodontia	-2.9304	0.07725	-3.0819	-2.7790	<.0001
Tooth_IDc*Group	U2	hypodontia	U6	hypodontia	-4.9159	0.06665	-5.0466	-4.7852	<.0001
Tooth_IDc*Group	U2	hypodontia	U7	hypodontia	-4.9430	0.08708	-5.1138	-4.7723	<.0001
Tooth_IDc*Group	U3	control	U4	control	-1.2329	0.06205	-1.3546	-1.1113	<.0001
Tooth_IDc*Group	U3	control	U5	control	-1.3543	0.06458	-1.4810	-1.2277	<.0001
Tooth_IDc*Group	U3	control	U6	control	-3.2007	0.06097	-3.3202	-3.0811	<.0001
Tooth_IDc*Group	U3	control	U7	control	-3.0863	0.07258	-3.2287	-2.9440	<.0001
Tooth_IDc*Group	U3	hypodontia	U4	hypodontia	-0.9546	0.06716	-1.0863	-0.8229	<.0001
Tooth_IDc*Group	U3	hypodontia	U5	hypodontia	-1.1615	0.07459	-1.3077	-1.0152	<.0001
Tooth_IDc*Group	U3	hypodontia	U6	hypodontia	-3.1469	0.06454	-3.2735	-3.0204	<.0001
Tooth_IDc*Group	U3	hypodontia	U7	hypodontia	-3.1741	0.08479	-3.3403	-3.0078	<.0001
Tooth_IDc*Group	U4	control	U5	control	-0.1214	0.06000	-0.2391	-0.00373	0.0432
Tooth_IDc*Group	U4	control	U6	control	-1.9677	0.05610	-2.0778	-1.8577	<.0001
Tooth_IDc*Group	U4	control	U7	control	-1.8534	0.06897	-1.9886	-1.7182	<.0001
Tooth_IDc*Group	U4	hypodontia	U5	hypodontia	-0.2068	0.07086	-0.3458	-0.06789	0.0035
Tooth_IDc*Group	U4	hypodontia	U6	hypodontia	-2.1923	0.06006	-2.3101	-2.0745	<.0001
Tooth_IDc*Group	U4	hypodontia	U7	hypodontia	-2.2194	0.08169	-2.3796	-2.0592	<.0001
Tooth_IDc*Group	U5	control	U6	control	-1.8464	0.05891	-1.9619	-1.7308	<.0001
Tooth_IDc*Group	U5	control	U7	control	-1.7320	0.07098	-1.8712	-1.5928	<.0001

Effect	Tooth_IDc	Group	_Tooth_IDc	_Group	Estimate	StdErr	Lower	Upper	Probt
Tooth_IDc*Group	U5	hypodontia	U6	hypodontia	-1.9855	0.06841	-2.1196	-1.8513	<.0001
Tooth_IDc*Group	U5	hypodontia	U7	hypodontia	-2.0126	0.08765	-2.1845	-1.8407	<.0001
Tooth_IDc*Group	U6	control	U7	control	0.1143	0.06798	-0.01896	0.2477	0.0927
Tooth_IDc*Group	U6	hypodontia	U7	hypodontia	-0.02714	0.07947	-0.1830	0.1287	0.7328

Model 7. Linear mixed-effects model of CH Dimension versus Hypodontia/Control and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	CH_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	Levels	Values
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	50
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2624
Number of Observations Not Used	1212

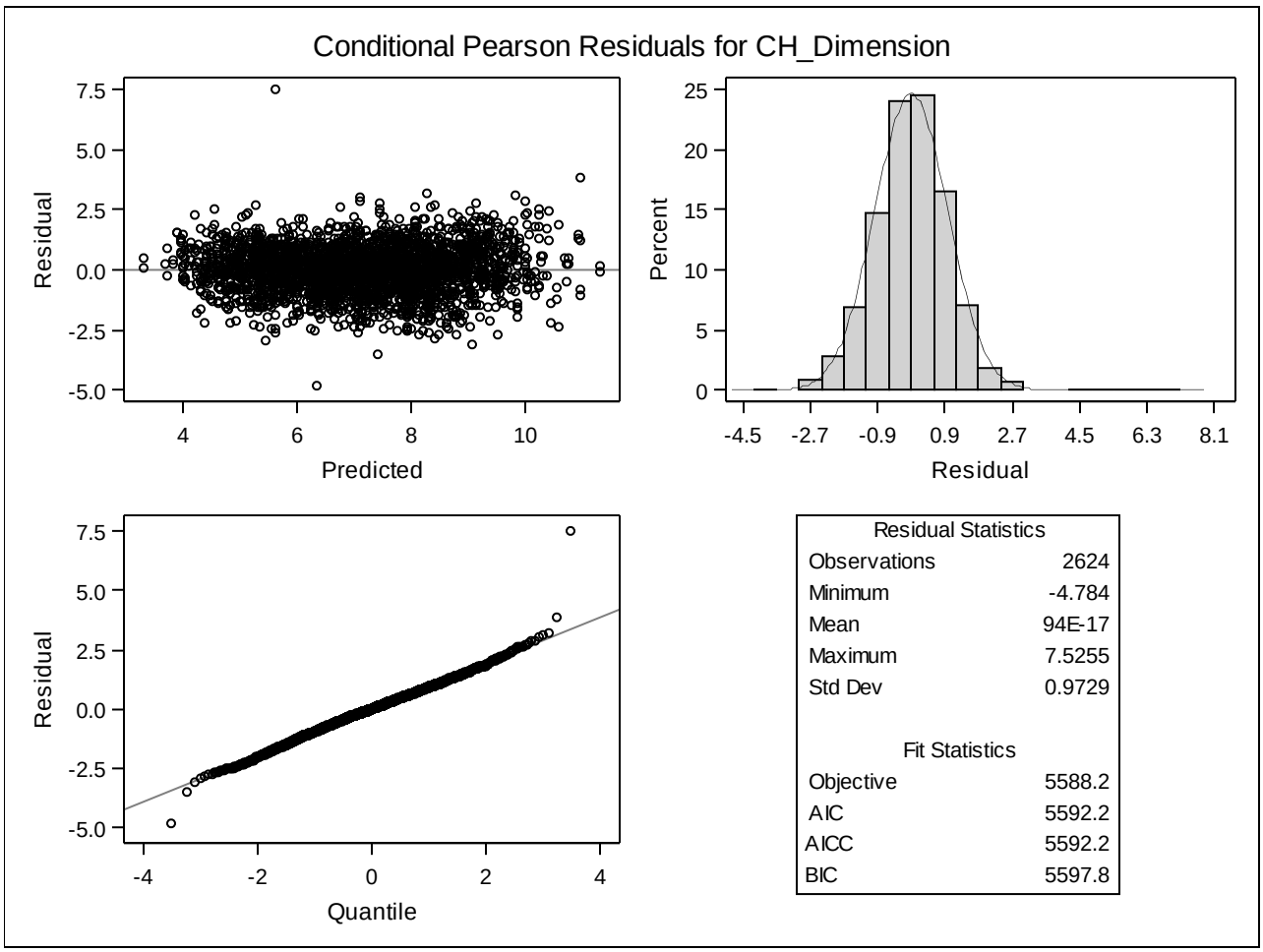
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.3950
Residual		0.4147

Fit Statistics	
-2 Res Log Likelihood	5588.2
AIC (Smaller is Better)	5592.2
AICC (Smaller is Better)	5592.2
BIC (Smaller is Better)	5597.8

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2477	8.67	0.0033
Tooth_IDc	13	2477	786.76	<.0001
Tooth_IDc*Group	13	2477	1.64	0.0673
Age_days	1	2477	31.64	<.0001
Sex	1	2477	4.71	0.0302
Ethnicity_Polynesian	1	2477	0.00	0.9983



Outcome CH dimension: Marginal means

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	L1	control	7.9817	0.1441	7.6992	8.2642
Tooth_IDc*Group	L1	hypodontia	7.4856	0.1323	7.2262	7.7451
Tooth_IDc*Group	L2	control	7.8781	0.1452	7.5933	8.1629
Tooth_IDc*Group	L2	hypodontia	7.6592	0.1332	7.3981	7.9204
Tooth_IDc*Group	L3	control	8.7718	0.1457	8.4862	9.0575
Tooth_IDc*Group	L3	hypodontia	8.5488	0.1336	8.2869	8.8107
Tooth_IDc*Group	L4	control	7.7016	0.1449	7.4175	7.9858
Tooth_IDc*Group	L4	hypodontia	7.3185	0.1342	7.0554	7.5817
Tooth_IDc*Group	L5	control	6.7231	0.1480	6.4330	7.0132
Tooth_IDc*Group	L5	hypodontia	6.2989	0.1559	5.9932	6.6045
Tooth_IDc*Group	L6	control	6.2269	0.1438	5.9448	6.5090
Tooth_IDc*Group	L6	hypodontia	5.9506	0.1318	5.6921	6.2090
Tooth_IDc*Group	L7	control	6.0645	0.1537	5.7630	6.3659

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	L7	hypodontia	5.5054	0.1468	5.2176	5.7932
Tooth_IDc*Group	U1	control	9.4977	0.1437	9.2160	9.7794
Tooth_IDc*Group	U1	hypodontia	9.0597	0.1314	8.8020	9.3174
Tooth_IDc*Group	U2	control	7.5727	0.1444	7.2896	7.8557
Tooth_IDc*Group	U2	hypodontia	7.1370	0.1406	6.8613	7.4128
Tooth_IDc*Group	U3	control	8.5784	0.1497	8.2848	8.8721
Tooth_IDc*Group	U3	hypodontia	8.1375	0.1384	7.8660	8.4090
Tooth_IDc*Group	U4	control	6.8530	0.1453	6.5680	7.1379
Tooth_IDc*Group	U4	hypodontia	6.5675	0.1343	6.3041	6.8310
Tooth_IDc*Group	U5	control	5.8810	0.1488	5.5893	6.1728
Tooth_IDc*Group	U5	hypodontia	5.4443	0.1439	5.1622	5.7264
Tooth_IDc*Group	U6	control	5.2545	0.1438	4.9726	5.5364
Tooth_IDc*Group	U6	hypodontia	4.9750	0.1312	4.7177	5.2324
Tooth_IDc*Group	U7	control	4.9911	0.1550	4.6871	5.2951
Tooth_IDc*Group	U7	hypodontia	4.9431	0.1554	4.6385	5.2478

Outcome CH dimension: Differences of marginal means: control versus hypodontia

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L1	hypodontia	0.4961	0.1449	0.2120	0.7802	0.0006
Tooth_IDc*Group	L2	control	L2	hypodontia	0.2189	0.1471	-0.06952	0.5073	0.1368
Tooth_IDc*Group	L3	control	L3	hypodontia	0.2230	0.1474	-0.06603	0.5120	0.1304
Tooth_IDc*Group	L4	control	L4	hypodontia	0.3831	0.1475	0.09394	0.6723	0.0094
Tooth_IDc*Group	L5	control	L5	hypodontia	0.4242	0.1712	0.08852	0.7599	0.0133
Tooth_IDc*Group	L6	control	L6	hypodontia	0.2763	0.1441	-0.00630	0.5590	0.0553
Tooth_IDc*Group	L7	control	L7	hypodontia	0.5591	0.1673	0.2309	0.8872	0.0008
Tooth_IDc*Group	U1	control	U1	hypodontia	0.4380	0.1436	0.1565	0.7195	0.0023
Tooth_IDc*Group	U2	control	U2	hypodontia	0.4356	0.1525	0.1366	0.7347	0.0043
Tooth_IDc*Group	U3	control	U3	hypodontia	0.4410	0.1558	0.1354	0.7465	0.0047
Tooth_IDc*Group	U4	control	U4	hypodontia	0.2854	0.1480	-0.00470	0.5756	0.0538
Tooth_IDc*Group	U5	control	U5	hypodontia	0.4368	0.1603	0.1224	0.7511	0.0065
Tooth_IDc*Group	U6	control	U6	hypodontia	0.2795	0.1435	-0.00202	0.5610	0.0517
Tooth_IDc*Group	U7	control	U7	hypodontia	0.04792	0.1762	-0.2975	0.3934	0.7856

Outcome CH dimension: Differences of marginal means: tooth comparisons

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L2	control	0.1036	0.08499	-0.06306	0.2703	0.2230
Tooth_IDc*Group	L1	control	L3	control	-0.7901	0.08568	-0.9581	-0.6221	<.0001
Tooth_IDc*Group	L1	control	L4	control	0.2801	0.08465	0.1141	0.4461	0.0010
Tooth_IDc*Group	L1	control	L5	control	1.2586	0.08988	1.0824	1.4349	<.0001
Tooth_IDc*Group	L1	control	L6	control	1.7548	0.08253	1.5930	1.9167	<.0001
Tooth_IDc*Group	L1	control	L7	control	1.9173	0.09892	1.7233	2.1112	<.0001
Tooth_IDc*Group	L1	control	U1	control	-1.5159	0.08219	-1.6771	-1.3548	<.0001
Tooth_IDc*Group	L1	control	U2	control	0.4091	0.08346	0.2454	0.5727	<.0001
Tooth_IDc*Group	L1	control	U3	control	-0.5967	0.09236	-0.7778	-0.4156	<.0001
Tooth_IDc*Group	L1	control	U4	control	1.1288	0.08520	0.9617	1.2958	<.0001
Tooth_IDc*Group	L1	control	U5	control	2.1007	0.09112	1.9220	2.2794	<.0001
Tooth_IDc*Group	L1	control	U6	control	2.7272	0.08237	2.5657	2.8888	<.0001
Tooth_IDc*Group	L1	control	U7	control	2.9907	0.1009	2.7927	3.1886	<.0001
Tooth_IDc*Group	L1	hypodontia	L2	hypodontia	-0.1736	0.09017	-0.3504	0.003208	0.0543
Tooth_IDc*Group	L1	hypodontia	L3	hypodontia	-1.0632	0.09032	-1.2403	-0.8861	<.0001
Tooth_IDc*Group	L1	hypodontia	L4	hypodontia	0.1671	0.09148	-0.01227	0.3465	0.0679
Tooth_IDc*Group	L1	hypodontia	L5	hypodontia	1.1868	0.1225	0.9465	1.4270	<.0001
Tooth_IDc*Group	L1	hypodontia	L6	hypodontia	1.5351	0.08788	1.3628	1.7074	<.0001
Tooth_IDc*Group	L1	hypodontia	L7	hypodontia	1.9802	0.1097	1.7651	2.1953	<.0001
Tooth_IDc*Group	L1	hypodontia	U1	hypodontia	-1.5740	0.08723	-1.7451	-1.4030	<.0001
Tooth_IDc*Group	L1	hypodontia	U2	hypodontia	0.3486	0.1004	0.1517	0.5455	0.0005
Tooth_IDc*Group	L1	hypodontia	U3	hypodontia	-0.6518	0.09763	-0.8433	-0.4604	<.0001
Tooth_IDc*Group	L1	hypodontia	U4	hypodontia	0.9181	0.09165	0.7384	1.0978	<.0001
Tooth_IDc*Group	L1	hypodontia	U5	hypodontia	2.0414	0.1057	1.8341	2.2486	<.0001
Tooth_IDc*Group	L1	hypodontia	U6	hypodontia	2.5106	0.08704	2.3399	2.6813	<.0001
Tooth_IDc*Group	L1	hypodontia	U7	hypodontia	2.5425	0.1210	2.3052	2.7798	<.0001
Tooth_IDc*Group	L2	control	L3	control	-0.8937	0.08756	-1.0654	-0.7220	<.0001
Tooth_IDc*Group	L2	control	L4	control	0.1765	0.08658	0.006715	0.3463	0.0416
Tooth_IDc*Group	L2	control	L5	control	1.1550	0.09172	0.9752	1.3349	<.0001
Tooth_IDc*Group	L2	control	L6	control	1.6512	0.08472	1.4851	1.8174	<.0001
Tooth_IDc*Group	L2	control	L7	control	1.8137	0.1005	1.6165	2.0108	<.0001
Tooth_IDc*Group	L2	control	U1	control	-1.6195	0.08438	-1.7850	-1.4541	<.0001
Tooth_IDc*Group	L2	control	U2	control	0.3055	0.08561	0.1376	0.4733	0.0004
Tooth_IDc*Group	L2	control	U3	control	-0.7003	0.09410	-0.8848	-0.5158	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L2	control	U4	control	1.0252	0.08710	0.8544	1.1960	<.0001
Tooth_IDc*Group	L2	control	U5	control	1.9971	0.09293	1.8149	2.1793	<.0001
Tooth_IDc*Group	L2	control	U6	control	2.6236	0.08456	2.4578	2.7895	<.0001
Tooth_IDc*Group	L2	control	U7	control	2.8871	0.1026	2.6859	3.0882	<.0001
Tooth_IDc*Group	L2	hypodontia	L3	hypodontia	-0.8896	0.09157	-1.0692	-0.7100	<.0001
Tooth_IDc*Group	L2	hypodontia	L4	hypodontia	0.3407	0.09278	0.1588	0.5227	0.0002
Tooth_IDc*Group	L2	hypodontia	L5	hypodontia	1.3604	0.1231	1.1190	1.6018	<.0001
Tooth_IDc*Group	L2	hypodontia	L6	hypodontia	1.7087	0.08943	1.5333	1.8841	<.0001
Tooth_IDc*Group	L2	hypodontia	L7	hypodontia	2.1538	0.1105	1.9372	2.3705	<.0001
Tooth_IDc*Group	L2	hypodontia	U1	hypodontia	-1.4004	0.08880	-1.5746	-1.2263	<.0001
Tooth_IDc*Group	L2	hypodontia	U2	hypodontia	0.5222	0.1016	0.3229	0.7215	<.0001
Tooth_IDc*Group	L2	hypodontia	U3	hypodontia	-0.4782	0.09874	-0.6719	-0.2846	<.0001
Tooth_IDc*Group	L2	hypodontia	U4	hypodontia	1.0917	0.09307	0.9092	1.2742	<.0001
Tooth_IDc*Group	L2	hypodontia	U5	hypodontia	2.2150	0.1066	2.0058	2.4241	<.0001
Tooth_IDc*Group	L2	hypodontia	U6	hypodontia	2.6842	0.08857	2.5106	2.8579	<.0001
Tooth_IDc*Group	L2	hypodontia	U7	hypodontia	2.7161	0.1218	2.4773	2.9549	<.0001
Tooth_IDc*Group	L3	control	L4	control	1.0702	0.08677	0.9000	1.2403	<.0001
Tooth_IDc*Group	L3	control	L5	control	2.0487	0.09177	1.8688	2.2287	<.0001
Tooth_IDc*Group	L3	control	L6	control	2.5449	0.08528	2.3777	2.7121	<.0001
Tooth_IDc*Group	L3	control	L7	control	2.7073	0.1006	2.5101	2.9046	<.0001
Tooth_IDc*Group	L3	control	U1	control	-0.7259	0.08499	-0.8925	-0.5592	<.0001
Tooth_IDc*Group	L3	control	U2	control	1.1991	0.08618	1.0302	1.3681	<.0001
Tooth_IDc*Group	L3	control	U3	control	0.1934	0.09430	0.008468	0.3783	0.0404
Tooth_IDc*Group	L3	control	U4	control	1.9189	0.08738	1.7475	2.0902	<.0001
Tooth_IDc*Group	L3	control	U5	control	2.8908	0.09295	2.7085	3.0730	<.0001
Tooth_IDc*Group	L3	control	U6	control	3.5173	0.08517	3.3503	3.6843	<.0001
Tooth_IDc*Group	L3	control	U7	control	3.7807	0.1026	3.5795	3.9820	<.0001
Tooth_IDc*Group	L3	hypodontia	L4	hypodontia	1.2303	0.09234	1.0492	1.4114	<.0001
Tooth_IDc*Group	L3	hypodontia	L5	hypodontia	2.2500	0.1229	2.0090	2.4909	<.0001
Tooth_IDc*Group	L3	hypodontia	L6	hypodontia	2.5983	0.08950	2.4228	2.7738	<.0001
Tooth_IDc*Group	L3	hypodontia	L7	hypodontia	3.0434	0.1103	2.8271	3.2597	<.0001
Tooth_IDc*Group	L3	hypodontia	U1	hypodontia	-0.5108	0.08886	-0.6851	-0.3366	<.0001
Tooth_IDc*Group	L3	hypodontia	U2	hypodontia	1.4118	0.1016	1.2125	1.6111	<.0001
Tooth_IDc*Group	L3	hypodontia	U3	hypodontia	0.4114	0.09824	0.2187	0.6040	<.0001
Tooth_IDc*Group	L3	hypodontia	U4	hypodontia	1.9813	0.09257	1.7998	2.1628	<.0001
Tooth_IDc*Group	L3	hypodontia	U5	hypodontia	3.1046	0.1064	2.8960	3.3131	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L3	hypodontia	U6	hypodontia	3.5738	0.08865	3.4000	3.7477	<.0001
Tooth_IDc*Group	L3	hypodontia	U7	hypodontia	3.6057	0.1213	3.3678	3.8436	<.0001
Tooth_IDc*Group	L4	control	L5	control	0.9785	0.09080	0.8005	1.1566	<.0001
Tooth_IDc*Group	L4	control	L6	control	1.4747	0.08424	1.3095	1.6399	<.0001
Tooth_IDc*Group	L4	control	L7	control	1.6372	0.09973	1.4416	1.8327	<.0001
Tooth_IDc*Group	L4	control	U1	control	-1.7960	0.08394	-1.9606	-1.6314	<.0001
Tooth_IDc*Group	L4	control	U2	control	0.1290	0.08514	-0.03799	0.2959	0.1300
Tooth_IDc*Group	L4	control	U3	control	-0.8768	0.09340	-1.0600	-0.6937	<.0001
Tooth_IDc*Group	L4	control	U4	control	0.8487	0.08637	0.6793	1.0180	<.0001
Tooth_IDc*Group	L4	control	U5	control	1.8206	0.09200	1.6402	2.0010	<.0001
Tooth_IDc*Group	L4	control	U6	control	2.4471	0.08413	2.2822	2.6121	<.0001
Tooth_IDc*Group	L4	control	U7	control	2.7106	0.1017	2.5110	2.9101	<.0001
Tooth_IDc*Group	L4	hypodontia	L5	hypodontia	1.0196	0.1233	0.7778	1.2615	<.0001
Tooth_IDc*Group	L4	hypodontia	L6	hypodontia	1.3680	0.09064	1.1902	1.5457	<.0001
Tooth_IDc*Group	L4	hypodontia	L7	hypodontia	1.8131	0.1111	1.5952	2.0310	<.0001
Tooth_IDc*Group	L4	hypodontia	U1	hypodontia	-1.7412	0.09000	-1.9176	-1.5647	<.0001
Tooth_IDc*Group	L4	hypodontia	U2	hypodontia	0.1815	0.1028	-0.02005	0.3830	0.0775
Tooth_IDc*Group	L4	hypodontia	U3	hypodontia	-0.8190	0.09922	-1.0135	-0.6244	<.0001
Tooth_IDc*Group	L4	hypodontia	U4	hypodontia	0.7510	0.09345	0.5677	0.9342	<.0001
Tooth_IDc*Group	L4	hypodontia	U5	hypodontia	1.8742	0.1070	1.6644	2.0841	<.0001
Tooth_IDc*Group	L4	hypodontia	U6	hypodontia	2.3435	0.08979	2.1674	2.5196	<.0001
Tooth_IDc*Group	L4	hypodontia	U7	hypodontia	2.3754	0.1224	2.1354	2.6153	<.0001
Tooth_IDc*Group	L5	control	L6	control	0.4962	0.08946	0.3208	0.6716	<.0001
Tooth_IDc*Group	L5	control	L7	control	0.6586	0.1036	0.4554	0.8618	<.0001
Tooth_IDc*Group	L5	control	U1	control	-2.7746	0.08915	-2.9494	-2.5997	<.0001
Tooth_IDc*Group	L5	control	U2	control	-0.8496	0.09028	-1.0266	-0.6725	<.0001
Tooth_IDc*Group	L5	control	U3	control	-1.8553	0.09807	-2.0476	-1.6630	<.0001
Tooth_IDc*Group	L5	control	U4	control	-0.1299	0.09139	-0.3091	0.04936	0.1555
Tooth_IDc*Group	L5	control	U5	control	0.8421	0.09631	0.6532	1.0309	<.0001
Tooth_IDc*Group	L5	control	U6	control	1.4686	0.08936	1.2934	1.6438	<.0001
Tooth_IDc*Group	L5	control	U7	control	1.7320	0.1056	1.5250	1.9391	<.0001
Tooth_IDc*Group	L5	hypodontia	L6	hypodontia	0.3483	0.1217	0.1096	0.5870	0.0043
Tooth_IDc*Group	L5	hypodontia	L7	hypodontia	0.7935	0.1360	0.5267	1.0602	<.0001
Tooth_IDc*Group	L5	hypodontia	U1	hypodontia	-2.7608	0.1213	-2.9987	-2.5229	<.0001
Tooth_IDc*Group	L5	hypodontia	U2	hypodontia	-0.8382	0.1317	-1.0964	-0.5799	<.0001
Tooth_IDc*Group	L5	hypodontia	U3	hypodontia	-1.8386	0.1282	-2.0901	-1.5872	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L5	hypodontia	U4	hypodontia	-0.2687	0.1237	-0.5111	-0.02618	0.0299
Tooth_IDc*Group	L5	hypodontia	U5	hypodontia	0.8546	0.1335	0.5928	1.1164	<.0001
Tooth_IDc*Group	L5	hypodontia	U6	hypodontia	1.3239	0.1211	1.0864	1.5613	<.0001
Tooth_IDc*Group	L5	hypodontia	U7	hypodontia	1.3557	0.1456	1.0703	1.6412	<.0001
Tooth_IDc*Group	L6	control	L7	control	0.1624	0.09851	-0.03074	0.3556	0.0993
Tooth_IDc*Group	L6	control	U1	control	-3.2708	0.08182	-3.4312	-3.1103	<.0001
Tooth_IDc*Group	L6	control	U2	control	-1.3458	0.08310	-1.5087	-1.1828	<.0001
Tooth_IDc*Group	L6	control	U3	control	-2.3515	0.09206	-2.5321	-2.1710	<.0001
Tooth_IDc*Group	L6	control	U4	control	-0.6261	0.08485	-0.7924	-0.4597	<.0001
Tooth_IDc*Group	L6	control	U5	control	0.3459	0.09070	0.1680	0.5237	0.0001
Tooth_IDc*Group	L6	control	U6	control	0.9724	0.08200	0.8116	1.1332	<.0001
Tooth_IDc*Group	L6	control	U7	control	1.2358	0.1006	1.0386	1.4331	<.0001
Tooth_IDc*Group	L6	hypodontia	L7	hypodontia	0.4451	0.1088	0.2318	0.6585	<.0001
Tooth_IDc*Group	L6	hypodontia	U1	hypodontia	-3.1091	0.08639	-3.2785	-2.9397	<.0001
Tooth_IDc*Group	L6	hypodontia	U2	hypodontia	-1.1865	0.09959	-1.3818	-0.9912	<.0001
Tooth_IDc*Group	L6	hypodontia	U3	hypodontia	-2.1869	0.09685	-2.3768	-1.9970	<.0001
Tooth_IDc*Group	L6	hypodontia	U4	hypodontia	-0.6170	0.09088	-0.7952	-0.4388	<.0001
Tooth_IDc*Group	L6	hypodontia	U5	hypodontia	0.5063	0.1049	0.3005	0.7121	<.0001
Tooth_IDc*Group	L6	hypodontia	U6	hypodontia	0.9755	0.08614	0.8066	1.1445	<.0001
Tooth_IDc*Group	L6	hypodontia	U7	hypodontia	1.0074	0.1202	0.7717	1.2431	<.0001
Tooth_IDc*Group	L7	control	U1	control	-3.4332	0.09821	-3.6258	-3.2406	<.0001
Tooth_IDc*Group	L7	control	U2	control	-1.5082	0.09922	-1.7028	-1.3137	<.0001
Tooth_IDc*Group	L7	control	U3	control	-2.5140	0.1061	-2.7220	-2.3059	<.0001
Tooth_IDc*Group	L7	control	U4	control	-0.7885	0.1002	-0.9850	-0.5920	<.0001
Tooth_IDc*Group	L7	control	U5	control	0.1834	0.1046	-0.02177	0.3886	0.0798
Tooth_IDc*Group	L7	control	U6	control	0.8100	0.09835	0.6171	1.0028	<.0001
Tooth_IDc*Group	L7	control	U7	control	1.0734	0.1128	0.8522	1.2945	<.0001
Tooth_IDc*Group	L7	hypodontia	U1	hypodontia	-3.5543	0.1083	-3.7667	-3.3418	<.0001
Tooth_IDc*Group	L7	hypodontia	U2	hypodontia	-1.6316	0.1191	-1.8652	-1.3980	<.0001
Tooth_IDc*Group	L7	hypodontia	U3	hypodontia	-2.6321	0.1159	-2.8593	-2.4048	<.0001
Tooth_IDc*Group	L7	hypodontia	U4	hypodontia	-1.0621	0.1113	-1.2804	-0.8439	<.0001
Tooth_IDc*Group	L7	hypodontia	U5	hypodontia	0.06114	0.1223	-0.1786	0.3009	0.6171
Tooth_IDc*Group	L7	hypodontia	U6	hypodontia	0.5304	0.1082	0.3183	0.7425	<.0001
Tooth_IDc*Group	L7	hypodontia	U7	hypodontia	0.5623	0.1349	0.2977	0.8269	<.0001
Tooth_IDc*Group	U1	control	U2	control	1.9250	0.08272	1.7628	2.0872	<.0001
Tooth_IDc*Group	U1	control	U3	control	0.9192	0.09168	0.7395	1.0990	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	U1	control	U4	control	2.6447	0.08451	2.4790	2.8104	<.0001
Tooth_IDc*Group	U1	control	U5	control	3.6166	0.09040	3.4394	3.7939	<.0001
Tooth_IDc*Group	U1	control	U6	control	4.2432	0.08166	4.0830	4.4033	<.0001
Tooth_IDc*Group	U1	control	U7	control	4.5066	0.1003	4.3100	4.7032	<.0001
Tooth_IDc*Group	U1	hypodontia	U2	hypodontia	1.9226	0.09900	1.7285	2.1168	<.0001
Tooth_IDc*Group	U1	hypodontia	U3	hypodontia	0.9222	0.09626	0.7334	1.1110	<.0001
Tooth_IDc*Group	U1	hypodontia	U4	hypodontia	2.4922	0.09025	2.3152	2.6691	<.0001
Tooth_IDc*Group	U1	hypodontia	U5	hypodontia	3.6154	0.1044	3.4106	3.8202	<.0001
Tooth_IDc*Group	U1	hypodontia	U6	hypodontia	4.0847	0.08554	3.9169	4.2524	<.0001
Tooth_IDc*Group	U1	hypodontia	U7	hypodontia	4.1165	0.1198	3.8816	4.3515	<.0001
Tooth_IDc*Group	U2	control	U3	control	-1.0058	0.09270	-1.1875	-0.8240	<.0001
Tooth_IDc*Group	U2	control	U4	control	0.7197	0.08570	0.5517	0.8878	<.0001
Tooth_IDc*Group	U2	control	U5	control	1.6916	0.09148	1.5122	1.8710	<.0001
Tooth_IDc*Group	U2	control	U6	control	2.3182	0.08294	2.1555	2.4808	<.0001
Tooth_IDc*Group	U2	control	U7	control	2.5816	0.1013	2.3831	2.7801	<.0001
Tooth_IDc*Group	U2	hypodontia	U3	hypodontia	-1.0005	0.1080	-1.2122	-0.7887	<.0001
Tooth_IDc*Group	U2	hypodontia	U4	hypodontia	0.5695	0.1028	0.3680	0.7711	<.0001
Tooth_IDc*Group	U2	hypodontia	U5	hypodontia	1.6928	0.1160	1.4654	1.9201	<.0001
Tooth_IDc*Group	U2	hypodontia	U6	hypodontia	2.1620	0.09884	1.9682	2.3558	<.0001
Tooth_IDc*Group	U2	hypodontia	U7	hypodontia	2.1939	0.1296	1.9397	2.4481	<.0001
Tooth_IDc*Group	U3	control	U4	control	1.7255	0.09384	1.5415	1.9095	<.0001
Tooth_IDc*Group	U3	control	U5	control	2.6974	0.09908	2.5031	2.8917	<.0001
Tooth_IDc*Group	U3	control	U6	control	3.3239	0.09190	3.1437	3.5042	<.0001
Tooth_IDc*Group	U3	control	U7	control	3.5874	0.1076	3.3763	3.7985	<.0001
Tooth_IDc*Group	U3	hypodontia	U4	hypodontia	1.5700	0.09924	1.3754	1.7646	<.0001
Tooth_IDc*Group	U3	hypodontia	U5	hypodontia	2.6932	0.1121	2.4734	2.9130	<.0001
Tooth_IDc*Group	U3	hypodontia	U6	hypodontia	3.1625	0.09606	2.9741	3.3508	<.0001
Tooth_IDc*Group	U3	hypodontia	U7	hypodontia	3.1943	0.1266	2.9462	3.4425	<.0001
Tooth_IDc*Group	U4	control	U5	control	0.9719	0.09250	0.7905	1.1533	<.0001
Tooth_IDc*Group	U4	control	U6	control	1.5985	0.08469	1.4324	1.7645	<.0001
Tooth_IDc*Group	U4	control	U7	control	1.8619	0.1022	1.6614	2.0623	<.0001
Tooth_IDc*Group	U4	hypodontia	U5	hypodontia	1.1232	0.1071	0.9133	1.3332	<.0001
Tooth_IDc*Group	U4	hypodontia	U6	hypodontia	1.5925	0.09003	1.4160	1.7691	<.0001
Tooth_IDc*Group	U4	hypodontia	U7	hypodontia	1.6244	0.1223	1.3846	1.8641	<.0001
Tooth_IDc*Group	U5	control	U6	control	0.6266	0.09060	0.4489	0.8042	<.0001
Tooth_IDc*Group	U5	control	U7	control	0.8900	0.1066	0.6809	1.0990	<.0001

Effect	Tooth_IDc	Group	_Tooth_IDc	_Group	Estimate	StdErr	Lower	Upper	Probt
Tooth_IDc*Group	U5	hypodontia	U6	hypodontia	0.4693	0.1042	0.2649	0.6736	<.0001
Tooth_IDc*Group	U5	hypodontia	U7	hypodontia	0.5011	0.1326	0.2411	0.7612	0.0002
Tooth_IDc*Group	U6	control	U7	control	0.2634	0.1004	0.06651	0.4603	0.0088
Tooth_IDc*Group	U6	hypodontia	U7	hypodontia	0.03187	0.1197	-0.2028	0.2665	0.7900

Model 8. Linear mixed-effects model of Modules versus Hypodontia/Control and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	Modules
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	Levels	Values
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	50
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2510
Number of Observations Not Used	1326

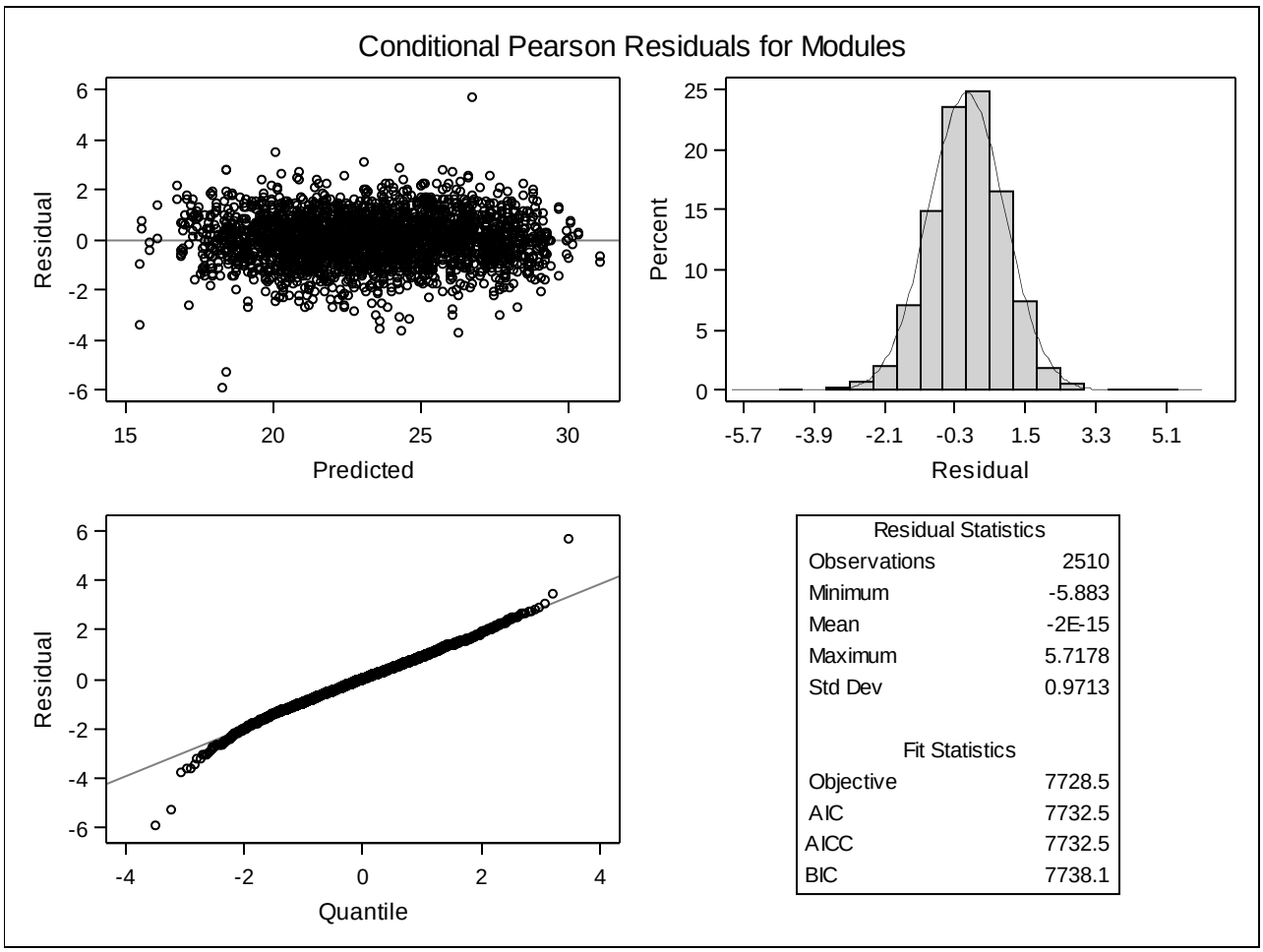
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	1.4642
Residual		1.0615

Fit Statistics	
-2 Res Log Likelihood	7728.5
AIC (Smaller is Better)	7732.5
AICC (Smaller is Better)	7732.5
BIC (Smaller is Better)	7738.1

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2363	18.45	<.0001
Tooth_IDc	13	2363	1303.93	<.0001
Tooth_IDc*Group	13	2363	1.68	0.0590
Age_days	1	2363	16.26	<.0001
Sex	1	2363	8.28	0.0041
Ethnicity_Polynesian	1	2363	0.31	0.5771



Outcome Modules: Marginal means

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	L1	control	19.7084	0.2696	19.1797	20.2370
Tooth_IDc*Group	L1	hypodontia	18.5934	0.2455	18.1121	19.0748
Tooth_IDc*Group	L2	control	20.3378	0.2708	19.8068	20.8687
Tooth_IDc*Group	L2	hypodontia	19.7403	0.2469	19.2562	20.2244
Tooth_IDc*Group	L3	control	23.2672	0.2732	22.7315	23.8030
Tooth_IDc*Group	L3	hypodontia	22.4246	0.2478	21.9388	22.9105
Tooth_IDc*Group	L4	control	23.0947	0.2706	22.5639	23.6254
Tooth_IDc*Group	L4	hypodontia	22.1883	0.2482	21.7015	22.6751
Tooth_IDc*Group	L5	control	22.8386	0.2745	22.3002	23.3769
Tooth_IDc*Group	L5	hypodontia	21.7866	0.2797	21.2382	22.3350
Tooth_IDc*Group	L6	control	28.0767	0.2691	27.5490	28.6045
Tooth_IDc*Group	L6	hypodontia	27.3315	0.2448	26.8513	27.8116
Tooth_IDc*Group	L7	control	27.6226	0.2972	27.0398	28.2055

Effect	*Tooth_IDc*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Group	L7	hypodontia	26.0937	0.2872	25.5306	26.6569
Tooth_IDc*Group	U1	control	25.5078	0.2687	24.9808	26.0348
Tooth_IDc*Group	U1	hypodontia	24.4736	0.2443	23.9945	24.9528
Tooth_IDc*Group	U2	control	20.7257	0.2697	20.1968	21.2546
Tooth_IDc*Group	U2	hypodontia	19.6789	0.2587	19.1715	20.1863
Tooth_IDc*Group	U3	control	24.7415	0.2780	24.1965	25.2866
Tooth_IDc*Group	U3	hypodontia	23.6771	0.2548	23.1775	24.1768
Tooth_IDc*Group	U4	control	23.3838	0.2709	22.8526	23.9150
Tooth_IDc*Group	U4	hypodontia	22.1883	0.2493	21.6995	22.6771
Tooth_IDc*Group	U5	control	22.2125	0.2757	21.6718	22.7532
Tooth_IDc*Group	U5	hypodontia	21.1604	0.2619	20.6469	21.6739
Tooth_IDc*Group	U6	control	27.3091	0.2689	26.7818	27.8364
Tooth_IDc*Group	U6	hypodontia	26.4069	0.2444	25.9277	26.8861
Tooth_IDc*Group	U7	control	26.6587	0.2922	26.0858	27.2316
Tooth_IDc*Group	U7	hypodontia	25.9396	0.2819	25.3868	26.4923

Outcome Modules: Differences of marginal means: control versus hypodontia

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L1	hypodontia	1.1149	0.2642	0.5968	1.6330	<.0001
Tooth_IDc*Group	L2	control	L2	hypodontia	0.5975	0.2672	0.07359	1.1213	0.0254
Tooth_IDc*Group	L3	control	L3	hypodontia	0.8426	0.2696	0.3139	1.3713	0.0018
Tooth_IDc*Group	L4	control	L4	hypodontia	0.9064	0.2678	0.3812	1.4316	0.0007
Tooth_IDc*Group	L5	control	L5	hypodontia	1.0520	0.3025	0.4589	1.6451	0.0005
Tooth_IDc*Group	L6	control	L6	hypodontia	0.7453	0.2629	0.2298	1.2608	0.0046
Tooth_IDc*Group	L7	control	L7	hypodontia	1.5289	0.3288	0.8841	2.1737	<.0001
Tooth_IDc*Group	U1	control	U1	hypodontia	1.0341	0.2622	0.5199	1.5484	<.0001
Tooth_IDc*Group	U2	control	U2	hypodontia	1.0468	0.2763	0.5051	1.5885	0.0002
Tooth_IDc*Group	U3	control	U3	hypodontia	1.0644	0.2810	0.5133	1.6155	0.0002
Tooth_IDc*Group	U4	control	U4	hypodontia	1.1955	0.2690	0.6680	1.7230	<.0001
Tooth_IDc*Group	U5	control	U5	hypodontia	1.0521	0.2860	0.4912	1.6130	0.0002
Tooth_IDc*Group	U6	control	U6	hypodontia	0.9022	0.2620	0.3883	1.4161	0.0006
Tooth_IDc*Group	U7	control	U7	hypodontia	0.7191	0.3191	0.09342	1.3448	0.0243

Outcome Modules: Differences of marginal means: tooth comparisons

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L1	control	L2	control	-0.6294	0.1368	-0.8977	-0.3610	<.0001
Tooth_IDc*Group	L1	control	L3	control	-3.5589	0.1414	-3.8362	-3.2816	<.0001
Tooth_IDc*Group	L1	control	L4	control	-3.3863	0.1370	-3.6550	-3.1176	<.0001
Tooth_IDc*Group	L1	control	L5	control	-3.1302	0.1447	-3.4140	-2.8464	<.0001
Tooth_IDc*Group	L1	control	L6	control	-8.3684	0.1335	-8.6302	-8.1065	<.0001
Tooth_IDc*Group	L1	control	L7	control	-7.9143	0.1840	-8.2751	-7.5534	<.0001
Tooth_IDc*Group	L1	control	U1	control	-5.7994	0.1326	-6.0595	-5.5394	<.0001
Tooth_IDc*Group	L1	control	U2	control	-1.0173	0.1347	-1.2815	-0.7532	<.0001
Tooth_IDc*Group	L1	control	U3	control	-5.0332	0.1504	-5.3280	-4.7383	<.0001
Tooth_IDc*Group	L1	control	U4	control	-3.6754	0.1372	-3.9445	-3.4064	<.0001
Tooth_IDc*Group	L1	control	U5	control	-2.5041	0.1467	-2.7918	-2.2165	<.0001
Tooth_IDc*Group	L1	control	U6	control	-7.6007	0.1329	-7.8614	-7.3401	<.0001
Tooth_IDc*Group	L1	control	U7	control	-6.9503	0.1757	-7.2949	-6.6057	<.0001
Tooth_IDc*Group	L1	hypodontia	L2	hypodontia	-1.1469	0.1463	-1.4337	-0.8600	<.0001
Tooth_IDc*Group	L1	hypodontia	L3	hypodontia	-3.8312	0.1469	-4.1193	-3.5431	<.0001
Tooth_IDc*Group	L1	hypodontia	L4	hypodontia	-3.5948	0.1482	-3.8855	-3.3042	<.0001
Tooth_IDc*Group	L1	hypodontia	L5	hypodontia	-3.1931	0.1986	-3.5826	-2.8036	<.0001
Tooth_IDc*Group	L1	hypodontia	L6	hypodontia	-8.7380	0.1421	-9.0167	-8.4594	<.0001
Tooth_IDc*Group	L1	hypodontia	L7	hypodontia	-7.5003	0.2080	-7.9082	-7.0924	<.0001
Tooth_IDc*Group	L1	hypodontia	U1	hypodontia	-5.8802	0.1416	-6.1578	-5.6026	<.0001
Tooth_IDc*Group	L1	hypodontia	U2	hypodontia	-1.0855	0.1646	-1.4082	-0.7627	<.0001
Tooth_IDc*Group	L1	hypodontia	U3	hypodontia	-5.0837	0.1589	-5.3953	-4.7721	<.0001
Tooth_IDc*Group	L1	hypodontia	U4	hypodontia	-3.5949	0.1497	-3.8884	-3.3013	<.0001
Tooth_IDc*Group	L1	hypodontia	U5	hypodontia	-2.5670	0.1707	-2.9018	-2.2321	<.0001
Tooth_IDc*Group	L1	hypodontia	U6	hypodontia	-7.8134	0.1411	-8.0902	-7.5367	<.0001
Tooth_IDc*Group	L1	hypodontia	U7	hypodontia	-7.3461	0.1998	-7.7380	-6.9543	<.0001
Tooth_IDc*Group	L2	control	L3	control	-2.9295	0.1435	-3.2108	-2.6481	<.0001
Tooth_IDc*Group	L2	control	L4	control	-2.7569	0.1392	-3.0298	-2.4840	<.0001
Tooth_IDc*Group	L2	control	L5	control	-2.5008	0.1468	-2.7887	-2.2129	<.0001
Tooth_IDc*Group	L2	control	L6	control	-7.7390	0.1360	-8.0057	-7.4723	<.0001
Tooth_IDc*Group	L2	control	L7	control	-7.2849	0.1853	-7.6483	-6.9214	<.0001
Tooth_IDc*Group	L2	control	U1	control	-5.1700	0.1353	-5.4353	-4.9048	<.0001
Tooth_IDc*Group	L2	control	U2	control	-0.3879	0.1373	-0.6572	-0.1187	0.0048
Tooth_IDc*Group	L2	control	U3	control	-4.4038	0.1522	-4.7023	-4.1053	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L2	control	U4	control	-3.0460	0.1394	-3.3194	-2.7727	<.0001
Tooth_IDc*Group	L2	control	U5	control	-1.8747	0.1487	-2.1664	-1.5831	<.0001
Tooth_IDc*Group	L2	control	U6	control	-6.9713	0.1356	-7.2372	-6.7055	<.0001
Tooth_IDc*Group	L2	control	U7	control	-6.3209	0.1774	-6.6687	-5.9731	<.0001
Tooth_IDc*Group	L2	hypodontia	L3	hypodontia	-2.6843	0.1493	-2.9771	-2.3916	<.0001
Tooth_IDc*Group	L2	hypodontia	L4	hypodontia	-2.4480	0.1506	-2.7433	-2.1526	<.0001
Tooth_IDc*Group	L2	hypodontia	L5	hypodontia	-2.0463	0.1998	-2.4380	-1.6545	<.0001
Tooth_IDc*Group	L2	hypodontia	L6	hypodontia	-7.5912	0.1450	-7.8756	-7.3067	<.0001
Tooth_IDc*Group	L2	hypodontia	L7	hypodontia	-6.3534	0.2092	-6.7637	-5.9432	<.0001
Tooth_IDc*Group	L2	hypodontia	U1	hypodontia	-4.7333	0.1440	-5.0157	-4.4509	<.0001
Tooth_IDc*Group	L2	hypodontia	U2	hypodontia	0.06138	0.1670	-0.2660	0.3888	0.7132
Tooth_IDc*Group	L2	hypodontia	U3	hypodontia	-3.9368	0.1611	-4.2528	-3.6209	<.0001
Tooth_IDc*Group	L2	hypodontia	U4	hypodontia	-2.4480	0.1523	-2.7466	-2.1494	<.0001
Tooth_IDc*Group	L2	hypodontia	U5	hypodontia	-1.4201	0.1726	-1.7586	-1.0816	<.0001
Tooth_IDc*Group	L2	hypodontia	U6	hypodontia	-6.6666	0.1438	-6.9487	-6.3845	<.0001
Tooth_IDc*Group	L2	hypodontia	U7	hypodontia	-6.1993	0.2013	-6.5941	-5.8045	<.0001
Tooth_IDc*Group	L3	control	L4	control	0.1726	0.1428	-0.1074	0.4525	0.2269
Tooth_IDc*Group	L3	control	L5	control	0.4287	0.1500	0.1346	0.7228	0.0043
Tooth_IDc*Group	L3	control	L6	control	-4.8095	0.1403	-5.0846	-4.5344	<.0001
Tooth_IDc*Group	L3	control	L7	control	-4.3554	0.1877	-4.7235	-3.9873	<.0001
Tooth_IDc*Group	L3	control	U1	control	-2.2406	0.1397	-2.5145	-1.9666	<.0001
Tooth_IDc*Group	L3	control	U2	control	2.5415	0.1416	2.2639	2.8192	<.0001
Tooth_IDc*Group	L3	control	U3	control	-1.4743	0.1554	-1.7791	-1.1695	<.0001
Tooth_IDc*Group	L3	control	U4	control	-0.1166	0.1431	-0.3972	0.1640	0.4153
Tooth_IDc*Group	L3	control	U5	control	1.0547	0.1517	0.7572	1.3522	<.0001
Tooth_IDc*Group	L3	control	U6	control	-4.0419	0.1400	-4.3164	-3.7673	<.0001
Tooth_IDc*Group	L3	control	U7	control	-3.3915	0.1798	-3.7440	-3.0389	<.0001
Tooth_IDc*Group	L3	hypodontia	L4	hypodontia	0.2364	0.1502	-0.05815	0.5309	0.1157
Tooth_IDc*Group	L3	hypodontia	L5	hypodontia	0.6381	0.1996	0.2467	1.0295	0.0014
Tooth_IDc*Group	L3	hypodontia	L6	hypodontia	-4.9068	0.1457	-5.1926	-4.6211	<.0001
Tooth_IDc*Group	L3	hypodontia	L7	hypodontia	-3.6691	0.2092	-4.0793	-3.2589	<.0001
Tooth_IDc*Group	L3	hypodontia	U1	hypodontia	-2.0490	0.1447	-2.3327	-1.7653	<.0001
Tooth_IDc*Group	L3	hypodontia	U2	hypodontia	2.7457	0.1670	2.4183	3.0731	<.0001
Tooth_IDc*Group	L3	hypodontia	U3	hypodontia	-1.2525	0.1605	-1.5672	-0.9378	<.0001
Tooth_IDc*Group	L3	hypodontia	U4	hypodontia	0.2363	0.1519	-0.06145	0.5341	0.1198
Tooth_IDc*Group	L3	hypodontia	U5	hypodontia	1.2642	0.1723	0.9264	1.6021	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L3	hypodontia	U6	hypodontia	-3.9823	0.1442	-4.2651	-3.6994	<.0001
Tooth_IDc*Group	L3	hypodontia	U7	hypodontia	-3.5149	0.2006	-3.9083	-3.1215	<.0001
Tooth_IDc*Group	L4	control	L5	control	0.2561	0.1459	-0.03005	0.5422	0.0794
Tooth_IDc*Group	L4	control	L6	control	-4.9821	0.1358	-5.2484	-4.7157	<.0001
Tooth_IDc*Group	L4	control	L7	control	-4.5280	0.1849	-4.8905	-4.1655	<.0001
Tooth_IDc*Group	L4	control	U1	control	-2.4131	0.1353	-2.6784	-2.1479	<.0001
Tooth_IDc*Group	L4	control	U2	control	2.3690	0.1372	2.0999	2.6380	<.0001
Tooth_IDc*Group	L4	control	U3	control	-1.6469	0.1518	-1.9445	-1.3493	<.0001
Tooth_IDc*Group	L4	control	U4	control	-0.2891	0.1388	-0.5614	-0.01689	0.0374
Tooth_IDc*Group	L4	control	U5	control	0.8822	0.1479	0.5922	1.1721	<.0001
Tooth_IDc*Group	L4	control	U6	control	-4.2144	0.1356	-4.4803	-3.9486	<.0001
Tooth_IDc*Group	L4	control	U7	control	-3.5640	0.1768	-3.9108	-3.2173	<.0001
Tooth_IDc*Group	L4	hypodontia	L5	hypodontia	0.4017	0.1998	0.009860	0.7936	0.0445
Tooth_IDc*Group	L4	hypodontia	L6	hypodontia	-5.1432	0.1467	-5.4309	-4.8555	<.0001
Tooth_IDc*Group	L4	hypodontia	L7	hypodontia	-3.9055	0.2100	-4.3173	-3.4936	<.0001
Tooth_IDc*Group	L4	hypodontia	U1	hypodontia	-2.2854	0.1457	-2.5711	-1.9996	<.0001
Tooth_IDc*Group	L4	hypodontia	U2	hypodontia	2.5094	0.1683	2.1793	2.8395	<.0001
Tooth_IDc*Group	L4	hypodontia	U3	hypodontia	-1.4889	0.1616	-1.8057	-1.1721	<.0001
Tooth_IDc*Group	L4	hypodontia	U4	hypodontia	-0.00002	0.1526	-0.2993	0.2993	0.9999
Tooth_IDc*Group	L4	hypodontia	U5	hypodontia	1.0279	0.1730	0.6887	1.3671	<.0001
Tooth_IDc*Group	L4	hypodontia	U6	hypodontia	-4.2186	0.1452	-4.5033	-3.9339	<.0001
Tooth_IDc*Group	L4	hypodontia	U7	hypodontia	-3.7513	0.2022	-4.1477	-3.3548	<.0001
Tooth_IDc*Group	L5	control	L6	control	-5.2382	0.1435	-5.5196	-4.9567	<.0001
Tooth_IDc*Group	L5	control	L7	control	-4.7841	0.1900	-5.1566	-4.4116	<.0001
Tooth_IDc*Group	L5	control	U1	control	-2.6692	0.1430	-2.9496	-2.3889	<.0001
Tooth_IDc*Group	L5	control	U2	control	2.1129	0.1448	1.8289	2.3968	<.0001
Tooth_IDc*Group	L5	control	U3	control	-1.9030	0.1586	-2.2141	-1.5919	<.0001
Tooth_IDc*Group	L5	control	U4	control	-0.5452	0.1462	-0.8320	-0.2585	0.0002
Tooth_IDc*Group	L5	control	U5	control	0.6261	0.1541	0.3238	0.9283	<.0001
Tooth_IDc*Group	L5	control	U6	control	-4.4705	0.1433	-4.7515	-4.1895	<.0001
Tooth_IDc*Group	L5	control	U7	control	-3.8201	0.1818	-4.1767	-3.4636	<.0001
Tooth_IDc*Group	L5	hypodontia	L6	hypodontia	-5.5449	0.1975	-5.9322	-5.1576	<.0001
Tooth_IDc*Group	L5	hypodontia	L7	hypodontia	-4.3072	0.2460	-4.7895	-3.8248	<.0001
Tooth_IDc*Group	L5	hypodontia	U1	hypodontia	-2.6871	0.1967	-3.0727	-2.3014	<.0001
Tooth_IDc*Group	L5	hypodontia	U2	hypodontia	2.1077	0.2152	1.6857	2.5296	<.0001
Tooth_IDc*Group	L5	hypodontia	U3	hypodontia	-1.8906	0.2085	-2.2994	-1.4817	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	L5	hypodontia	U4	hypodontia	-0.4017	0.2013	-0.7965	-0.00695	0.0461
Tooth_IDc*Group	L5	hypodontia	U5	hypodontia	0.6262	0.2161	0.2023	1.0500	0.0038
Tooth_IDc*Group	L5	hypodontia	U6	hypodontia	-4.6203	0.1963	-5.0052	-4.2354	<.0001
Tooth_IDc*Group	L5	hypodontia	U7	hypodontia	-4.1530	0.2393	-4.6222	-3.6838	<.0001
Tooth_IDc*Group	L6	control	L7	control	0.4541	0.1830	0.09520	0.8130	0.0132
Tooth_IDc*Group	L6	control	U1	control	2.5690	0.1318	2.3106	2.8274	<.0001
Tooth_IDc*Group	L6	control	U2	control	7.3511	0.1338	7.0887	7.6134	<.0001
Tooth_IDc*Group	L6	control	U3	control	3.3352	0.1495	3.0421	3.6283	<.0001
Tooth_IDc*Group	L6	control	U4	control	4.6929	0.1361	4.4260	4.9599	<.0001
Tooth_IDc*Group	L6	control	U5	control	5.8643	0.1455	5.5789	6.1496	<.0001
Tooth_IDc*Group	L6	control	U6	control	0.7677	0.1321	0.5087	1.0267	<.0001
Tooth_IDc*Group	L6	control	U7	control	1.4181	0.1748	1.0754	1.7607	<.0001
Tooth_IDc*Group	L6	hypodontia	L7	hypodontia	1.2377	0.2069	0.8320	1.6435	<.0001
Tooth_IDc*Group	L6	hypodontia	U1	hypodontia	2.8578	0.1401	2.5832	3.1325	<.0001
Tooth_IDc*Group	L6	hypodontia	U2	hypodontia	7.6525	0.1633	7.3322	7.9729	<.0001
Tooth_IDc*Group	L6	hypodontia	U3	hypodontia	3.6543	0.1577	3.3451	3.9636	<.0001
Tooth_IDc*Group	L6	hypodontia	U4	hypodontia	5.1432	0.1486	4.8519	5.4345	<.0001
Tooth_IDc*Group	L6	hypodontia	U5	hypodontia	6.1711	0.1697	5.8382	6.5039	<.0001
Tooth_IDc*Group	L6	hypodontia	U6	hypodontia	0.9246	0.1395	0.6510	1.1982	<.0001
Tooth_IDc*Group	L6	hypodontia	U7	hypodontia	1.3919	0.1985	1.0026	1.7812	<.0001
Tooth_IDc*Group	L7	control	U1	control	2.1149	0.1825	1.7570	2.4727	<.0001
Tooth_IDc*Group	L7	control	U2	control	6.8969	0.1839	6.5362	7.2577	<.0001
Tooth_IDc*Group	L7	control	U3	control	2.8811	0.1943	2.5001	3.2621	<.0001
Tooth_IDc*Group	L7	control	U4	control	4.2388	0.1850	3.8761	4.6016	<.0001
Tooth_IDc*Group	L7	control	U5	control	5.4101	0.1912	5.0351	5.7852	<.0001
Tooth_IDc*Group	L7	control	U6	control	0.3135	0.1827	-0.04470	0.6718	0.0862
Tooth_IDc*Group	L7	control	U7	control	0.9639	0.2128	0.5466	1.3813	<.0001
Tooth_IDc*Group	L7	hypodontia	U1	hypodontia	1.6201	0.2060	1.2160	2.0242	<.0001
Tooth_IDc*Group	L7	hypodontia	U2	hypodontia	6.4148	0.2220	5.9795	6.8502	<.0001
Tooth_IDc*Group	L7	hypodontia	U3	hypodontia	2.4166	0.2171	1.9909	2.8423	<.0001
Tooth_IDc*Group	L7	hypodontia	U4	hypodontia	3.9054	0.2113	3.4911	4.3197	<.0001
Tooth_IDc*Group	L7	hypodontia	U5	hypodontia	4.9333	0.2251	4.4918	5.3749	<.0001
Tooth_IDc*Group	L7	hypodontia	U6	hypodontia	-0.3132	0.2058	-0.7167	0.09043	0.1282
Tooth_IDc*Group	L7	hypodontia	U7	hypodontia	0.1542	0.2467	-0.3295	0.6379	0.5320
Tooth_IDc*Group	U1	control	U2	control	4.7821	0.1329	4.5214	5.0427	<.0001
Tooth_IDc*Group	U1	control	U3	control	0.7662	0.1488	0.4745	1.0580	<.0001

Effect	*Tooth_IDc*	*Group*	*_Tooth_IDc*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Group	U1	control	U4	control	2.1240	0.1355	1.8583	2.3896	<.0001
Tooth_IDc*Group	U1	control	U5	control	3.2953	0.1449	3.0111	3.5795	<.0001
Tooth_IDc*Group	U1	control	U6	control	-1.8013	0.1312	-2.0585	-1.5441	<.0001
Tooth_IDc*Group	U1	control	U7	control	-1.1509	0.1742	-1.4926	-0.8092	<.0001
Tooth_IDc*Group	U1	hypodontia	U2	hypodontia	4.7947	0.1624	4.4762	5.1133	<.0001
Tooth_IDc*Group	U1	hypodontia	U3	hypodontia	0.7965	0.1567	0.4891	1.1039	<.0001
Tooth_IDc*Group	U1	hypodontia	U4	hypodontia	2.2853	0.1475	1.9961	2.5746	<.0001
Tooth_IDc*Group	U1	hypodontia	U5	hypodontia	3.3132	0.1689	2.9821	3.6444	<.0001
Tooth_IDc*Group	U1	hypodontia	U6	hypodontia	-1.9332	0.1388	-2.2055	-1.6610	<.0001
Tooth_IDc*Group	U1	hypodontia	U7	hypodontia	-1.4659	0.1980	-1.8542	-1.0777	<.0001
Tooth_IDc*Group	U2	control	U3	control	-4.0158	0.1503	-4.3105	-3.7212	<.0001
Tooth_IDc*Group	U2	control	U4	control	-2.6581	0.1374	-2.9276	-2.3887	<.0001
Tooth_IDc*Group	U2	control	U5	control	-1.4868	0.1466	-1.7743	-1.1993	<.0001
Tooth_IDc*Group	U2	control	U6	control	-6.5834	0.1333	-6.8448	-6.3220	<.0001
Tooth_IDc*Group	U2	control	U7	control	-5.9330	0.1757	-6.2774	-5.5886	<.0001
Tooth_IDc*Group	U2	hypodontia	U3	hypodontia	-3.9982	0.1772	-4.3458	-3.6507	<.0001
Tooth_IDc*Group	U2	hypodontia	U4	hypodontia	-2.5094	0.1695	-2.8418	-2.1770	<.0001
Tooth_IDc*Group	U2	hypodontia	U5	hypodontia	-1.4815	0.1891	-1.8524	-1.1106	<.0001
Tooth_IDc*Group	U2	hypodontia	U6	hypodontia	-6.7280	0.1622	-7.0461	-6.4098	<.0001
Tooth_IDc*Group	U2	hypodontia	U7	hypodontia	-6.2607	0.2151	-6.6825	-5.8388	<.0001
Tooth_IDc*Group	U3	control	U4	control	1.3577	0.1519	1.0598	1.6556	<.0001
Tooth_IDc*Group	U3	control	U5	control	2.5290	0.1602	2.2149	2.8432	<.0001
Tooth_IDc*Group	U3	control	U6	control	-2.5676	0.1491	-2.8600	-2.2751	<.0001
Tooth_IDc*Group	U3	control	U7	control	-1.9172	0.1863	-2.2825	-1.5519	<.0001
Tooth_IDc*Group	U3	hypodontia	U4	hypodontia	1.4888	0.1628	1.1696	1.8081	<.0001
Tooth_IDc*Group	U3	hypodontia	U5	hypodontia	2.5167	0.1820	2.1599	2.8735	<.0001
Tooth_IDc*Group	U3	hypodontia	U6	hypodontia	-2.7298	0.1564	-3.0364	-2.4232	<.0001
Tooth_IDc*Group	U3	hypodontia	U7	hypodontia	-2.2624	0.2091	-2.6725	-1.8523	<.0001
Tooth_IDc*Group	U4	control	U5	control	1.1713	0.1480	0.8811	1.4616	<.0001
Tooth_IDc*Group	U4	control	U6	control	-3.9253	0.1358	-4.1915	-3.6590	<.0001
Tooth_IDc*Group	U4	control	U7	control	-3.2749	0.1769	-3.6217	-2.9280	<.0001
Tooth_IDc*Group	U4	hypodontia	U5	hypodontia	1.0279	0.1742	0.6863	1.3696	<.0001
Tooth_IDc*Group	U4	hypodontia	U6	hypodontia	-4.2186	0.1471	-4.5069	-3.9302	<.0001
Tooth_IDc*Group	U4	hypodontia	U7	hypodontia	-3.7513	0.2029	-4.1491	-3.3534	<.0001
Tooth_IDc*Group	U5	control	U6	control	-5.0966	0.1453	-5.3815	-4.8117	<.0001
Tooth_IDc*Group	U5	control	U7	control	-4.4462	0.1834	-4.8059	-4.0865	<.0001

Effect	Tooth_IDc	Group	_Tooth_IDc	_Group	Estimate	StdErr	Lower	Upper	Probt
Tooth_IDc*Group	U5	hypodontia	U6	hypodontia	-5.2465	0.1683	-5.5766	-4.9164	<.0001
Tooth_IDc*Group	U5	hypodontia	U7	hypodontia	-4.7792	0.2181	-5.2068	-4.3515	<.0001
Tooth_IDc*Group	U6	control	U7	control	0.6504	0.1745	0.3083	0.9925	0.0002
Tooth_IDc*Group	U6	hypodontia	U7	hypodontia	0.4673	0.1977	0.07966	0.8550	0.0182

Model 9. For hypodontia patients only: Linear mixed-effects model of MD Dimension versus Missing tooth and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	MD_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	Levels	Values
Patient_ID	56	LF163 LF171 LF174 LF192 LF193 LF223 LF228 30.04.14 LF233 LF236 LF241 LF246 LF265A LF266A LF270 LF271A LF277 LF278A LF279a LF285a LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF308A LF312A LF320 LF321A LF324 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF380A LF381 LF384a LF386A LF387a LF389A LF390A 31.08.10 LF394 LF395A LF398A LF401 LF411 LF417 LF445 LF458 LF463 LF488A
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Missing_tooth	2	0 1

Dimensions	
Covariance Parameters	2
Columns in X	40
Columns in Z per Subject	1
Subjects	56
Max Obs per Subject	26

Number of Observations	
Number of Observations Read	1876
Number of Observations Used	1136
Number of Observations Not Used	740

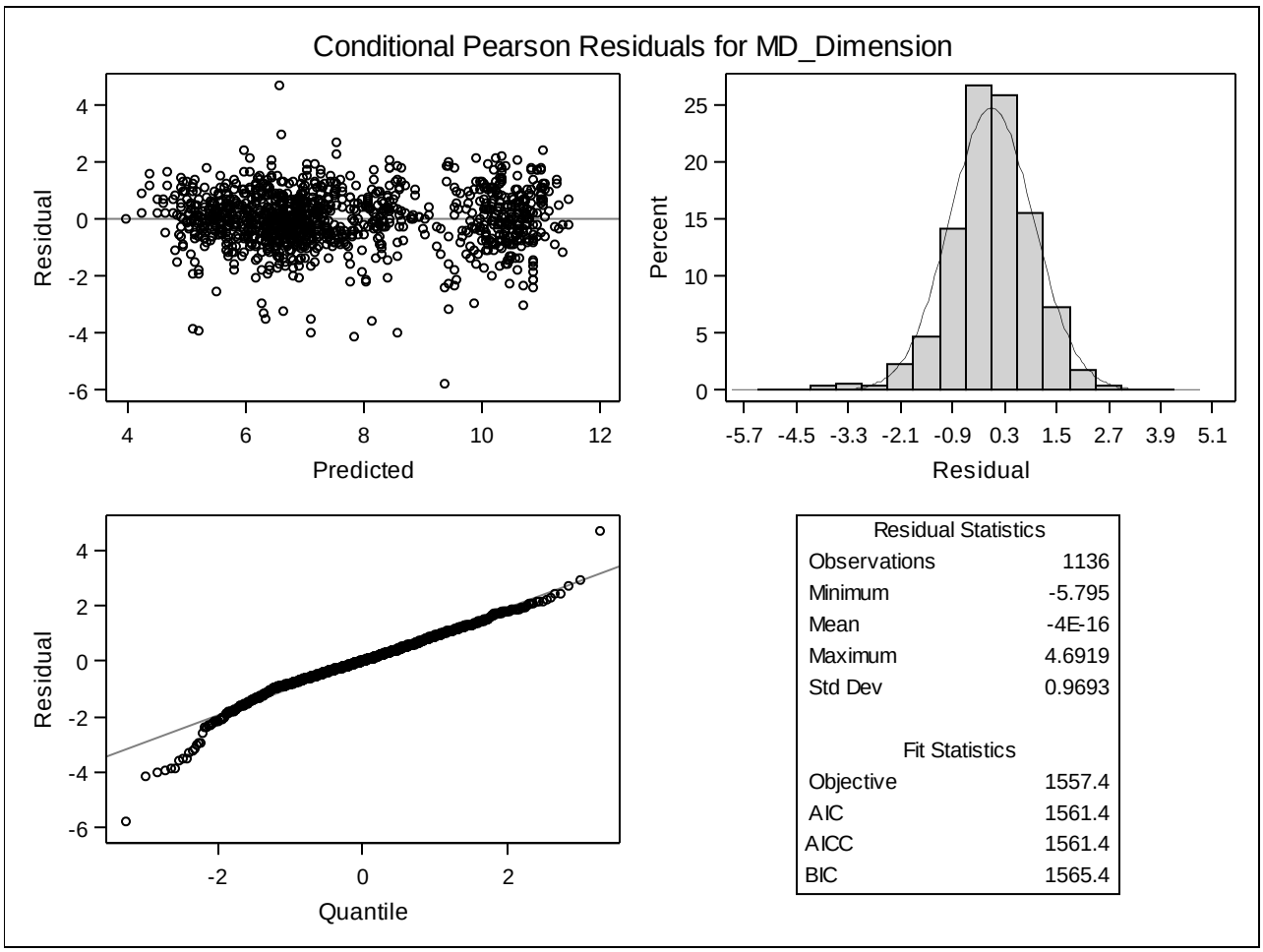
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.1412
Residual		0.1916

Fit Statistics	
-2 Res Log Likelihood	1557.4
AIC (Smaller is Better)	1561.4
AICC (Smaller is Better)	1561.4
BIC (Smaller is Better)	1565.4

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Missing_tooth	1	1063	1.88	0.1712
Tooth_IDc	13	1063	1290.93	<.0001
Tooth_IDc*Missing_to	3	1063	4.90	0.0022
Age_days	1	1063	0.93	0.3349
Sex	1	1063	2.82	0.0937
Ethnicity_Polynesian	1	1063	1.03	0.3100



Outcome MD dimension: Marginal means

Effect	*Tooth_IDc*	*Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Missing_to	L1	0	5.2251	0.08681	5.0547	5.3954
Tooth_IDc*Missing_to	L1	1	5.3888	0.4534	4.4991	6.2785
Tooth_IDc*Missing_to	L2	0	5.7532	0.08693	5.5827	5.9238
Tooth_IDc*Missing_to	L2	1	5.7387	0.2697	5.2094	6.2679
Tooth_IDc*Missing_to	L3	0	6.6674	0.08752	6.4956	6.8391
Tooth_IDc*Missing_to	L4	0	6.9570	0.08874	6.7829	7.1311
Tooth_IDc*Missing_to	L5	0	6.9582	0.1050	6.7521	7.1643
Tooth_IDc*Missing_to	L5	1	7.1541	0.4528	6.2657	8.0426
Tooth_IDc*Missing_to	L6	0	10.7938	0.08690	10.6233	10.9643
Tooth_IDc*Missing_to	L7	0	10.2704	0.1067	10.0611	10.4798
Tooth_IDc*Missing_to	U1	0	8.3619	0.08628	8.1926	8.5312
Tooth_IDc*Missing_to	U2	0	6.3633	0.09307	6.1807	6.5459
Tooth_IDc*Missing_to	U2	1	4.9774	0.3257	4.3383	5.6164
Tooth_IDc*Missing_to	U3	0	7.5719	0.09098	7.3933	7.7504

Effect	*Tooth_IDc*	*Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Missing_to	U4	0	6.7062	0.08919	6.5312	6.8812
Tooth_IDc*Missing_to	U5	0	6.5690	0.09559	6.3814	6.7565
Tooth_IDc*Missing_to	U6	0	10.3663	0.08660	10.1964	10.5363
Tooth_IDc*Missing_to	U7	0	9.8448	0.1048	9.6391	10.0504

Outcome MD dimension: Differences of marginal means: no missing tooth vs missing tooth

Effect	*Tooth_IDc*	*Missing_tooth*	*_Tooth_IDc*	*_Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Missing_to	L1	0	L1	1	-0.1637	0.4494	-1.0455	0.7181	0.7157
Tooth_IDc*Missing_to	L2	0	L2	1	0.01458	0.2625	-0.5004	0.5296	0.9557
Tooth_IDc*Missing_to	L5	0	L5	1	-0.1960	0.4531	-1.0850	0.6930	0.6654
Tooth_IDc*Missing_to	U2	0	U2	1	1.3859	0.3223	0.7535	2.0184	<.0001

Model 10. For hypodontia patients only: Linear mixed-effects model of BL Dimension versus Missing tooth and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	BL_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information		
Class	*Levels*	*Values*
Patient_ID	56	LF163 LF171 LF174 LF192 LF193 LF223 LF228 30.04.14 LF233 LF236 LF241 LF246 LF265A LF266A LF270 LF271A LF277 LF278A LF279a LF285a LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF308A LF312A LF320 LF321A LF324 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF380A LF381 LF384a LF386A LF387a LF389A LF390A 31.08.10 LF394 LF395A LF398A LF401 LF411 LF417 LF445 LF458 LF463 LF488A
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Missing_tooth	2	0 1

Dimensions	
Covariance Parameters	2
Columns in X	40
Columns in Z per Subject	1
Subjects	56
Max Obs per Subject	27

Number of Observations	
Number of Observations Read	1876
Number of Observations Used	1114
Number of Observations Not Used	762

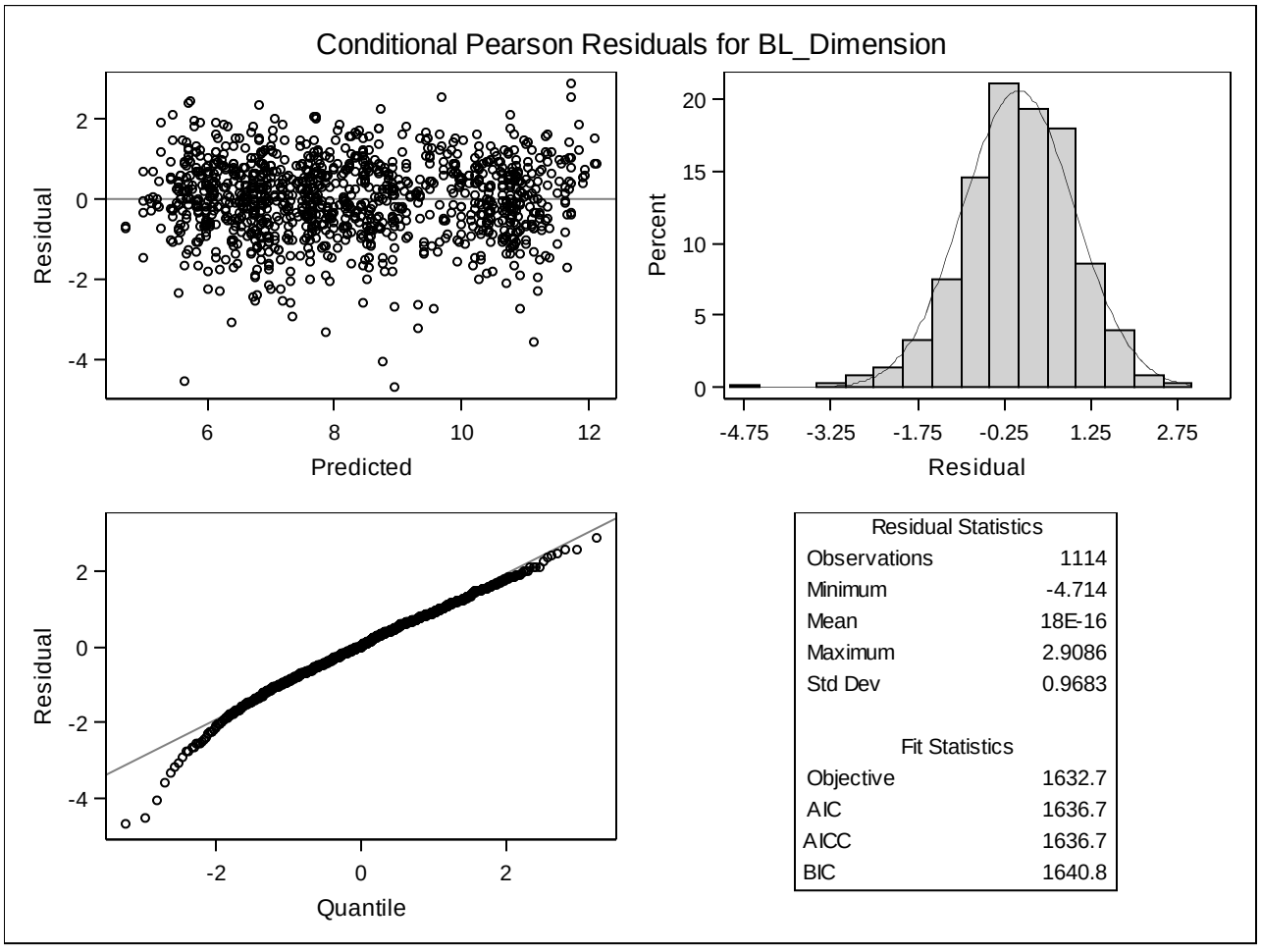
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	*Subject*	*Estimate*
Intercept	Patient_ID	0.2118
Residual		0.2075

Fit Statistics	
-2 Res Log Likelihood	1632.7
AIC (Smaller is Better)	1636.7
AICC (Smaller is Better)	1636.7
BIC (Smaller is Better)	1640.8

Type 3 Tests of Fixed Effects

Effect	*Num DF*	*Den DF*	*F Value*	*Pr > F*
Missing_tooth	1	1041	0.04	0.8444
Tooth_IDc	13	1041	1073.69	<.0001
*Tooth_IDc*Missing_to*	3	1041	1.54	0.2038
Age_days	1	1041	2.65	0.1039
Sex	1	1041	1.56	0.2121
Ethnicity_Polynesian	1	1041	0.33	0.5633



Outcome BL dimension: Marginal means

Effect	*Tooth_IDc*	*Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Missing_to	L1	0	5.8675	0.1032	5.6650	6.0700
Tooth_IDc*Missing_to	L1	1	6.2943	0.4745	5.3632	7.2255
Tooth_IDc*Missing_to	L2	0	6.2983	0.1041	6.0940	6.5026
Tooth_IDc*Missing_to	L2	1	6.4889	0.2848	5.9300	7.0478
Tooth_IDc*Missing_to	L3	0	7.1624	0.1041	6.9581	7.3667
Tooth_IDc*Missing_to	L4	0	7.8831	0.1044	7.6781	8.0880
Tooth_IDc*Missing_to	L5	0	8.4965	0.1198	8.2615	8.7316
Tooth_IDc*Missing_to	L5	1	8.5837	0.3465	7.9038	9.2636
Tooth_IDc*Missing_to	L6	0	10.5921	0.1029	10.3903	10.7940
Tooth_IDc*Missing_to	L7	0	10.1710	0.1164	9.9425	10.3994
Tooth_IDc*Missing_to	U1	0	7.0254	0.1028	6.8237	7.2272
Tooth_IDc*Missing_to	U2	0	6.1506	0.1096	5.9355	6.3658
Tooth_IDc*Missing_to	U2	1	5.2898	0.4797	4.3485	6.2310
Tooth_IDc*Missing_to	U3	0	7.9208	0.1075	7.7098	8.1318
Tooth_IDc*Missing_to	U4	0	8.8741	0.1048	8.6685	9.0796
Tooth_IDc*Missing_to	U5	0	9.0816	0.1106	8.8645	9.2986
Tooth_IDc*Missing_to	U6	0	11.0722	0.1023	10.8715	11.2728
Tooth_IDc*Missing_to	U7	0	11.0964	0.1189	10.8631	11.3297

Outcome BL dimension: Differences of marginal means: no missing tooth vs missing tooth

Effect	*Tooth_IDc*	*Missing_tooth*	*_Tooth_IDc*	*_Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Missing_to	L1	0	L1	1	-0.4268	0.4679	-1.3450	0.4914	0.3619
Tooth_IDc*Missing_to	L2	0	L2	1	-0.1906	0.2735	-0.7273	0.3460	0.4860
Tooth_IDc*Missing_to	L5	0	L5	1	-0.08714	0.3434	-0.7610	0.5868	0.7997
Tooth_IDc*Missing_to	U2	0	U2	1	0.8609	0.4744	-0.07003	1.7918	0.0699

Model 11. For hypodontia patients only: Linear mixed-effects model of CH Dimension versus Missing tooth and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	CH_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	56	LF163 LF171 LF174 LF192 LF193 LF223 LF228 30.04.14 LF233 LF236 LF241 LF246 LF265A LF266A LF270 LF271A LF277 LF278A LF279a LF285a LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF308A LF312A LF320 LF321A LF324 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF380A LF381 LF384a LF386A LF387a LF389A LF390A 31.08.10 LF394 LF395A LF398A LF401 LF411 LF417 LF445 LF458 LF463 LF488A
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Missing_tooth	2	0 1

Dimensions	
Covariance Parameters	2
Columns in X	40
Columns in Z per Subject	1
Subjects	56
Max Obs per Subject	27

Number of Observations	
Number of Observations Read	1876

Number of Observations	
Number of Observations Used	1132
Number of Observations Not Used	744

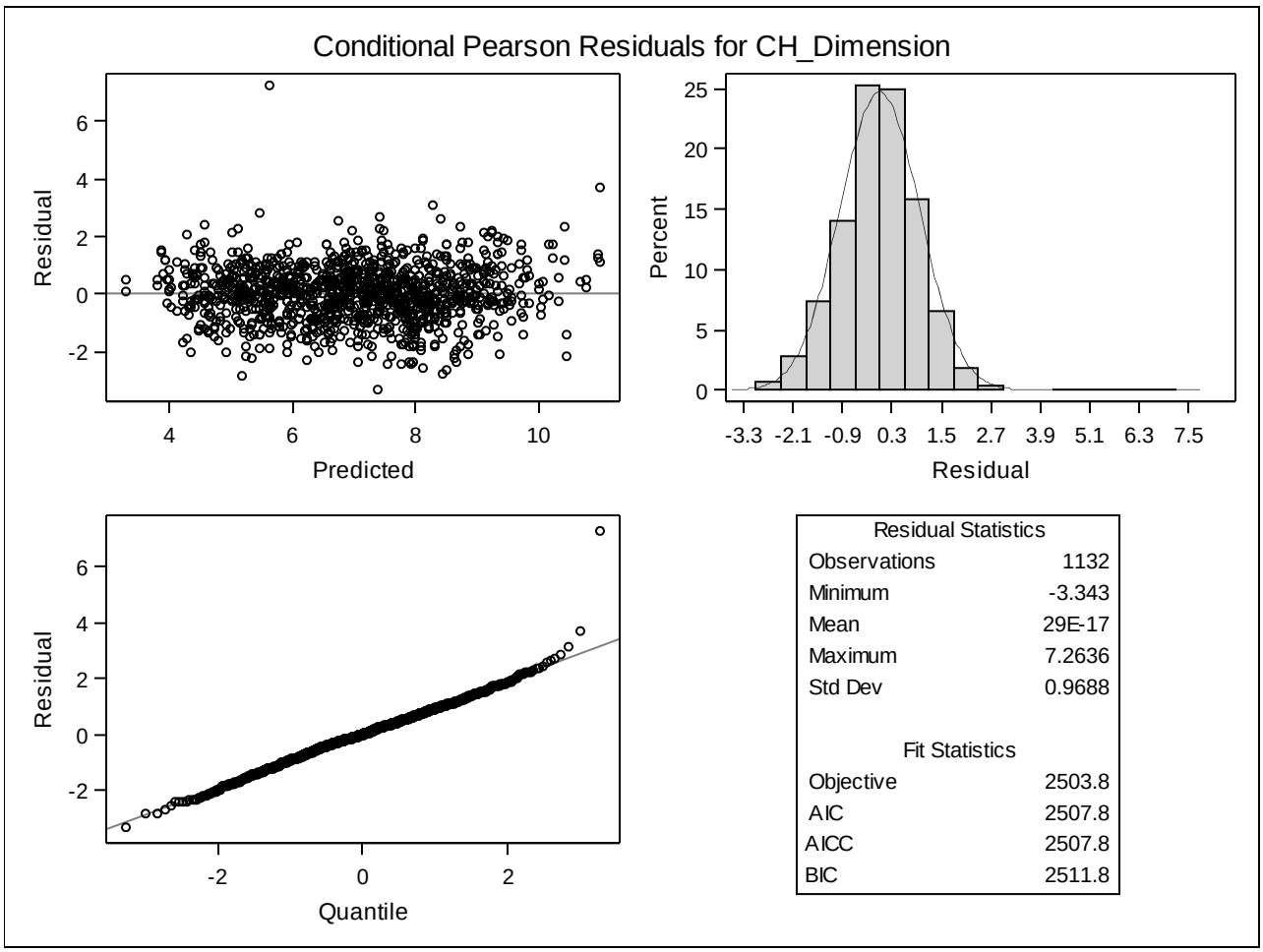
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.4694
Residual		0.4438

Fit Statistics	
-2 Res Log Likelihood	2503.8
AIC (Smaller is Better)	2507.8
AICC (Smaller is Better)	2507.8
BIC (Smaller is Better)	2511.8

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Missing_tooth	1	1059	0.80	0.3722
Tooth_IDc	13	1059	311.53	<.0001
Tooth_IDc*Missing_to	3	1059	2.83	0.0373
Age_days	1	1059	18.92	<.0001
Sex	1	1059	1.53	0.2157
Ethnicity_Polynesian	1	1059	0.42	0.5154



Outcome CH dimension: Marginal means

Effect	*Tooth_IDc*	*Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Missing_to	L1	0	7.5494	0.1529	7.2493	7.8495
Tooth_IDc*Missing_to	L1	1	7.6427	0.6943	6.2802	9.0051
Tooth_IDc*Missing_to	L2	0	7.6898	0.1541	7.3874	7.9922
Tooth_IDc*Missing_to	L2	1	8.2172	0.4173	7.3983	9.0361
Tooth_IDc*Missing_to	L3	0	8.5954	0.1541	8.2930	8.8977
Tooth_IDc*Missing_to	L4	0	7.3944	0.1545	7.0912	7.6976
Tooth_IDc*Missing_to	L5	0	6.3784	0.1779	6.0294	6.7274
Tooth_IDc*Missing_to	L5	1	6.1132	0.5073	5.1178	7.1086
Tooth_IDc*Missing_to	L6	0	6.0172	0.1524	5.7181	6.3163
Tooth_IDc*Missing_to	L7	0	5.5387	0.1666	5.2119	5.8656
Tooth_IDc*Missing_to	U1	0	9.1246	0.1520	8.8262	9.4229
Tooth_IDc*Missing_to	U2	0	7.2310	0.1616	6.9140	7.5480
Tooth_IDc*Missing_to	U2	1	5.9326	0.5015	4.9485	6.9166

Effect	*Tooth_IDc*	*Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Missing_to	U3	0	8.1919	0.1584	7.8810	8.5028
Tooth_IDc*Missing_to	U4	0	6.6204	0.1549	6.3165	6.9242
Tooth_IDc*Missing_to	U5	0	5.4867	0.1646	5.1637	5.8097
Tooth_IDc*Missing_to	U6	0	5.0379	0.1519	4.7399	5.3359
Tooth_IDc*Missing_to	U7	0	4.9688	0.1754	4.6246	5.3129

Outcome CH dimension: Differences of marginal means: no missing tooth vs missing tooth

Effect	*Tooth_IDc*	*Missing_tooth*	*_Tooth_IDc*	*_Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Missing_to	L1	0	L1	1	-0.09327	0.6842	-1.4359	1.2494	0.8916
Tooth_IDc*Missing_to	L2	0	L2	1	-0.5274	0.4000	-1.3122	0.2574	0.1876
Tooth_IDc*Missing_to	L5	0	L5	1	0.2652	0.5026	-0.7210	1.2513	0.5979
Tooth_IDc*Missing_to	U2	0	U2	1	1.2984	0.4909	0.3352	2.2617	0.0083

Model 12. For hypodontia patients only: Linear mixed-effects model of Modules versus Missing tooth and tooth number (combined) interaction, adjusting forage, Sex and ethnicity and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	Modules
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	56	LF163 LF171 LF174 LF192 LF193 LF223 LF228 30.04.14 LF233 LF236 LF241 LF246 LF265A LF266A LF270 LF271A LF277 LF278A LF279a LF285a LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF308A LF312A LF320 LF321A LF324 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF380A LF381 LF384a LF386A LF387a LF389A LF390A 31.08.10 LF394 LF395A LF398A LF401 LF411 LF417 LF445 LF458 LF463 LF488A
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Missing_tooth	2	0 1

Dimensions	
Covariance Parameters	2
Columns in X	40
Columns in Z per Subject	1
Subjects	56
Max Obs per Subject	25

Number of Observations	
Number of Observations Read	1876
Number of Observations Used	1077
Number of Observations Not Used	799

Convergence criteria met.

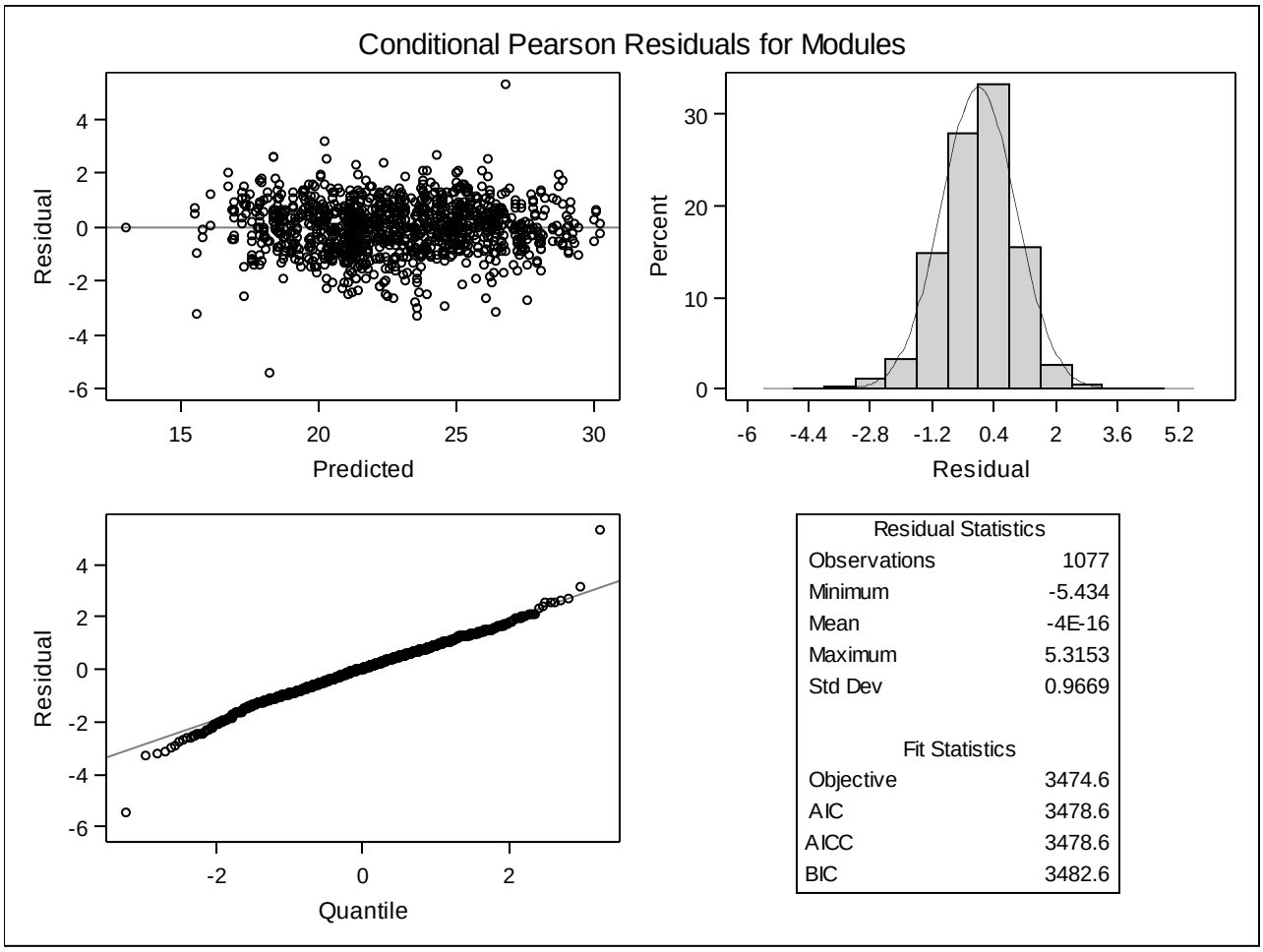
Covariance Parameter Estimates

Cov Parm	*Subject*	*Estimate*
Intercept	Patient_ID	1.7980
Residual		1.2238

Fit Statistics	
-2 Res Log Likelihood	3474.6
AIC (Smaller is Better)	3478.6
AICC (Smaller is Better)	3478.6
BIC (Smaller is Better)	3482.6

Type 3 Tests of Fixed Effects

Effect	*Num DF*	*Den DF*	*F Value*	*Pr > F*
Missing_tooth	1	1004	4.35	0.0373
Tooth_IDc	13	1004	414.09	<.0001
*Tooth_IDc*Missing_to*	3	1004	8.91	<.0001
Age_days	1	1004	8.84	0.0030
Sex	1	1004	2.41	0.1207
Ethnicity_Polynesian	1	1004	0.49	0.4848



Outcome Modules: Marginal means

Effect	*Tooth_IDc*	*Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*
Tooth_IDc*Missing_to	L1	0	18.6116	0.2911	18.0405	19.1828
Tooth_IDc*Missing_to	L1	1	19.3676	1.1620	17.0873	21.6478
Tooth_IDc*Missing_to	L2	0	19.7308	0.2930	19.1559	20.3058
Tooth_IDc*Missing_to	L2	1	20.4531	0.7081	19.0636	21.8426
Tooth_IDc*Missing_to	L3	0	22.4322	0.2932	21.8568	23.0076
Tooth_IDc*Missing_to	L4	0	22.2374	0.2935	21.6614	22.8133
Tooth_IDc*Missing_to	L5	0	21.8500	0.3275	21.2072	22.4927
Tooth_IDc*Missing_to	L5	1	21.9150	1.1601	19.6385	24.1916
Tooth_IDc*Missing_to	L6	0	27.3754	0.2904	26.8056	27.9452
Tooth_IDc*Missing_to	L7	0	26.1144	0.3327	25.4617	26.7672
Tooth_IDc*Missing_to	U1	0	24.5012	0.2897	23.9326	25.0697
Tooth_IDc*Missing_to	U2	0	19.8085	0.3047	19.2105	20.4064
Tooth_IDc*Missing_to	U2	1	13.9110	1.1748	11.6057	16.2163
Tooth_IDc*Missing_to	U3	0	23.7084	0.2998	23.1202	24.2967
Tooth_IDc*Missing_to	U4	0	22.2067	0.2949	21.6280	22.7853
Tooth_IDc*Missing_to	U5	0	21.1605	0.3084	20.5553	21.7656
Tooth_IDc*Missing_to	U6	0	26.4402	0.2899	25.8714	27.0090
Tooth_IDc*Missing_to	U7	0	25.9061	0.3285	25.2615	26.5507

Outcome Modules: Differences of marginal means: no missing tooth vs missing tooth

Effect	*Tooth_IDc*	*Missing_tooth*	*_Tooth_IDc*	*_Missing_tooth*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Tooth_IDc*Missing_to	L1	0	L1	1	-0.7560	1.1368	-2.9867	1.4748	0.5062
Tooth_IDc*Missing_to	L2	0	L2	1	-0.7223	0.6653	-2.0280	0.5833	0.2779
Tooth_IDc*Missing_to	L5	0	L5	1	-0.06509	1.1460	-2.3139	2.1837	0.9547
Tooth_IDc*Missing_to	U2	0	U2	1	5.8975	1.1529	3.6351	8.1599	<.0001

Model 13. Linear mixed-effects model of MD Dimension versus Hypodontia/Control and Ethnicity interaction, adjusting forage, tooth_ID (combined) and Sex and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	MD_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2641
Number of Observations Not Used	1195

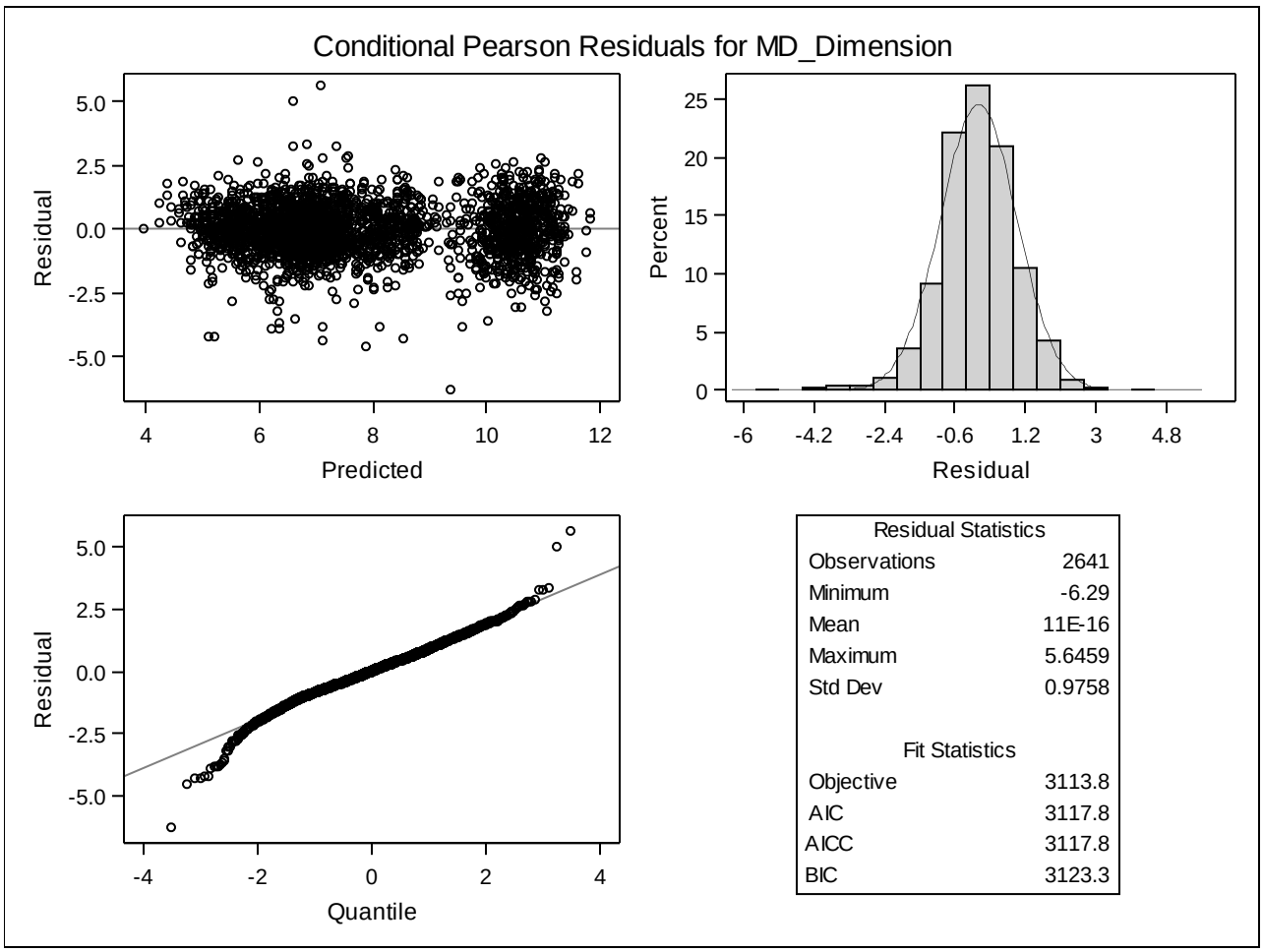
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.1214
Residual		0.1623

Fit Statistics	
-2 Res Log Likelihood	3113.8
AIC (Smaller is Better)	3117.8
AICC (Smaller is Better)	3117.8
BIC (Smaller is Better)	3123.3

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2506	5.36	0.0207
Ethnicity_Polynesian	1	2506	1.63	0.2024
Ethnicity_Poly*Group	1	2506	0.10	0.7535
Age_days	1	2506	2.18	0.1396
Tooth_IDc	13	2506	4024.63	<.0001
Sex	1	2506	7.44	0.0064



Outcome MD dimension: Marginal means

Effect	*Ethnicity_Polynesian*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Ethnicity_Poly*Group	non-polynesian	control	7.9787	0.04638	7.8877	8.0696
Ethnicity_Poly*Group	non-polynesian	hypodontia	7.6836	0.05124	7.5831	7.7841
Ethnicity_Poly*Group	polynesian	control	8.2157	0.2580	7.7098	8.7216
Ethnicity_Poly*Group	polynesian	hypodontia	7.8279	0.1298	7.5734	8.0824

Outcome MD dimension: Differences of marginal means: control versus hypodontia

Effect	*Ethnicity_Polynesian*	*Group*	*_Ethnicity_ Polynesian*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Ethnicity_Poly*Group	non-polynesian	control	non-polynesian	hypodontia	0.2951	0.06862	0.1606	0.4297	<.0001
Ethnicity_Poly*Group	polynesian	control	polynesian	hypodontia	0.3878	0.2869	-0.1749	0.9505	0.1767

Outcome MD dimension: Differences of marginal means: Non polynesian versus polynesian

Effect	*Ethnicity_Polynesian*	*Group*	*_Ethnicity_ Polynesian*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Ethnicity_Poly*Group	non-polynesian	control	polynesian	control	-0.2370	0.2625	-0.7517	0.2777	0.3666
Ethnicity_Poly*Group	non-polynesian	hypodontia	polynesian	hypodontia	-0.1443	0.1392	-0.4173	0.1287	0.3000

Model 14. Linear mixed-effects model of BL Dimension versus Hypodontia/Control and Ethnicity interaction, adjusting forage, tooth_ID (combined) and Sex and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	BL_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2605
Number of Observations Not Used	1231

Convergence criteria met.

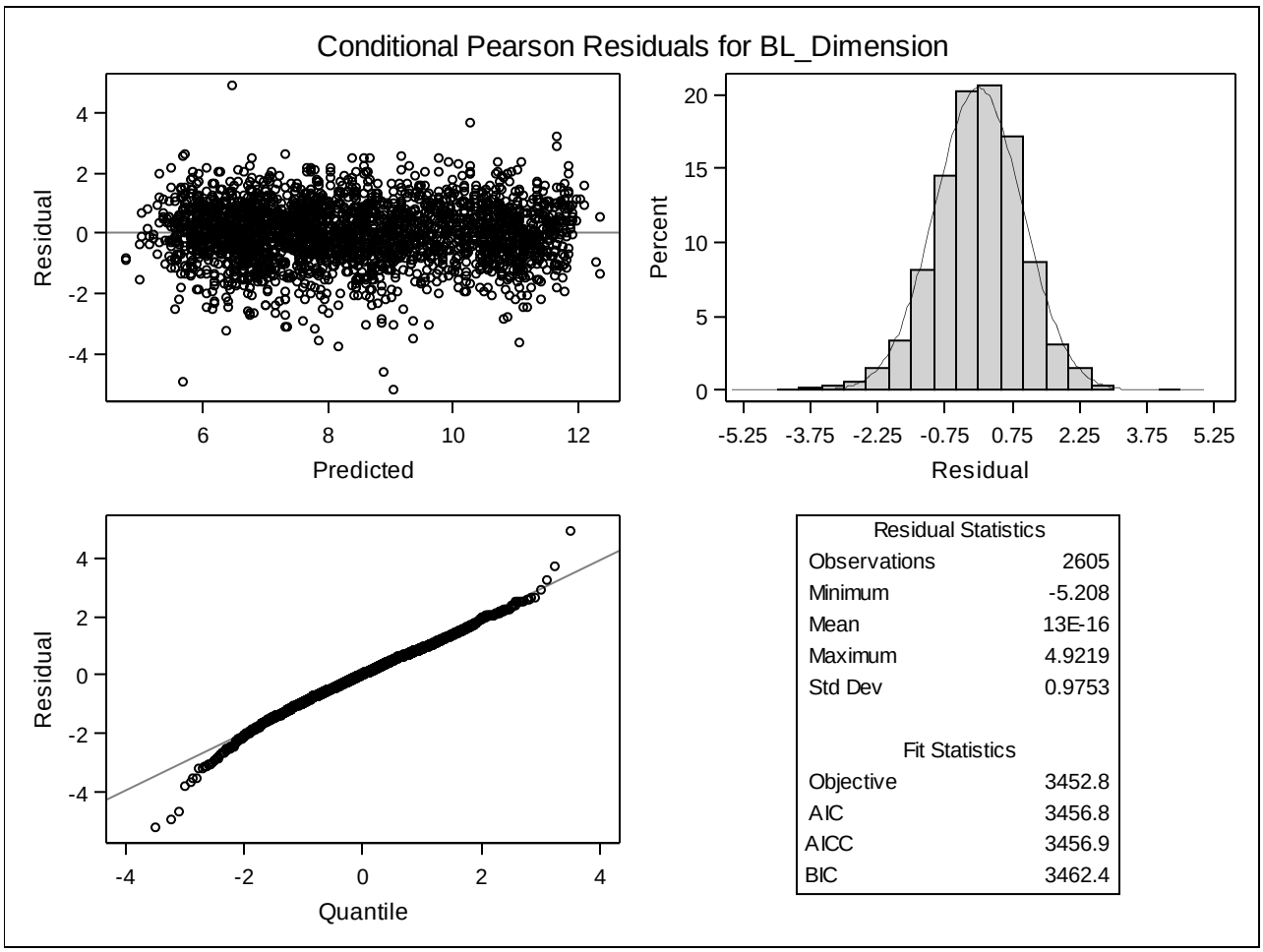
Covariance Parameter Estimates

Cov Parm	*Subject*	*Estimate*
Intercept	Patient_ID	0.1758
Residual		0.1860

Fit Statistics	
-2 Res Log Likelihood	3452.8
AIC (Smaller is Better)	3456.8
AICC (Smaller is Better)	3456.9
BIC (Smaller is Better)	3462.4

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2471	4.38	0.0365
Ethnicity_Polynesian	1	2471	0.53	0.4680
Ethnicity_Poly*Group	1	2471	0.09	0.7637
Age_days	1	2471	4.73	0.0298
Tooth_IDc	13	2471	3326.15	<.0001
Sex	1	2471	4.95	0.0262



Outcome BL dimension: Marginal means

Effect	*Ethnicity_Polynesian*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Ethnicity_Poly*Group	non-polynesian	control	8.6862	0.05552	8.5773	8.7950
Ethnicity_Poly*Group	non-polynesian	hypodontia	8.3701	0.06131	8.2498	8.4903
Ethnicity_Poly*Group	polynesian	control	8.8692	0.3089	8.2634	9.4749
Ethnicity_Poly*Group	polynesian	hypodontia	8.4469	0.1552	8.1425	8.7513

Outcome BL dimension: Differences of marginal means: control versus hypodontia

Effect	*Ethnicity_Polynesian*	*Group*	*_Ethnicity_ Polynesian*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Ethnicity_Poly*Group	non-polynesian	control	non-polynesian	hypodontia	0.3161	0.08213	0.1551	0.4772	0.0001
Ethnicity_Poly*Group	polynesian	control	polynesian	hypodontia	0.4223	0.3434	-0.2510	1.0956	0.2189

Outcome BL dimension: Differences of marginal means: Non polynesian versus polynesian

Effect	Ethnicity_Polynesian	Group	_Ethnicity_ Polynesian	_Group	Estimate	StdErr	Lower	Upper	Probt
Ethnicity_Poly*Group	non-polynesian	control	polynesian	control	-0.1830	0.3142	-0.7991	0.4331	0.5603
Ethnicity_Poly*Group	non-polynesian	hypodontia	polynesian	hypodontia	-0.07682	0.1664	-0.4031	0.2495	0.6444

Model 15. Linear mixed-effects model of CH Dimension versus Hypodontia/Control and Ethnicity interaction, adjusting forage, tooth_ID (combined) and Sex and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	CH_Dimension
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	Levels	Values
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2624
Number of Observations Not Used	1212

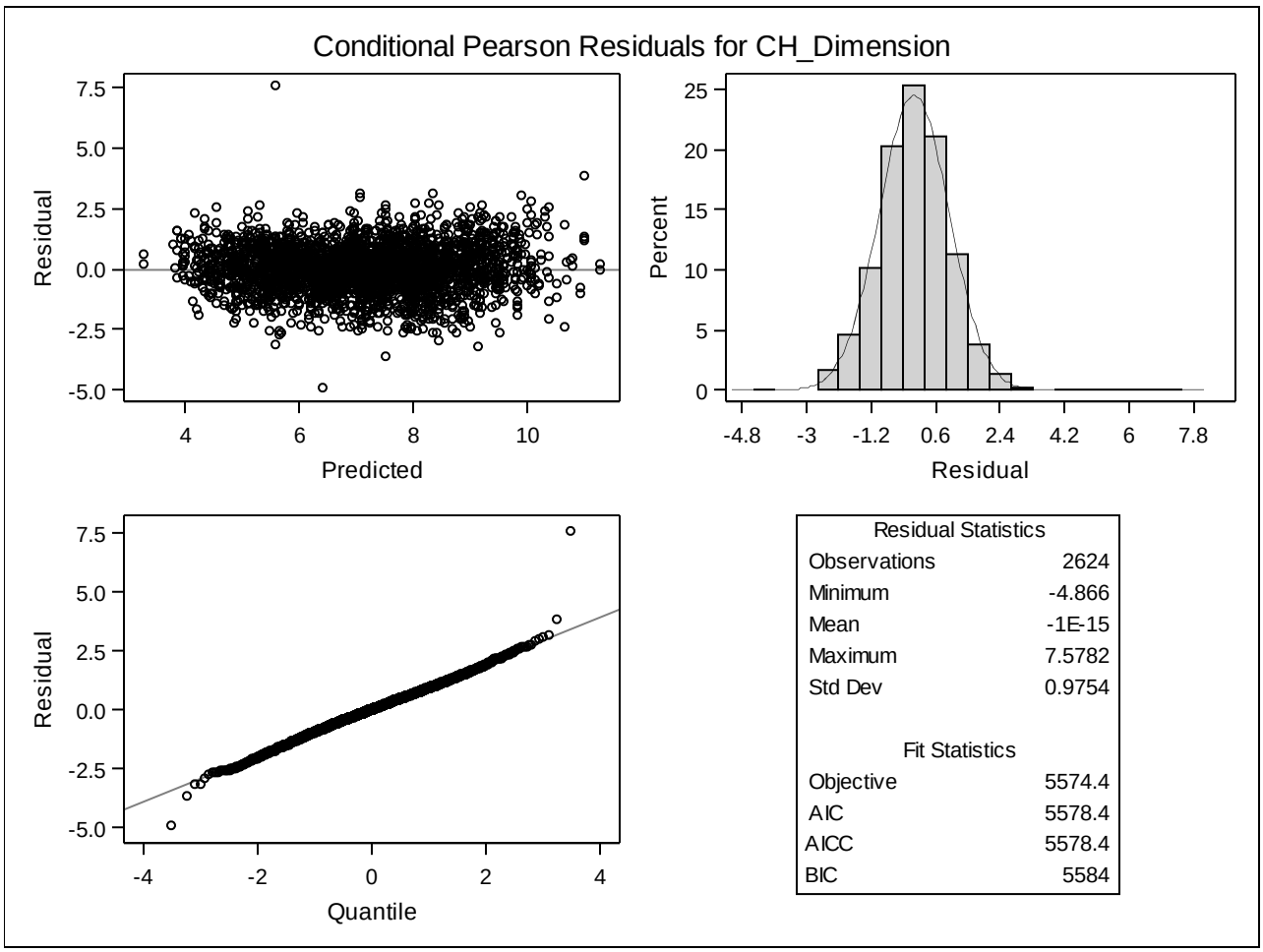
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	0.3967
Residual		0.4161

Fit Statistics	
-2 Res Log Likelihood	5574.4
AIC (Smaller is Better)	5578.4
AICC (Smaller is Better)	5578.4
BIC (Smaller is Better)	5584.0

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2490	0.39	0.5347
Ethnicity_Polynesian	1	2490	0.20	0.6527
Ethnicity_Poly*Group	1	2490	0.63	0.4273
Age_days	1	2490	31.57	<.0001
Tooth_IDc	13	2490	796.07	<.0001
Sex	1	2490	5.03	0.0250



Outcome CH dimension: Marginal means

Effect	*Ethnicity_Polynesian*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Ethnicity_Poly*Group	non-polynesian	control	7.1522	0.08337	6.9887	7.3157
Ethnicity_Poly*Group	non-polynesian	hypodontia	6.7773	0.09199	6.5969	6.9577
Ethnicity_Poly*Group	polynesian	control	6.8209	0.4637	5.9117	7.7301
Ethnicity_Poly*Group	polynesian	hypodontia	6.8668	0.2331	6.4098	7.3239

Outcome CH dimension: Differences of marginal means: control versus hypodontia

Effect	*Ethnicity_Polynesian*	*Group*	*_Ethnicity_ Polynesian*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Ethnicity_Poly*Group	non-polynesian	control	non-polynesian	hypodontia	0.3749	0.1233	0.1332	0.6167	0.0024
Ethnicity_Poly*Group	polynesian	control	polynesian	hypodontia	-0.04597	0.5154	-1.0566	0.9647	0.9289

Outcome CH dimension: Differences of marginal means: Non polynesian versus polynesian

Effect	*Ethnicity_Polynesian*	*Group*	*_Ethnicity_ Polynesian*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Ethnicity_Poly*Group	non-polynesian	control	polynesian	control	0.3313	0.4716	-0.5934	1.2561	0.4824
Ethnicity_Poly*Group	non-polynesian	hypodontia	polynesian	hypodontia	-0.08955	0.2498	-0.5795	0.4003	0.7200

Model 16. Linear mixed-effects model of Modules versus Hypodontia/Control and Ethnicity interaction, adjusting forage, tooth_ID (combined) and Sex and controlling for clustering on Patient ID (multiple teeth per patient)

The Mixed Procedure

Model Information	
Data Set	WORK.TEETH
Dependent Variable	Modules
Covariance Structure	Variance Components
Subject Effect	Patient_ID
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Class Level Information

Class	*Levels*	*Values*
Patient_ID	121	LF162 LF163 LF171 LF174 LF176 LF177 LF183 LF184 LF192 LF193 LF198 LF199 LF204 LF207 LF210 LF211 LF222 LF223 LF225 LF227 LF228 30.04.14 LF231 LF233 LF236 LF237 LF239 LF240 LF241 LF242 LF246 LF260 LF265A LF266A LF270 LF271A LF272 LF274 LF277 LF278A LF279a LF282A 5.2.09 LF285a LF286 LF287a LF289A LF290 LF291 LF293A LF298A LF300a LF304a LF305 LF306A LF307 LF308A LF312A LF316 LF319A LF320 LF321A LF324 LF325 LF327 LF332 LF336 LF347a 29/03/11 LF351a LF354a LF355A 24.03.14 LF359A LF363 LF365 LF366 LF374 LF375 LF376 LF377 LF380A LF381 LF382 LF384a LF386A LF387a LF388 LF389A LF390A 31.08.10 LF394 LF395A LF396 LF398A LF399 LF401 LF406 LF407 LF411 LF415 LF417 LF422 LF423 LF429 LF434 LF444 LF445 LF447 LF450 LF453 LF458 LF463 LF470 LF472 LF476 LF485 LF486 LF488A LF489 LF496 LF497 LF501 LF505 LF509 LF510
Tooth_IDc	14	L1 L2 L3 L4 L5 L6 L7 U1 U2 U3 U4 U5 U6 U7
Sex	2	F M
Ethnicity_Polynesian	2	non-polynesian polynesian
Group	2	control hypodontia

Dimensions	
Covariance Parameters	2
Columns in X	26
Columns in Z per Subject	1
Subjects	121
Max Obs per Subject	28

Number of Observations	
Number of Observations Read	3836
Number of Observations Used	2510
Number of Observations Not Used	1326

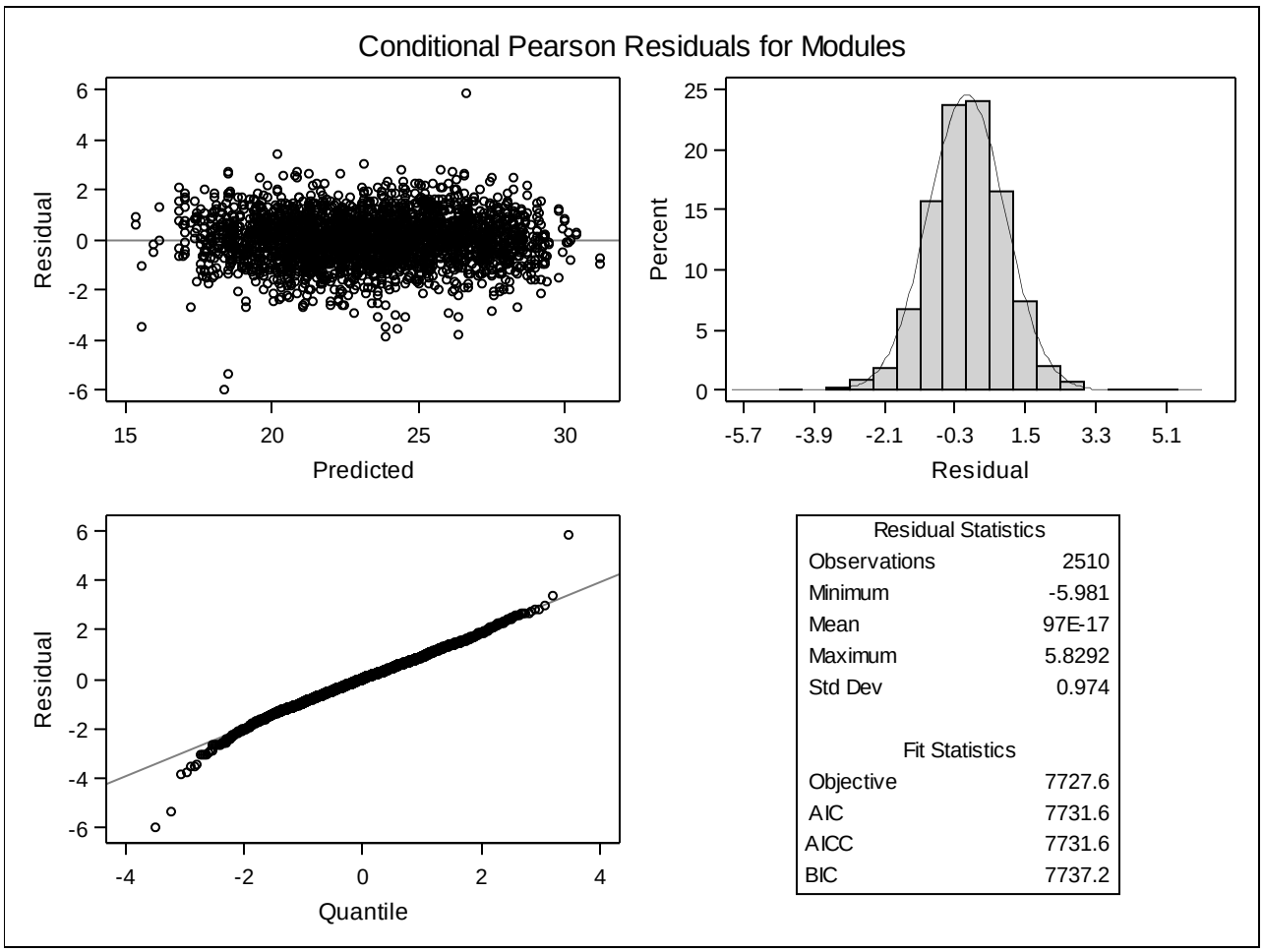
Convergence criteria met.

Covariance Parameter Estimates		
Cov Parm	Subject	Estimate
Intercept	Patient_ID	1.4752
Residual		1.0655

Fit Statistics	
-2 Res Log Likelihood	7727.6
AIC (Smaller is Better)	7731.6
AICC (Smaller is Better)	7731.6
BIC (Smaller is Better)	7737.2

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
Group	1	2375	3.11	0.0777
Ethnicity_Polynesian	1	2375	0.14	0.7101
Ethnicity_Poly*Group	1	2375	0.02	0.8889
Age_days	1	2375	16.14	<.0001
Tooth_IDc	13	2375	1316.38	<.0001
Sex	1	2375	8.24	0.0041



Outcome Modules: Marginal means

Effect	*Ethnicity_Polynesian*	*Group*	*Estimate*	*StdErr*	*Lower*	*Upper*
Ethnicity_Poly*Group	non-polynesian	control	23.8401	0.1598	23.5266	24.1535
Ethnicity_Poly*Group	non-polynesian	hypodontia	22.8748	0.1762	22.5292	23.2204
Ethnicity_Poly*Group	polynesian	control	23.9603	0.8870	22.2208	25.6998
Ethnicity_Poly*Group	polynesian	hypodontia	23.1368	0.4463	22.2615	24.0120

Outcome Modules: Differences of marginal means: control versus hypodontia

Effect	*Ethnicity_Polynesian*	*Group*	*_Ethnicity_ Polynesian*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Ethnicity_Poly*Group	non-polynesian	control	non-polynesian	hypodontia	0.9653	0.2362	0.5021	1.4284	<.0001
Ethnicity_Poly*Group	polynesian	control	polynesian	hypodontia	0.8236	0.9861	-1.1101	2.7572	0.4037

Outcome Modules: Differences of marginal means: Non polynesian versus polynesian

Effect	*Ethnicity_Polynesian*	*Group*	*_Ethnicity_ Polynesian*	*_Group*	*Estimate*	*StdErr*	*Lower*	*Upper*	*Probt*
Ethnicity_Poly*Group	non-polynesian	control	polynesian	control	-0.1203	0.9022	-1.8895	1.6490	0.8940
Ethnicity_Poly*Group	non-polynesian	hypodontia	polynesian	hypodontia	-0.2620	0.4783	-1.1999	0.6760	0.5840