3D GEOMETRIC MORPHOMETRIC ANALYSIS OF TOOTH SHAPE IN HYPODONTIA

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Abstract

Assessment of tooth morphology is essential in the diagnosis and management of hypodontia patients. Several techniques have been used to quantify tooth shape in hypodontia patients and these have revealed smaller tooth dimensions and anomalous tooth shapes in these patients when compared with controls. However, previous studies have mainly used 2D images and have thus provided limited information. The present study adopted a novel three-dimensional geometric morphometric technique to quantify the crown morphology and sizes of teeth of hypodontia patients and compare them with those of control patients. Allometric variations were also investigated in order to determine whether there was any association between the size and shape of teeth.

Landmarks were recorded on each clinical crown of all the permanent teeth, apart from third molars, of 3D scanned study models of hypodontia and control subjects. The study sample comprised 120 hypodontia patients (40 patients with mild, 40 with moderate and 40 with severe hypodontia) and 40 age- and sex-matched controls. Procrustes superimposition was utilized to scale and superimpose the landmark coordinate data and were then subjected to principal component analysis (PCA). Subsequently, shape differences were tested statistically using multivariate statistics.

Size variation was for the most part found to be significant, especially when the control subjects were compared to the hypodontia groups. The anterior teeth were more affected than the posterior. Generally speaking, the size differences became greater as the severity of the hypodontia increased. The pattern was virtually the same for both sexes. With regard to shape, most teeth were affected by the hypodontia, although the pattern was less clear. When allometry was taken into account, the pattern of size/shape relationship was found to be significant for most teeth, particularly in the anterior region, and shape differences were still significant after controlling, when possible, for allometry.

It was found that the degree of variation in tooth shape was associated with the degree of severity of the hypodontia. The findings of the study therefore indicate that quantitative measurement of the tooth shape in hypodontia patients may enhance the multidisciplinary management of those patients.

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Awards

- First place, Sarnat Craniofacial Biology Award 2010. International Association of Dental Research (IADR), General Session, Barcelona, Spain, 14th-17th July 2010.
- Distinguished achievement award 2011. The 5th Saudi International conference, Coventry, UK, 23rd-26th June, 2011.
- Second best poster award in medical science 2011. The 5th Saudi International conference, Coventry, UK, 23rd-26th June, 2011.
- NEPG Runner's up poster prize 2011. The North East Post-graduate Research Conference, Newcastle, UK, 21st October, 2011.

Publications

- Validation of a 3D laser scanner for odontometric measurements. *K. KHALAF, I. AL SHAHRANI, W. DIRKS, and N.J.A. JEPSON, J Dent Res 88 (*Spec Iss *B): 146 (BSDR), 2009* (www.dentalresearch.org).
- 3D Analysis of Tooth Shape in Hypodontia. *I. AL SHAHRANI, W. DIRKS, K. KHALAF, and N.J.A. JEPSON, J Dent Res 89 (*Spec Iss *B): 3521, 2010* (www.dentalresearch.org).

Presentations

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- **Oral:** 3D geometric morphometrics tooth shape analysis in hypodontia from the North East of England. North East Postgraduate Conference, Newcastle, UK, 5th November, 2010.
- **Poster:** 3D Geometric Morphometrics Tooth Shape Analysis in Hypodontia. 3D User group, Cardiff, UK, 12th November, 2010.

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- **Poster:** 3D analysis to describe tooth shape in hypodontia patients. Saudi International Conference 2011. Coventry, UK, 23rd – 26th June 2011.
- **Oral:** 3D Geometric Morphometrics Tooth Shape Analysis in Hypodontia. 15th International Symposium on Dental Morphology. Newcastle upon Tyne, UK, 24th – 27th August 2011.
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- **Oral:** 3D Quantitative Tooth Shape Analysis in Hypodontia. British Society for Oral and Dental Research (BSODR), Unilever Poster Competition, Sheffield, UK, 13th – 15th September 2011.
- **Poster:** 3D quantitative tooth shape analysis in hypodontia from the North East of England. North East Postgraduate Conference, Newcastle, UK, 21st October, 2011.

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Introduction

The term 'hypodontia' refers to the congenital absence of teeth. Hypodontia is the most frequently occurring dental anomaly (Brook, 1984; Dhanrajani, 2002; McKeown *et al.*, 2002; Kirzioglu *et al.*, 2005; Wu *et al.*, 2007). The prevalence of hypodontia has been estimated at between 2 and 10% of the population in the permanent dentition, excluding third molars (Polder *et al.*, 2004). Second premolars and upper lateral incisors are the most frequently missing teeth. Females are more often affected than males (Brook, 1984). Hypodontia is not an isolated trait but occurs in conjunction with other dental anomalies such as aplasia of second premolars, or small size of maxillary lateral incisors (Baccetti, 1998).

The precise aetiology and pathogenesis of the congenital absence of teeth is still unclear (Vastardis, 2000; Mostowska *et al.*, 2003; Polder *et al.*, 2004). However, it appears that it is the result of environmental, epigenetic or genetic factors or a combination of these causes. Brook (1984) suggests a multifactorial model in which polygenic factors play a major part but environmental factors are included. Recently, Brook (2009) reviewed the aetiology of dental anomalies and emphasized the complexity of the dental development process. This a multilevel process that takes place at both molecular and cellular levels, which interact to produce a clinical outcome. It is also multidimensional as it grows and develops on three axes: x, y, and z, and in the fourth dimension of time. The process is, in addition, a long-term process and might be affected by various factors: genetic, epigenetic or environmental factors (Brook, 2009). Variations in the size and shape of the remaining teeth have also been found to be associated with hypodontia (Brook, 1984; Schalk-van der Weide *et al.*, 1992; Schalk-van der Weide and Bosman, 1996).

Many studies have indicated an association between anomalies in tooth number and form and other dental anomalies (Brook, 1984; Schalk-van der Weide *et al.*, 1992; Schalk-van der Weide and Bosman, 1996; McKeown *et al.*, 2002). These dental anomalies can create differences in maxillary and mandibular dental arch lengths which may result in malocclusion and complicate treatment planning. Orthodontic management of hypodontia patients requires multidisciplinary care, either to close the spaces where there are missing teeth or to open up these spaces and then replace the missing teeth to achieve aesthetic and functional occlusion (Jepson *et al.*, 2003; Rashedi, 2003; Forgie *et al.*, 2005; Holt and Drake, 2008). Both options may require reshaping some teeth to change their size and shape. A good knowledge of the size and the exact shape of each tooth (in 3D) in each

category of hypodontia (mild, moderate, severe) will therefore help in reshaping teeth or in determining how much the spaces need to be opened to allow the restorative replacement of the missing teeth, in order to achieve harmony in intra- and inter-arch relationships. Furthermore, knowledge of the shape will offer additional insights which will help in choosing the correct bracket prescriptions for hypodontia patients, since the present prescriptions are designed for people with normal size and shape of teeth.

Several techniques have been proposed to quantify tooth size and shape. Some of these techniques involve the use of traditional morphometrics such as linear measurements (MD and BL) and have revealed smaller tooth dimensions in patients with hypodontia than in controls (Rune and Sarnas, 1974; Schalk-van der Weide *et al.,* 1992; Schalk-van der Weide and Bosman, 1996); another researcher measured the size in two dimensions and found that patients with severe hypodontia (6 or more teeth missing) had a slightly greater reduction in tooth size than control subjects (Brook, 1984).

The use of linear measurements only gives limited data, mainly about size, and does not describe variations in tooth shape or form. Recently, image analysis systems have been developed that overcome some of the shortcomings of manual techniques (Brook *et al.,* 2002). Further advances in digital imaging and scanning have aided the process of taking measurements and also make it possible to record landmark locations as coordinates. Bookstein (1996) led the development of geometric morphometrics to analyse shape and called the new methodology 'morphometric syntheses'. Robinson and colleagues (2001; 2002) used these ideas to study tooth form in 2 dimensions (x, y coordinates) from a photographic image. They introduced a formal definition of shape and demonstrated its application in the study of tooth morphology. A high resolution scanner was used by Kieser (2007) to analyse anterior tooth shape but he only used it in two dimensions. Thus, although previous investigators have described tooth shape, they have built their methodology in 2-dimensional planes; the result of this 2D analysis of a 3D object is that they have provided only partial and rather limited descriptions of shape. Therefore, an investigation of a large number of subjects divided into subgroups of patients with differing degrees of severity of hypodontia using 3D geometric morphometric analysis may contribute to our understanding of the aetiology and pathogenesis of hypodontia. The use of geometric morphometric techniques in conjunction with multivariate analysis has had a great impact on biological studies, since it allows a comprehensive analysis of variations in biological shape. An important feature of these techniques is that they allow

the non-destructive 3D capture of the geometry of the morphological structure and preserve this information throughout the analysis (Adams *et al.*, 2004). In addition, geometric methods permit the quantification of differences in size as well as in shape; this cannot be accomplished using traditional methods (Monteiro *et al.*, 2002).

The aim of the current study was to apply a novel 3D geometric morphometric technique to quantify the crown size, shape and allometric variation of the remaining teeth of hypodontia subgroups using scanned study models of these teeth. These teeth would be compared to those of control subjects with full dentition of a similar age to the hypodontia subjects, with both groups having similar proportions of male and female subjects.

This thesis is divided into five chapters. The following first chapter contains a review of the relevant literature, divided into several sections and subsections, and then a summary of the literature review. Chapter two includes a statement of the problem and a discussion of the overall aims, objectives, secondary aims and null hypotheses of the study. Chapter three describes the study population and the materials and methods used in the research. The measurement of errors conducted to evaluate the new 3D system and investigator reliability are also described in this chapter. Chapter four consists of four parts: the first part provides a description of the study population; in the second part, detailed findings for one tooth (the lower left first molar) are presented; part three contains a summary of the findings for all teeth together, and in part four 3D visualizations of all shape differences for all teeth between the groups are provided. In chapter five the methodology and the main findings are discussed, presenting the conclusions of the project and making recommendations for future research.

Chapter 1 Literature Review

1.1 Hypodontia

1.1.1 Terminology

Hypodontia is generally defined as the developmental absence of one or more teeth, excluding the third molars, either in the primary or permanent dentition. Researchers have used a variety of terminology to describe the condition, such as a reduction in teeth number, teeth aplasia, congenitally missing teeth, absence of teeth, agenesis of teeth, and lack of teeth (Hunstadbraten, 1973; Brook, 1974; Jorgenson, 1980; Zhu *et al.*, 1996; Dhanrajani, 2002; McKeown *et al.*, 2002; Kirzioglu *et al.*, 2005; Wu *et al.*, 2007; Swinnen *et al.*, 2008; Brook *et al.*, 2009a; Brook *et al.*, 2009b). The missing teeth are those which have failed to erupt clinically in the oral cavity and even in radiographs there is no sign of the teeth starting to appear; the cause is usually disturbance during the early stages of tooth development (Jorgenson, 1980; Pemberton *et al.*, 2005). Hypodontia is one of the most common human dental developmental anomalies (Brook, 1974; Hobkirk and Brook, 1980; Jorgenson, 1980; Vastardis, 2000; Kirzioglu *et al.*, 2005; Pemberton *et al.*, 2005; Wu *et al.*, 2007; De Coster *et al.*, 2009).

1.1.2 Classification

Many methods of classification have been employed in the literature (Brook, 1974; Hobkirk and Brook, 1980; Schalk-van der Weide *et al.*, 1992; Goodman *et al.*, 1994; Schalk-van der Weide and Bosman, 1996; Vastardis, 2000; Brook *et al.*, 2002; Dhanrajani, 2002; Mostowska *et al.*, 2003; Nunn *et al.*, 2003; Polder *et al.*, 2004; Kirzioglu *et al.*, 2005; Pemberton *et al.*, 2005; Cobourne, 2007; Wu *et al.*, 2007).

Some researchers have found the congenital absence of teeth to occur either as an isolated family form or as an intermittent form. The inherited form could be either autosomal-dominant, autosomal-recessive, or an X-linked trait (Mostowska *et al.*, 2003).

Others have defined the congenital absence of teeth according to the number of missing teeth (Brook, 1974; Burzynski and Escobar, 1983; van der Weide *et al.*, 1993; Goodman *et al.*, 1994; Vastardis, 2000; Nunn *et al.*, 2003; Cobourne, 2007; Wu *et al.*, 2007). *Hypodontia* refers to the condition where there is an absence of fewer than six teeth The term *Oligodontia* is usually used to describe a larger number of missing teeth (six or more). *Anodontia* is the complete absence of teeth.

Dhanrajani (2002) classified hypodontia according to the severity of the condition following the method of previous researchers (Hobkirk and Brook, 1980; Brook, 1984). He used 'mild to moderate hypodontia' to denote agenesis of two to five teeth, and referred to the absence of six or more teeth, excluding the third molars, as 'severe hypodontia'. 'Oligodontia' in this scheme is the absence of multiple teeth, usually associated with systemic disorders (Dhanrajani, 2002). Many other researchers have used similar methods of classifying the congenital absence of teeth (Brook *et al.*, 2002; Hobkirk *et al.*, 2011). In general, they identify three categories of hypodontia, excluding third molars, as follows:

- *Mild* with 1 or 2 missing teeth.
- *Moderate* with 3 – 5 missing teeth.
- *Severe* with 6 or more missing teeth.

Hypodontia is also classified as either isolated hypodontia or syndromic hypodontia. Isolated hypodontia refers to those cases without syndromes (Arte *et al.*, 2001; Tan *et al.*, 2011). Thus, hypodontia can occur either as part of a syndrome or as a non-syndromic, familial form; in the latter it occurs as an isolated trait, affects variable numbers of teeth and appears either sporadically or as an inherited condition within a family pedigree (Pemberton *et al.*, 2005; Cobourne, 2007).

1.1.3 Prevalence

Primary dentition

The prevalence of hypodontia in the primary dentition is found to be very low. The range has generally been between 0.1 and 0.9% of the population (Brook, 1974; Daugaard-Jensen *et al.*, 1997; Wu *et al.*, 2007). The chance of having the permanent successors missing is, by contrast, very high (Daugaard-Jensen *et al.*, 1997; Wu *et al.*, 2007). In a study involving a sample of Saudi children, the teeth found to be missing most frequently in the primary dentition were the upper and lower lateral incisors (Salama and Abdel-Megid, 1994). Larmour (2005) and colleagues reviewed many previous studies and found the prevalence of hypodontia in primary dentition was between 0.5% in the Icelandic population and 2.4% in the Japanese population.

Permanent dentition

Populational differences

The occurrence of tooth agenesis varies in the permanent dentition. Polder and colleagues (2004) used meta-analysis and found that the prevalence of missing permanent teeth varies from 2.2% to 10.1%, excluding third molars, which are absent in around 20% of individuals in the recorded population. The highest prevalence of the hypodontia was found in Australian Caucasians, at 6.3%, followed by European descent (5.5%) and then North American Caucasians (3.9%). Polder et al (2004) also showed the prevalence in African Americans (3.8%), Saudi Arabs (2.5%) and Chinese (6.9%) but they did not include these in their meta-analysis, since according to them the samples used in studies of these populations were too small. Another review has shown that the prevalence of hypodontia apart from the third molars varied between 2.6% in Saudi Arabia and 11.3% in Ireland, while in the United Kingdom it was found to be between 4% and 4.5% (Larmour *et al.*, 2005; Shimizu and Maeda, 2009). The authors suggest that these variations in prevalence may result from a) the different age groups in the samples, since in younger groups there might be some teeth which are still to erupt, whereas in older patients teeth might have been extracted; b) differences in sampling methodology; c) populational differences, and d) differences in the diagnostic criteria employed (Larmour *et al.*, 2005; Shimizu and Maeda, 2009). In a study conducted in 1974, it was found that the prevalence rate in British children was 3.5-6.5% in the permanent dentition, excluding third molars (Brook, 1974).

Variations have been found in the prevalence of hypodontia between different populations; in some African and indigenous Australian populations the prevalence was found to be 1%, but it could be as high as 30% in Japanese populations (Sofaer, 1975). In African Americans, it has been estimated to be 7.7% (Jorgenson, 1980). Also, in Scandinavian children, the prevalence of agenesis in the permanent dentition is reported to be 6-8% (Bjerklin *et al.*, 2008). In the American population, hypodontia is more common in whites than in blacks, and the number of missing teeth is also higher in whites than in blacks (Harris and Clark, 2008). In the Indian population the prevalence of hypodontia has recently been found to be 4.19% (Gupta *et al.*, 2011). The prevalence of tooth agenesis in the Turkish orthodontic population has been found to be 4.6% (Celikoglu *et al.*, 2010), and 6.4% in the Brazilian orthodontic population (Gomes *et al.*, 2010); by contrast, in Thai populations it is as high as 26.1% (Kositbowornchai, 2011).

It is clear from all the studies mentioned above that the prevalence of missing teeth varies among different populations. These differences found in prevalence may not be true populational differences, however, but could be the result of variations in sampling methodology, data collection methods and participants' ages (Wu *et al.*, 2007).

Sex differences

A possible relationship between tooth agenesis and sex has been investigated. There have been studies which have found higher incidences of tooth agenesis in females (Brook, 1974; Vastardis, 2000; Mattheeuws *et al.*, 2004; Polder *et al.*, 2004). Polder's (2004) meta-analysis found a male to female ratio of 1:1.4. Brook (1974) summarised the findings of numerous studies which evaluated the effect of sex on hypodontia in the permanent dentition, and concluded that hypodontia is less common in males than in females, the ratio being 1:1.5. Recently, Mattheeuws (2004) reviewed nineteen papers from a total of 42 studies on the subject and reported that girls tended to have a slightly higher occurrence of missing teeth than boys of the same age. Another review showed that occurrence was higher in females than in males, with a ratio of 3:2 (Larmour *et al.*, 2005). In American white children, it was found that more girls (63%) had hypodontia than boys (37%) (Harris *et al.*, 2011), while among the Irish population the ratio of girls to boys with hypodontia was 1.3:1 (Hashem *et al.*, 2010).

Distribution of missing teeth in hypodontia

The tooth most commonly found to be missing is the third molar. Lynham (1990) found the third molar to be missing in one fifth of the Australian population. With regard to the remaining 28 teeth, meta-analysis has revealed that the teeth most commonly affected are the mandibular second premolars (41%), maxillary lateral incisors (23%), maxillary second premolars (21%), and the mandibular incisors (6%) (Polder *et al.*, 2004). In the Australian population, apart from the third molars, the most commonly affected teeth have been found to be the second premolars and upper lateral incisors (Hunstadbraten, 1973; Schalk-van der Weide *et al.*, 1992). In African Americans, it is the mandibular second premolars which have been found to be missing most frequently (Jorgenson, 1980), while among the Japanese the most frequently missing tooth was the mandibular second premolar (23.7%), followed by the maxillary second premolar (21.5%), maxillary lateral incisor (17.2%) and mandibular first incisor (14.0%) (Yamada *et al.*, 2010). The same pattern has recently been reported in the Irish population (Hashem *et al.*, 2010), whereas in American white children the most commonly missing teeth apart from the

third molars were the second premolars (50%), lateral incisors (23%) and maxillary second premolars (15%) (Harris *et al.*, 2011). Davis (1987) found that in Asian populations the mandibular lateral incisors were the most affected. By contrast, in all UK studies the most frequently affected teeth are the mandibular second premolars, while in all population studies the mandibular second premolars and the maxillary lateral incisors are the teeth most commonly found to be missing. Some researchers have found the maxillary permanent canine to be missing but the instances of this are very rare (Larmour *et al.*, 2005). Hypodontia of the maxillary central incisors, canines or first permanent molars is rare, occurring principally in cases of severe hypodontia (Hobkirk and Brook, 1980).

The most common congenitally absent teeth in the European population are the third molars, followed by the mandibular second premolars, the maxillary lateral incisors and lastly the maxillary second premolars (Grahnen, 1956; Bassett, 1997). It has been found that 9-37% of different populations have the third molars missing (Bishara, 1999). It has been proposed that if the third molars were congenitally absent then the probability of having other missing teeth is 13 times greater (Bailit, 1975; Harris and Clark, 2008). The prevalence of missing mandibular second premolars is around 2.8%, while maxillary lateral incisor agenesis is in the range of 1-1.6% (Grahnen, 1956). There appears to be a degree of symmetry in the absence of all teeth except the maxillary lateral incisors, where the absence of the left lateral was more common than the right (Bailit, 1975). In a review article it has been suggested that asymmetrical hypodontia is predominant (Shimizu and Maeda, 2009). Unilateral missing teeth are more common than bilateral teeth, although not in the upper lateral incisors (Polder *et al.*, 2004). However, Hashem et al (2010) found no evidence of symmetry of missing teeth between the right and left sides among an Irish population. Another group of researchers has revealed that congenital absence commonly affects just one tooth of a pair, not both, which means that hypodontia occurs unilaterally. They have also found no suggestion in these data of directional asymmetry (Harris *et al.*, 2011). However, among the Chinese population a different pattern has been found, the most commonly affected teeth being the lower incisors, followed by the upper second premolars and then the upper lateral incisors (Davis, 1987). All the review studies have shown that mild hypodontia is the most common, affecting 80% of those who have the condition (Polder *et al.*, 2004; Larmour *et al.*, 2005; Wu *et al.*, 2007; Harris and Clark, 2008).

Recently, a study presented a pattern for the missing teeth in non-syndromic severe hypodontia. The common patterns in the upper arch are agenesis of the lateral incisors and of both premolars, with a percentage of 13%, and in the lower arch the pattern is agenesis of all mandibular premolars, with a percentage of 11.5% (Tan *et al.*, 2011).

1.1.4 Dental anomalies associated with hypodontia

Many dental characteristics have been reported to be associated with hypodontia, including microdontia, canine impaction, taurodontism, transposition and rotation of teeth, and hypoplastic alveolar bone (Schalk-van der Weide *et al.*, 1992; Goodman *et al.*, 1994; Peck *et al.*, 1996; Schalk-van der Weide and Bosman, 1996; Baccetti, 1998; McKeown *et al.*, 2002; Peck *et al.*, 2002; Brook *et al.*, 2009a; Brook *et al.*, 2009b). Microdontia (reduction in tooth size) is considered one of the most common dental anomalies. It is common to see hypodontia of a maxillary lateral incisor on one side and a peg-shaped lateral incisor on the other side (Schalk-van der Weide *et al.*, 1992; Schalk-van der Weide and Bosman, 1996; Garib *et al.*, 2009; Garib *et al.*, 2010; Gupta *et al.*, 2011; Kositbowornchai, 2011). It has been noted that even relatives of hypodontia patients commonly have relatively reduced tooth size even if they do not have hypodontia (Schalk-van der Weide and Bosman, 1996; McKeown *et al.*, 2002). It has also been reported that hypodontia is associated with palatally impacted canines (Peck *et al.*, 1996), and that there was a 26% increase in the transposition of the maxillary canine and first premolar in cases of maxillary lateral incisors agenesis (Peck *et al.*, 1996). There is also a relationship between tooth rotation and hypodontia. Pirinen (1996) and Baccetti (1998) suggested that if there is a unilateral maxillary lateral incisor or premolar agenesis, it is more likely that the corresponding teeth on the other side will be rotated. Other researchers have found an increase of 10.8% in taurodontism of mandibular first molars associated with severe hypodontia (Lai and Seow, 1989; Schalk-Van Der Weide *et al.*, 1993; Gupta *et al.*, 2011). Goodman and her colleagues (1994) found that the failure of the alveolar bone to develop may create an increased freeway space in the range of 10-15 mm. Furthermore, many researchers have reported delayed formation and eruption of permanent teeth, small teeth (Garn and Lewis, 1970), ectopic eruption of first permanent molars, infraposition of primary molars (Bjerklin *et al.*, 1992; Baccetti, 1998; Garib *et al.*, 2009), short root anomaly, invaginations in incisors (Apajalahti *et al.*, 1999; Gupta *et al.*, 2011), distoangulation of mandibular second premolars (Garib *et al.*, 2009) and palatally displaced canines (Pirinen *et al.*, 1996; Baccetti, 1998; Garib *et al.*, 2009).

1.1.5 Skeletal pattern in hypodontia cases

There are not usually any noticeable changes to or effects on the skeletal pattern in the mild types of hypodontia, but it may be possible to see changes in cases of severe hypodontia. It has been reported that individuals with severe hypodontia or oligodontia associated with hypohidrotic ectodermal dysplasia had a flat or concave facial profile, obtuse nasolabial angle, retrognathic maxilla, reduced anterior face height and mandiblular plane angle, and reduced facial vertical height (Bondarets and McDonald, 2000).

1.1.6 Aetiology

From the literature it is evident that the aetiology of hypodontia is varied and that genetic, epigenetic and environmental factors may be contributory factors (Brook, 1984; Rushmah, 1992; Stockton *et al.*, 2000; Vastardis, 2000; Mostowska *et al.*, 2003; Brook, 2009; Parkin *et al.*, 2009; Shimizu and Maeda, 2009; Townsend *et al.*, 2009b). As with other conditions, the causes of missing teeth can be classified into general and local. The general category includes cases where there is a genetic cause, particularly syndromes such as Down syndrome, cleft lip and palate and ectodermal dysplasia. Local factors that result in hypodontia include early irradiation of tooth germs, hormonal and metabolic influences, trauma, osteomyelitis, and unintended removal of a tooth germ during the extraction of a primary tooth (Nunn *et al.*, 2003). Many researchers have suggested models and concepts of tooth agenesis (Butler, 1939; Dahlberg, 1945; Sofaer *et al.*, 1971; Osborn, 1978; Brook, 1984; Sharpe, 1995; Mitsiadis and Smith, 2006). These models and concepts have been reviewed recently and incorporated into a single model from a clinical perspective (Townsend *et al.*, 2009a). This model will be discussed briefly at the end of the following section.

Genetic factors

All previous studies on monozygotic or bizygotic twins claim that dental development, including both the size and the shape of teeth, is governed principally by genetic processes, in which hundreds of genes take part (Kondo and Townsend, 2006; Townsend *et al.*, 2008; Brook *et al.*, 2009a; Townsend *et al.*, 2009b). The evidence for genetic control is more significant in the aetiology of hypodontia and the occurrence among individuals related to hypodontia patients is higher than in the general population (Grahnen, 1956; Stockton *et al.*, 2000; Vastardis, 2000; Arte *et al.*, 2001; Mostowska *et al.*, 2003; Tallon-Walton *et al.*, 2007; Bailleul-Forestier *et al.*, 2008; Shimizu and Maeda,

2009; Tan *et al.*, 2011). Many other studies have been done on genetic diseases. These studies have been classified in various ways according to the affected tooth structure (enamel vs. dentine), by their specificity (syndromic vs. non-syndromic) and also by their pattern of inheritance: autosomal dominant, autosomal recessive, or X-linked recessive (Bailleul-Forestier *et al.*, 2008). There are numerous reports in the literature on the clinical genetics of tooth agenesis. Shimizu and Maeda have recently reviewed genetic studies which deal with hypodontia in human and mouse models. They report that non-syndromic or familial hypodontia is more common than the syndromic type and that it might follow autosomal dominant, autosomal recessive or X-linked patterns of inheritance (Shimizu and Maeda, 2009).

Grahnen, in his family study in Sweden, reported that hypodontia is determined by genetic factors (Grahnen, 1956). However, among the subjects of Grahnen's study, the type of inheritance in the majority of cases of familial hypodontia seems to have been autosomal dominant. Furthermore, some types of hypodontia, such as peg-shaped upper lateral incisors, are claimed to be the result of modifying genes (Grahnen, 1956; Alvesalo and Portin, 1969).

Advances in the fields of molecular biology and human genetics have enlarged our understanding of tooth development, by exploring the important role played by homeobox genes in tooth formation and craniofacial development (Shimizu and Maeda, 2009). Many researchers have found a direct relation between tooth formation and some of the regulatory homeobox genes: MSX1, PAX9 and AXIN2 (Vastardis, 2000; Arte *et al.*, 2001; Mostowska *et al.*, 2006; Cobourne, 2007; Shimizu and Maeda, 2009; Nakatomi *et al.*, 2010). MSX1 (Muscle segment homeobox 1) is essential in mediating epithelial-mesenchymal interaction during tooth development and has been found to be associated with familial hypodontia and certain forms of syndromic hypodontia (Arte *et al.*, 2001; Cobourne, 2007). MSX1 mutations predominantly affect second premolars and third molars (Shimizu and Maeda, 2009). However, some other genetics studies have not found any correlation between MSX1 and premolar hypodontia (Arte *et al.*, 1996; Shimizu and Maeda, 2009). PAX9 (Paired box gene 9) is also expressed in the prospective mesenchymal compartment of developing teeth. This gene has been identified in association with variable forms of hypodontia that affect the posterior region, particularly molar teeth (Thesleff, 2000; Mostowska *et al.*, 2003; Tallon-Walton *et al.*, 2007). The PAX9 gene has also been found to be associated with different forms of oligodontia

(Mostowska *et al.*, 2006). AXIN2 (Axis inhibition protein-2) mutations are associated with hypodontia and involve a wider range of tooth types (Cobourne, 2007).

Although previous studies have provided evidence for the role played by genetic factors in causing hypodontia, there is as yet no clear understanding of the genetics underlying this condition.

Environmental factors

Although, as discussed above, it appears that tooth agenesis is frequently caused by genetic factors, occasionally hypodontia can be associated with environmental factors. Major environmental factors such as infection of the tooth bud or trauma (Gullikson, 1975), or extraction of the preceding primary tooth, have been found to be associated with hypodontia owing to their effect on dental and organ development. Somatic diseases such as syphilis, scarlet fever and rickets are also associated with hypodontia, as are nutritional disturbances during pregnancy or infancy. Smoking during pregnancy, maternal medications, irradiation at an early age that may result in glandular and dental dysfunction are also implicated (Graber, 1978; Vastardis, 2000). Developing teeth are irreversibly affected by multiagent chemotherapy and radiation therapy. However, the effect of irradiation has been found to be more severe than that of chemotherapeutic agents (Näsman *et al.*, 1997).

Tooth agenesis models

Developmental defects in teeth have always been the subject of a great deal of interest on the part of researchers. Many studies have investigated and interpreted these defects using evolutionary and anatomic models such as Butler's (1939) field theory, odontogenic polarity, Sofaer and colleagues' (1971) model of compensatory tooth size interactions, Osborn's clone concept (Osborn, 1978) or the new discoveries in molecular biology which incorporate genetic factors (Mitsiadis and Smith, 2006). Many researchers have reviewed these theories and models and incorporated them into clinical research (Vastardis, 2000; Townsend *et al.*, 2009a).

Butler's (1939) theory attempts to explain why certain teeth have a greater tendency not to form than others. He hypothesized that the human dentition can be divided into 3 morphologic fields, corresponding to incisors, canines and premolars/molars. Within each field, one **"**key**"** tooth is presumed to be stable; distal teeth within the field become progressively less stable. Considering each quadrant separately, the key tooth in the

molar/premolar field would be the first molar. Based on Butler's theory, the third molar and the first premolar would be predicted to be most variable in size and shape. Clinical epidemiology supports this view for the third molar, but not for the first premolar (Bailit, 1975). Dahlberg (1945) applied Butler's concept to the human dentition and separated the premolar region from the molar region, so that in each quadrant four fields are present: incisor, canine, premolar and molar. Each field has its most stable tooth located mesially while the least stable tooth is positioned distally. He applied this concept only to the permanent dentition, and not to the primary dentition, however.

Clayton (1956) observed 3557 human subjects. The age sample was ranged between 3 – 12 years and found the frequent missing teeth were the posterior teeth. He hypothesized that the teeth most often missing were "vestigial organs" which had little practical value for modern man. In the evolutionary process, these teeth have come to provide no selective advantage for the species and have hence been lost.

From the results of a study done on Hawaiian children, Sofaer et al. (1971) proposed an association between missing teeth and smaller teeth. They suggested that a compensatory interaction occurs during tooth development which results in variations in the expression and occurrence of tooth agenesis among children. In cases where the lateral incisors were absent, the central incisors were found to be larger than normal. In individuals with peg-shaped lateral incisors, the central incisor was smaller than average. Sofaer et al. (1971) postulated that tooth agenesis occurred as a result of insufficient primordia for tooth germ initiation. However, they also postulated that the peg-shaped lateral incisor occurred subsequently as a result of poor nutrition with sufficient primordia.

Osborn (1978) adopted a new concept in which each particular class is moderated by a single clone within pre-programmed cells. This single clone leads to the development of the whole class by inducing the dental lamina and allows the cells to grow distally tooth after tooth: e.g., a molar clone. Each clone has the ability to stop the other teeth in the class erupting, right up to the last tooth in the class. The interesting point about clone theory, unlike the field theory, is that tooth shape is determined from the moment the primordium has been initiated (Cobourne and Mitsiadis, 2006).

Although the clone theory explains how a single clone is able to grow and form teeth – as, for example, the molar clone can grow and then form the other molar teeth, a recent study has criticized this theory as it does not explain the development of the dentition as a

whole (Townsend *et al.*, 2009a). However, the clone and field concepts are not mutually contradictory but can be viewed as complementary concepts which help us to understand the morphogenetic fields within the human dentition (Townsend *et al.*, 2009a). Line (2001) claims that understanding how genotypic changes are translated into phenotypic changes during evolution is one of the challenges facing modern biology. He hypothesized a relative molecular morphogenetic field to determine the relative influence of different genes (*MSX1* and *PAX9*) in families affected with hypodontia, rather than limiting the concept to the expression of a single gene. He reported that morphogenetic fields associated with MSX1 and PAX9 were not limited to a single tooth class or to a consistent pattern. Furthermore, Mitsiadis and Smith (2006) suggested that teeth may be affected by gene mutations resulting in either size reduction or complete tooth loss. They claimed that an interaction combines the field, clone and odontogenic homeobox models. This interaction plays an important role in tooth development. Townsend et al. (2009a) reviewed all these concepts and claimed that changes in the concept of the morphogenetic fields may support the multifactorial concept that has been proposed by Brook (1984; 2009).

It has recently been reported that the pattern of crown dimensions varies from tooth to tooth depending on which population group is being studied (Brook *et al.*, 2009c). Brook et al. also found that in each tooth type the tooth that forms last is usually smaller and more variable in the mesiodistal dimension. They claim that the overall pattern follows the latest concept of the morphogenetic field, as discussed above (Townsend *et al.*, 2009a).

Other investigators (Rushmah, 1992; Nik-Hussein and Abdul Majid, 1996) concluded that the developmental causes of hypodontia lie in the following:

- Disruption or obstruction of the lingual or distal outgrowth of the tooth bud cells from the dental lamina.
- Space limitation.
- Functional abnormalities of the dental epithelium.
- Failure in the initiation of the underlying mesenchyme.

The exact aetiology of these conditions is still being debated. They could be caused by environmental factors or genetic factors or a combination of the two (Rushmah, 1992).

Researchers have suggested that the areas of embryonic fusion may be more susceptible to epigenetic influences and that this could lead to hypodontia (Svinhufvud *et al.*, 1988). For instance, the maxillary lateral incisor develops in the area of fusion between the lateral and median nasal processes. Another example is the mandibular second premolar that develops at the distal end of the primary dental lamina. Both of these teeth are the teeth most commonly missing. A third site of frequent tooth agenesis is the midline of the mandible where the two lower central incisors develop and the two mandibular processes fuse (Svinhufvud *et al.*, 1988).

Kjaer and colleagues (1994; 1997) have explained the location of tooth agenesis by neural developmental fields in the jaws (incisor field, canine/premolar, and molar field). The region within a single field where innervation occurs last is more likely to manifest tooth agenesis.

Multifactorial aetiology

A single model has been proposed relating tooth size (microdontia and megadontia) and number (hypodontia and supernumerary teeth) (Brook, 1984). The model explains the aetiology and the associations of each anomaly. Figure 1.1 illustrates the model as the x-axis represents variations in tooth number and size while the y-axis shows the frequency of these variations in the population. The model consists of two curves representing the two sexes, one tail indicating hypodontia and microdontia and the other tail representing supernumerary teeth and megadontia.

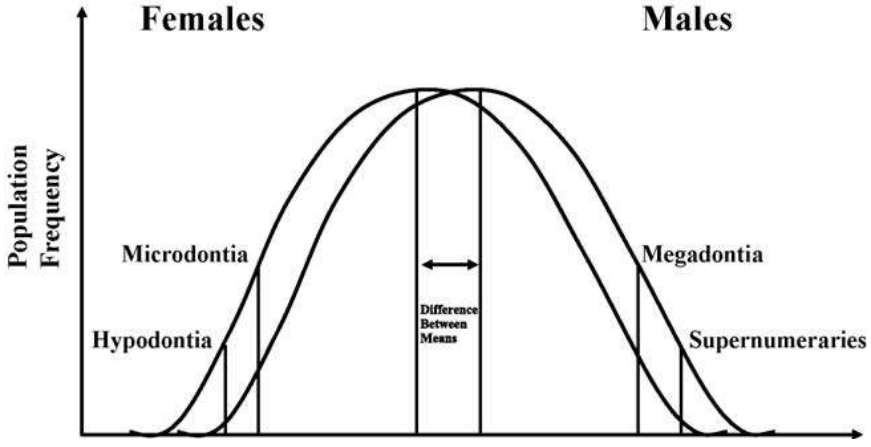

Figure 1.1 Brook's multifactorial model (1984). Reprinted from Brook (2009) with permission from Elsevier Science accessed on 23/01/2012.

The model shows a higher prevalence of hypodontia and microdontia in female subjects and a higher prevalence of supernumerary teeth and megadontia in male subjects (Brook, 1984). This kind of correlation between hypodontia and microdontia in the female subjects on one hand and between supernumerary teeth and megadontia in male subjects on the other hand has been proven by many studies (Ooshima *et al.*, 1996; Schalk-van der Weide and Bosman, 1996; Brook *et al.*, 2002; McKeown *et al.*, 2002; Parkin *et al.*, 2009). The model is multifactorial as it proposes the amount of polygenic influence and the amount of environmental influence in each individual case (Brook, 1984). Although the model is a theoretical one, it has a direct relevance to clinical practice. It emphasizes the fact that common anomalies such as missing teeth represent part of a continuous spectrum of inter-related dental phenotypes that are influenced by a combination of genetic, epigenetic and environmental factors (Townsend *et al.*, 2005). Recent reviews on genetic and environmental factors and on the morphogenetic field theory have supported this concept (Townsend *et al.*, 2009a; Townsend *et al.*, 2009b). Townsend et al (2009a) reviewed the concept of the morphogenetic theory within the dentition that has been presented and readdressed by many authors (Butler, 1939; Dahlberg, 1945; Osborn, 1978; Sharpe, 1995). They proposed that the field, clone and homeobox code models could all be incorporated into a single model to explain dental patterning and viewed as complementary rather than contradictory (Townsend *et al.*, 2009a). This proposal is compatible with the unifying aetiological model developed by Brook (1984). Nevertheless, studies from twins and their families have been applied using different approaches to investigate genetic and environmental influences on human dental variation (Townsend *et al.*, 2009b). These different approaches showed different ontogenetic and phylogenetic influences. Epigenetic factors are also proposed as important in explaining differences in the dentitions of monozygotic co-twins (Townsend *et al.*, 2009b).

Recently, Brook (2009) has reviewed the current knowledge about the aetiological reasons behind dental anomalies and readdressed the unifying aetiological model that has been proposed earlier (Brook, 1984). He claims that the aetiology of dental anomalies is a multifactorial and complex and requires the dental developmental process to be considered on multiple levels, multiple dimensions and as a progression on time. This process is a multilevel process, taking place on both molecular and cellular levels, which then interact to produce a clinical outcome. It is also multidimensional as it grows and develops on three different spatial dimensions: x, y and z, and in the fourth dimension of

time. The process also occurs over a long period and might be affected by different factors, such as genetic or epigenetic factors (when alterations in the gene expression are not accompanied by alterations to the nucleotide), or environmental factors (Brook, 2009).

1.1.7 Syndromic hypodontia

More than 120 syndromes listed in the On-line Mendelian Inheritance in Man (OMIM) database are associated with tooth anomalies (Schalk-van der Weide and Bosman, 1996; McKusick, 2007). The London dysmorphology database reported 150 syndromes as being associated with hypodontia (Winter and Baraitser, 2001). The absence of many teeth is commonly associated with specific syndromes or systematic abnormalities and is particularly related to ectodermal dysplasia (Goodman and Gorlin, 1970). Nevertheless, hypodontia is a very common dental anomaly in patients with oral and facial clefts, Rieger syndrome, Down syndrome (trisomy 21), Witkop syndrome, van der Woude syndrome, Book syndrome, Hemifacial microsomia and many others (Arte *et al.*, 2001; Hobkirk *et al.*, 2011).

In addition to inherited defects, tooth agenesis could occur as a result of somatic diseases such as syphilis, scarlet fever, rickets, or nutritional disturbances during pregnancy or infancy which might affect tooth and other organ development. Also, glandular dysfunction could occur as a result of cranial irradiation in the very early stage of development and this can then lead to dental anomalies (Vastardis, 2000).

1.1.8 Clinical implications

Hypodontia has significant clinical implications as it can seriously affect a person's physical and emotional status. The scenario is worse if the missing teeth are located in the anterior region for aesthetic reasons. Furthermore, management of the condition is made difficult by problems of diagnosis, the severity of the tooth absence, and the general effect on the remaining teeth and dental occlusion. Although the the severity of hypodontia varies among members of the same population, as mentioned above, it is still necessary to provide good care and treatment as these patients may be suffering from psychological problems.

The prime motivating factor for individuals seeking orthodontic treatment is aesthetics. Some hypodontia patients seek treatment to manage depression caused by the

deterioration in their appearance and/or functions. Hypodontia requires great care with extensive and complex treatments.

Unfortunately, there is no established formal procedure to manage patients with hypodontia. Their management may necessitate the help of many specialities. Treatment might range from single restorations to surgery and multiple restorations (Valle *et al.*, 2011). Management will depend upon the pattern and severity of tooth absence, the amount of spaces present and, of course, the patient's attitude. The general principle in management is to deal with the space within the dental arches: i.e., a space closure in less severe cases, while prosthetic replacement as well as some orthodontic tooth movement: i.e., redistribution of space, is usually the case in extensive conditions. Different options and methods of treatment have been suggested, including orthodontic movement and/or restorative replacements in the form of dentures, crowns, bridges, auto-transplantation and dental implants. Many factors should be evaluated before the commencement of management. These include the age of the patient, the dental occlusion, soft tissue and skeletal patterns and the facial morphology of hypodontia, the number, colour and morphology of the remaining teeth, the location of the absence, amount of alveolar ridge, oral hygiene, interest of the patient motivation, expectation of treatment, team/patient interaction and time as well as the cost of treatment. Furthermore, from an orthodontic perspective, variations in the size and shape of teeth with abnormal morphology may lead to incorrect bracket placement, since the standardised brackets are still being used for hypodontia patients. The use of standardised brackets may lead to different root angulation, inappropriate crown rotation and unequal torque between teeth.

1.1.9 Management of hypodontia

As mentioned previously, hypodontia is not an easy condition to manage. Many studies have shown the importance of the role of interdisciplinary teams in the management of hypodontia (Carter *et al.*, 2003; McNamara *et al.*, 2006; Wu *et al.*, 2007; Brough *et al.*, 2010; Al-Anezi, 2011; Valle *et al.*, 2011). A recent book by Hobkirk and colleagues (2011) provides a comprehensive review for clinicians about the available options for the management of hypodontia adopting a multidisciplinary approach.

The clinical management of hypodontia requires careful multidisciplinary planning and has financial implications. A number of procedures can be carried out to cope with patients' wishes and which take into account their age. The cooperation between the different specialities in the team provides a wide variety of expertise which is not easy to

find in one individual and the delivery of the treatment requires great care to meet the objectives of the treatment (Hobkirk *et al.*, 2011). At one of the international conferences on hypodontia, an international agreement was announced about who should be on the team. The conclusion was that the members of the team should include the following: general dental practitioners, dental nurses, orthodontists, paediatric dentists, prosthodontists, oral and maxillofacial surgeons, specialist laboratory technicians, clinical psychologists, clinical geneticists, dermatologists, speech and language therapists (Hobkirk *et al.*, 2006). This is the ideal team, but in many situations it is impossible to assemble such a team. Several papers have been published focusing on the importance and the role of the interdisciplinary team in the care of hypodontia patients both functionally and aesthetically (Jepson *et al.*, 2003; McNamara *et al.*, 2006; Simeone *et al.*, 2007; Worsaae *et al.*, 2007). This multidisciplinary approach is often costly but the benefits outweigh the cost. This approach maximises the clinical outcomes for patients.

When deciding on a course of treatment, the space within both arches should be taken into consideration. The space should be considered in three dimensions: mesially, between both crowns and their roots; vertically, between both arches, and transversally, within and between dental arches. These considerations are also influenced by the fourth dimension, which is time: i.e., patient development and growth (Hobkirk *et al.*, 2011). A good multidisciplinary team should take all these factors into consideration at the diagnosis and treatment planning stages. For instance, a restorative dentist should evaluate the available distance between the teeth, each dental implant requiring a minimum distance of 6 mm (Mirabella *et al.*, 2011). The orthodontist also should evaluate the alveolar ridge condition before moving teeth. In long-term treatment planning the number of remaining teeth, their size, morphology and development, available space and the condition of the alveolar ridge are of importance. All of the above indicate the need on the one hand to obtain more comprehensive patterns of the size and morphology of the teeth of hypodontia patients by, for instance, using 3D measurement methods, and on the other hand to determine in what way such patients differ from individuals without this condition. Both these aspects form the subject of the current research.

1.1.10 Variation in hypodontia

Tooth size variation

Many studies in the dental literature have reported an association between hypodontia and microdontia of the remaining teeth (Rantanen, 1956; Alvesalo and Portin, 1969; Garn and Lewis, 1970; Lavelle, 1970; Baum and Cohen, 1971c; Sofaer *et al.*, 1971; Rune and Sarnas, 1974; Brook, 1984; Harris and Bailit, 1988; Ooshima *et al.*, 1988; Schalk-van der Weide and Bosman, 1996; Brook *et al.*, 2002; McKeown *et al.*, 2002; Harris, 2003; Brook *et al.*, 2009a; Brook *et al.*, 2009b; Yamada *et al.*, 2010; Mirabella *et al.*, 2011; Yaqoob *et al.*, 2011). A reduction in tooth size was found in many members of the Hailuoto population in Finland, and this was found to be associated with hypodontia (Alvesalo and Portin, 1969). Lavelle (1970) reported a crown size reduction in hypodontia subjects compared to control subjects. He also found that the arch was smaller in the hypodontia group. Baum and Cohen (1971c) found a significant generalized decrease in crown size in a mesiodistal direction in agenesis groups when compared to control subjects.

The pattern of size reduction in hypodontia cases has also been tested. Rantanen (1956) found that when an upper lateral incisor is developmentally absent on one side, the other side often presents with a smaller in size lateral incisor tooth. Another group of researchers studied the tooth size discrepancy in the anterior region in 17,000 schoolchildren in Hawaii. They reported that when the maxillary lateral incisor was congenitally absent on one side, the adjacent central incisor was larger in size than its counterpart, suggesting a possible compensatory local interaction affecting the size of the adjacent tooth (Sofaer *et al.*, 1971). Garn and Lewis (1970) measured the mesiodistal diameters of all teeth, excluding third molars, for two hypodontia groups. The first group consisted of 82 subjects who had hypodontia of one or more third molars, while the second group consisted of 19 subjects with multiple absence of the lateral incisors and second premolars. They reported that the permanent teeth were smaller in both groups compared with the controls. They also found an association between the severity of hypodontia and the reduction in crown size of the remaining teeth. Another study investigated the differences in the size of four or more teeth in hypodontia and control groups (Rune and Sarnas, 1974). They found a significantly greater reduction in tooth size in hypodontia subjects than in the control subjects, with no significant difference between boys and girls.

Many other researchers have found that the reduction in size is associated with the degree of severity of the condition. Brook (1984) suggested a relationship between hypodontia and microdontia of the remaining teeth. He reported that the more severe the hypodontia the greater the reduction in tooth size. Another clinical study also showed a direct correlation between hypodontia and reduction in the size of the teeth (Ooshima *et al.*, 1988). A reduction in the tooth dimensions of relatives of patients with severe hypodontia has also been revealed (Schalk-van der Weide and Bosman, 1996). McKeown and colleagues (2002) also found reduced tooth dimensions of some teeth in relatives of hypodontia patients. Furthermore, they compared the crown dimensions of hypodontia patients and their relatives on the one hand and those of a group of control subjects on the other. They found that both the hypodontia patients and their relatives had a smaller tooth size when compared to the control subjects. The degree of reduction in size was also found to be associated with the degree of severity of hypodontia. The closest group to the control group was the relatives of the hypodontia patients, while the group most affected by reduction in tooth size was the group of patients with severe hypodontia (Brook *et al.*, 2002).

Conversely, patients with supernumerary teeth have been shown to have increased tooth dimensions (Khalaf *et al.*, 2009b; Khalaf *et al.*, 2009c). One group of researchers therefore investigated crown size in individuals with hypodontia and those with supernumerary teeth. Their aim was to find any link between hypodontia, supernumerary teeth and crown size. All tooth measurements and mesiodistal and buccolingual dimensions were recorded manually using an electronic calliper. Their findings were compatible with the multifactorial model, as the hypodontia groups showed a reduction in tooth size when compared to a control group, while the supernumerary group showed larger tooth dimensions in relation to their control subjects (Brook *et al.*, 2009b). Brook and colleagues also used a modern imaging system to investigate the crown dimensions of the remaining teeth for those hypodontia patients with a known PAX9 mutation. Mesiodistal (MD), buccolingual (BL), area and perimeter measurements were recorded for all remaining teeth. They found an association between reduction in tooth size and missing teeth in the family members of patients affected by PAX9 mutation (Brook *et al.*, 2009a).

Harris introduced a multivariate statistical approach (Harris and Bailit, 1988; Harris, 2003) to human odontometrics. He measured the mesiodistal and buccolingual crown

dimensions for all the permanent teeth excluding third molars in 100 American whites and 100 American blacks with equal gender distribution (Harris, 2003). He classified the variation into seven classes: race, arcade, tooth type, tooth surface (mesial, distal), dimension and residual term. The most varied class was tooth type, accounting for 82.8% of the variation, with very low values found for the other classes. The variation within tooth type was among all teeth.

Recent studies have also measured crown dimensions in hypodontia patients and have come to similar conclusions: that tooth size reduction is associated with hypodontia. Mirabella et al. (2011) investigated the size differences (mesiodistal length only) between patients with congenitally missing lateral incisors; both types unilateral and bilateral agenesis. They found narrower teeth on their sample compared to those with no missing teeth, with the exception of the maxillary first molars. No differences were found in tooth size reduction between patients with unilateral or bilateral congenitally missing teeth. Yaqoob et al. (2011) claim that the relationship between moderate or severe hypodontia and generalized microdontia is well established, but that there has been little research into the association between mild hypodontia and microdontia. They investigated differences in size using mesiodistal length (MD) only and found that tooth size reduction is associated with mild hypodontia as well. Conversely, Yamada et al. (2010) found that agenesis of one or two teeth is associated with larger remaining teeth. They recorded the crown diameters from 100 Japanese males using plaster models. Subjects with agenesis were divided into three groups: the first group contained individuals with one missing tooth; the second included patients with two teeth missing, and the last group consisted of those with three or more missing teeth; a reference group acted as a control sample. The first group showed increased tooth size in comparison to the control subjects; the teeth of the second group showed a tendency to be larger than those of the control subjects, although the differences were not significant; however, by contrast, the severe hypodontia group showed a progressive reduction in tooth size when compared to the control subjects. Yamada et al. (2010) suggested a complex relationship between tooth size and dental agenesis and referred this to local compensatory interaction affecting the tooth size. In their study, participants' ages were ranged from 10 to 30 years which is a huge range of age on male subjects only. In addition, the study used undefined control subjects that have been used in a previous study with no information about it. Also, they did not study molar teeth. All of these factors might affect their conclusion.

Tooth shape variation

Shape alteration of the remaining teeth has been reported to be associated with hypodontia (Davies, 1968; Alvesalo and Portin, 1969; Foster and Van Roey, 1970; Lavelle, 1970; Sofaer *et al.*, 1971; Ooshima *et al.*, 1996; Kondo and Townsend, 2006). Davies (1968) reported the frequency of subjects with hypodontia and/or peg-shaping of one or more teeth as 22.2%. A relationship between a peg-shaped upper lateral incisor on one side and the absence of the contralateral tooth was subsequently found (Alvesalo and Portin, 1969). This finding suggested that hereditary genetics may play a role in the aetiology of a missing tooth in hypodontia patients who have peg-shaped upper lateral incisors. Sofaer and colleagues (1971) found that there is a higher prevalence of peg-shaped lateral incisors on the left than on the right side. This is also accompanied by smaller central incisors. It is more common to see the remaining teeth tending to be smaller when a peg-shaped lateral incisor tooth is present (Ooshima *et al.*, 1996). Conical teeth or alterations in the shape of the remaining teeth were usually associated with the degree of severity of hypodontia (Foster and Van Roey, 1970).

A direct relationship between alteration in tooth shape and the malformation that occurs within hypodontia has been reported in the dental literature. The deficiency of cusps in human teeth is also documented as being associated with hypodontia. It has been noticed that the palatal cusps of the posterior teeth - mainly the upper first premolar and upper first permanent molars - were usually affected and malformed (Foster and Van Roey, 1970). Lavelle (1970) also reported that 8% of his sample of hypodontia patients with third molars missing lacked the distolingual cusp of the first molar. Kondo and Townsend (2006) aimed to measure the areas of the four main cusps and the area of the Carabelli cusp, in addition to the crown dimensions. They found the first forming paracone displaying the least variation, and the last forming Carabelli cusp showing the greatest. The presence and absence of the Carabelli cusp has an effect on the shape of the molar teeth.

Different methods adopted to quantify tooth shape differences are described in the dental literature (Axelsson and Kirveskari, 1983; Robinson *et al.*, 2001; Brook *et al.*, 2002; Agenter *et al.*, 2009). Axelsson and Kirviskari (1983) used tooth shape ratio (crown indices) to describe the crown shape of members of different populations (North-east Iceland) using normal subjects. Another group of researchers used a modern imaging system to show the differences in tooth shape between hypodontia and control subjects

(Brook *et al.*, 2002). They found that tooth shape was different for teeth 12, 21, 22 and 32, with the crown taper from gingival margin to incisal edge increasing with the severity of the hypodontia. Agenter et al. (2009) claimed that tooth shape could be evaluated indirectly following Peck and Peck's concept (1975), which uses the MD/BL ratio as an indicator of tooth shape. They claimed that the ratios are intercorrelated and that one dimension has an indirect effect on the other. Robinson et al. (2001) studied tooth form applying the Procrustes technique in two dimension plane images following Brook et al. (1998). They reported shape differences between hypodontia and control subjects in the position of the incisal corners of the upper central incisors. The teeth of the hypodontia groups were more tapered in shape.

Allometric variation

The similarity in shape between objects of different sizes called isometry. In biology, many anatomical structures such as teeth are not isometric in nature due to the fact that huge number of morphological and physiological variables is different between tested groups. These non-isomteric differences referred to as allometric variation (Schmidt-Nielsen, 1984). Allometric variation could be related to any scaled variables relative to the body size but in this study allometric variation referred to the morphological variation that was caused by size variation or could be due the relation between size and shape when both calculated separately (Mosimann, 1970).

Allometry has three different types (Fleagle, 1999). These types are:

- **Growth allometry:** the study of ontogenetic shape changes in relation to the size.
- **Intraspecific or static allometry:** the study of shape changes in adults within the same population at the same time with regard to size differences.
- **Interspecific or evolutionary allometry:** the study of shape changes between different populations among different evolutionary lineages with regard to size differences.

Allometry can be tested by using the following equation

$$y = a.x^b$$

$$\log y = \log a + b \log x$$

This statement is the simplest form representing allometric variation as a regression line when two variables (i.e. size and shape of teeth) are plotted on logarithmic coordinates. The exponent *b* represents the slope of the straight line. The slope equals 1.0 when tooth size varies in relation to the tooth shape is isometric, which is rare in biological studies. The slope could be positive when tooth size varies and has an effect on tooth shape and this called positive allometry. Also, the slope could be negative when the tooth size varies but has a negligible effect on tooth shape and this called negative allometry (Schmidt-Nielsen, 1984). In geometric morphometric studies, the same regression approach is used with landmarks configuration which can be related to the centroid size by multivariate regression. A number of geometric morphometrics freeware programs are available to perform and test allometric variation (Viscosi and Cardini, 2011).

Many allometric studies have been done in many different disciplines (Klingenberg, 1996; Kondo and Natori, 2002; Cardini *et al.*, 2010; Singleton *et al.*, 2011; Viscosi and Cardini, 2011). However, few studies have been done in the dental field. A research group integrated the internal crown surface features and the morphology of the crown outline to examine the morphological variation of hominin lower second premolars using geometric morphometrics (Martinón-Torres *et al.*, 2006). They used multivariate regression analysis of shape on size to test for allometry. The result indicates a slight but significant allometry that accounts for 7.5% of the overall variation. The outlines tend to circular with central intra-crown structures in the smaller premolars, whereas larger premolar outlines are rectangular with displaced intracrown structures mesially and prominent lingual surfaces. This finding indicates that morphology of these premolars is influenced by the dental size, whereas a previous study showed that lower second premolar crown morphology is not affected by size (Bailey and Lynch, 2005). Another study implemented geometric morphometric methods to explore the morphological variability of hominin upper first molar. To test for allometry, they have explored the influence of cusp size of the molar shape using multivariate regression (Gómez-Robles *et al.*, 2007). The result indicates a significant size effect with a very small allometric variation that accounts for just 3.02% of the observed variation. The shape of larger molars was with regular contours while those smaller molars are compressed with rhomboidal occlusal polygons.

Odontometric variations

A number of variations in tooth size have been widely reported and this has given rise to important findings and conclusions. These variations could be related to many factors,

such as differences between different population groups as well as gender differences, difference of various types of occlusion, and body size. However, all variations might be manipulated by the interaction of genetic, epigenetic and environmental factors. This interaction may have a direct or indirect impact on the development of the dentition. Garn et al. (1980) reported that the size of the dentition could be affected by a number of genes, not just a single gene. Small tooth dimensions could also be linked to poor maternal conditions during pregnancy and small birth size.

Populational variation

The dimensions of teeth are not the same in different populations. While smaller tooth dimensions can be seen in European populations than in Chinese, larger tooth dimensions are observed in Australian Aboriginals and Africans (Bailit, 1975; Perzigian, 1976; Yuen *et al.*, 1997). Brook et al. (2009c) compared tooth variability between four different populations. The measurements were manual measurements of the mesiodistal crown dimensions. The Southern Chinese showed the largest crown dimension while the Romano-British crown dimensions were the smallest. However, a variable pattern was noticeable within all populations. It was noted that Europeans have narrower anterior teeth and broader posterior teeth. Conversely, Africans and Australian Aboriginals have shorter and broader anterior teeth in conjunction with longer and narrower posterior teeth (Harris and Rathbun, 1991).

Sex variation

Sex was considered as an important factor in tooth dimension variations. Females were found to have narrower recorded crown dimensions than males (Moorrees *et al.*, 1957). Other researchers obtained the same finding for both tooth size and shape (Garn *et al.*, 1967; Garn and Lewis, 1970). There were sex differences in the mesiodistal and buccolingual dimensions, with the latter being bigger than the former. Lavelle (1975) reported that males generally had larger tooth sizes than females. Kondo and Townsend (2006) measured the overall crown size and areas of individual cusps and their finding also showed sexual dimorphism, with values in males exceeding those in females. On the other hand, other studies have not found any sexual dimorphism in their samples (Mirabella *et al.*, 2011; Yaqoob *et al.*, 2011).

Symmetry in tooth dimension

Although the bilateral symmetry of the dentition is theorized to be genetically determined, it has been suggested that environmental conditions also play a role (Bailit *et al.*, 1970).

In a study including 500 models, variations in tooth size between the left and right sides of each model of the dentition were found in 90% of subjects (Ballard, 1944). In Africans, the differences in tooth size were even larger (Kieser and Groeneveld, 1988). Sex differences with regard to the asymmetry in tooth size were negligible. While in one study females showed greater asymmetry than males (Niswander and Chung, 1965), in another study the converse was found (Garn *et al.*, 1966). It was observed that the asymmetry followed the morphogenetic classes of teeth, with the distal teeth showing less symmetry than the mesial teeth (Khalaf *et al.*, 2009b).

1.2 Measurement of tooth size and shape

Traditional morphometric methods, such as measurements of length, depth or width, along with modern morphometric methods such as geometric morphometric methods (GMM), are now implemented widely in all biological sciences (Zelditch *et al.*, 2004). Traditional morphometric data have the ability to provide information about size, but less about shape because many of the measurements overlap or run in similar directions (Bernal, 2007). Another problem with traditional morphometrics is that it measures size rather than shape. This does not mean that no shape information is obtained, but all information about shape is in the form of ratios. Another limitation of traditional morphometrics is that the measurements offer no information about the geometry of the object. On the other hand, an important feature of geometric morphometrics is that it draws an informative picture about the tested object. However, there are also limitations associated with geometric morphometrics, such as the cost of the equipment needed to obtain three-dimensional coordinates, the fact that it is time-consuming to use, and the difficulty of interpreting the results using two-dimensional media such as journal pages (Zelditch *et al.*, 2004).

In the following sections, a review of both the traditional and modern morphometrics that have been used to measure tooth size and shape is presented.

1.2.1 Measurement of tooth size

Most traditional morphometrics use linear techniques such as mesiodistal dimension, buccolingual dimension and occlusogingival dimension, while others have used indices to represent size (Kieser *et al.*, 1985). Many orthodontists today practise some form of odontometry as part of their routine case diagnosis (Peck and Peck, 1975). On the other hand, many others in different disciplines use different tools to describe size using GMM (Zelditch *et al.*, 2004).

Metrical and non-metrical variations are usually differentiated in studies investigating tooth morphology. All aspects that are measured directly are known as metrical (i.e., the mesiodistal crown diameters of teeth), while non-metrical variations involve scoring or describing the presence, absence and degree of development or form visually (Hillson, 1996). The complexity of non-metric aspects is related mainly to difficulty in assessment, as a standardized test is required.

Mesiodistal dimension

There are several terms used to refer to the mesiodistal diameter of the crown: tooth width (Moorrees *et al.*, 1957), mesiodistal width (Bolton, 1958), tooth breadth (Lundstrom, 1955) and mesiodistal crown diameter (Lavelle, 1968). Moorrees and colleagues (1957) defined mesiodistal dimension as the greatest distance between the contact points while holding callipers parallel to both the occlusal and vestibular surfaces, while Kieser et al. (1985) defined it as the maximum distance between the contact points of a tooth in normoocclusion (Kieser *et al.*, 1985). Difficulties can arise in the case of rotation or displacement of teeth (Moorrees *et al.*, 1957).

Other researchers defined the MD dimension by measuring a line between the mesial and distal contact points of each crown when the teeth are in the normal occlusion (Goose, 1963; Wolpoff, 1971). Interestingly, the majority of researchers have stated that the mesiodistal dimension line is the maximum distance between contact points or points where contact happens. However, teeth with marked approximal and occlusal attrition may be excluded (Kieser, 1990). Others consider the mesiodistal line to be the largest distance between the normal contact points on the proximal regions of the tooth crowns, measured parallel to the occlusal plane (Lavelle, 1971). Holding callipers parallel to the occlusal and buccal surfaces has been suggested as a way of obtaining a more accurate measurement of the mesiodistal line (Moorrees *et al.*, 1957; Potter *et al.*, 1981; Axelsson and Kirveskari, 1983).

Buccolingual dimension

There are various names for this dimension, such as the buccolingual crown diameter (Lavelle, 1968), or breadth (Kieser *et al.*, 1985). The maximum BL dimension of the tooth as taken perpendicular to the MD dimension has been considered as the reference for their measurement (Moorrees *et al.*, 1957; Lavelle, 1971; Potter *et al.*, 1981; Axelsson and Kirveskari, 1983). According to Lavelle (1972), this was the distance between the buccal and lingual crown convexities, measured at right angles to the mesiodistal crown diameter, the greatest distance being recorded.

Occlusogingival dimension

The occlusogingival line is rarely referred to in the dental literature. Bolton (1958) used the term ‘incisogingival height’ to describe this dimension. It has also been called crown height (Lavelle, 1968; Volchansky *et al.*, 1981) and is usually taken from the buccal surface. Lavelle (1968) used this dimension in premolars, canines and incisors, from the

point on the upper surface of the crown above the lowest point of the amelocemental junction or free gingival margin. In molars, on the other hand, the measurement was taken from between the tip of the mesiolingual cusp to the lowest point on the amelocemental junction or free gingival margin. It was the distance between the occlusal line and the cementoenamel junction (Volchansky *et al.*, 1981).

Dental indices

The buccolingual and mesiodistal dimensions can be used together as indices to define crown morphology. One researcher suggested using the crown index to investigate the shape of the tooth crown (Lavelle, 1968). This is the ratio of the buccolingual and mesiodistal crown dimensions expressed as a percentage. The crown module was defined as the sum of the mesiodistal and buccolingual crown dimensions divided by two (Lavelle, 1968). The crown area or the robustness index is the product of the mesiodistal and buccolingual dimensions (Lavelle, 1968). The crown index is used more frequently than other indices. These indices, however, do not take into account variations and alterations in the actual crown morphology.

As described here, most of these methods have used traditional orthodontic measurements to describe tooth size, but these old- fashioned techniques may incorporate measurement bias during application.

Centroid size

Studies in the geometric morphometric field usually measure size by calculating centroid size as a step to describing shape. Kendall's definition of shape mentions scale as one of the effects that need to be removed before describing shape differences between groups (Kendall, 1977). Scale refers to the definition of size which is based on inter-landmark distances (Zelditch *et al.*, 2004). Many geometric studies have described size using this concept, which is based on calculating the centre of the object by measuring the distance between each landmark and the centroid (Robinson *et al.*, 2001; Zelditch *et al.*, 2004; Bernal, 2007; Viscosi and Cardini, 2011). Viscosi and Cardini (2011) published an introductory paper for beginners that suggests a simple and in some aspects simplistic protocol using landmarks and Procrustes methods.

1.2.2 Measurement of tooth shape

Tooth shape can be measured in different ways depending on the data source. Measurement methods can be either qualitative or quantitative. Qualitative methods measure tooth shape subjectively: e.g., tooth taper, cusp numbers or Carabelli's trait (Turner *et al.*, 1991). Quantitative methods are those using landmark-based techniques such as geometric morphometrics. Landmark-based methods may be further subdivided into either distance methods, outline methods or landmark configuration methods (Bookstein, 1997b; Adams *et al.*, 2004).

Qualitative methods

Tooth taper

Many previous studies describe tooth shape qualitatively according to its morphology. Barker (1973) stated that the morphology of the maxillary lateral incisor is variable. The crown varies from being very small to an ovoid form or peg-shaped lateral incisors. Peg-shaped lateral incisors were described by Le Bot and Salmon (1977) as those having a conical crown shape, which is associated with a reduction in diameter from 'the cervix to the incisal edge'. The area higher than the proximal surfaces in the direction of the incisal edge describes the tooth taper. Lateral incisor morphology was scored by Turner et al. (1991) using different levels, ranging from normal to peg-shaped lateral. However, Turner's scoring is highly subjective and may not cover the whole range of differences between upper lateral incisors. Additional measurements of the taper of the crown may produce a more accurate picture of lateral incisor variations. Khalaf and colleagues (2009c) introduced a method of examining the taper degree at 25, 50 and 75 percentiles with 2D tools using the image analysis system.

Cusp numbers

Molar crown morphology is reported not to vary in contralateral teeth (Garn *et al.*, 1966). Variations between males and females with regard to the molar crown size and cusp numbers in different populations have been reported (Dahlberg, 1961; Garn *et al.*, 1966). Axelsson and Kirveskari (1983) found that the upper first molars have the greatest stability of crown shape, while the upper lateral and lower incisor teeth show the most variation. The crowns of upper molars have four main cusps. An additional cusp, Carabelli's cusp, may arise from the palatal crown side below the mesiopalatal cusp (Harris and Bailit, 1980). However, five cusps can generally be seen in permanent lower molars. On some occasions, a sixth cusp may be seen close to the distobuccal cusp at the

lingual aspect of the crown (Hillson, 1996). The premolar crowns consist of two cusps: one buccal and one lingual. In some cases, there are two or three small lingual cusps (Hillson, 1996).

Carabelli's trait

Carabelli's trait is the most commonly known non-metric trait. Carabelli's trait is a small cusp on the mesiopalatal corner of upper molars. It is absent in some and present in other individuals in different forms. There has been controversy regarding Carabelli trait expression and upper molar size. Recently, Harris (2007) concluded that Carabelli's trait is developmentally correlated with crown size, but with no apparent alteration of cusp arrangements.

Quantitative Methods

The quantitative approach to describing shape depends mainly on landmarks and is called geometric morphometrics. This method solves many of the problems associated with traditional methods of measurement (Zelditch *et al.*, 2004).

Morphometrics

Morphometrics, the study of the geometrical form of organisms, combines themes from biology, geometry and statistics (Bookstein, 1986). Traditionally, morphometrics was the application of either univariate or multivariate statistical analysis to quantitative data such as angles or indices (Adams *et al.*, 2004). Multivariate morphometrics is a combination of multivariate statistics and quantitative morphology, which shows results in a scatter plot or graphs without visulizing the actual shape of the object. Recently, a shift has occurred in the field, based on the geometry of the object itself, which means that information about the geometry of the object is preserved throughout the analyses. This new approach, called geometric morphometrics (GMM), is based mainly on landmark configuration, will be described later (James and Marcus, 1993).

1.3 Geometric morphometrics

The use of geometric morphometric techniques with the aid of multivariate analysis has had a great impact on biological studies since it allows a comprehensive analysis of variations in biological shape. Data from morphometric studies usually include geometric locations of landmarks, points that correspond biologically to form. In some applications, one measures configurations of landmark points by variables that express aspects of the size and shape of single specimens, such as distances or ratios of distances (Bookstein, 1997a).

Many researchers have made enormous efforts to improve the field of geometric morphometrics. Bookstein (1984; 1986; 1996) reviewed the background of geometric morphometrics and also showed the applications of this new method. Adams and colleagues (2004) updated the method again, reviewed its application and clarified its potential.

Numerous books have been published on geometric morphometrics. The most comprehensive of these was `Statistical shape analysis' by Dryden and Mardia (1998). Other books which have been published in the field are coded by colour:

- 'Red book': Morphometrics in evolutionary biology, Bookstein et al. (1985)
- 'Blue book': Proceedings of the Michigan workshop in morphometrics, Rohlf and Bookstein (1990).
- 'Black book': Contributions to morphometrics, Marcus et al. (1993).
- 'White book': Advances in morphometrics, Marcus et al. (1996).
- 'Green book': the primer by Zelditch et al. (2004).

Furthermore, many workshops are being run from time to time all around the world by experts in the field like Paul O'Higgins and Andrea Cardini. Also, for those who would like to know more about geometric morphometrics, there is an excellent source of information on shape analysis on the Stony Brook website at the State University of New York, which is moderated and monitored by F. J. Rohlf, F. L. Bookstein and D. E. Slice:

http://life.bio.sunysb.edu/morph/ (accessed on 12th January 2011). There is also a universal mailing list for all people interested in geometric morphometrics via: http://www.morphometrics.org/morphmet.html (accessed on 12th January 2011).

1.3.1 Geometric morphometrics analysis

Geometric morphometrics is widely used to answer anthropological questions about craniofacial form, with a few studies in the dental field also employing this method. An important feature of these techniques is that they allow the non-destructive 3D capture of the geometry of the morphological structure and preserve this information throughout analysis (Adams *et al.*, 2004). In addition, geometric methods are able to allow for quantifying differences in size as well as in shape; this cannot be accomplished using traditional methods (Monteiro *et al.*, 2002).

Geometric morphometrics distinguishes the form of an object from the shape by scaling to unit size. As shape can be defined as the geometric properties of a configuration of points that are invariant to changes in translation, rotation and scale, this variety of morphometry deals with the relationship between landmarks in three dimensions (Kendall, 1977). It also links the set of measurements with the shape of the object. The form of the object is recorded as the coordinates of defining features, i.e., landmarks (Hennessy and Stringer, 2002). The landmark coordinates for a set of objects are typically transformed into points in the shape space (Kendall, 1984), via scaling and alignment procedures known as generalized Procrustes analysis (Rohlf, 1999). For each object, the transformed coordinates represent a single point in the shape space.

Landmarks

Landmarks are discrete anatomical loci that can be recognized as the same loci in all objects in the study (Zelditch *et al.*, 2004). Landmarks play a fundamental role in geometric morphometrics, so it is important to understand their function in a shape analysis. A quantitative study should capture at least as much information as a qualitative study. Bookstein classified landmarks into three categories: Type 1, Type 2 and Type 3. Type 1 landmarks include points in space at which three structures meet, such as the bony sutures. Type 2 landmarks include tips of extrusions and valleys of invaginations, such as tips of predatory structures – claws and teeth. Type 3 by definition refers to information at diverse, finitely separated locations, such as end points of diameters or centroids (Bookstein, 1991). To explain this classification further, Types 1 and 2 are considered to be anatomical landmarks, while Type 3 landmarks are mathematical ones such as maximal curvature.

Zelditch (2004) described the ideal criteria for choosing landmarks as follows: they should be homologous anatomical loci, should not alter their topological positions relative

to other landmarks, should provide adequate coverage of the morphology, be found repeatedly and reliably, and lie within the same plane. Landmark locations, moreover, are registered as two- or three-dimensional coordinates according to the methods that have been used. Moreover, if the same landmark was collected from different objects, it is referred to as a corresponding landmark (Richtsmeier *et al.*, 2002).

It is widely accepted that landmarks are utilized in direct and indirect anthropometry (Farkas, 1981; Tiddeman *et al.*, 2000). Any measurement of distances and angles between anthropometric landmarks using callipers and angular measurements is considered to be direct anthropometry. On the other hand, indirect anthropometry is the measurement of the human form from recorded images of the subject. It can be based on two- or three-dimensional images with a consequent complexity of analytical methods. The indirect method has an advantage in data collection and offers the opportunity to create an archive of original data that can be re-examined. The only shortcoming of this method is the possible distortion of the dimensions of the subject. This will depend on the type of imaging process used.

Landmark-based GMM (Rohlf and Marcus, 1993; Adams *et al.*, 2004; Zelditch *et al.*, 2004) capture the form of a structure using Cartesian coordinates of a configuration of points. These points must have a one to one correspondence in the specimens to be compared. The type of correspondence (topographical, anatomical, developmental etc.) depends on the scientific questions being asked (Oxnard and O'Higgins, 2009). There is no absolute landmark configuration on any given structure and the choice of the configuration must be meaningful in terms of the specific hypothesis being tested (Klingenberg *et al.*, 2002). Therefore, the choice of landmarks is a crucial step in the analysis (Robinson *et al.*, 2002). On the other hand the use of outline methods such as semi-landmarks, which have equally spaced points on the object's contour and do not depend on the explicit identification of anatomical landmarks (Adams *et al.*, 2004), makes it possible to obtain a large amount of information on surfaces but presents problems in terms of biological interpretation and the large number of variables they produce (Viscosi and Cardini, 2011). Increasing the number of points used to describe a structure quantitatively may also lead to problems in parametric statistical testing, as the number of variables easily becomes larger than the sample size, which makes some tests impossible, assumptions more difficult to test, and estimates of parameters (e.g., means and variances) problematic.

In recent years the increased availability of 3D data capture systems and powerful computer hardware has encouraged the design of new computer techniques for processing 3D data and the adoption of such techniques for both clinical and non-clinical applications. Tiddeman and colleagues (2000) used Morphoanalysis - a software package that employs a standardized framework for quantitative craniofacial assessment in a three-dimensional modality. Wiley and colleagues (2005) in cooperation with the NYCEP Morphometrics Group (NMG) introduced a free software program called Landmark.exe. Landmark.exe allows researchers to input different file formats from different scanner types and it is also compatible with 2D and 3D data. It has many features depending on the researcher's interest, but its main purpose is to place landmarks easily, accurately and with a high level of repeatability.

Three-dimensional shape analysis

The shape of an object can be represented by a number of points called landmarks. These landmarks, as described earlier, should be selected uniformly and according to each object type: e.g., tooth type, since they should represent the shape within and between each population. For any methods, the configuration of landmarks extracted as coordinates depends on the data type: e.g., x and y for two-dimensional and x, y and z for three-dimensional data.

To obtain a clear idea about the shape of any object, size must be defined very accurately. In the current study, size is defined as centroid size, which is calculated as the square root of the sum of the squared distances of each landmark from the configuration's centre (Bookstein, 1997b).

To become generally applicable in clinical assessment, the currency of shape analysis will need to be made comprehensive to the clinician. Different 3D shape analyses have been reported in the literature: e.g., Procrustes superimposition analysis (Dryden and Mardia, 1998), finite element scaling morphometry (FEM) (Richtsmeier *et al.*, 2002), mesh diagram analysis (Ferrario *et al.*, 1999), and Euclidean distance matrix analysis (EDM) (Lele and Richtsmeier, 1991). Procrustes superimposition analysis has become widely used and applied to data acquired using a variety of imaging methods, since it eliminates non-shape variation from the configuration of landmarks (Hennessy and Moss, 2001). Procrustes analysis is a method of superimposition that rotates, translates and scales configurations of 3D landmarks to a position of maximal agreement while retaining shape. The three steps in Procrustes analysis are as follows: firstly, all the objects are

scaled to a centroid size of 1.0 to eliminate the isometric size effect on coordinates. Secondly, all landmark configurations are moved to a common position in a way that shifts the centroid of the configurations to the 0, 0, 0 coordinates. Finally, the objects are then rotated to an overall best fit around the centroid. A criticism of geometric morphometrics concerns the arbitrariness of the choice of alignment procedure, but it has been demonstrated that the choice of registration method is unimportant if the variation in shape is small (Lele and Richtsmeier, 1991; O'Higgins and Jones, 1998).

Another approach to the statistical analysis of landmark coordinates, Euclidean distance matrix analysis (EDMA), has been developed. This method avoids registration and analyses the inter-landmark distances derived from the coordinates (Lele and Richtsmeier, 1991). EDMA, however, does not allow the direct visualization of results of the statistical analysis. Rohlf (1999) has criticized it for its lack of statistical power and its potential to produce misleading coordinates.

In the current study, Procrustes superimposition analysis was chosen as it made it possible to separate the non-shape components, which then made it possible to compare samples using multivariate inferential techniques and to produce graphical displays in order to visualize variations in shape.

Principal component analysis (PCA) is one of those multivariate techniques and was first introduced about 100 years ago (Näsman *et al.*, 1997). The main idea of PCA is to reduce the data dimensionality especially when they consist of a large number of interrelated variables. Moreover, it is a technique that explores the overall variation without looking into any group structure. Principal components (PCs) are statistically uncorrelated, which means they are ordered according to the maximum shape variation by creating a new coordinate system. The first PC describes the maximum shape variation, followed by the second, followed by the third and so on (Näsman *et al.*, 1997). PCs can be inspected and examined separately as they are uncorrelated and the first few PCs usually give a clear idea about the shape of the examined object. Also, each PC (eigenvalues) indicates the percentage of variance in relation to the total variance (Viscosi and Cardini, 2011).

Many researchers have suggested using standard multivariate methods, and then statistical analyses are carried out on the resultant PCs to investigate size, shape and allometry within and between groups (Winter and Baraitser, 2001; Garib *et al.*, 2010; Viscosi and Cardini, 2011). In the current study, three-dimensional geometric morphometrics was

used in conjunction with modern data collection and analysis techniques, in which there have been tremendous advances, as described above.

Software

Geometric morphometrics analysis has a number of software programs. Each of them has a particular objective and performs a specific function. Most of these software programs are available for free through the State University of New York (SUNY) at Stony Brook website: http://life.bio.sunysb.edu/morph/index.html (accessed on 12th January 2011).

Software programs are classified according to their main role. Some are used for data collection, shape coordination or multivariate analysis. Others can be used for comprehensive analysis.

In the current study, a number of free pieces of software were used: Meshlab software (Cignoni *et al.*, 2008) was used to convert image format and landmarks.exe (Wiley *et al.*, 2005) was used to place landmarks; MorphoJ (Klingenberg, 2011) and Morphologika were then used to perform geometric morphometric analysis (O'Higgins and Jones, 1998). The details of each piece of software will be explained in chapter three.

1.4 Geometric morphometrics studies:

The geometric morphometrics of the shape variation described by the principal components can be visualized, since the landmark configuration of a hypothetical specimen can be displayed by computer graphics (Hennessy and Stringer, 2002). These displacements can be represented in various ways: in two dimensions (2D) mainly by thin-plate splines (Bookstein, 1989; O'Higgins and Dryden, 1993), and in three dimensions (3D) by vectors (Slice, 1996), by warping a wireframe or rendered representation (Penin *et al.*, 2002), or by transformation grids (O'Higgins and Jones, 1998). However, the transformation grids are currently the most popular method.

1.4.1 Craniofacial application

The principal advantages of geometric morphometrics analysis over the traditional approaches are that it provides a shape space in which geometry is preserved and which can be interpreted statistically. Many studies have been published in the field of primate craniometry, using a variety of methods to generate shape coordinates and shape analysis, followed by graphical representation (Bookstein, 1997b; Hennessy and Stringer, 2002).

Bookstein (1997b) introduced a combination of Procrustes analysis and thin-plate splines for the multivariate analysis of curving outlines in samples of MRI images of 25 human brains. He concluded that it is important to use three-dimensional (3D) tools to establish a reliable shape analysis. Many similar studies have been conducted using two dimensions (2D), including sexual dimorphism of African and Roman-British groups (Lynch *et al.*, 1996); comparison of African, Australian, Chinese and Australian human groups (Wood and Lynch, 1996); and sexual dimorphism in *Pan, Gorilla* and *Pongo* (O'Higgins and Dryden, 1993).

Other examples of three-dimensional studies are comparisons of *Pan* and *Pongo* (Penin and Baylac, 1999); shape differences between two American human groups (Ross *et al.*, 1999); growth of *Cercocebus torquatus* (O'Higgins and Jones, 1998); and comparison of chimpanzees' and bonobos' crania (Lieberman *et al.*, 2007). Nevertheless, a recent work investigates the relationship between cranial size and shape of the *Liang Bua hominins* and the association pattern of the size on shape among various taxa using three-dimensional (3D) geometric morphometrics method (GMM) (Baab and McNulty, 2009). Furthermore, 3D GMM has been used to investigate the shape of the face and skull in humans (Badawi-Fayad and Cabanis, 2007; Franklin *et al.*, 2007a; Franklin *et al.*, 2007b; Mitteroecker and Bookstein, 2008).

1.4.2 Dental application

Tooth morphology has long been studied using traditional morphometrics. Advances in digital imaging and scanning have aided the process of taking such measurements and have also made it possible to record the location of landmarks as coordinates. Robinson and colleagues (2001; 2002) used these ideas to study tooth form in two-dimensional (x, y) coordinates from a photographic image. They introduced a formal definition of shape and demonstrated its application in the study of tooth morphology. A high resolution scanner was used to analyse anterior tooth shape but they only used it in two dimensions. Although they described the shape, their methodology used two-dimensional planes; this 2D analysis of a 3D object meant that they provided only a partial and rather limited description of shape (Kieser *et al.*, 2007).

Others have used the advantages of geometric morphometrics to analyse and investigate the effect of different types of mechanics on the treatment of class II division 1 malocclusion (Singh, 2002; Singh and Thind, 2003). Soft tissue facial profiles were compared using cephalometry, followed by Euclidean distance matrix (EDMA) and thin-

plate spline (TPS) analyses after Procrustes superimposition. They all demonstrated improvements in facial profile (Singh, 2002; Singh and Thind, 2003).

Some researchers have compared traditional and newer geometric morphometric techniques for the analysis of the size and shape of human molars (Bernal, 2007), while others have attempted to use geometric morphometrics to study dental arch form (Camporesi *et al.*, 2006). Furthermore, geometric morphometrics has been used on 3D tooth surface reconstruction and has been shown to be efficient for the recovery of tooth shape given crown information (Buchaillard *et al.*, 2007). Smith et al. (2007) mathematically assessed the curvature of the upper anterior teeth along the facial axis of the clinical crown in two dimensions. They concluded that the most prominent area of curvature was around the middle region and slightly towards the incisal edge of the tooth (Smith *et al.*, 2007).

Recently, Gomez-Robles and his colleagues compared 105 upper first molars (Gómez-Robles *et al.*, 2007) and 106 first premolars (Gómez-Robles *et al.*, 2008) from several hominin species using standardized occlusal surface pictures of the study sample. Using geometric morphometrics, they captured the spatial aspects of morphological variation by configurations of landmarks, then used generalized Procrustes superimposition to produce a mean configuration of the sample. Finally, the shape of a Procrustes registered landmark configuration was defined by the entirety of its residual coordinates (Gómez-Robles *et al.*, 2007; Gómez-Robles *et al.*, 2008). They emphasized the ability of geometric morphometric techniques precisely to assess morphological differences and have recommended the use of three-dimensional (3D) tools, avoiding possible complications derived from the analysis of 2D images (Gómez-Robles *et al.*, 2007; Gómez-Robles *et al.*, 2008).

Another group of researchers compared a new orientation method with those proposed in the literature (Benazzi *et al.*, 2009). This method is based on three points identified on the cervical line. They argue that an orientation system is a first step toward the creation of a virtual set of hominoid and fossil human first molars and provide guidelines as to how to extend the new methodology to other teeth (Benazzi *et al.*, 2009). They concluded that 3D geometric models offer the ideal solution for comparison of the various orientation systems since they permit objective and easily repeatable analytical methods (Benazzi *et al.*, 2009).

1.5 Methods for the determination of tooth dimensions

Various methods of measuring the dimensions of the human dentition are described in the literature. Each of these methods has advantages, disadvantages and limitations. The subjective resolution of technical problems is always associated with measurement techniques: e. g., calliper placement on crowded teeth. Dental models are used to obtain two- or three-dimensional analyses. The techniques are either traditional or advanced methods, and these methods involve either direct (digital callipers) or indirect measurement (laser scanning, radiographs, photographs).

Manual techniques involving the use of dividers, sliding, vernier or dial callipers, or a Boley gauge, allow only linear measurements to be obtained (Moorrees *et al.*, 1957; Bolton, 1958; Hunter and Priest, 1960; Garn and Lewis, 1970; Lavelle, 1970; Richardson and Malhotra, 1975). It has been suggested that the type of measuring instrument used plays a role in determining the accuracy of the measurements obtained.

Brook developed an image analysis technique to describe tooth dimensions using a dental study cast (Brook *et al.*, 1983). Linear, perimeter and area measurements of tooth crowns are obtained from video images of buccal and occlusal surfaces. Using this technique, Brook et al. (1986) measured the mesiodistal dimensions of the teeth of 50 male students. A comparison was made between this technique and the manual method. In general, the image analysis produced more variability than did the manual method.

Three-dimensional imaging has evolved a great deal and has found applications in orthodontics. In 3D dental imaging, a set of anatomical data is collected using diagnostic imaging equipment; it is processed by a computer and then displayed on a 2D monitor to give the illusion of depth. Depth perception causes the image to appear in 3D (Hajeer *et al.*, 2004a). 3D images are a reliable way to archive study models, producing durable images without any fear of loss or damage to the original casts. Furthermore, ease of access, transfer, and the accuracy of image capture techniques has been reported (Bell *et al.*, 2003; Santoro *et al.*, 2003; Quimby *et al.*, 2004). Also, it helps any clinician in diagnosis and in making a treatment plan (Hajeer *et al.*, 2004b).

One of these 3D imaging tools is the 3D study model scanner (3Shape R-640T). The scanning of a dental cast is performed using an optical scanning system, in which laser planes are projected onto the object. High-resolution digital cameras acquire images of the lines created on the cast. Later on, processing software automatically processes the

images and creates accurate and fully surfaced 3D models. The scanner captures the full geometry of the dental cast in one scanning session with high accuracy, including any undercuts present on the original study model. Consistently high levels of precision are guaranteed by projective geometry and a novel calibration of the laser, cameras and axes. A combination of rotation, translation and tilting of the model during scanning ensures that the model geometry is given maximum exposure to the cameras and laser. The accuracy of the 3Shape 3D scanner applied to study models was not measured by the researcher but was estimated to be 0.2mm, based on information provided by the manufacturer (3Shape, 2009).

1.5.1 Reliability of measurements

Reliability has been defined as "the extent to which a measurement and its technique are consistent" (Kieser, 1990: p.7). Precision and accuracy are the two aspects of reliability. Accuracy is better described as validity; it refers to how close the measured value is to the actual value. Precision, on the other hand, is more commonly known as reproducibility; it refers to the repeatability of measurements (Kieser, 1990: p.7).

There is no agreement in the literature regarding what is the best method of accurately quantifying the reliability of measurement error caused by the instrument used or by personal inconsistency. This may be the result of differences between study purposes and the techniques used in the investigation. However, there are some ways of minimizing those differences: for instance, accurate identification of landmarks (Robinson *et al.*, 2002) and a thorough training of the investigator (Harris and Smith, 2009). Anrnqvist and Martensson (1998) identified three types of error in GMM studies: methodological error, instrumental error and personal error. Methodological errors are those which occur during preparation such as preparing a specimen, taking an impression of teeth, or casting procedures. These steps can only be taken once for ethical and practical reasons and are irreversible (Arnqvist and Martensson, 1998). On the other hand, the other errors - instrumental (e.g., scanning) and personal (e.g., digitization), are the main levels of error that need to be quantified. In geometric morphometrics studies, quantification of the measurement of errors at different levels has been introduced using a modified version of the conventional analysis of variance (ANOVA), called a Procrustes ANOVA. This was introduced by Klingenberg and has also been incorporated with MorphoJ software to quantify the measurement of error. A Procrustes ANOVA is used to assess the relative magnitudes of measurement error from repeat measurements (Klingenberg and McIntyre,

1998; Klingenberg *et al.*, 2002). Recently, Harris and Smith (2009) reviewed the available statistical approaches that have been used to quantify measurement error. They reported that the incorporation of repeated measurements into the statistical design has improved with the newly established computer methods.

Previous studies have not found any significant differences between inter-observor errors and intra-observer error (Bailey *et al.*, 2004). Other researchers have examined repeatability and relative accuracy and these have been found to be less than 10 μm and less than 6 μm respectively (Persson *et al.*, 2006; Vlaar and van der Zel, 2006). To increase the validity of the research findings, the probability of rejecting null hypotheses when they are not true, errors need to be controlled for (Smith *et al.*, 2009). Smith et al. suggested using either an interclass correlation coefficient to estimate the repeatability of measurements or using Dahlberg's d (1940). However, when they investigated measurement errors in the repeated measurement of their study models, they found no significant errors in the reliability of linear measurements of scanned images when compared to those obtained from dental casts (Smith *et al.*, 2009). The results of tests of measurement error in the present study were congruent with the findings of the studies mentioned above and confirm the finding that 3D scanned images are accurate and provide excellent material for the investigation of human teeth variability.

1.6 Summary of literature review

The congenital absence of one or more teeth is known as hypodontia. The incidence of hypodontia involving the permanent teeth ranges between 2 and 10% of the global human population (Polder *et al.*, 2004); this does not include the absence of wisdom teeth. Hypodontia can affect any tooth with different levels of severity (Grahnen, 1956; Hunstadbraten, 1973).

It has been reported that hypodontia is isolated in relation to its aetiology and clinical aspects. The literature demonstrates an association between tooth number, size and shape (Rantanen, 1956; Alvesalo and Portin, 1969; Lavelle, 1970; Sofaer *et al.*, 1971; Brook, 1974; Brook, 1984; Lai and Seow, 1989; Schalk-van der Weide and Bosman, 1996; Baccetti, 1998).

A number of models have been suggested in regard to the causes of hypodontia; however, these causes are still unclear. Many studies have provided evidence for genetic, epigenetic or environmental causes behind hypodontia. Brook (1984) suggested a single model describing the aetiology and explained the distribution of anomalies of tooth number and size for both sexes. Limited progress has been made in our understanding of the aetiology of hypodontia. Researchers have attributed this to two reasons (Townsend *et al.*, 2009a): the first involves the complexity of the aetiology and the interlink between genetic, epigenetic and environmental factors (Brook, 2009); secondly, the lack of a quantitative method, such as a 3D method, that may be used to quantify tooth form accurately and comprehensively may help to explain why different authors have reached different conclusions. Indeed, Brook (2009b) points out that clinical practice always requires a knowledge of tooth shape and not just of tooth size; they recommend using data from 3D imaging techniques to obtain accurate information about tooth form, since all previous studies tend to use a traditional morphometrics based on linear tools only. The new method of 3D geometric morphometrics used in the current study will allow accurate and detailed description of crown size and shape in hypodontia subjects and thus overcome the shortcomings of previous studies. Furthermore, the present study of tooth size and shape in 3D will allow us to know what is the ideal tooth size and shape in hypodontia patients, including height, length and width. Previous studies have mainly emphasized the MD and BL dimensions. Knowledge of other tooth size parameters, such as tooth height, for example, is important in hypodontia subjects, as this will dictate the level of gingival

margin, which is particularly important when the patient has a high smile line, for example.

Chapter 2 Aims and Objectives

2.1 Statement of the problem

A great deal of research has been conducted over the past few years in an attempt to identify the causes of hypodontia. However, only a limited amount of information has been obtained owing to the limitations of the methods used in the research. Previous researchers have used traditional methods that were not able to quantify tooth size and shape robustly. In some cases the methodology was able to describe size but not to explain tooth shape quantitatively. Also, no study has yet quantified tooth morphology in a comprehensive pattern in regard to the sample, severity of the condition, age of the candidates and their sexes, or in 3D. Given the advances in modern imaging systems and taking into account most previous recommendations, a new 3D imaging system should be introduced in order to be able to quantify tooth morphology in a comprehensive manner and to visualize shape variation in teeth between different groups easily. The aim of this research was thus to investigate crown morphology variation within and between hypodontia groups. It is hoped that this investigation will have some clinical value and that it will give rise to new research questions regarding the aetiology of hypodontia.

The present study adopted a novel three-dimensional geometric morphometric technique to quantify the crown morphology of teeth and their sizes. The study also investigated allometric variations in order to determine whether there was any association between the size and shape of teeth.

2.2 Null hypotheses

- There are no size differences between hypodontia and control subjects.
- There are no shape differences between hypodontia and control subjects.
- There are no size effects on shape in hypodontia or control subjects.

2.3 Overall aim

The overall aim of this study was to investigate tooth size, shape and allometry in subjects with hypodontia and to compare these with control subjects of the same age and sex using 3-dimensional (3D) geometric morphometrics. The hypodontia group was subdivided into three groups according to the number of missing teeth.

2.4 Aims

2.4.1 First aim

To develop a new method based on geometric morphometric analysis to quantify the size and shape of teeth in three dimensions.

Null hypothesis

Geometric morphometric methods are neither applicable nor useful in quantifying tooth size and shape.

2.4.2 Second aim

To determine whether there are significant differences in 3D tooth size between hypodontia patients and matched control subjects.

Null hypothesis

There are no significant differences in 3D tooth size between hypodontia and control subjects.

2.4.3 Third aim

To determine whether there are significant differences in 3D tooth size between mild, moderate and severe hypodontia subgroups.

Null hypothesis

There are no significant differences in 3D tooth size between mild, moderate and severe hypodontia subgroups.

2.4.4 Fourth aim

To demonstrate the pattern of size differences between the teeth of hypodontia patients and those of control subjects.

Null hypothesis

There is no pattern of size differences between the teeth of hypodontia patients and those of control subjects.

2.4.5 Fifth aim

To assess whether there are significant differences in 3D tooth shape between hypodontia patients and matched control subjects.

Null hypothesis

There are no significant differences in 3D tooth shape between hypodontia patients and controls.

2.4.6 Sixth aim

To determine whether there are significant differences in 3D tooth shape between mild, moderate and severe hypodontia subgroups.

Null hypothesis

There are no significant differences in 3D tooth shape between mild, moderate and severe hypodontia subgroups.

2.4.7 Seventh aim

To demonstrate the pattern of shape differences between the teeth of hypodontia patients and control subjects.

Null hypothesis

There is no visible pattern of shape differences between the teeth of hypodontia patients and control subjects.

2.4.8 Eighth aim

To determine if there is a significant difference in 3D tooth allometry between hypodontia patients and control subjects.

Null hypothesis

There are no significant differences in 3D tooth allometry between hypodontia and control subjects.

2.4.9 Ninth aim

To determine sexual dimorphism of tooth size and shape.

Null hypothesis

There is no sexual dimorphism of tooth size and shape.

Chapter 3 Materials and Methods

3.1 Material

3.1.1 Study design

This research project is a retrospective cross-sectional case-controlled study designed to compare the crown morphology of the permanent dentition of hypodontia and control subjects using modern three-dimensional geometric morphometric analysis techniques. Each tooth type, tooth size and tooth shape of male and female hypodontia subjects was compared with that of subjects who had a full complement of permanent teeth. The aim of the study was therefore to investigate three-dimensional differences and variations in crown morphology across groups representing differing degrees of severity of the disease, as well as those in healthy individuals, and to determine whether there was any difference between females and males.

3.1.2 Sample size calculation

The size of the sample used in the present study was similar to that of samples in previous studies which employed linear measurements. Brook and his colleagues (2002), for example, suggest that a comparison between two groups of 20 will give an 80% power to detect a size difference of 0.90 mm. They found that it is reasonable to expect size differences of this magnitude.

3.1.3 Study population

The study population comprised male and female subjects aged between 12 and 18 years old: one group with hypodontia (hypodontia group) and the other with a normal complement of permanent teeth (control group). Hypodontia patients were selected from the patient database associated with the multi-disciplinary Hypodontia Clinic, Newcastle Dental Hospital. Control patients were selected from among orthodontic patients attending consultant clinics and postgraduate orthodontic teaching clinics. Their ages were taken from the dates shown on their pre-treatment dental casts. The total sample size was one hundred and sixty subjects.

The hypodontia subjects were further divided into three groups that represented varying degrees of severity of hypodontia - mild, moderate and severe. All groups were balanced with regard to sex, age and group size.

The following definitions and criteria were used to select subjects for the study groups:

- **Mild hypodontia (Group M):** Cases with hypodontia of one or two teeth, excluding the third molars (20 males and 20 females).
- **Moderate hypodontia (Group D):** Cases with hypodontia of three to five teeth, excluding the third molars (20 males and 20 females).
- **Severe hypodontia (Group S):** Cases with hypodontia of six or more teeth, excluding the third molars (20 males and 20 females).
- **Control group (Group C):** Cases with a full complement of permanent dentition (20 males and 20 females).

3.1.4 Inclusion criteria

Subjects for both hypodontia and control groups were collected according to the following criteria:

- **Location:** From one demographic area (north-east England).
- **Ethnicity:** European descent.
- **Sex:** Both sexes.
- **Age:** Similar ages (12 – 18 years old).
- **Orthodontic treatment:** No history of orthodontic treatment.
- **Teeth condition:** Slight attrition or dental wear.
- **Occlusion type:** No selection of particular dental occlusion or skeletal pattern was made.
- **Study models:** Good quality study models were required for all subjects; thus, any defective study models would be excluded.
- Patients with any syndrome: Not included.

3.1.5 Ethical approval

Ethical approval for the study was granted by the County Durham & Tees Valley 1 Research Ethics Committee. In order to recruit subjects for the control group, information sheets were produced and sent to both the children concerned and their parents. The written consent of parents/guardians of control group subjects was obtained before the start of the data collection. No further consent was required for the hypodontia subjects, however, since the data for these subjects were collected anonymously from the main Newcastle Dental Hospital database.

3.1.6 Sampling methodology

A tooth was recorded as congenitally absent when the tooth could not be detected on the study models and the dental records of the patient confirmed that the tooth had not been extracted.

Only pre-treatment study models of the maxillary and mandibular arches were used to examine tooth size and shape. Study models had already been made for all participants as part of a routine orthodontic assessment.

On accepting the candidate for inclusion, the name, sex, date of birth, date of the impression of study models, and the presence or absence of teeth in each subject was ascertained. Each subject was then given a code number to allow the measurements to be undertaken 'blind'.

3.2 Methods

The study utilized a modern three-dimensional geometric morphometric analysis technique to obtain measurements of tooth size and shape for the whole sample. Validation of the new three-dimensional technique against manual measurement was obtained and published by the British Society for Oral and Dental Research (BSODR) (Khalaf *et al.*, 2009a) .

The following are the main system components used in the present study (Figure 3.1):

- Three-dimensional dental scanner (R640) (3Shape, 2009).
- Personal computer.
- Software (Figure 3.2)
    - ✓ *Orthoanalyzer (3Shape, 2009) - Adjusts scanned images.*
    - ✓ *MeshLab v1.2.1 (Cignoni et al., 2008) - Converts scanned images.*
    - ✓ *Landmark.exe (Wiley et al., 2005) - Landmark identification.*
    - ✓ *MorphoJ 1.02c (Klingenberg, 2011) – Geometric morphometrics and statistical analysis.*
    - ✓ *Past 2.06 (Hammer et al., 2001) - Statistical analysis.*
    - ✓ *Morphologika2 v2.5 (O'Higgins and Jones, 2006) – Shape visualization.*
    - ✓ *SPSS 18.0 (Pallant, 2007) - Statistical analysis.*

Figure 3.1 Main system tools

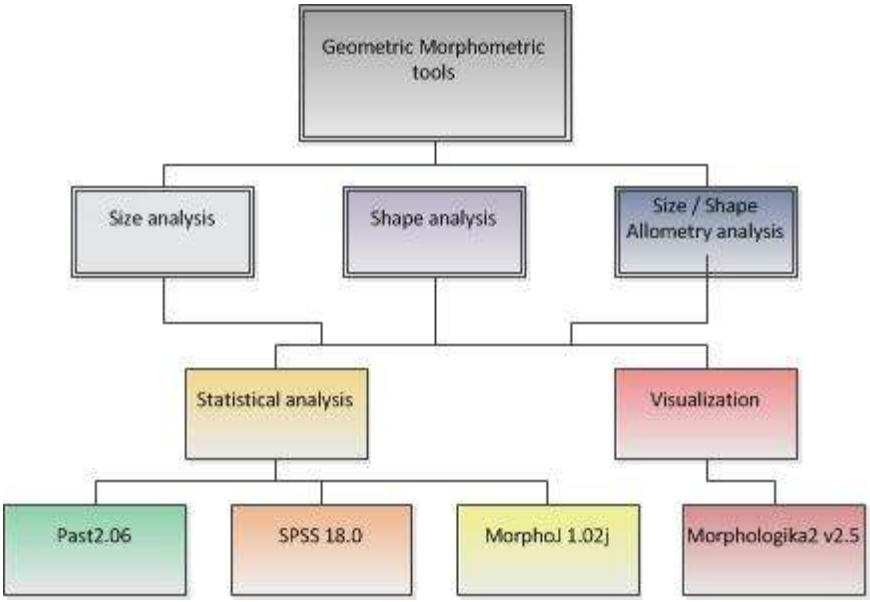

Figure 3.2 Project software

Three main processes were involved in this project, as follows (Figure 3.3):

- Data collection, as described above
- Data acquisition
- Data analysis

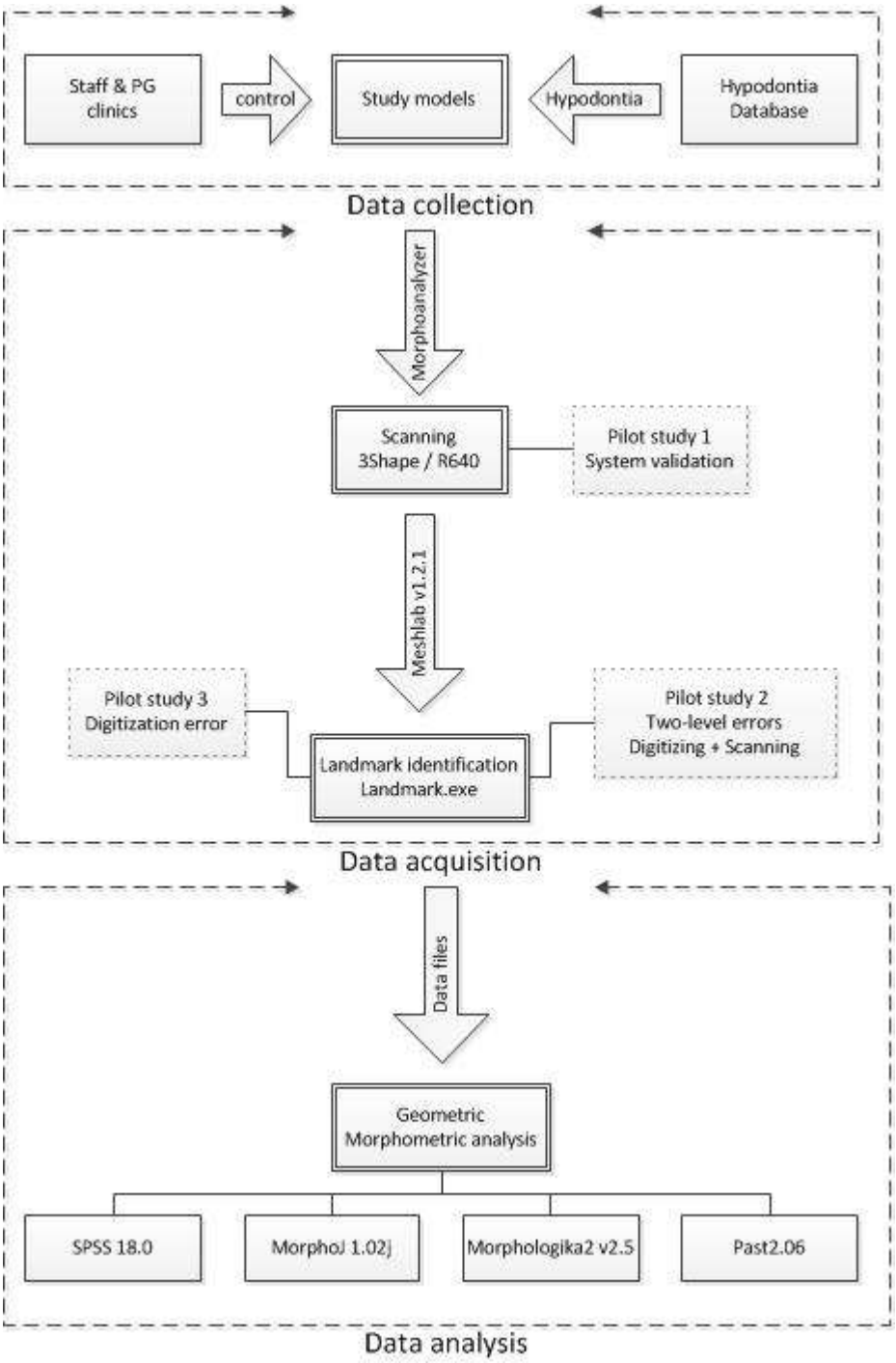

Figure 3.3 Methodological steps

3.2.1 Data acquisition

Scanning process

The scanning of a dental study model was performed using an optical scanning system (R640), in which laser planes were projected onto the object. High-resolution digital cameras acquire images of the lines created on the study model. The R640's processing

software automatically processed the images and created accurate and fully surfaced 3D models. There are four main elements to the R640 scanner:

- 2 x High resolution CCD cameras
- 1 x Laser projector
- 1 x Articulating table

Scanning procedure

The model was positioned on the articulating table and the laser projected an image of a line/series of points onto the surface of the model. This was performed in darkness so that what was visible to the cameras was a red line on the surface of the model. The two cameras were positioned at an angle of approximately 30 degrees on either side of the projected image (Figure 3.4).

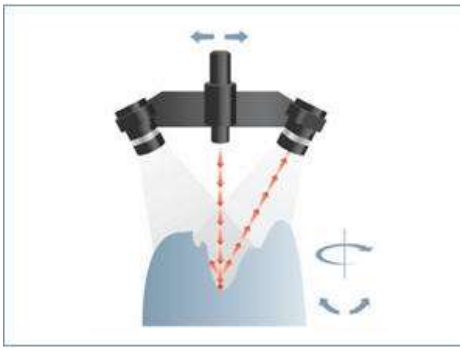

Figure 3.4 Two-sided camera with laser projector in the middle (3Shape, 2009)

Two scanning processes had to be executed during the complete cycle involved in generating the full digital study models, as shown in Figure 3.5 below.

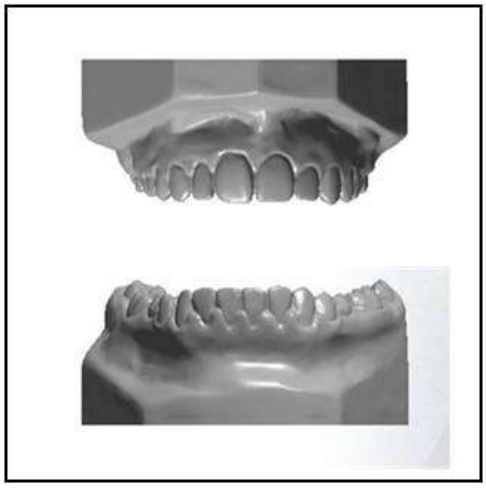

Figure 3.5 Full digital upper and lower models

The first of these was the process by which many thousands of points are created in a three-dimensional space. Each of these points has x, y and z coordinates and make up the "point cloud" (Figure 3.6).

Figure 3.6 Model creation: point cloud and post-processing (3Shape, 2009)

The second process was a software process that converted the point cloud into a series of triangles. Each triangle was constructed from three adjacent points in the point cloud. This process does not require the model to be placed in the scanner as the process is performed on the completed point cloud. When the triangles are created, algorithms which perform an extrapolating function add curvature to the triangular surfaces to mimic the smoothness and fluidity of naturally occurring surfaces. The resulting scanned models were saved in *STL format which was converted into *PLY using MeshLab v1.2.1 (Cignoni *et al*., 2008). The time taken to scan an upper or lower model was approximately 2min 15sec. The time required for post-processing an upper or lower model was approximately 1min.

Calibration of the Scanner

There were two steps involved in calibrating the scanner. First, the scanner was used to measure an object of known dimensions and software was then used to compare the measurements made during the scan with the pre-defined actual dimensions of the calibration standard.

Second, each of the cameras was exposed to the pattern of holes produced by a high accuracy 'dot box'; this 'box' contains a light source which shines through an opaque sheet of plastic which has an array of clear circular holes accurately and evenly spaced across its surface. The software compares the image acquired by the camera with the known pattern of the 'dot box'. The calibration standard and the 'dot box' are shown in figure 3.7 below.

Figure 3.7 The calibration tools for the scanner

During both calibration cycles, the accuracy of the cameras, the drive motors and the accuracy of the encoders which measure the motor positions were all measured. Any discrepancy between the measured values and the true values was recorded and used for compensation purposes by the software. The manufacturer suggests performing a calibration test every two weeks. In this study the calibration was performed on every scanning cycle.

Landmark definition and identification

Anatomical landmarks provide the core information on morphology in geometric morphometrics. They have to be accurately defined, precise and relate to the same anatomical features in every specimen (Robinson *et al*., 2002; Oxnard and O'Higgins, 2009).

In this research project, landmarks were defined according to tooth type or according to morphological class. Most of the landmarks were of Type I (anatomical evidence) and some were of Type II (geometric evidence) (Robinson *et al.*, 2002; Zelditch *et al.*, 2004). The different classes used in this project are detailed in tables 3.1-3.3.

The landmarks were digitized by the same person (Figure 3.8) using the PLY* file in landmark.exe (Wiley *et al*., 2005) and the coordinates were later exported as simple data text files. The data text files with the landmark coordinates were modified as required by the specific format of the programs used for the geometric morphometric analyses. Formats of various programs are described in the help manuals/user guides. A data text file consists of the configuration of a matrix (*k x m*) in which the *k* rows represent landmarks while the *m* columns represent dimensions. The shape of a configuration matrix depends on the particular task or software that is being used - for more details on this see Zelditch et al. (2004, p.76). In this project a configuration of matrix was used

which was compatible with both the types of geometric morphometric software that were being employed (Morphologika and MorphoJ). Landmark reproducibility was estimated taking into account both scanning and digitization errors and digitization error alone (measurement of errors section - at the end of this chapter).

Landmarks	Definition
(1) and (2)	mesial and distal endpoints of MD (contact points)
(3) and (4)	gingival and incisal endpoints of the LACC (point of bisection of incisal edge by BL)
(5) and (6)	corners of mesial and distal sides and incisal edge
(7) and (8)	ends of mesial and distal papillae from the buccal side
(9)	buccal endpoint of BL

Table 3.1 Upper & lower anterior teeth landmark defintions

Landmarks	Definition
(1) and (2)	mesial and distal endpoints of MD (contact points)
(3)	buccal endpoint of BL
(4) and (5)	mesial and distal pits/fissure junctions
(6) and (7)	lingual and labial cusp-tips
(8) and (9)	mesial and distal endpoints of maximum labial cusp width (corners of buccal cusps)
(10) and (12)	ends of mesial and distal papillae from the buccal side
(11)	halfway between (10) and (12) along the gingival margin from the buccal side

Table 3.2 Upper & lower premolar teeth landmark defintions

Landmarks	Definition
(1) and (2)	mesial and distal endpoints of MD (contact points)
(3)	buccal endpoint of BL
(4) and (5)	mesial and distal lingual cusp-tips
(6) and (7)	mesial and distal labial cusp-tips
(8)	distobuccal cusp tip (only lower first molar)
(9)–(12)	outer mesial, inner mesial, central and distal pits *
(13) and (15)	ends of mesial and distal papillae from the buccal side
(14)	halfway between (14) and (16) along the gingival margin from the buccal side
(16)	occlusal limit of buccal groove
(17)	occlusal limit of distobuccal groove (only lower first molar)
(18)	occlusal limit of lingual groove

Table 3.3 Upper and lower molar teeth landmarks defintions. * The number of pits differs according to molar type

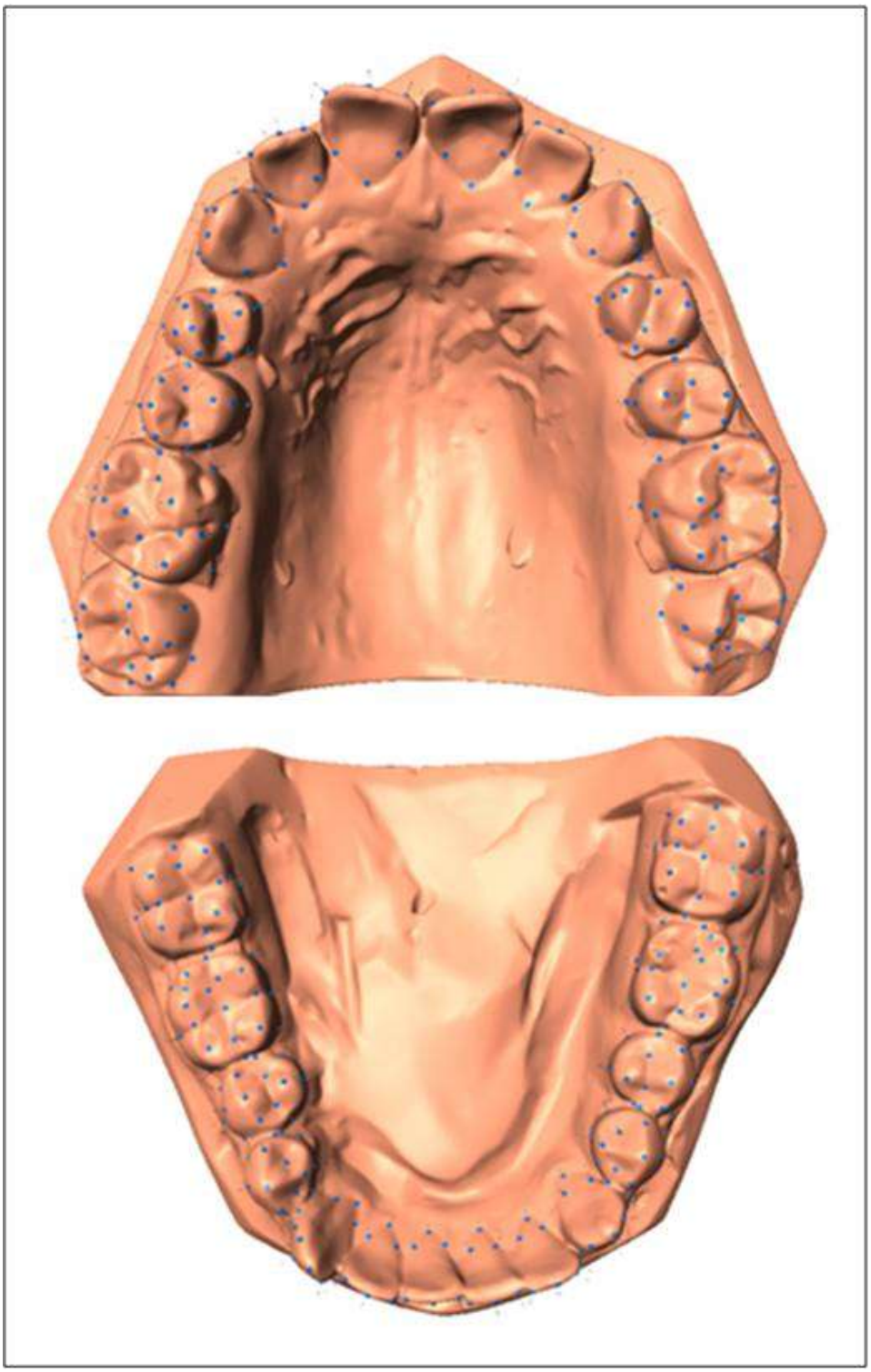

Figure 3.8 Selected landmarks on all teeth

3.2.2 Data analysis

Geometric Morphometrics: size and shape variables

Geometric morphometrics is a set of statistical methods designed to analyse biological form using Cartesian coordinates of anatomical landmarks (O'Higgins and Jones, 1998; Adams *et al.*, 2004; Sanfilippo *et al.*, 2009). Accounts of applications in orthodontics have started to appear in the literature (Robinson *et al*., 2001; Halazonetis, 2004). The aim of geometric morphometrics is to extract relevant information and discard information that is not of interest. In this research, centroid size - the square root of the sum of the squared distances from each landmark to the centroid of the configuration (Bookstein, 1997b; Dryden and Mardia, 1998) - was used to represent crown size. Shape variables were computed by scaling landmark configurations to unit centroid size and minimizing translational and rotational differences across all individuals using a least squares method called generalized Procrustes analysis (GPA) (Rohlf and Slice, 1990). GPA superimposed shape data can be described as points in a 3k -7 dimensional shape space, where *k* is the number of landmarks. The removal of 'information' in the GPA results in the loss of seven degrees of freedom (one for scale, three for translational axes and another three degrees for rotational planes) (Zelditch *et al*., 2004). For example, a lower left first molar has 54 coordinates (18 landmarks x 3 dimensions); however, in shape space 7 coordinates are lost, so the number of remaining coordinates is 37, and this is also the case with the other teeth. Shape matching considers the total configuration of landmarks, rather than individual landmarks; e.g., the lower first molar has 18 landmarks with three coordinates on each landmark, and a total of 36 variables. This means we have only one shape unit rather than 36 variables. This approach is different from those adopted in traditional morphometrics, where each variable is treated separately. It may seem unclear to treat the entire shape as a single unit, but according to Zelditch (2004), the rigour and power of these methods and their ability to visualize shape variation graphically overcomes this problem. Again, for any shape a number of dimensions are lost during GPA. The Procrustes shape space is a non-Euclidean curved space which has to be projected into a tangent Euclidean space to perform statistical analyses (O'Higgins and Jones, 1998). The approximation of the tangent space to the Procrustes shape space is akin to the approximation of the curvature of the Earth on a flat map. The main difference is that the curvature in the shape space is multi-dimensional (being a sphere only for configurations of three landmarks). In the same way that the curvature appears negligible when mapping

a small region of the Earth, the curvature of the shape space generally also appears negligible, because the portion of the shape space occupied by biological variation tends to be tiny compared to the space of all possible configurations of *k* landmarks (Slice, 2001).

Shape variation can be further divided into allometric and non-allometric variation using a multivariate analysis of covariance approach. Allometry is the study of size-related shape changes: differences in shape which are explained by size in a multivariate regression of total shape onto the natural logarithm of centroid size - the predictions slope of this regression are the allometric trajectory (Cardini and Elton, 2008a).

Procrustes superimposition

In the current research, the data for each tooth (i.e., the raw x, y and z coordinates of the landmarks) were loaded into MorphoJ 1.02j, and shape coordinates were computed by performing a GPA (simply called 'Procrustes fit' in MorphoJ) (Figure 3.9). The shape differences between the landmark configurations of two individual teeth can be quantified by their Procrustes distance, which is approximately the square root of the sum of the squared distances between pairs of corresponding landmarks. Centroid size was saved as a separate variable for testing size differences. Statistical analyses are univariate for size but must be multivariate for shape, i.e., performed on all shape variables. This is because shape is inherently multivariate: even with the simplest shape, a triangle (which has 6 coordinates in a 2-dimensional GPA), although four dimensions are lost when variation in size, translation (on the x and y axes) and rotation (on the xy plane) have been removed, still has two coordinates remaining to describe its shape.

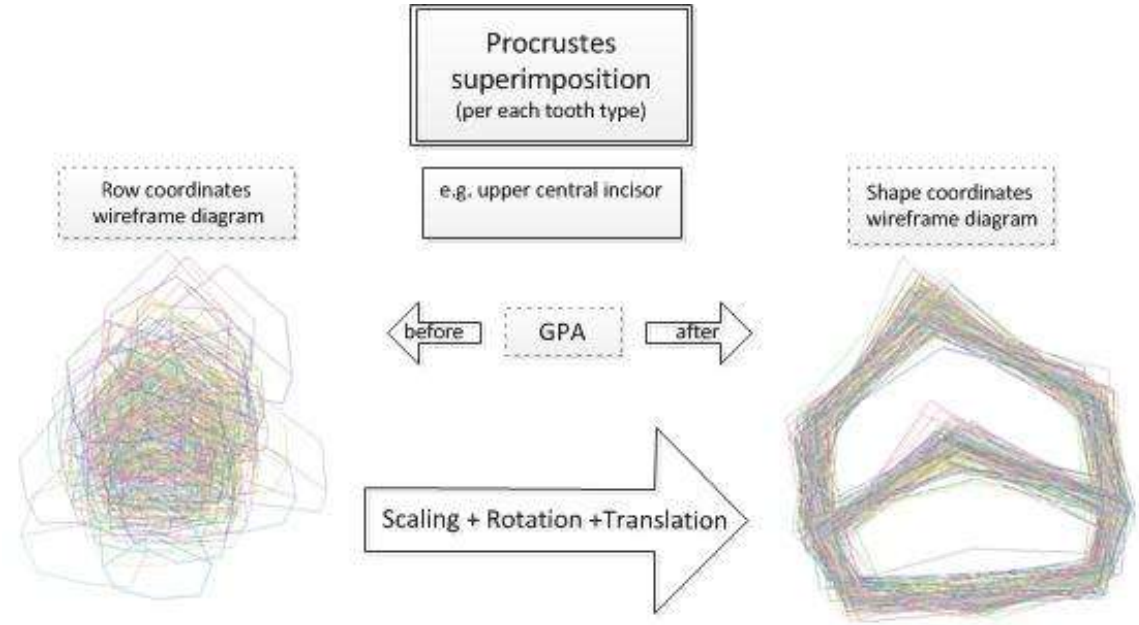

Figure 3.9 Procrustes superimposition for upper central incisor

Outliers

The data were checked for outliers by examining PCA scatter plots. This was done for both on the total sample and within each population sample. The presence of outliers was investigated also by inspecting the vector of the Procrustes shape distances between the data of two individual teeth and the mean shape. Outliers might represent extreme biological variation or be related to errors in data collection; if present, careful checking should be undertaken as they can critically affect analytical results.

Principal component analysis

A geometric morphometric method has the ability to describe the diversity between different shapes. Two methods are usually used to do this: principal component analysis (PCA) and canonical variates analysis (CVA). PCA was used in this research since it simplifies the data and makes it easier for the investigator to interpret findings by creating new coordinate systems that are linear representations of the original data, uncorrelated to each other. It results in the production of fewer variables to be explained. The reduced number of variables achieved by PCA is adequate and able to show any variation within the sample without affecting the overall result. This makes the presentation of the results easier. Furthermore, PCA gives an overall description of the data, but this should be viewed with caution and should not be misused. Clusters of individuals can be explained in PC plots but these clusters do not represent evidence of statistical significance.

However, PC scores are typically the shape coordinates that are used to investigate shape and allometric variation when tested by multivariate statistics (Zelditch *et al*., 2004).

A PCA using the variance covariance matrix of the shape coordinates was performed to summarize shape variables in a small number of principal components that explain most of the total sample variance in this research. PCs can also be used to explore patterns of variation regardless of groups (Figure 3.10). If groups separate well on the first few PCs, this is a strong indication that the specimens occupy different regions of the shape space. If these differences are statistically significant, the significance value will need to be tested using multivariate tests for group differences (see the following section).

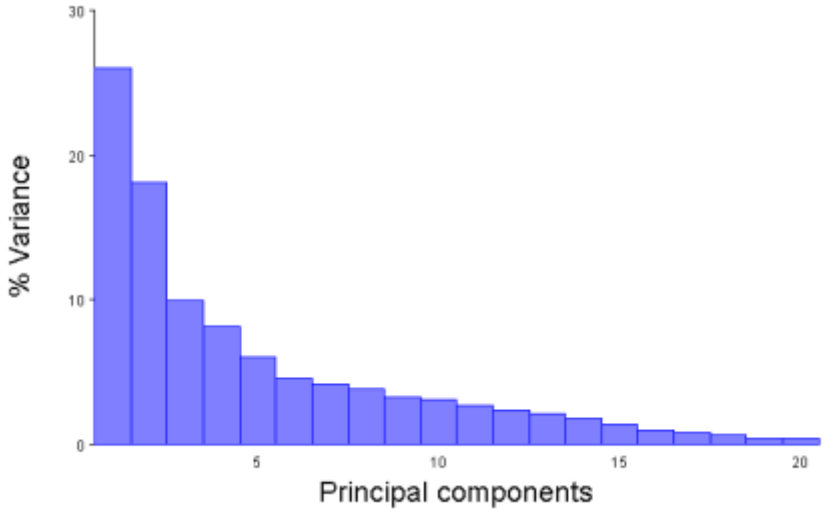

Figure 3.10 **The percentage of shape variance explained by each PC. The first PC has the maximum variation followed by the second one and so on.**

In this research, a PCA was used to reduce the dimensionality in the data. The number of PCs to be retained for the statistical shape analysis was selected by measuring the correlation between the matrix of Procrustes shape distances in the full shape space and pairwise Euclidean distances in the reduced shape space (3, 6, 9 principal components, and so on). Computations of distances and matrix correlations were performed in Past 2.06 freeware program, which plotted correlation coefficients onto the number of components using types of scree plots in order to determine how many variables accounted for most of the shape variation (Figure 3.11). A detailed description of this process can be found in Cardini et al. (2010). The ‘elbow’ in the plot suggests the

minimum number of PCs that should be retained before the loss of information in the higher order PCs (which are excluded) becomes so large that it appreciably changes the relationships between specimens in the reduced shape space compared to the relationships between them in the full Procrustes shape space. Thus, with regard to the data of the current research, if we take the lower right first molar as an example, the first 20 principal components of shape explained 84.0% of the total variance, had a correlation with distances in the full shape space of 0.98, and so were selected for use in all subsequent analyses relating to that tooth.

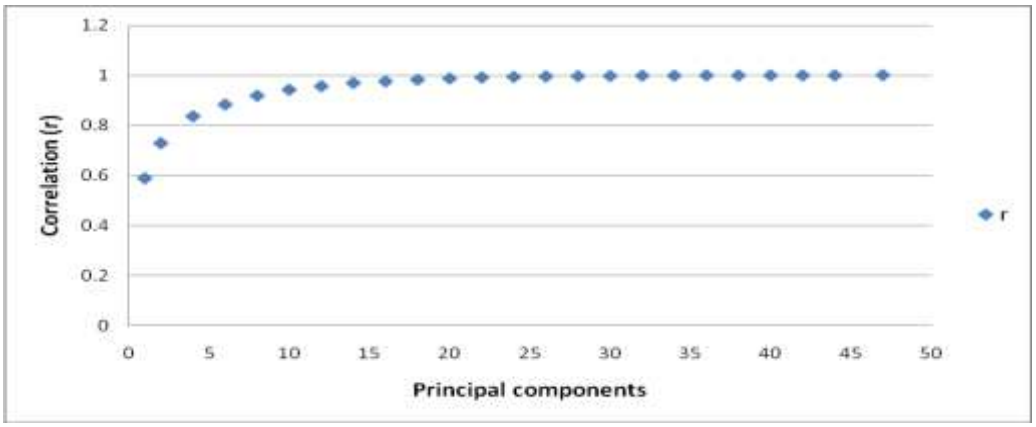

Figure 3.11 **Correlation between matrices of Euclidean distances computed from 3, 6, 9 etc. PCs and the matrix of Procrustes distances in the full shape space.**

A PCA was used to account for the actual shape variation in the total sample of real specimens and also to visualize the main trends in relative differences between groups using PC scatter plots showing the mean shapes of the teeth of the control and hypodontia groups. Mean shape similarity relationships were also summarized using a cluster analysis in Past 2.06 (Cardini and Elton, 2008b).

Statistical tests

Size and shape

When testing any hypothesis, the corresponding research question could be very simple: for instance, comparing one continuous variable in one categorical variable (sex: males and females); or it might be very complex: for instance, comparing multivariate continuous variables (shape coordinates) between multiple categorical variables (sex by groups). In this study, a statistical framework was created for each hypothesis to answer the corresponding question. It was necessary to use multivariate analysis to compare

shape as each landmark has three dimensions (x, y and z coordinates). When testing allometry - groups differ in shape when they differ in size - it is recommended that multivariate regression be used. Size difference is tested by a univariate test because size is a one-dimensional variable.

Four main analytical techniques were used: analysis of variance (two-way ANOVA sex by groups) was used for size, while multivariate analyses of variance (MANOVA) and covariance (MANCOVA) and discriminant analyses (DA) were used for shape. In this research, the two-way ANOVA was used to test the hypothesis that there would be no differences in centroid size means across groups. The groups could be either control or hypodontia groups (the two sexes were analysed separately). The two-way ANOVA not only allowed group differences to be tested but also enabled the researcher to determine whether the pattern (i.e., the magnitude and direction) of sexual dimorphism, if present and significant, was similar across all control and hypodontia groups (non-significant interaction term) This was crucial to deciding whether sex was statistically significant and whether to pool females and males or instead to perform analyses on each sex separately.

The MANOVA procedure allows the researcher to model the values of multiple dependent variables (shape coordinates), based on their relationships to categorical variables (groups and sex). The principle is the same as in the ANOVA but it is extended to enable the researcher to test many variables simultaneously.

The MANCOVA procedure is similar to that of the MANOVA, but we are now also controlling for a continuous predictor. The predictor or covariate in this study was centroid size. If the pattern of size-related shape variation (i.e., allometry) was found to be the same across all control and hypodontia groups, then it would be possible to hold it constant while testing group differences. This would make it possible to determine whether differences in shape between groups, when present, were simply due to size differences and the covariation of shape with size.

In this research, a predictive DA was used to construct a model that would enable us to discriminate most accurately according to a least square criterion among control and hypodontia groups. The main aim was therefore to classify individuals in groups according to the stage of the disease. In DA, group predictions are based on a jacknife cross-validation. Thus, in this research each individual was excluded in turn, and the discriminant functions were computed using all the other individuals; finally these

functions were used to compute the discriminant score for the one case which had been left out. The same process was repeated for all cases. This avoids the circularity of a standard DA, where a specimen is classified based on functions built on samples which included that same specimen, a procedure which inevitably leads to 'overlay optimistic' results.

All the above-mentioned techniques are based on a number of assumptions: mainly, normality and homogeneity of variance-covariance (homoscedasticity) and independence of observations. Normality and homoscedasticity were tested using, respectively, the Shapiro-Wilk and Levene's tests for the univariate case (size) and the Box's test for homoscedasticity for the multivariate data (shape).

Besides MANOVAs, post-hoc tests for the overall statistical significance of group differences were performed for both univariate size and multivariate shape to find out which groups differed from the others. The post-hoc tests were computed in MorphoJ 1.02j using pairwise permutation tests for mean group size or shape distances. It is important to bear in mind the fact that increasing the number of tests, increases the rate of Type I error, which means that the null hypothesis may be rejected when it should not be. A Holm's sequential Bonferroni correction between groups and sex, with a pairwise comparison test, was therefore used to control for Type I errors (informally speaking, these occur when the tests suggest that there is a difference when in truth there is none, a mistake which becomes more difficult to avoid when conducting multiple tests). It works by adjusting the significance values, by establishing the *alpha* level. Using Holm's method, the observed significance values are arranged in an ascending order. In this study there were four groups, which meant there would be six pairwise comparisons. The smallest p-value of the six tests had to be smaller than the nominal significance threshold (0.05) divided by the total number of tests: i.e., 0.05/6 = 0.0083, in order to be significant. If this value was not significant, none of the others would be. A detailed explanation can be found in Holm (1979).

For all pairwise tests, in addition to *p*, the magnitude of the differences being tested was estimated as the percentage of explained variance. This was computed using group dummy variables and a regression approach, as described in (Cardini and Elton, 2008a).

The steps of both the size and shape analysis are summarized in figures 3.12 – 3.13

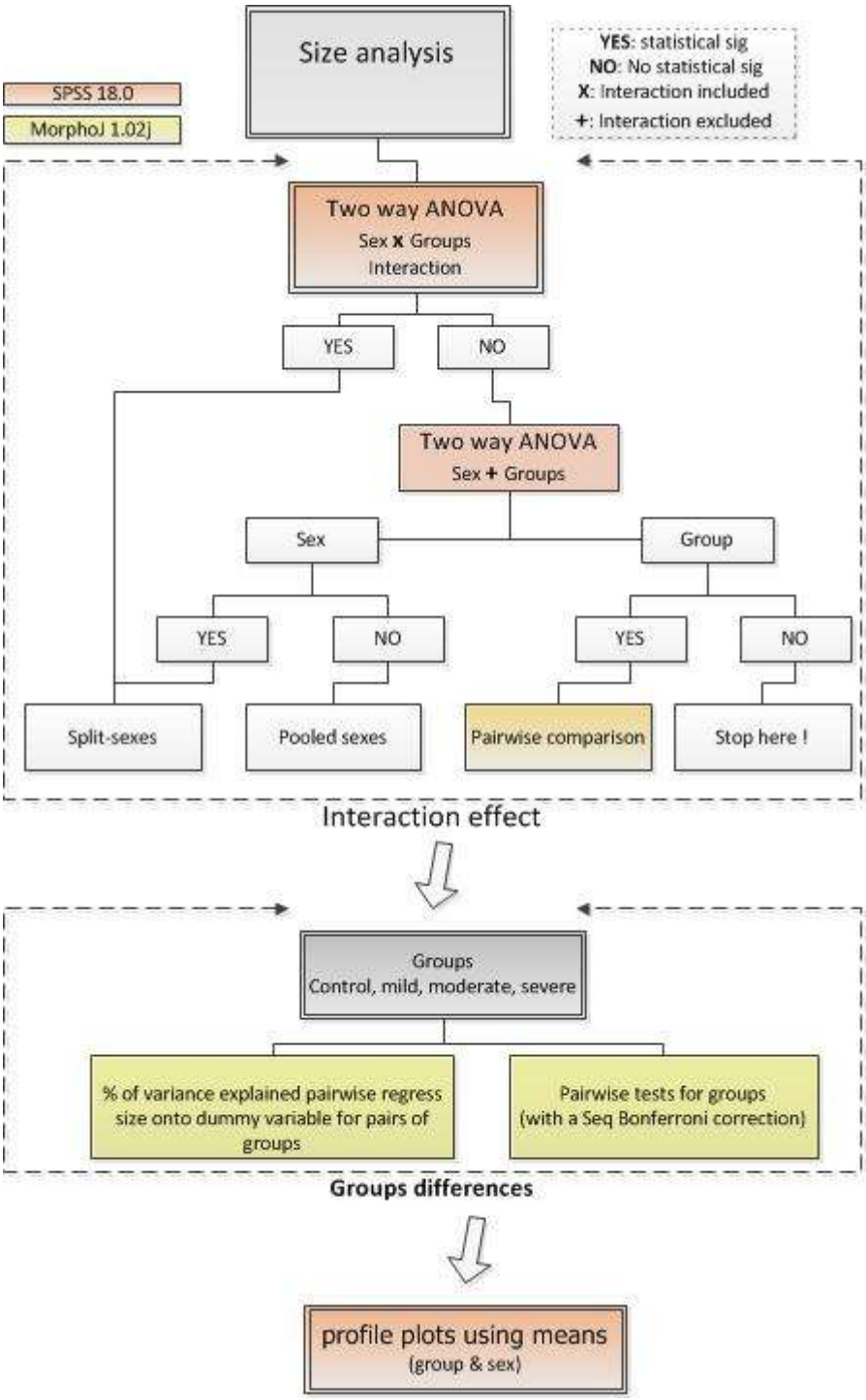

Figure 3.12 Size analysis statistical model

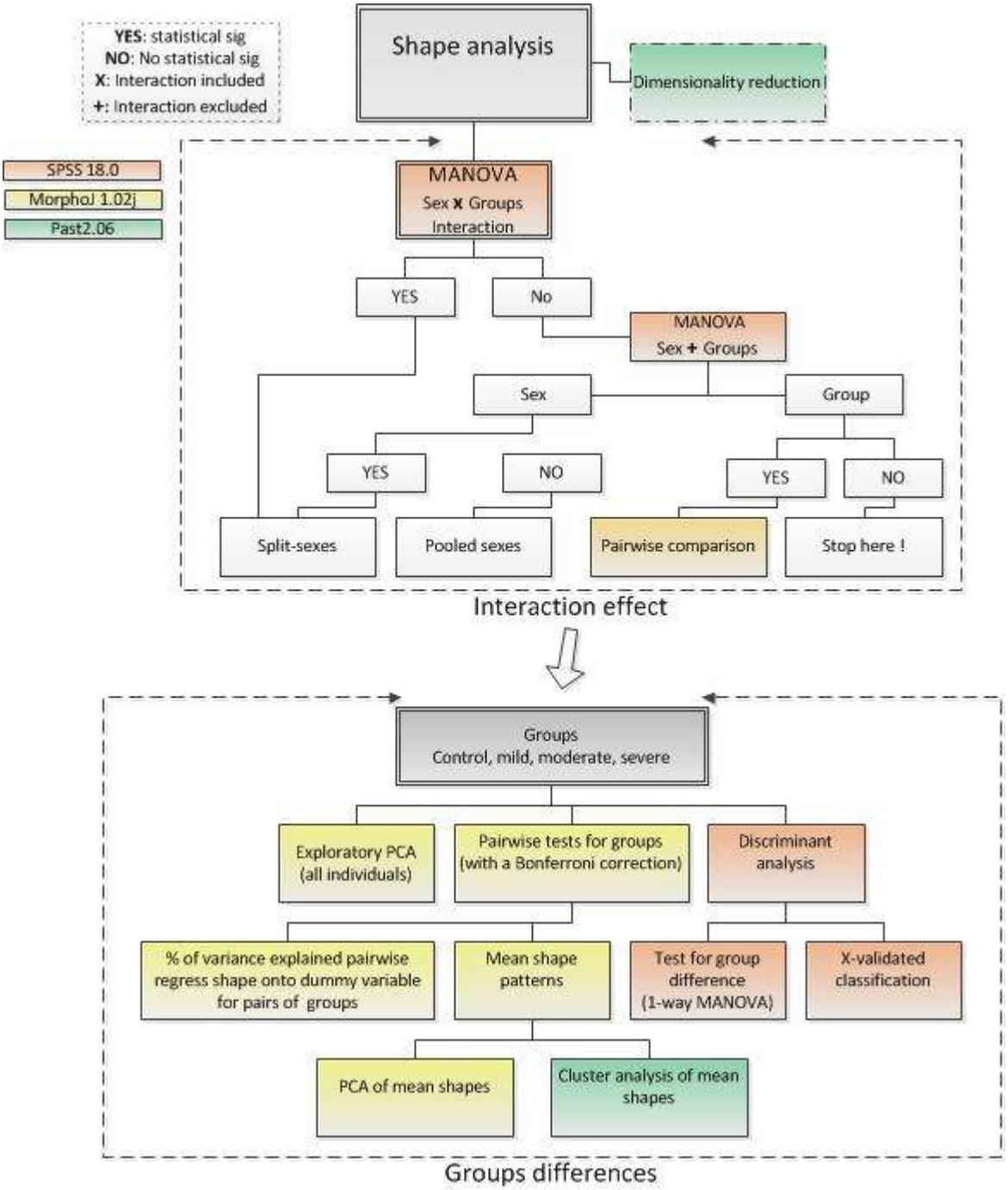

Figure 3.13 Shape analysis statistical model

Allometry

The effect of size on shape (allometry) was examined. First, shape was tested by multivariate regressions onto size within each of the groups (Cardini and Elton, 2008b). If a significant trend was found in at least some of the groups, a multivariate analysis of covariance (MANCOVA) was performed using shape coordinates as a dependent variables, the control and hypodontia samples as groups and centroid size as the covariate. Differences in slopes of allometric trajectories were tested by examining the interaction between the groups and the covariate. If the slopes were not significant (groups x centroid size), the MANCOVA was repeated after removing the interaction term. Then, if the differences between the groups were significant, this indicated that the allometric pattern was the same but laterally transposed (parallel allometric trajectories). This means that differences were found within the groups when the effect of allometry was held constant. In this case, size-corrected shapes could be calculated in MorphoJ and used for replicating the series of tests (DA and pairwise comparisons) previously performed on full shapes. On the other hand, if no significant differences were found within the groups in the MANCOVA, from which the interaction had been excluded, this indicated that all the differences (if any) were allometric and were therefore related to the extension or truncation of a common size-related shape trajectory (Elton *et al*., 2010).

The steps of the analysis of allometric and non-allometric shape differences are summarized in Figure 3.14.

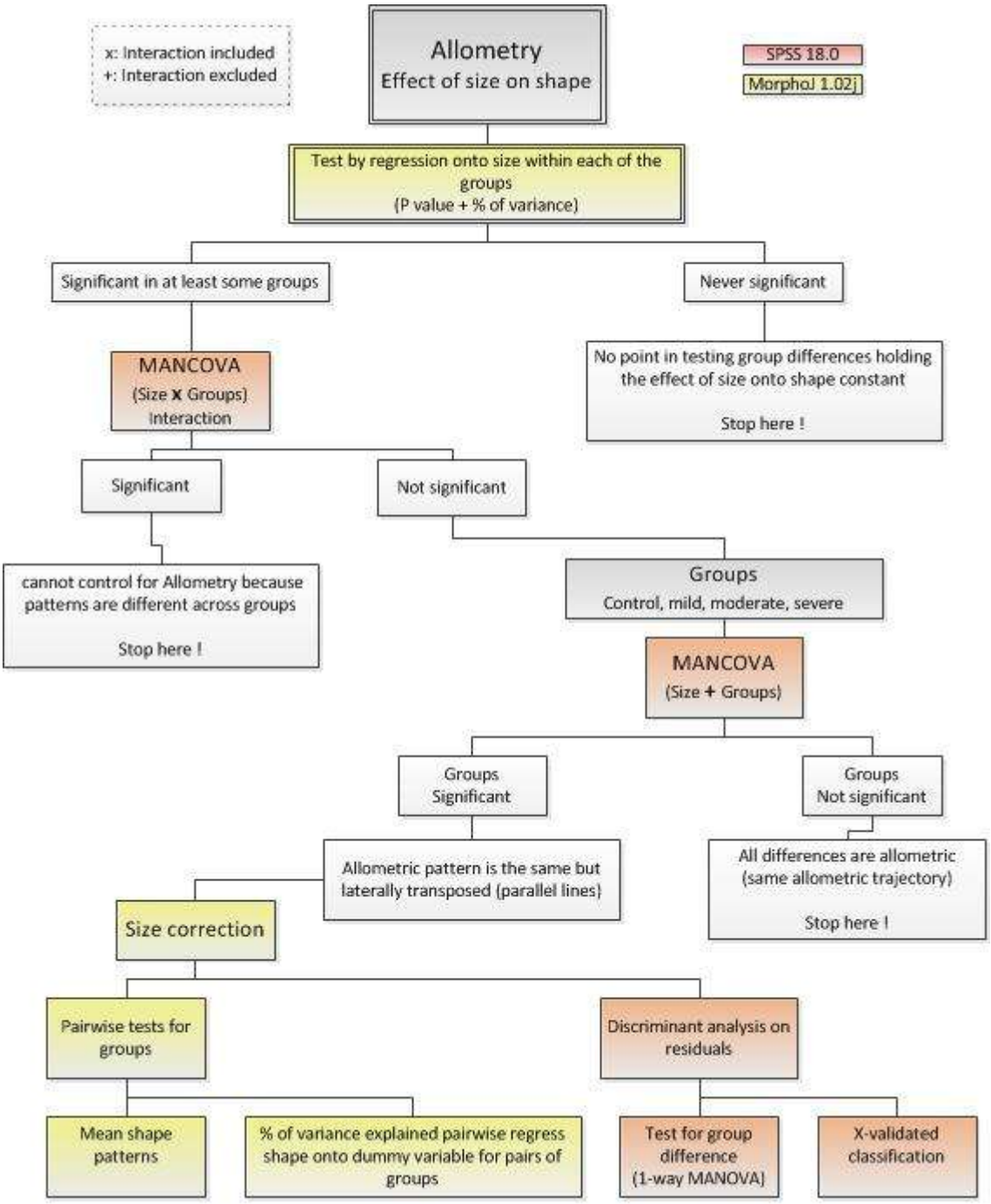

Figure 3.14 Allometry analysis statistical model

Shape transformations

The main directions of shape variation were visualized using diagrams. These included wireframes (a set of lines connecting pairs of landmarks), surface rendering and thin-plate spline (TPS) deformation grids. The grids were computed using an interpolation technique and, in three dimensions, they were reflected onto planes through the volume defined by the landmark configuration. By warping grids, differences between a reference or the starting shape and a target shape can be better emphasized. It produces vectors of coefficients which can be used to predict how grid lines may change because of the warping. Generally, in this study, the starting shape was the control mean shape and the target shape was one of the hypodontia groups mean shapes. The shapes for each group were computed, and they were then imported into Morphologika2 v2.5 in order to carry out visualization of mean shapes.

Measurement of errors

Systematic and random errors are the two main types of error which can occur when employing any research methodology (Kieser, 1990). Both types of error should be tested for and kept to a minimum. Since the system employed in the current study was entirely new, an assessment of the new system was carried out in order to investigate the validity of the scanner. The intra-class correlation coefficient (ICC) was used to assess intra-operator repeatability and inter-operator reproducibility (Kieser, 1990). Furthermore, a full day's training was delivered by an expert from the company that supplied the scanner for members of the research team. A two-phase reliability test was also conducted. In Phase I the digitization error was assessed, and in Phase II both scanning and digitization errors were investigated. A Procrustes ANOVA (Klingenberg and McIntyre, 1998; Klingenberg *et al*., 2002) was performed using MorphoJ 1.02j to test the measurement error that occurred in either the scanning or the digitization steps when analysing size and shape variation. The variance explained by any of the main effects (scanning or digitization) reflects the measurement error and it is estimated on the basis of the differences found between repetitions of the procedure.

Validation of a 3D laser scanner for odontometric measurements

The accuracy of the new 3D laser scanner, used to obtain 3-dimensional measurements, was tested against that of the manual method of measurement by:

- Investigating intra-observer repeatability.
- Investigating inter-observer reproducibility.

The researcher and another operator from the research team scanned 20 randomly selected study models. Two permanent tooth types (the upper right central incisor and the upper left first molar) were used to carry out the measurements. These were the mesiodistal (MD), buccolingual (BL) and incisogingival (IG) or occlusogingival (OG) dimensions. Initially, each of the two operators agreed on the criteria to measure the mesiodistal (MD) and buccolingual (BL) dimensions: the MD was obtained from the proximal contact points when the peaks of the calliper arms were directed from the buccal aspect and positioned as perpendicular as possible to the long axis of the clinical crown for each tooth. In situations where there was difficulty in placing the calliper beaks: e.g., tooth crowding, the measurements were taken from the occlusal or lingual aspect. The BL was taken from the most prominent points of the buccal and lingual (palatal) surfaces of the tooth crowns. For the manual measurements, the calliper was held in a vertical position to the occlusal plane with the arms as parallel as possible to the long axis of the crown. For the 3D measurements, on the other hand, all linear measurements were made on the computer screen. All the measurements using both the manual method and the 3D laser scanner were taken on two separate occasions at an interval of two weeks.

The difference between the measurements made by the investigator on the first and second occasions indicated intra-observer repeatability, and the differences between the first occasion measurements obtained by the investigator and by a second operator indicated inter-observer reproducibility.

Intra- and inter-operator reliability were assessed using the intra-class correlation coefficient (ICC). The results showed that inter-operator reliability for all variables ranged from 0.77-0.90 and 0.75-0.94 for the manual and 3D methods respectively (Table 3.4). Intra-operator reliability for both the manual and 3D method and for all variables ranged from 0.69-0.88 for operator 1 and 0.68-86 for operator 2 (Table 3.5). The intra- and inter-operator reliability was substantial or excellent for all but two of the variables. These two variables were the IG of the upper right central incisor for operator 1, with an

inter-operator reproducibility of 0.69, and the MD of the upper right central incisor for operator 2, with an inter-operator reproducibility of 0.68.

	Upper right central incisor		
	Mesiodistal (MD)	**Buccolingual (BL)**	**Incisogingival (IG)**
Inter-Operator Manual	0.81	0.77	0.89
Inter-Operator 3D	0.89	0.80	0.90
	Upper left first molar		
	Mesiodistal (MD)	**Buccolingual (BL)**	**Incisogingival (IG)**
Inter-Operator Manual	0.79	0.80	0.90
Inter-Operator 3D	0.87	0.75	0.94

Table 3.4 Inter-Operator reliability for the manual and 3D methods using intra-class correlation coefficient (ICC)

	Upper right central incisor		
	Mesiodistal (MD)	**Buccolingual (BL)**	**Incisogingival (IG)**
Operator 1	0.76	0.78	0.69
Operator 2	0.68	0.57	0.77
	Upper left first molar		
	Mesiodistal (MD)	**Buccolingual (BL)**	**Incisogingival (IG)**
Operator 1	0.85	0.83	0.88
Operator 2	0.78	0.86	0.79

Table 3.5 Inter-Method reliability of operators 1 and 2 using intra-class correlation coefficient (ICC)

Two matters relating to scanner repetitions are worth discussing here: absolute error and scanner reproducibility. The absolute error is produced by the scanner manufacturer. All the study models were scanned using a 3Shape D700 3D scanner. Before each scanning cycle, the scanner was calibrated according to the manufacturer's instructions. Reproducibility error has to be assessed. Harris and Smith (2009) reviewed total measurement errors and the statistical tests commonly used to assess these errors. They reported that incorporation of repeated measures into the statistical design has improved with the newly established computer methods. Previous studies have not found any significant differences between inter-observor errors and intra-observer error (Bailey *et al*., 2004). Other researchers have examined repeatability and relative accuracy and found these to be less than 10 µm and less than 6 µm respectively (Persson *et al.*, 2006; Vlaar and van der Zel, 2006). According to Smith et al. (2009), to increase power, the probability of rejecting null hypotheses when they are not true, errors need to be

controlled for. They suggested using either an interclass correlation coefficient to estimate repeatability of measurements or using Dahlberg's d. However, when they investigated measurement errors in the repeated measurement of their study models, they did not find any significant errors in the reliability of linear measurements of scanned images when compared to those obtained from dental casts (Smith *et al.*, 2009). The results of tests of measurement error in the present study were congruent with the findings of these studies and confirmed that 3D scanned images are accurate and provide excellent material for the investigation of human teeth variability.

Validation of landmark reproducibility (digitization error only)

The operator measured six permanent teeth from 20 sets of maxillary and mandibular casts taken from the study population. The selected teeth were an upper right first molar, an upper right central incisor, an upper left first premolar, a lower left first molar, a lower left canine and a lower right second premolar. These teeth were scanned using the R640 3D laser scanner, and then the landmarks for each tooth were identified on each scanned image on two separate occasions at an interval of two weeks using landmarks.exe software. The saved data files were then subjected to a Procrustes analysis. The details of all these steps were described earlier in this chapter (Landmark definition and identification). Intra-operator reproducibility at the digitization stage was assessed using a Procrustes ANOVA.

Only the results for the upper left first premolar are presented here since the same principle was followed for the rest of the teeth. For size, the main effect of individuals was statistically significant and explained about 97.60% of total sum of squares. The digitization effect for the centroid size (2.4%) was negligible, as indicated by the high significance of individual variation compared to measurement error (Table 3.6). The average variance related to digitization error for centroid size among the selected teeth was 5.3% (result not shown).

Results of shape showed that the digitization effect was also negligible (11.5%) in relation to the (88.5%) individual variation (Table 3.7). The average variance displayed by digitization error for shape among the selected teeth was 12.9 % (result not shown).

Effect	% explained	SS	MS	df	F	P
Individual	97.60	23.514722	1.237617	19	42.73	<.0001
Digitization error	2.40	0.57923	0.028962	20		

Table 3.6 **Digitization error of overall size for upper left first premolar. In this and all other tables for measurement errors, (%) percentage of variance explained, (SS) sums of squares, (MS) mean squares, (df) degrees of freedom, F statistics and parametric *P*-values for each of the effects found in the ANOVA.**

Effect	% explained	SS	MS	df	F	P
Individual	88.52	0.7229861	0.000928	779	8.12	<.0001
Digitization error	11.48	0.0937363	0.000114	820		

Table 3.7 **Digitization error of shape for upper left first premolar**

Total error measurements (scanner and digitization)

All the steps, i.e. the scanning and digitization, were repeated in two separate sessions at an interval of two weeks on a sample of 20 individuals for the same single tooth - the lower right first molar.

Intra-operator reproducibility at two levels was assessed using a Procrustes ANOVA to investigate scanning and digitization errors.

The digitization effect for centroid size as well the scanning effect was negligible, with a minimum variance explained compared to the total variance (Table 3.8). The total variance displayed by all effects for centroid size was 1.85 %.

The analysis of variance, using Procrustes sums of squares as a measure of overall variation in shape, showed that individual variation was significant in relation to both scanning and digitization effects (Table 3.9). This led to the conclusion that the total measurement effect (17.2%) was negligible, with a small variance explained compared to the individual variation.

Effect	% explained	SS	MS	df	F	P
Individual	98.15	71.323187	3.753852	19	163.67	<.0001
Scanner error	0.63	0.458709	0.022935	20	1.04	0.4447
Digitization error	1.22	0.883804	0.022095	40		

Table 3.8 **Total error of overall size for lower left first molar**

Effect	% explained	SS	MS	df	F	P
Individual	82.79	0.90107054	0.00080381	1121	14	<.0001
Scanner error	6.23	0.06775842	5.74224E-05	1180	1.13	0.006
Digitization error	10.98	0.11954161	5.06532E-05	2360		

Table 3.9 **Total error of shape for lower left first molar**

Anrnqvist and Martensson (1998) identified three types of error in GMM studies: methodological error, instrumental error and personal error. In this project we had three error components. The first of these was the impression and casting procedures. These steps were taken only once for ethical and practical reasons and were thus irreversible (Arnqvist and Martensson, 1998). The Newcastle dental hospital follows a standard protocol that has been shown to be accurate. Therefore only the main levels of error: instrumental error (scanning) and personal error (digitization) were tested and these were found to be negligible. The new system permits reproducible measurements for teeth in dental study casts. Furthermore, it shows the ability of the operator to produce highly reliable reproducible data through locating landmarks with precision and scanned images are obtained with accuracy using 3D dental scanner.

The individual variation in both measurements was large. This may indicate the complex interaction in the developmental process between genetic, epigenetic and different environmental factors (Brook, 2009).

Chapter 4 Results

Three main variation factors were considered in this project: size variation, shape variation and allometric variation. Comparisons were made with respect to these factors between the control subjects and the hypodontia groups and between the hypodontia groups themselves. Separate statistical models were constructed for each factor. For the most part, significant differences were found in size variation, especially when the control subjects were compared to the hypodontia groups. Generally, these differences became more pronounced as the severity of the hypodontia increased. The pattern was largely congruent in both sexes. With regard to shape, it was found that most teeth were affected by the hypodontia; however, the pattern was less clear in the posterior teeth when the hypodontia groups were compared one to the other, and the variance explained by group differences was smaller and less clearly correlated to the severity of the disease. When allometry was considered, the effect of size on shape was found to be significant for most teeth, particularly in the anterior region, and shape differences were still significant after controlling, when possible, for allometry.

This chapter consists of four parts: the first part provides a description of the study population; in the second part, detailed findings for one tooth (the lower left first molar) are presented; part three contains a summary of the findings for all teeth together, and in part four 3D visualizations of all shape differences for all teeth between the groups are provided.

4.1 Study population

Four groups were analysed: a group of control subjects and three hypodontia groups. The hypodontia groups were classified into three groups (mild, moderate and severe) according to the number of missing teeth. In total, 160 participants took part in the project. The subjects were distributed equally among the groups, each group representing 25% (40 subjects) of the total sample. The proportion of female to male subjects in each group was also equal: 50% (20 subjects) of each sex. The details are presented in Table 4.1 below.

Sex	Control (C)	Mild Hypodontia (M)	Moderate Hypodontia (D)	Severe Hypodontia (S)	Total
Female	20	20	20	20	80
Male	20	20	20	20	80
Total	40	40	40	40	160

Table 4.1 Distribution of sample size by group and sex

The age group of the sample was 12 – 18 years. This age group was selected in order to avoid any misdiagnosis of any of the teeth and also to avoid having to control for any other factors that might affect the enamel of the teeth, such as enamel wear or attrition or gingival recession. This age range was also chosen to make sure that the participants were old enough for us confidently to confirm the presence of each permanent tooth. The lower limit - 12 years - was chosen since this is generally the age at which one can be sure that the crown is completed, even in people who mature more slowly (Harris & Clark, 2008). The ages were calculated according to the age of the subject at the time the impression was made.

The average age for the whole sample was 14.03 years, with a standard deviation of 1.85 years. The mean age for the female sample was 14.04 years, with a minimum age of 13.4 years (in the severe hypodontia group) and a maximum of 14.5 years (in the mild hypodontia group). The mean age of the male sample was 14.02 years, with a minimum of 13.3 years, also in the severe hypodontia group, and a maximum of 14.3 years (in both the control and moderate hypodontia groups) (Table 4.2). It was considered that this uniformity of age range might help to avoid any measurement bias. In addition, older subjects could have been affected by crown attrition, enamel fracture and/or gingival recession.

Sex Mean (SD)	Control (C)	Mild Hypodontia (M)	Moderate Hypodontia (D)	Severe Hypodontia (S)	Total
Female	14.4 (2.2)	14.5 (1.7)	13.8 (1.7)	13.4 (1.6)	14.04 (1.85)
Male	14.3 (2.1)	14.1 (1.9)	14.3 (2.1)	13.3 (1.8)	14.02 (1.98)
Total	14.4 (2.2)	14.3 (1.8)	14.1 (1.9)	13.4 (1.7)	14.03 (1.91)

Table 4.2 Mean and standard deviations of age by group and sex

The frequency of hypodontia according to severity was almost equal between the sexes in all groups (Table 4.3).

Group	Tooth Absence no.	Frequency in females		Frequency in males	
		No.	%	No.	%
Mild Hypodontia (M)	1	4	20	3	15
	2	16	80	17	85
Moderate Hypodontia (D)	3	6	30	8	40
	4	8	40	6	30
	5	6	30	6	30
Severe Hypodontia (S)	6	8	40	9	45
	7	5	25	4	20
	8	4	20	3	15
	9	3	15	1	5
	11	0	0	1	5
	13	0	0	1	5
	14	0	0	1	5

Table 4.3 Frequency of hypodontia according to severity

The frequencies obtained for hypodontia according to location showed that mild hypodontia was located predominantly in the upper anterior region, 80% of female subjects and 85% of male subjects having two teeth missing. Moderate hypodontia was found less in the lower than in the upper anterior region, with an equal distribution between the sexes. By contrast severe hypodontia (between 6 and 8 teeth missing) was found to be distributed equally in all regions. The same pattern was noticed in both sexes (Table 4.4).

Tooth type / Region	Mild H (M)		Moderate H (D)		Severe H (S)	
	Female	Male	Female	Male	Female	Male
Upper anterior	27	24	25	30	26	23
Lower anterior	-	2	5	9	17	17
Upper posterior	1	1	20	16	29	26
Lower posterior	4	8	25	29	45	42

Table 4.4 Frequency of hypodontia according to location

In all the hypodontia groups, the tooth found to be missing most frequently was the upper lateral incisor, followed by the lower second premolars, then the upper second premolars. In the mild hypodontia groups the upper lateral incisor was the tooth most frequently missing, while in moderate and severe hypodontia subjects it was the lower second premolar. These findings on the frequency of missing teeth confirm those of previous studies (Table 4.5).

Tooth type	Mild H (M)		Moderate H (D)		Severe H (S)	
	Female	Male	Female	Male	Female	Male
U1	-	-	-	1	-	-
U2	25	23	19	21	17	15
U3	2	1	6	8	9	8
U4	-	-	6	4	10	13
U5	1	1	12	12	16	19
U6	-	-	2	-	3	4
U7	-	-	-	-	9	7
L1	-	2	5	9	13	11
L2	-	-	-	-	4	6
L3	-	-	-	-	-	-
L4	-	-	3	5	13	10
L5	4	8	20	23	27	21
L6	-	-	2	1	1	3
L7	-	-	-	-	5	8

Table 4.5 Most frequently missing teeth

4.2 Analysis for the lower left first molar tooth

Differences in tooth size (centroid size), shape (PC scores) and allometry (effect of size on shape) between hypodontia and control subjects were investigated using a geometric morphometric approach. The effects of the severity of hypodontia and sex on each dependent measurement were tested statistically. Since the study investigated multiple measurement variables of many different teeth, one tooth (lower left first molar) has been chosen as an example to demonstrate in detail the statistical procedures used for all the teeth. The main findings for the rest of the teeth will be summarized (section 4.3 Data summary) and for more details see Appendix I. The results of the statistical procedures in size, shape and allometry for all teeth apart from third molars are listed in Appendix II - Size analysis, Appendix III - Shape analysis and Appendix IV - Allometric analysis.

Geometric morphometrics analyses were performed using MorphoJ 1.02j, Morphologika2 v2.5 and Past 2.06. Statistical analyses were performed using SPSS 18.0 (See Figure 3.2).

The x, y and z coordinates of the recorded eighteen landmarks on the clinical crown of the lower left first molar (tooth # 36) were subjected to a Procrustes analysis to be scaled, translated and rotated to best fit. The Procrustes coordinates were then subjected to a principal component analysis (PCA). Figure 4.1 shows the selected landmarks and the mean shape with the corresponding texture map overlaid on the lower left first molar.

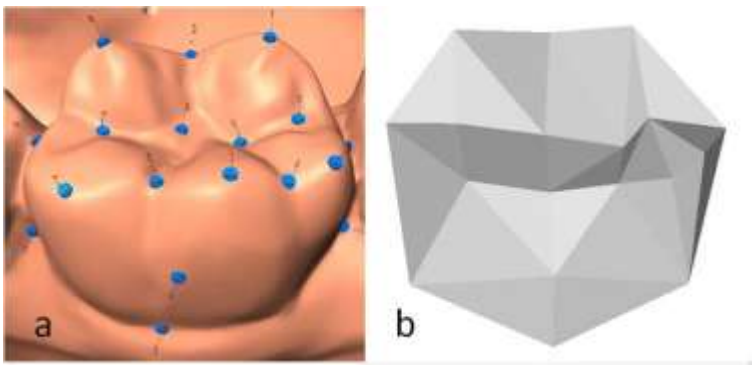

Figure 4.1 **Landmarks of lower left first molar: (a) scanned image (b) texture map**

4.2.1 Size analysis

Descriptive statistics computed for size with the groups split according to sex (i.e., the two sexes were treated separately) are given in Table 4.6. In the female subjects, a decrease in mean size was found moving from the control group, through the mild and moderate and up to the severe hypodontia groups (Figure 4.2). The same pattern can be seen for the male subjects. The average size found for male subjects was greater than that found for females across all the four groups. Although there were two outliers within the male mild hypodontia group, the smaller inter-quarter range for this group indicated that it was less varied than the others. The female moderate and male severe hypodontia groups had the largest size range, indicating that the data were more varied.

The coefficient of variation ranged between 5 – 7% for the female groups. The corresponding figures for male groups were between 4 - 9% (Table 4.6).

Sex	Groups	Mean	SD	CV (%)	N
Female	**control**	18.58	1.04	5.60	20
	mild	17.88	0.9	5.03	20
	moderate	17.84	1.11	6.22	20
	severe	17.51	1.17	6.68	19
Male	**control**	18.81	0.79	4.20	20
	mild	18.57	0.84	4.52	20
	moderate	18.39	1.09	5.93	19
	severe	17.82	1.53	8.59	15

Table 4.6 Descriptive statistics for size (centroid) for control and hypodontia groups by sex of the lower left first molar

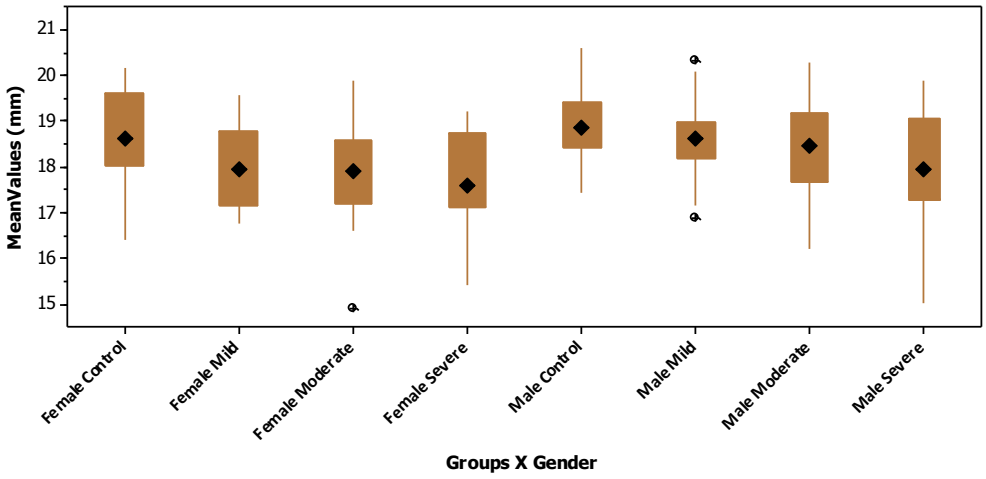

Figure 4.2 Boxplot of groups by sex of the lower left first molar

Size variation in groups and between sexes

The results of the ANOVA (groups by sex) for size indicated that there was no significant interaction of group by sex. This is suggested by the profile plots for mean size, which show almost parallel lines (Figure 4.3). The main effects of both group and sex were found to be significant (Table 4.7).

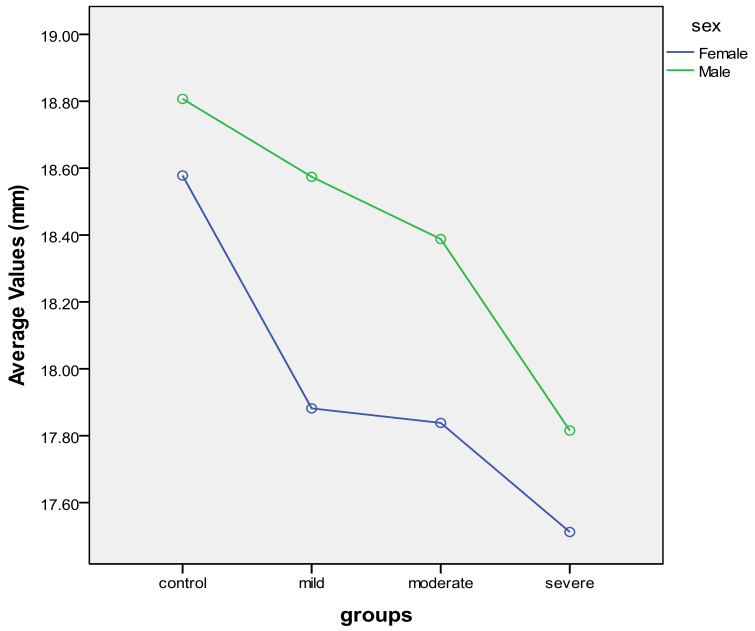

Figure 4.3 Average size of the lower left first molar by groups according to sex

Source	SS	df	MS	F	Sig.
groups	19.666	3	6.555	5.816	*0.001*
sex	7.463	1	7.463	6.621	*0.011*
groups * sex	1.353	3	0.451	0.4	0.753

Table 4.7 ANOVA of groups by sex of the lower left first molar

As there was no interaction effect of group by sex, the interaction term was removed and the ANOVA test was repeated. Again, the main effects of group and sex was found to be significant (Table 4.8).

Source	SS	df	MS	F	Sig.
groups	19.469	3	6.49	5.829	*0.001*
sex	7.682	1	7.682	6.899	*0.010*

Table 4.8 ANOVA of groups by sex without the interaction term

Because of this significant difference between the sexes, size was then examined within groups by sex. The results are presented in the following section. Non-parametric permutation tests were carried out pairwise with split-sex samples. With regard to the female groups, only the severe hypodontia group was found to differ significantly from the control group after a sequential Bonferroni correction, with 19.67% of the variance explained by group membership (Table 4.9). The same finding was found in the male groups, that severe hypodontia group showed significant differences in size as well, with 15.86% of the variance explained by group membership (Table 4.10).

	Control	Mild	Moderate	Severe
Control	-	11.52%	11.09%	19.67%
Mild	0.0358	-	3.21%	3.21%
Moderate	0.0355	0.2664	-	2.11%
Severe	*0.0050*	0.2764	0.3757	-

Table 4.9 Pairwise comparison of female group averages for size variation. In this and all other tables for pairwise tests, p values, estimated using 10 000 random permutations, are shown below the main diagonal and percentage of variance explained by group membership; p values significant after a sequential Bonferroni correction for multiple comparisons are shown in italics.

	Control	Mild	Moderate	Severe
Control	-	2.11%	4.87%	15.86%
Mild	0.3688	-	0.96%	9.68%
Moderate	0.1752	0.5562	-	4.83%
Severe	*0.0081*	0.0693	0.2137	-

Table 4.10 Pairwise comparison of male group averages for size variation

4.2.2 Shape analysis

A principal component analysis (PCA), which identifies the maximum variation within the sample, was performed in order to reduce the dimensionality in the analysis.

The first 20 principal components (PCs) explained approximately 84% of total shape variance, and the correlation of Euclidean distances based on these 20 PCs and Procrustes shape distances in the full shape space was larger than 0.98. The inverted scree-plot based on correlations between shape distances showed that the correspondence between the space of reduced dimensionality and the full shape space did not increase appreciably after including 20 PCs (Figure 4.4). Thus, the first 20 PCs were used for parametric tests of group differences.

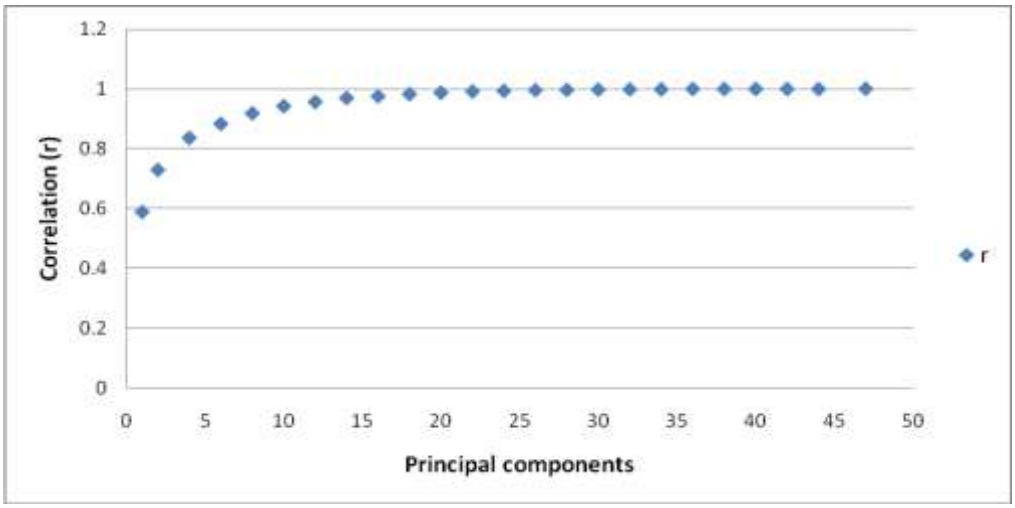

Figure 4.4 **Plot of the values of the correlation coefficient (r) between Procrustes distances and the Euclidian distances as a function of the number of PCs included, from 1 up to 47 PCs. 20 PCs, explaining 84% of the total variance, with *r* = 0.988, retained in the analysis of shape.**

The multivariate analysis of variance (MANOVA) sex by groups for shape (first 20 PCs) showed that all factors including their interaction were highly significant (Table 4.11).

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.	Eta Squared
groups	0.143	5.762	60	376.75	0.001	0.477
sex	0.698	2.723	20	126	0.001	0.302
groups * sex	0.491	1.69	60	376.75	*0.002*	0.211

Table 4.11 Shape variation: MANOVA of groups by sex of the lower left first molar

Group differences

Split-sex samples were used in all the analyses, because in the MANOVA sexual dimorphism was found to be significant and the pattern of group shape differences was different between the sexes (significant interaction). Pairwise tests for groups using Procrustes distance after a sequential Bonferroni correction nearly always showed significant differences. On average, differences explained 7-10% of shape variance.

For the female groups, significant differences were found in 100% of the pairwise comparisons across groups after a sequential Bonferroni correction, and on average 10% of the variance was explained by group membership (Table 4.12). Similarly, the largest differences were found between the mild and moderate/severe hypodontia groups, whereas those between the control and moderate/severe hypodontia groups were fairly small, although all were significant.

	Control	Mild	Moderate	Severe
Control	-	11.20%	6.61%	7.65%
Mild	*<.0001*	-	18.27%	18.27%
Moderate	*<.0001*	*<.0001*	-	6.65%
Severe	*<.0001*	*<.0001*	*0.0002*	-

Table 4.12 Pairwise tests for mean shape differences between female groups

The scatter plot of the first two PCs of shape showed a clear separation between the mild and severe hypodontia groups and a large overlap between the control and moderate hypodontia groups for PC1 (Figure 4.5). For PC2 and further PCs (not shown), the groups largely overlapped.

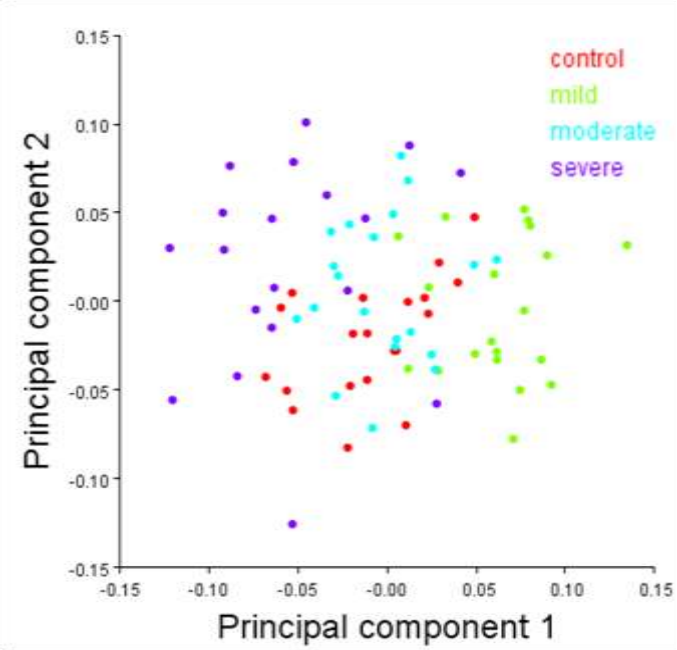

Figure 4.5 **Female groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables (16.46% and 11.74% of total shape variance respectively).**

In the male groups the results of all pairwise comparisons except one were found to be significant after a sequential Bonferroni correction, and on average 7.41% of the variance was explained by group membership. The only non-significant pairwise comparison was that between the mild and moderate hypodontia groups (Table 4.13). The largest differences were found between the control and severe hypodontia and also between the mild and severe hypodontia groups.

	Control	Mild	Moderate	Severe
Control	-	6.03%	5.82%	10.86%
Mild	*0.0022*	-	4.11%	10.68%
Moderate	*0.0006*	0.0370	-	6.95%
Severe	*<.0001*	*<.0001*	*0.0036*	-

Table 4.13 **Pairwise tests for mean shape differences between male groups**

The scatter plot of the first two PCs of shape showed a slight separation of the severe hypodontia groups and a large overlap between the control, mild and moderate hypodontia groups (Figure 4.6). For PC2 and further PCs (not shown), the groups largely overlapped.

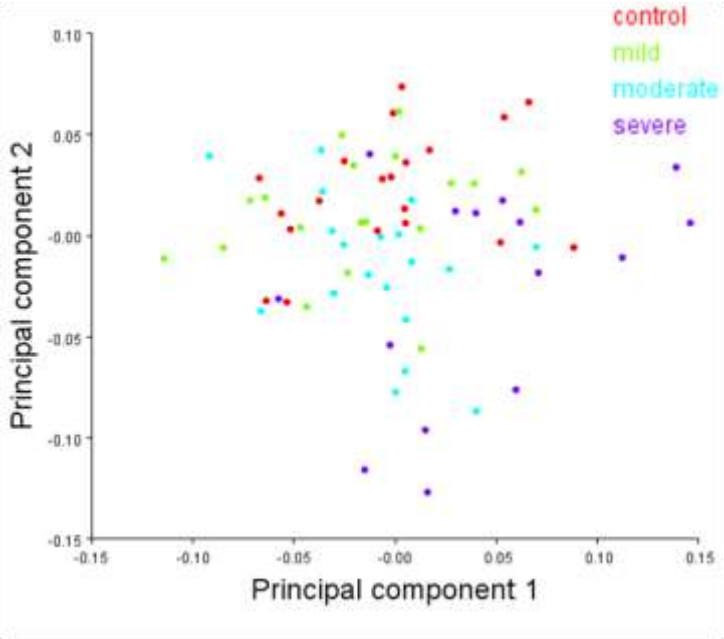

Figure 4.6 **Male groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables (16.99% and 10.98% of total shape variance respectively).**

Mean shape similarity relationships

Similarity relationships among groups per sex were summarized using a PCA on the matrix of mean shape variables. A mean shape is computed by taking the sample average of shape coordinates from the full set of shape variables. In females, PC1 differentiated the hypodontia groups progressively according to the increasing degree of severity, while PC2 separated the control group from the hypodontia groups (Figure 4.7).

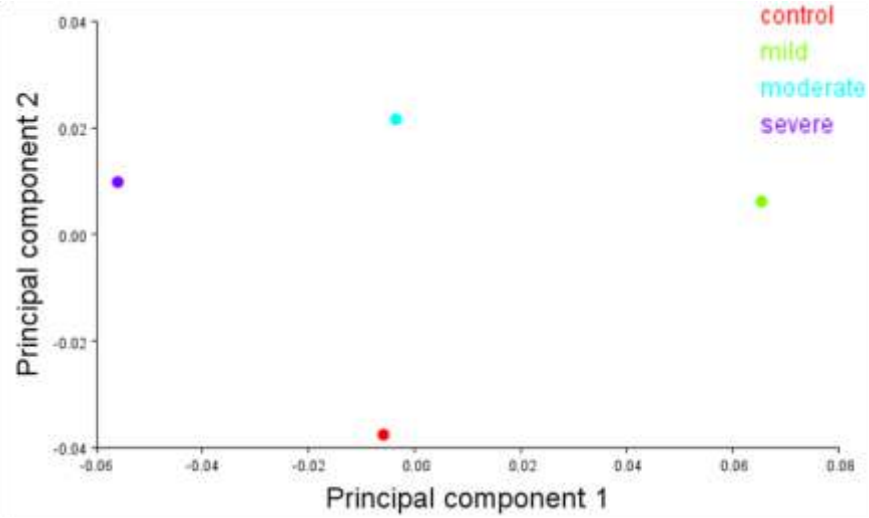

Figure 4.7 **Female groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables**

The hypodontia groups showed a progressive shortening at the gingival margin. In addition, the gingival margin became flatter, with a less bulbous labial surface as one moved from the mild toward the severe hypodontia groups. However, shape variation on the vertical axis can be summarized by comparing the control against the hypodontia groups. The hypodontia groups were found to have a flatter occlusal plane with smaller cusps when compared to the control subjects (Figure 4.8).

Figures 4.9 – 4.10 illustrate the same analysis was performed for the males. The results suggested the same group pattern and showed similar shape differences among groups.

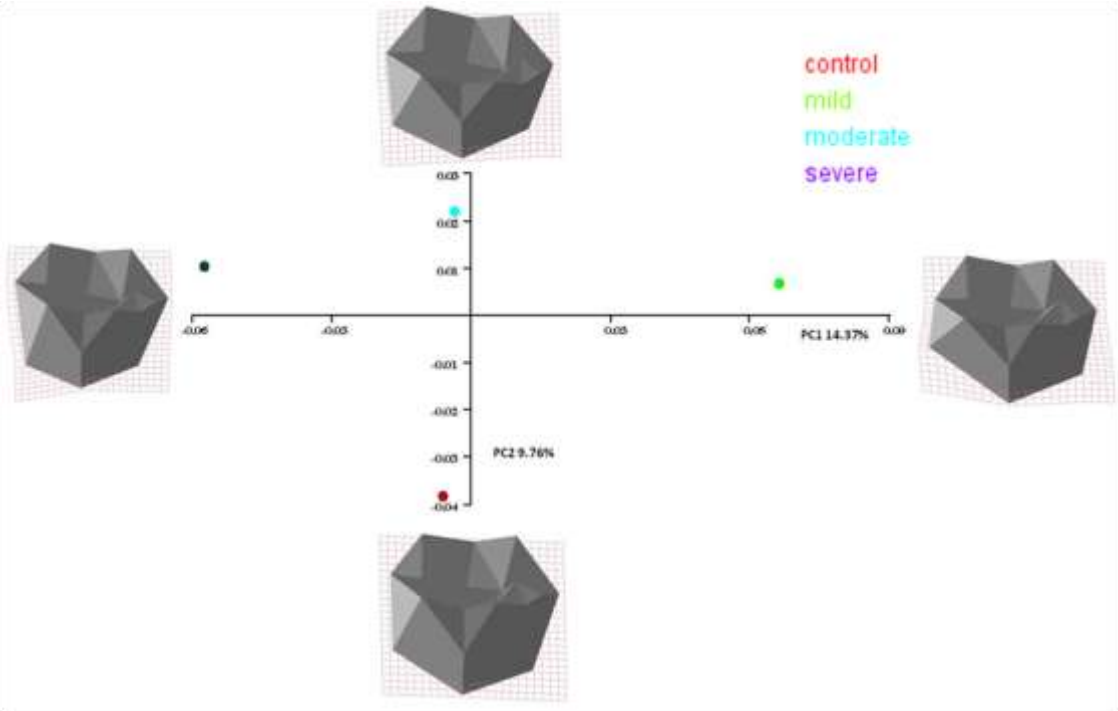

Figure 4.8 **Transformation grids for female groups mean shape using thin-plate spline derived from the difference between the reference form (control mean shape) and the various target forms (hypodontia groups' mean shape)**

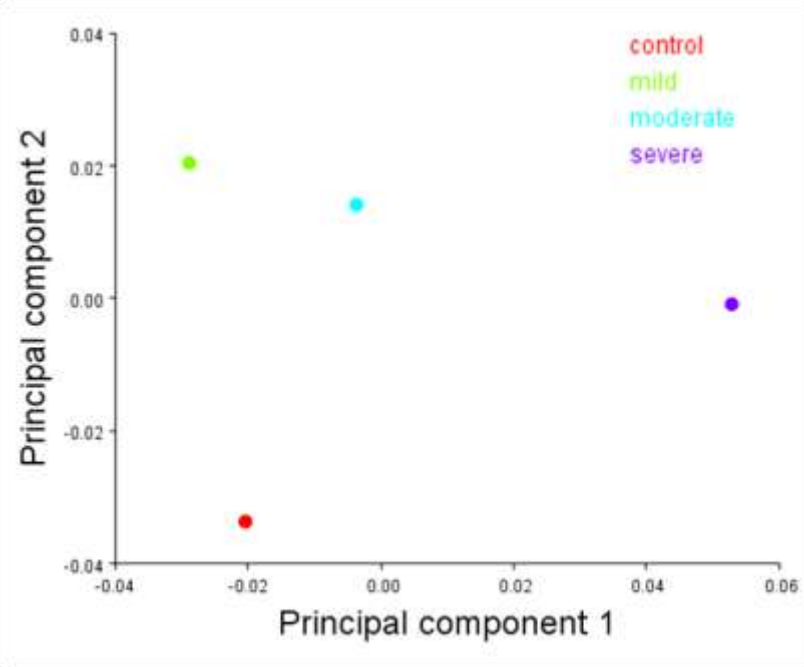

Figure 4.9 **Male groups mean shapes. Scatter plots of the first principal components (PCs) of shape variable**

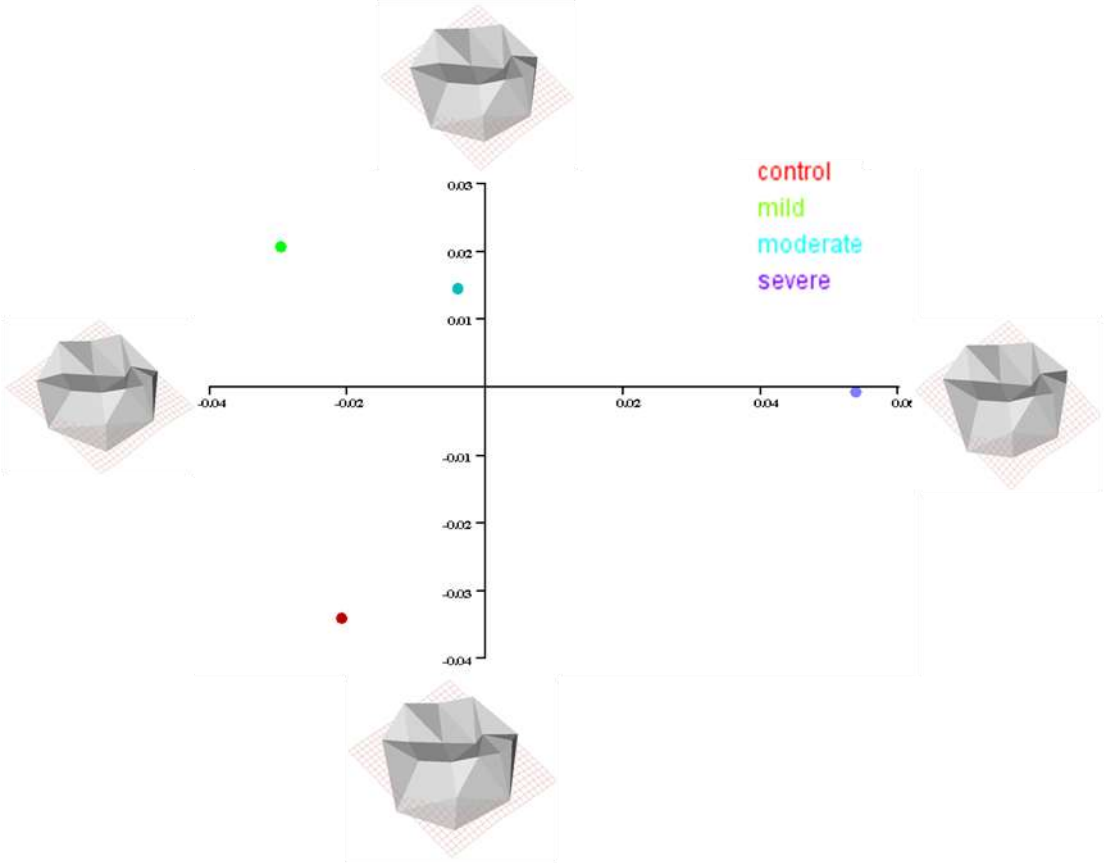

Figure 4.10 **Transformation grids for male groups mean shape using thin-plate spline derived from the difference between the reference form (control mean shape) and the various target forms (hypodontia groups' mean shape)**

Discriminant analyses

The results of the discriminant analyses were highly significant: females Wilks' λ = 0.062, $F_{60,168}$ = 4.299 with a p value of 0.0001; males Wilks' λ = 0.086, $F_{60,153}$ = 3.264 with a p value of 0.0001. Table 4.14 shows percentages of correctly classified cases according to subgroups in the discriminant analysis of shape. Overall, at least 85% of teeth were classified into the correct groups, with the percentage for females (89.73%) being slightly higher than that for males (79.25%). When the results were cross-validated, the percentages of correctly classified specimens dropped to just over 66% in females and 56% in males, which is better than would be expected by pure random chance (i.e., approximately 25%). Male moderate hypodontia was found to be misclassified when cross-validated against mild and severe hypodontia (25.1 and 33.3% respectively).

Groups	Sex			
	Female (%)		Male (%)	
	Analysis	Jacknife	Analysis	Jacknife
Control	90.0	70.0	95.0	80.0
Mild	100.0	70.0	75.0	65.0
Moderate	90.0	65.0	73.7	21.1
Severe	78.9	57.9	73.3	53.3

Table 4.14 Percentages of correctly classified specimens in discriminant analyses

4.2.3 Allometry

The effect of size on shape (allometry) was tested by regressing shape onto size (CS) within each of the eight groups (Table 4.15). The effect was found to be significant only in the male moderate hypodontia group with a p value of 0.0255 and about 9% of shape variance explained by size. With a sequential Bonferroni correction, however, the effect for this group was not found to be significant either. The allometric variance across all the eight groups ranged from a minimum of nearly 5% to a maximum of nearly 9%. Although the evidence for allometric variation was very weak, a MANCOVA model was used to test for differences after holding just a small effect of size on shape constant.

Sex	Groups	%	P value
Female	Control	7.05%	0.1171
	Mild	6.20%	0.2325
	Moderate	7.48%	0.0649
	Severe	5.37%	0.4877
Male	Control	6.31%	0.2102
	Mild	4.72%	0.5855
	Moderate	8.81%	*0.0255*
	Severe	8.51%	0.2569

Table 4.15 **Group regression onto size. P value, estimated using 10 000 random permutations**

MANCOVA

A MANCOVA conducted using the first 20 PCs of shape showed that there was no interaction effect of size on groups for either female or male subjects (Table 4.16). Thus, the effect of size on shape was similar across groups. The interaction term was therefore removed and the analysis repeated using only groups (without the interaction term) and the size covariate.

Sex	Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.	Eta Squared
Female	groups	0.407	0.915	60	155.974	0.647	0.259
	CS	0.638	1.472	20	52	0.133	0.362
	groups * CS	0.417	0.885	60	155.974	*0.701*	0.253
Male	groups	0.344	1.01	60	141.057	0.471	0.299
	CS	0.466	2.689	20	47	0.003	0.534
	groups * CS	0.347	1.001	60	141.057	*0.487*	0.297

Table 4.16 **MANCOVA of groups across sex onto size with interaction**

The results of the MANCOVA analysis without the interaction effect indicated that the main effect of group was highly significant for both females and males (Table 4.17). Allometric variation was small (similar in both sexes), but differences between groups for both male and female subjects were significant. This indicates that allometric patterns are similar but laterally transposed (i.e., with parallel lines shifted up or down relative to one another). To examine group variation further, when the effect of size on shape was held constant, shapes were ‘size-corrected’ and the test of group differences re-run.

Sex	Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.	Eta Squared
Female	groups	0.065	4.106	60	164.924	*0.001*	0.597
	CS	0.628	1.632	20	55	0.078	0.372
Male	groups	0.077	3.406	60	150.007	*0.001*	0.575
	CS	0.436	3.229	20	50	0.001	0.564

Table 4.17 MANCOVA of groups across sex onto size without interaction

‘Size-corrected’ pairwise comparisons

The results of the pairwise tests for group differences after controlling for allometry were exactly the same in both sexes as those for full shapes. This is consistent with the observation of a small and probably negligible effect of size on shape.

A significant difference was found between female groups across all possible pairwise comparisons after a sequential Bonferroni correction. The magnitude of group differences ranged between 7 – 18% among all groups (Table 4.18).

	control	mild	moderate	severe
control	-	12.20%	6.61%	7.65%
mild	*<.0001*	-	10.57%	18.27%
moderate	*0.0001*	*<.0001*	-	6.65%
severe	*0.0018*	*<.0001*	*0.0012*	-

Table 4.18 Pairwise tests for mean shape between female groups after size correction

A significant difference was also found between male groups across all possible pairwise comparisons, with the exception of the pairwise test between the mild and the moderate hypodontia groups. The difference between these two groups was found to be non-significant after a sequential Bonferroni correction. The magnitude of differences varied between 5 – 11% (Table 4.19).

	Control	Mild	Moderate	Severe
Control	-	6.03%	5.82%	10.86%
Mild	*0.0025*	-	4.11%	10.68%
Moderate	*0.0016*	0.045	-	6.95%
Severe	*<.0001*	*<.0001*	*0.0041*	-

Table 4.19 Pairwise tests for mean shape between males groups after size correction

Discriminant analyses

The results of the discriminant analyses were highly significant: females Wilks' λ = 0.069, $F_{60,168}$ = 4.053 with a p value of 0.0001; males Wilks' λ = 0.082, $F_{60,153}$ = 3.342 with a p value of 0.0001. Overall, at least 76% of teeth were correctly classified in a priori sub specific groups, the percentage for females (86%) again being slightly higher than that for males (84%). However, when the results were cross-validated, the percentages of correctly classified specimens dropped to slightly over 64% and 54% in female and male groups respectively (Table 4.20). The results of the 'size-corrected' shape analyses were virtually identical to those for the actual shape without size correction, which would be expected if the effect of size on shape were negligible.

Groups	Sex			
	Female (%)		Male (%)	
	Analysis	Jacknife	Analysis	Jacknife
Control	80.0	55.0	95.0	70.0
Mild	100.0	80.0	85.0	60.0
Moderate	90.0	65.0	73.7	31.6
Severe	73.7	52.6	80.0	53.3

Table 4.20 Percentages of correctly classified specimens in discriminant analyses after size correction

4.3 Data summary charts

This project utilized a comprehensive 3D technique to test the whole permanent dentition excluding third molars. The findings indicate that the landmarks-based method finds size, shape and allometric differences both within and between groups. Furthermore, the landmarks-based method shows differences in the mean group shapes and within-group variations.

In the previous section, an analysis of the lower left first molar was presented in order to demonstrate in detail the statistical procedures used for each of the teeth. For all other teeth, a summary of the data and the main findings are presented in this section. Standardized summary charts are used to illustrate the main statistical differences between the hypodontia groups and control subjects and also between the mild, moderate and severe hypodontia groups themselves. Detailed results may be found in the Appendices II, III and IV as mentioned earlier.

Ten summary charts, figures 4.11 to 4.20, are used to display the differences found among all groups of subjects. The first four figures illustrate the differences found in tooth (centroid) size between the control and the hypodontia groups and then within the hypodontia groups themselves. Results for female and male subjects are presented separately. The next four figures illustrate differences in tooth shape in like manner. The final two figures show the allometric differences with figure 4.19 showing the results for all comparisons for female groups, while figure 4.20 presents the results for all groups of male subjects.

Figure 4.11, and all other summary charts used to present the analysis, show 28 teeth divided into two sets of 14 teeth for the upper and lower jaws. The coloured bar on the left-hand side indicates the average variance explained by the pairwise tests among group members for each tooth. The colour ranges from yellow to red, which respectively correspond to ≤10% and ≥50% variance explained on average by group differences. Each tooth is coloured according to the average variation for that tooth. The letter P on a tooth indicates the use of pooled male and female data where no significant sexual dimorphism was evident. Asterisks are used to emphasize statistical significance after a sequential Bonferroni correction when testing one group against the other three: if there is no asterisk, none of the three comparisons was significant; *: 1 out of 3 comparisons was significant; **: 2 out of 3 comparisons were significant; ***: all were significant. All

possible pairwise comparisons were undertaken (e.g., control vs. each of the three hypodontia groups; mild hypodontia vs. moderate or severe etc.). In the comparisons between hypodontia and control subjects, three different colours are used for the asterisks: lime green for mild hypodontia vs. control subjects; sky blue for moderate hypodontia vs. control subjects, and dark blue for severe hypodontia vs. control subjects. For the comparisons among the hypodontia groups themselves, the colours used for the asterisks are as follows: pale blue for mild vs. moderate; lavender for mild vs. severe, and violet for moderate vs. severe.

4.3.1 Summary size analysis:

Comparisons between hypodontia groups and control subjects

Three upper teeth (the upper right second premolar, upper left first premolar and upper left first molar) and half of the lower teeth (lower premolars, lower left lateral incisor and lower left central incisors) were analysed with the sexes pooled, since sexual dimorphism was not significant.

Female

Figure 4.11 summaries comparisons between the female members of the hypodontia groups and the female control subjects. In the upper jaw, significant differences were found between the severe hypodontia group and the control subjects for all teeth. Significant differences were found between the moderate hypodontia group and the control subjects for 79% of the upper teeth. In the comparison between the control subjects and the mild hypodontia group, significant differences were found for 50% of all teeth. In the comparison between the female control subjects and the female members of the hypodontia groups, there was a tendency for the right side to have a higher variance than the left side, with almost the same number of pairwise comparisons indicating significance in group membership (e.g., for the lateral incisors, the pairwise groups on the right side had a higher variance than those on the left). The explained variances for the upper laterals and the upper first premolars on the right side were higher than those found for the corresponding teeth on the left side. The average variances for the upper right lateral incisor and upper left lateral incisor were 42.6% and 33.6% respectively; for the upper right first premolar and the upper left first premolar the variances were 45.9% and 33.2% respectively. Also, the percentage of average variance gradually increased moving from the posterior toward the anterior teeth .

In the lower jaw, highly significant differences were found between the severe hypodontia group and the control subjects for all teeth. In the comparison between the mild and moderate hypodontia groups and the control subjects, significant differences were found for 65 % and 85% respectively of the lower teeth. As in the upper jaw, the comparison between the female control subjects and the female members of the hypodontia groups suggested a higher variance in the anterior than in the posterior region. The average variance ranged between 20% and 33% among all teeth. The highest variance found was for the lower second premolars and the smallest was for the lower first molars.

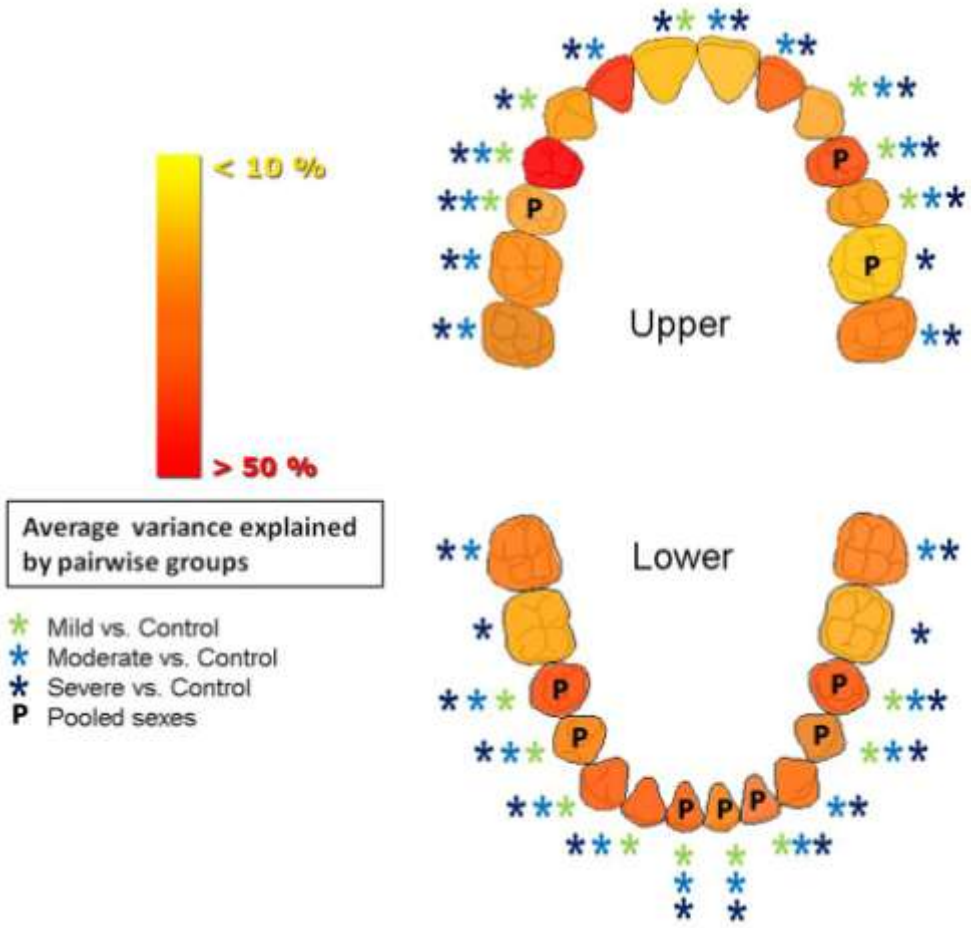

Figure 4.11 **Differences in tooth size between control and hypodontia groups for female subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

Male (Figure 4.12)

For the male subjects significant differences were found between the severe hypodontia group and the control subjects for all upper teeth; in the comparison with the moderate hypodontia group the differences were highly significant in 65% of the teeth. With the mild hypodontia group significant differences were found for only 35% of the teeth. The percentage of average variance gradually increased from the posterior teeth toward the anterior teeth as with the female subjects. The average variance ranged between 15 and 44%. The highest variances were for the upper right lateral incisor and the upper left canine, while the lowest was for the upper right first molar.

Highly significant differences were found between the severe hypodontia and the control groups for all teeth in the lower jaw. There were significant differences between the control subjects and the moderate hypodontia group in 85% of the lower teeth, while in the comparison with the mild hypodontia group the difference was significant for 50% of the teeth in the lower jaw. The comparison between the male control subjects and the male members of the hypodontia groups revealed a higher variance in the anterior than in the posterior region. The average variance ranged between 20 and 39% among all teeth. The highest was for the lower second premolars and lower right canine, while the lowest was for the lower first molars.

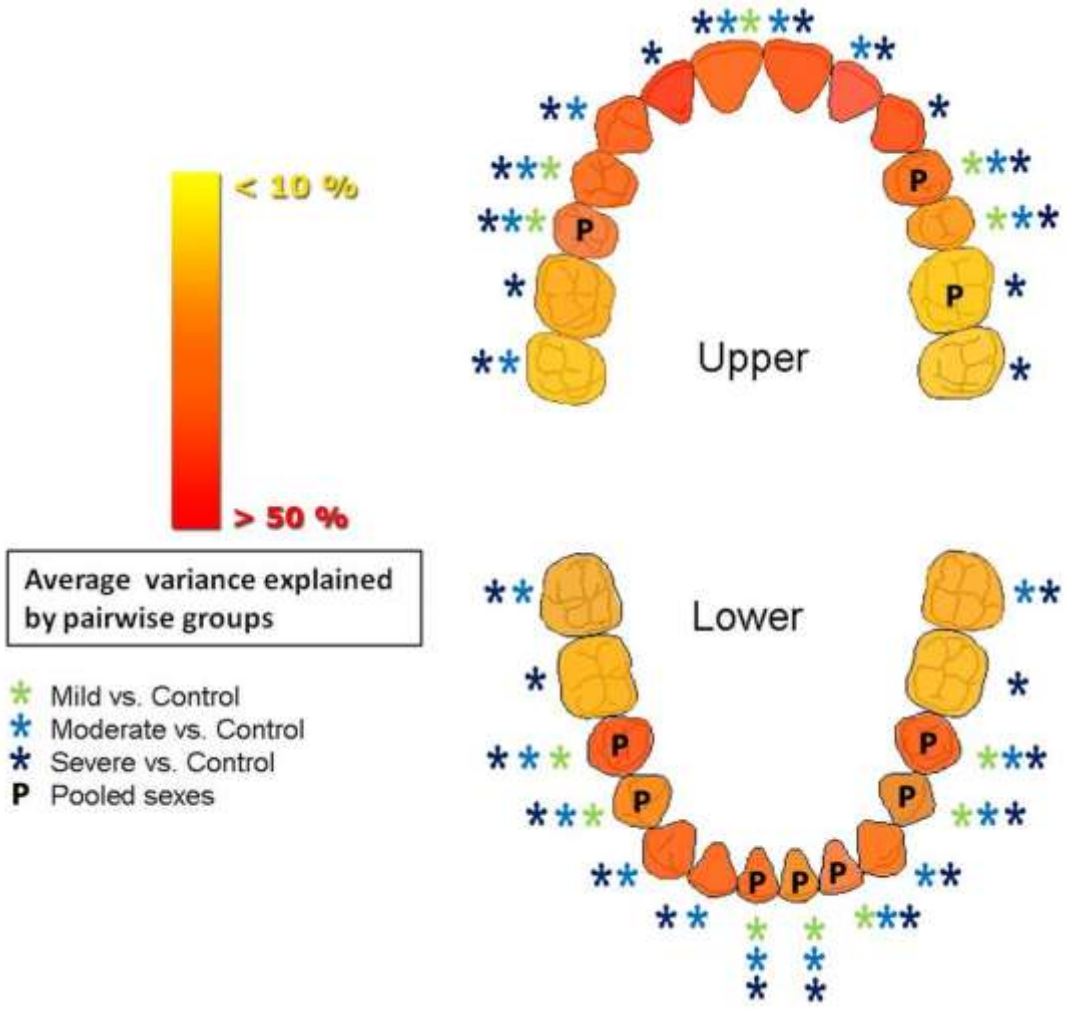

Figure 4.12 **Differences in tooth size between control and hypodontia groups for male subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

Comparisons between hypodontia groups

Three teeth in the upper jaw (the upper right second premolar, upper left first premolar and upper left first molar) and half of the teeth in the lower jaw (lower premolars, lower left lateral incisor and lower left central incisors) were analysed with the sexes pooled, since sexual dimorphism was not significant.

Female (Figure 4.13)

In the comparisons of the female members of the hypodontia groups, the only significant difference in the upper jaw was found between the mild and severe hypodontia groups, with a 16.6% explained variance in the upper left first premolar. In the lower jaw, the only significant differences were found between the lower second premolars and the lower left

lateral incisor. The average explained variance for these teeth was 20.5%. The highest variance found was for the lower left lateral incisor and the smallest was for the lower second premolars.

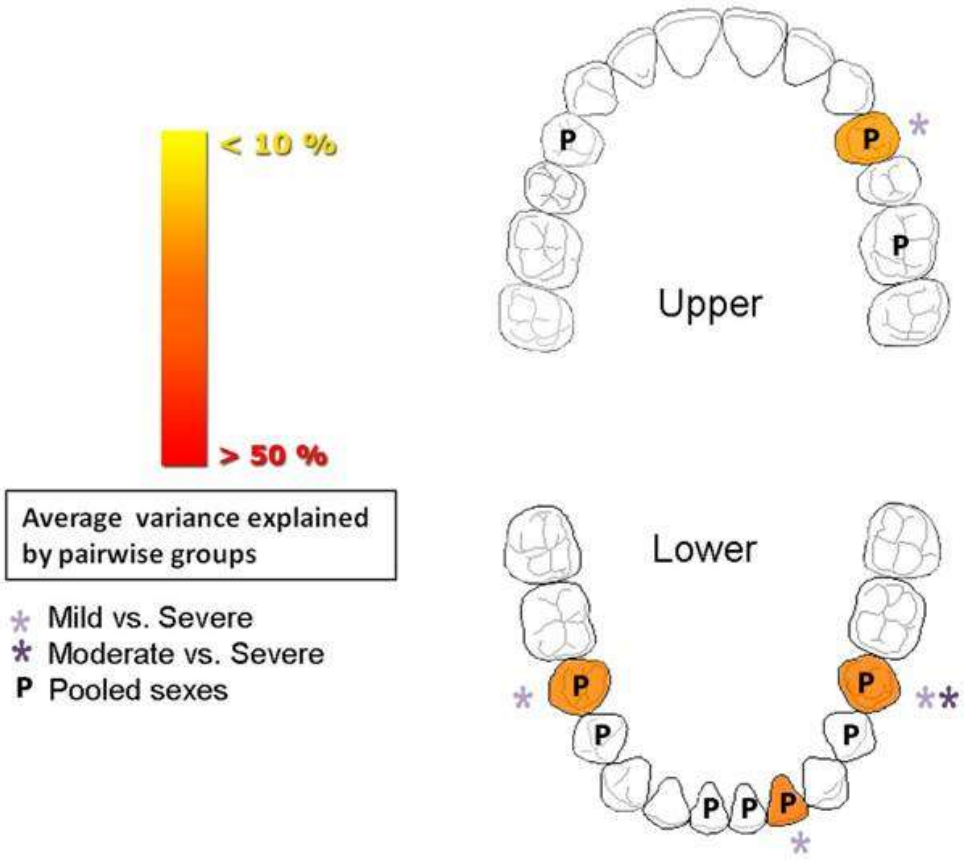

Figure 4.13 **Differences in tooth size within hypodontia groups for female subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

Male (Figure 4.14)

In the comparisons between the male hypodontia groups, significant differences were found for three teeth in the upper jaw: the upper central incisors and the upper left first premolar. The average variance ranged from 16.6% for the upper left first premolar to 28.7% for the upper central incisors. The highest variance found was for the upper right central incisor and the smallest was for the upper left first premolar.

Significant differences were found for six teeth in the lower jaw: the lower second premolars, the lower canines and the lower lateral incisors. The average variance ranged

from 16.7% for the lower left second premolar to 24.8% for the lower lateral incisors. The highest explained variance was for the lower left canine and the lowest was for the lower right canine.

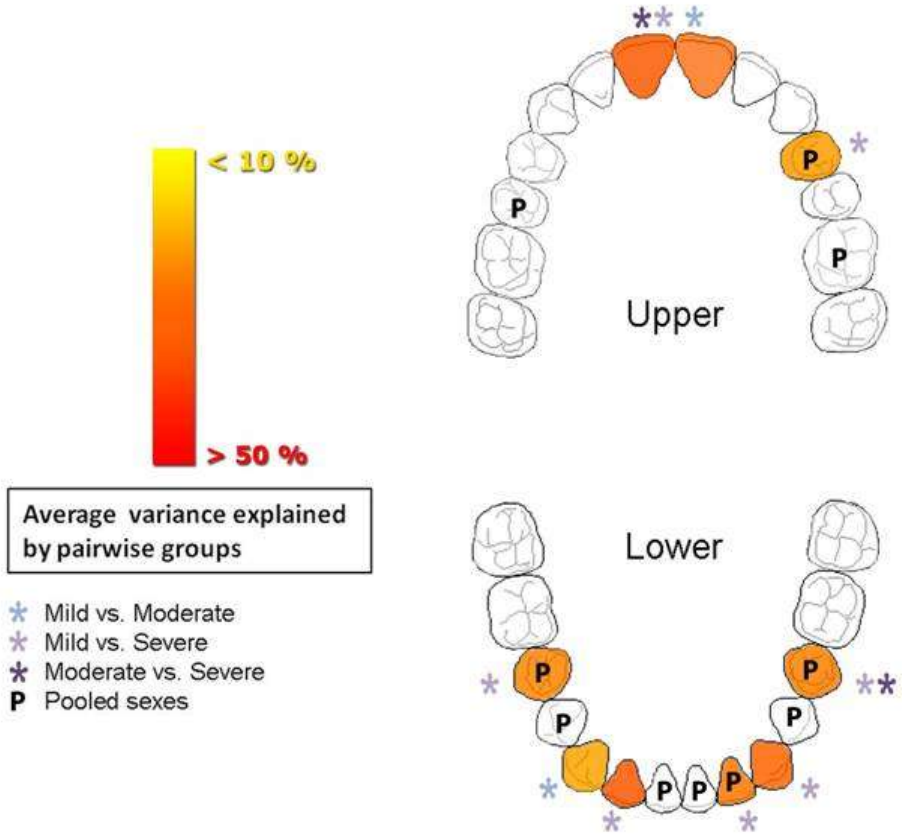

Figure 4.14 **Differences in tooth size within hypodontia groups for male subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

4.3.2 Summary shape analysis:

Comparisons between hypodontia groups and control subjects

All upper teeth except the upper right canine and eight lower teeth (the lower second molars, lower premolars, lower left canine and lower left lateral incisor) were analysed with the sexes pooled as since sexual dimorphism was not significant.

Female (Figure 4.15)

In the comparisons between the female hypodontia groups and the female control group, in the upper jaw, significant differences were found in almost all pairwise comparisons of all teeth. The differences between all hypodontia groups and the control subjects were significant, with the exception of the upper left central incisor in the mild hypodontia group. The average explained variance ranged between 3.7 and 9.0% of the total variation. The highest variance found was for the upper right second premolars and the smallest was for the upper right lateral incisor.

In the lower jaw, significant differences were found in at least one pairwise comparison for all teeth, with the greatest number being found in comparisons with the mild hypodontia group, followed by the severe group and lastly the group with moderate hypodontia, with 85%, 79% and 64% of the teeth respectively. The average explained variance ranged from 6 to 9.6% of the total variation. The highest variance found was for the lower right first molar and the smallest was for the lower central incisors.

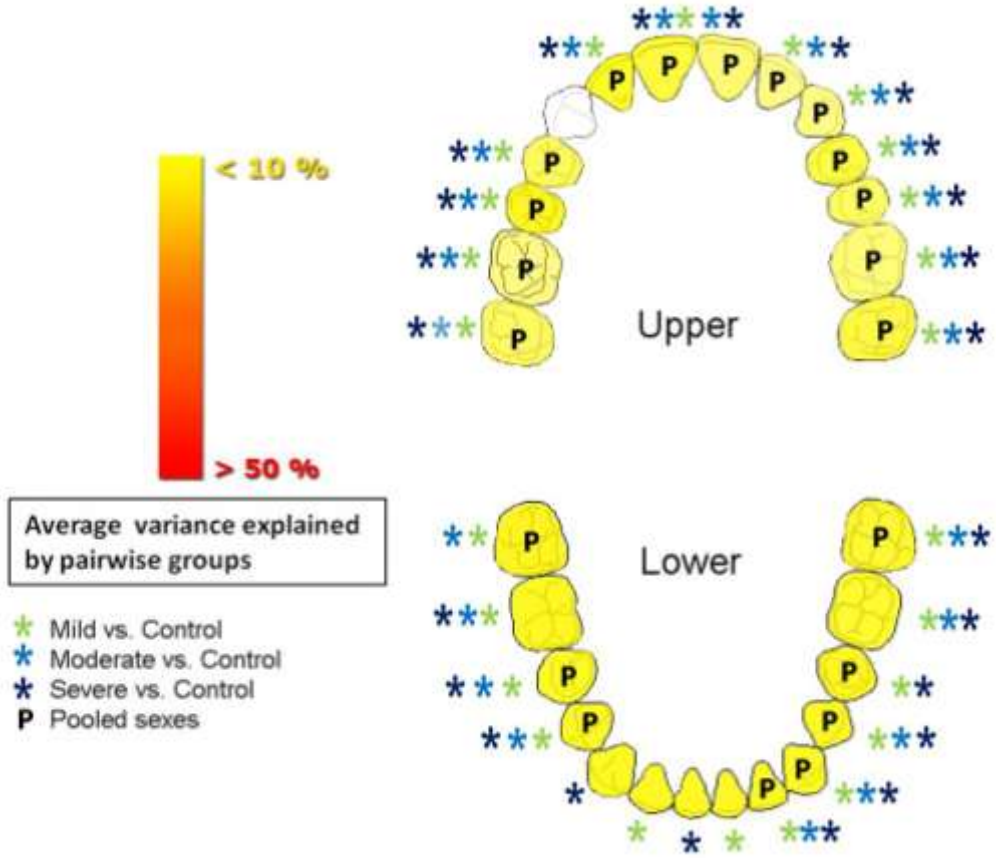

Figure 4.15 **Differences in tooth shape between control and hypodontia groups for female subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

Male (Figure 4.16)

Results for the upper arch are the same as for the female subjects presented above, given that all but one tooth, the upper right canine, were analysed with the sexes pooled. The result for the dimorphic tooth, the upper right canine, however, was not congruent with the results for the females. It showed significant differences in all pairwise comparisons. The average explained variance ranged from 3.7 to 9.2% of the total variation for all the teeth. The highest variance found was for the upper right canine and the smallest was for the upper right lateral incisor.

Significant differences were found in at least one pairwise comparison of each tooth in the lower jaw. In the comparison between the severe hypodontia and the control subjects, significant differences were found for all the teeth except the lower right second molar. With the moderate hypodontia group the difference was significant for 79% of the teeth, while with the mild hypodontia group it was significant for 72% of the teeth. The average

explained variance ranged from 6.8 to 16.5% of the total variation. The highest variance was for the lower right canine and the smallest was for the lower left lateral incisor.

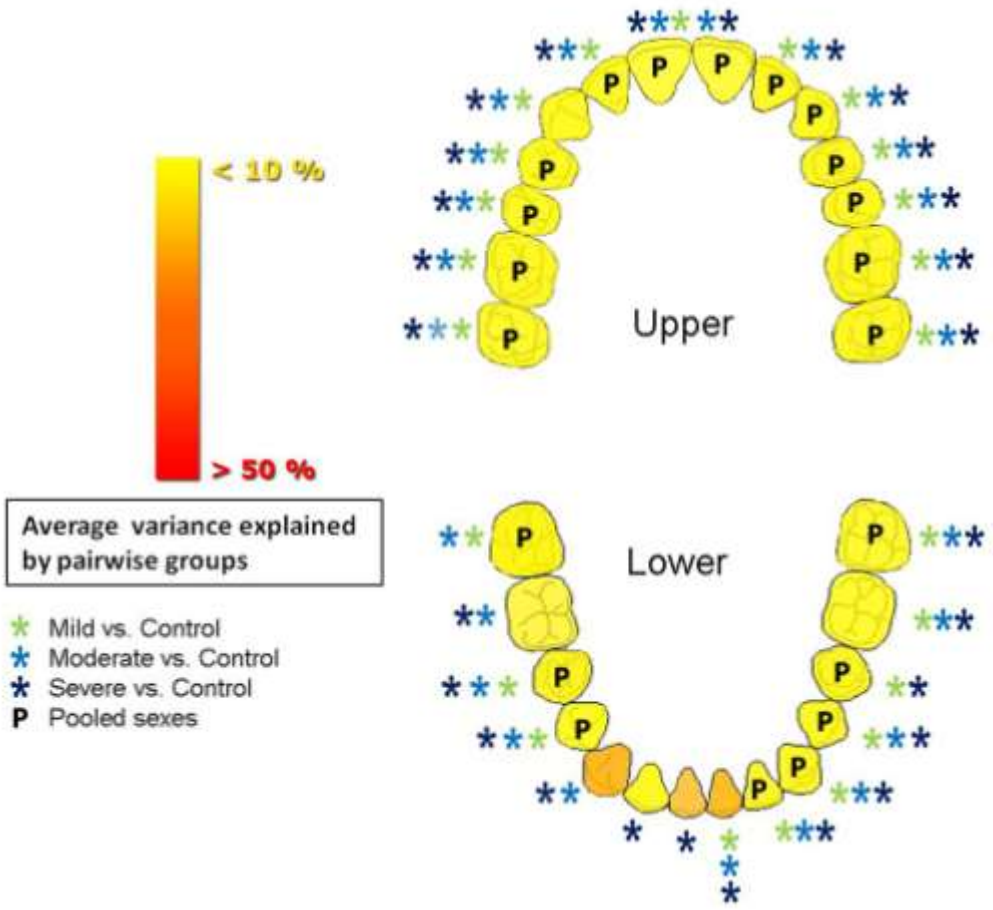

Figure 4.16 **Differences in tooth shape between control and hypodontia groups for male subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

Comparisons between hypodontia groups

All upper teeth, except the upper right canine, and eight lower teeth (the lower second molars, lower premolars, lower left canine and lower left lateral incisor) were analysed with the sexes pooled, since sexual dimorphism was not significant.

Female (Figure 4.17)

In the comparisons between the female subjects in the different hypodontia groups, in the upper jaw, all the shape differences were located in the posterior region, with the addition

of the upper right central incisor. In the comparison between the hypodontia groups, significant differences were found for 57% of the teeth, mainly posterior teeth, between the mild and severe hypodontia groups and also between the moderate and severe hypodontia groups. 0.05% of the shape differences were found between the mild and moderate hypodontia groups on the upper right central incisor. The average variance in the posterior region ranged between 4.9 and 14.6% of the total variation. The highest variances were for the upper right second premolar and the smallest was for the upper right central incisor.

In the lower jaw, all the shape differences were again found in the posterior teeth but with the addition of the lower left canine. In the comparison between the mild and moderate and also between the moderate and severe hypodontia groups, significant differences were found for 50% of the teeth. However, 64% of the shape differences were found in the comparison between the mild and severe hypodontia groups. The average variance ranged from 3.8 to 18.3% of the total variation. The highest variances were for the lower left first molar and the smallest was for the lower left canine.

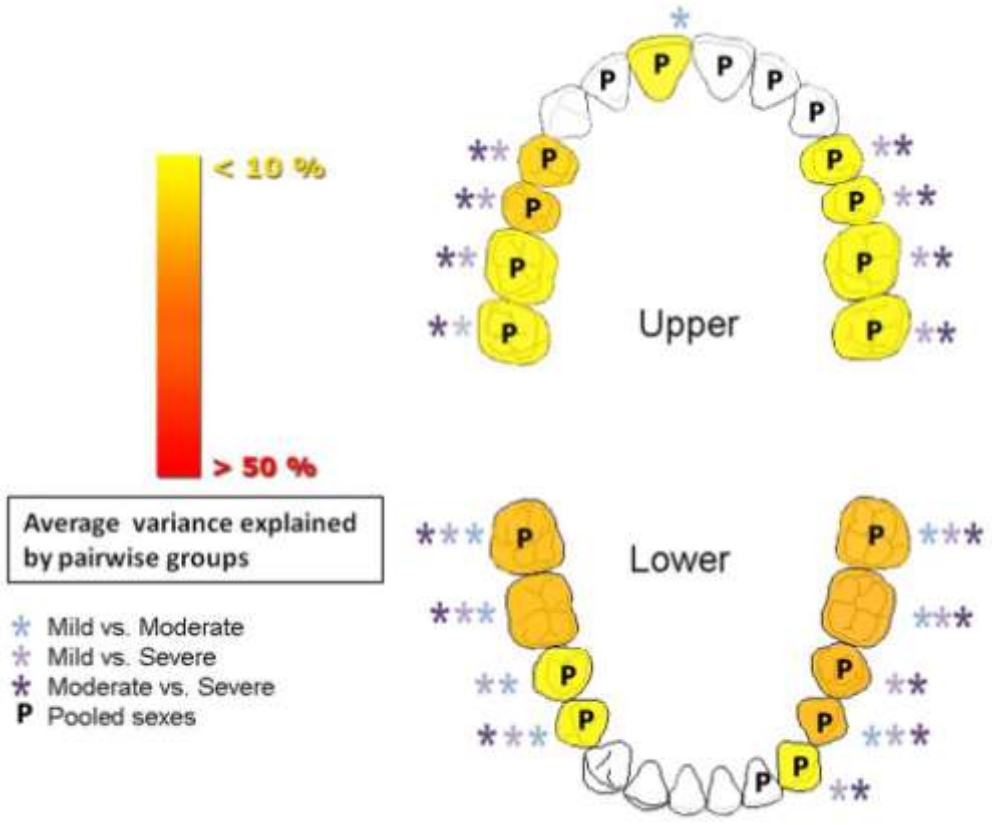

Figure 4.17 **Differences in tooth shape within hypodontia groups for female subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

Male (Figure 4.18)

In the upper jaw, the results were the same as for the female subjects presented above, given that all the shape differences were located in the posterior region, with the addition of the upper right central incisor. The average variance ranged between 3.5 and 15.8% of the total variation in the posterior region. The highest variances were for the upper right second premolar and the smallest was for the upper right central incisor.

In the lower jaw, shape differences were found in all the teeth except the lower incisors. In the comparison between the hypodontia groups, significant differences were found between the mild and moderate hypodontia groups, the moderate and severe hypodontia groups and between the mild and severe hypodontia groups, with 50%, 64% and 71% of the teeth respectively. The average variance ranged between 3.9 and 23.4% of the total variation. The highest shape variance explained within the hypodontia groups was found in the lower right canine while the lowest was found in the lower left canine.

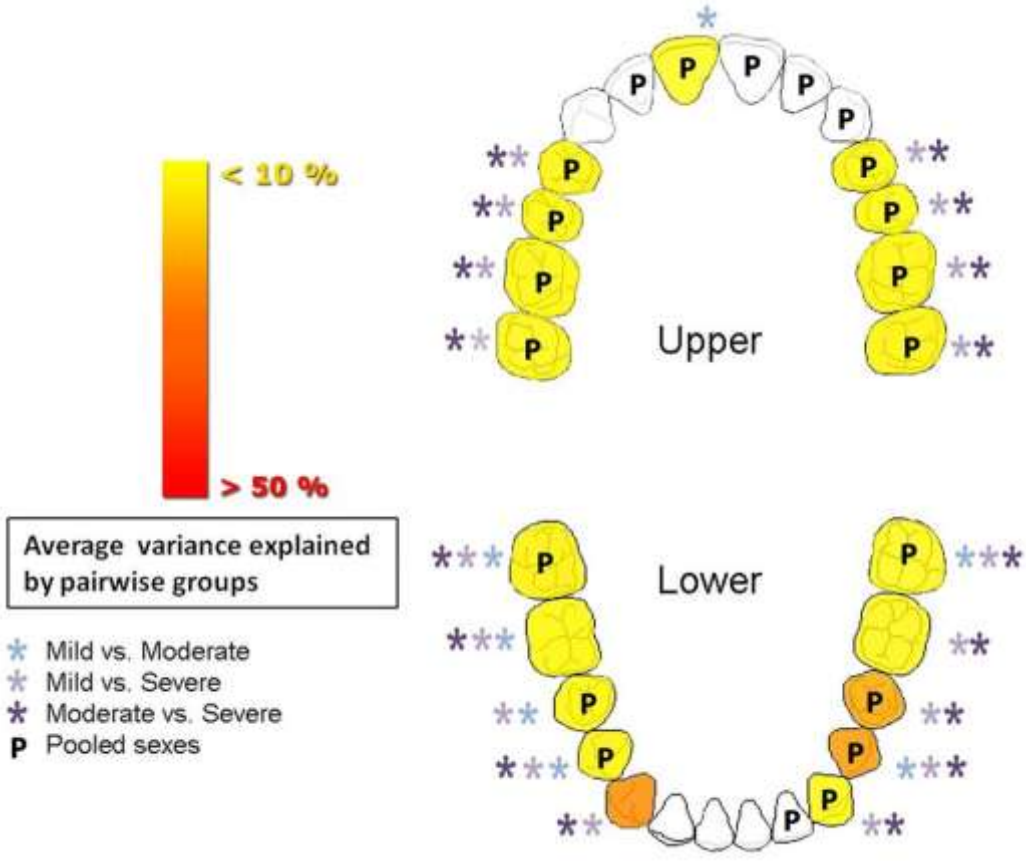

Figure 4.18 **Differences in tooth shape within hypodontia groups for male subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

4.3.3 Summary allometric variation

Allometric variations were tested within each group, and sexual dimorphism was also tested in order to decide whether or not to pool the sexes. The results obtained for sexual dimorphism and the allometric variations are presented in the following section. Depending on the allometric significance, a MANCOVA group by size was carried out in the same way as the MANOVA in the shape analysis presented in the first part of this chapter.

With regard to allometry, the effect of size on shape was found to be significant for most teeth, mainly in the anterior region, and shape differences were still significant after controlling, when possible, for allometry. The allometric variation was more significant in the lower anterior teeth than in the upper. The details of the allometric results are shown in the appendix.

Comparisons within all groups (control subjects and hypodontia groups)

All upper teeth, except the upper right canine, and eight lower teeth (the lower second molars, lower premolars, lower left canine and lower left lateral incisor) were analysed with the sexes pooled, since sexual dimorphism was not significant.

Female (Figure 4.19)

When testing allometry one group at a time among the female subjects, 71% of the teeth in the upper jaw showed significant allometric variation; the exceptions were the upper right lateral incisor, the upper left second premolar, and upper second molars. Allometric variations among the female control subjects were found in 50% of the teeth, while within the female mild hypodontia group variations were found in 57% of the teeth. In the moderate hypodontia group, allometric differences were found in only two teeth, while no allometric differences were found within the severe hypodontia group. The average explained variance ranged between 3.98 and 14.3% of the total variation. The highest variation was found in the upper left lateral incisor within the mild hypodontia group, while the lowest was found in the upper left first molar within the mild hypodontia group.

In the lower jaw, most of the allometric variation was found in the anterior teeth, and in some of the posterior teeth. Significant allometric variations were found within the control group and among members of the mild hypodontia, moderate hypodontia and severe hypodontia groups for 50%, 43%, 14% and 21% of the lower teeth respectively. The

average explained variance ranged from 5.38 and 17.5% of the total variation. The highest variation was found in the lower right canine within the severe hypodontia group, while the lowest was found in the lower right first premolar within the control group.

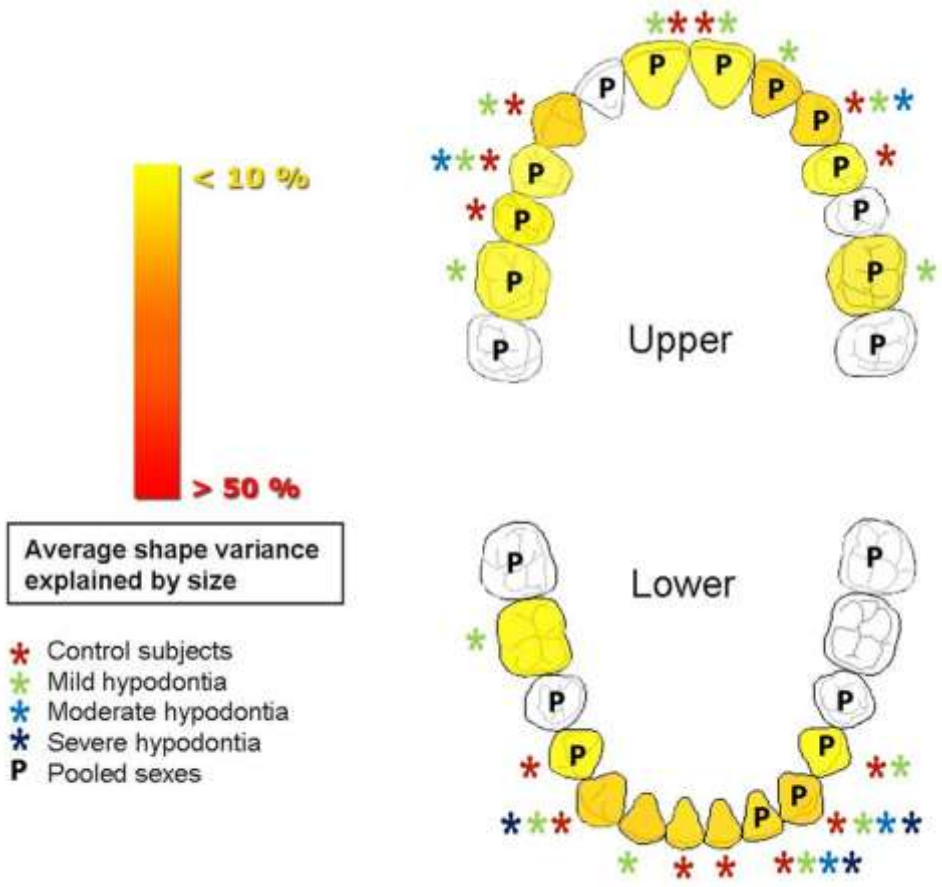

Figure 4.19 **Shape/size differences within control and hypodontia groups for the female subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

Male (Figure 4.20)

For the male subjects, in the upper jaw, allometric variation was found for 71% of teeth, as with the female subjects. Among the control subjects, allometric variation was found in 50% of the teeth, and within the mild hypodontia group allometric variation was found in 50% of the teeth as well. Within the moderate hypodontia group allometric variation was found for only two teeth, while no allometric variation was found in the severe hypodontia group. The average explained variance ranged between 3.98 and 17.2% of the total variation. The highest variation was found in the upper right canine within the

moderate hypodontia group, while the lowest was found in the upper left first molar within the mild hypodontia group.

In the lower jaw allometric variation was found for all lower teeth. This was mainly in the anterior region with the exception of the lower second premolars and lower second molars. Significant allometric variation was found within the control group and within the mild hypodontia, moderate hypodontia and severe hypodontia groups in 43%, 50%, 57% and 43% of the lower teeth respectively. The average variance ranged between 5.4 and 35.4% of the total variation. The highest variation was found in the lower left central incisors, while the lowest was found in the right first premolar within the control group.

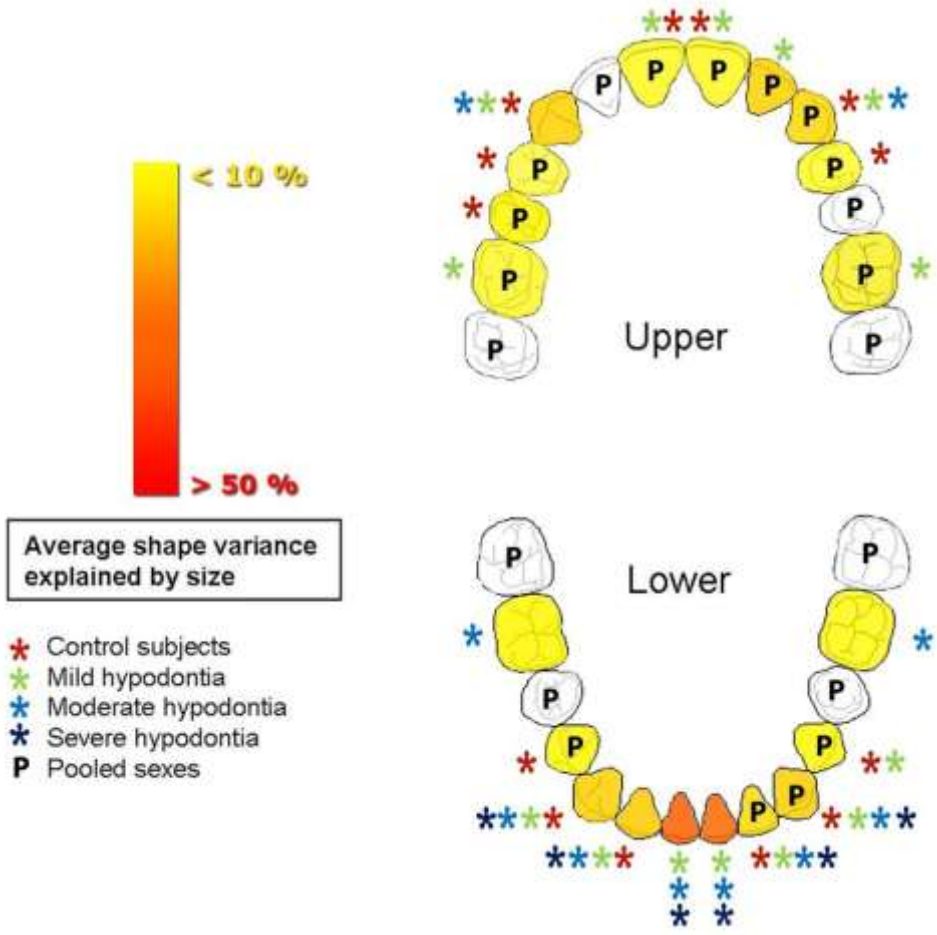

Figure 4.20 **Shape/size differences within control and hypodontia groups for the male subjects. (Pooled (P) male and female data were used for teeth where no significant sexual dimorphism was evident).**

4.3.4 Summary of the data analysis

Size variation was for the most part found to be significant, especially when the control subjects were compared to the hypodontia groups. The anterior teeth were more affected than posterior teeth. Among the female subjects teeth on the right side were more affected than those on the left. Sexual dimorphism was found less in the anterior than in the posterior region; thus the sexes were pooled more often for teeth in the anterior region. Generally, size differences with controls increased as the severity of the hypodontia increased. The pattern was largely congruent for both sexes.

With regard to shape, most teeth were affected in hypodontia but the pattern was less clear than for size particularly in posterior teeth. Within hypodontia groups the variance explained by group differences was smaller and less clearly correlated to the severity of the disease. Posterior teeth were found to be the most affected when the hypodontia groups were compared with each other.

When allometry was taken into account, the effect of size on shape was found to be significant for most teeth, particularly in the anterior region, and shape differences were still significant after controlling, when possible, for allometry.

4.4 Shape transformation

Shape differences between groups were examined using a PCA on the matrix of group mean shape variables. A mean shape was computed by taking the sample average of shape coordinates from the full set of shape variables. The analysis was performed for all 28 teeth using Morphologika2 v2.5. Similar shape differences between groups were found for the contralateral teeth in both dental arches. For this reason, in this section, the three-dimensional shape differences of the permanent teeth in the upper right and lower right quadrants only will be presented. In addition, the same analysis was performed on both sexes when there were significant differences between them. This suggested similar shape differences among the groups (for more details see appendix V – shape differences for the remaining teeth and appendix VI – DVD attached presents shape differences for all teeth in 3D).

The severe hypodontia group was chosen as a representative of the hypodontia groups to compare to the control since it had the most pronounced shape variation out of all the groups. However, a similar pattern was noticed for both the mild and moderate hypodontia groups.

Shape differences of the permanent teeth as viewed from the buccal and occlusal views (upper and lower posterior teeth) or from the buccal and lateral views (upper and lower anterior teeth) are described below.

The upper right second molar

Fifteen landmarks were selected on the upper right second molar (Figure 4.21).

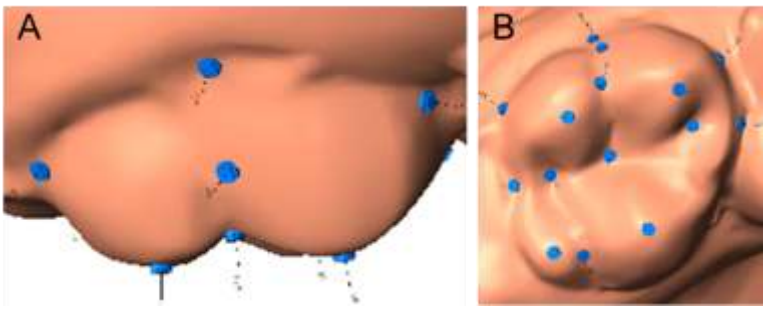

Figure 4.21 **Landmarks of upper right second molar (scanned image): A, Buccal view; B, Occlusal view.**

Buccal view

The mean shape of the severe hypodontia teeth showed a flatter gingival margin. Furthermore, the buccal cusp tips in the severe hypodontia teeth were less prominent than those in the controls. The proximal surfaces were more tapered towards the occlusal surface in the severe hypodontia group when compared to the control subjects (Figure 4.22, A & B).

Occlusal view

Shape variation of the occlusal surface can be summarized by comparing the mean shape of the severe hypodontia teeth with the controls. The hypodontia group had a more rectangular occlusal surface when compared to the control subjects (Figure 4.22, C & D).

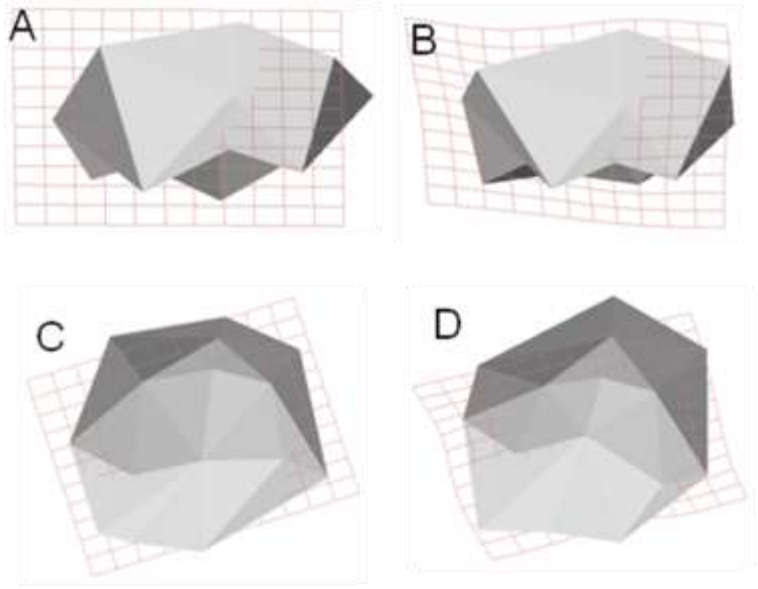

Figure 4.22 **Upper right second molar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

The upper right first molar

Fifteen landmarks were selected on the upper right first molar (Figure 4.23).

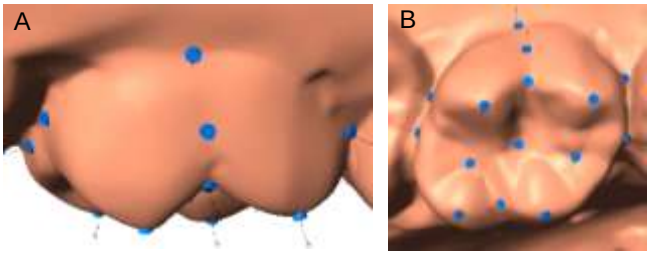

Figure 4.23 **Landmarks of upper right first molar (scanned image): A, Buccal view; B, Occlusal view.**

Buccal view

The mean shape of the teeth of the severe hypodontia group showed a flatter gingival margin. Furthermore, the buccal cusp tips in the severe hypodontia teeth were less prominent than in the controls. The proximal surfaces were less tapered towards the occlusal surface in the severe hypodontia group when compared to the control subjects (Figure 4.24, A & B).

Occlusal view

Shape variation of the occlusal surface can be summarized by comparing the severe hypodontia group with the control subjects. The teeth of the hypodontia group had a less bulbous buccal surface than those of the control subjects (Figure 4.24, C & D).

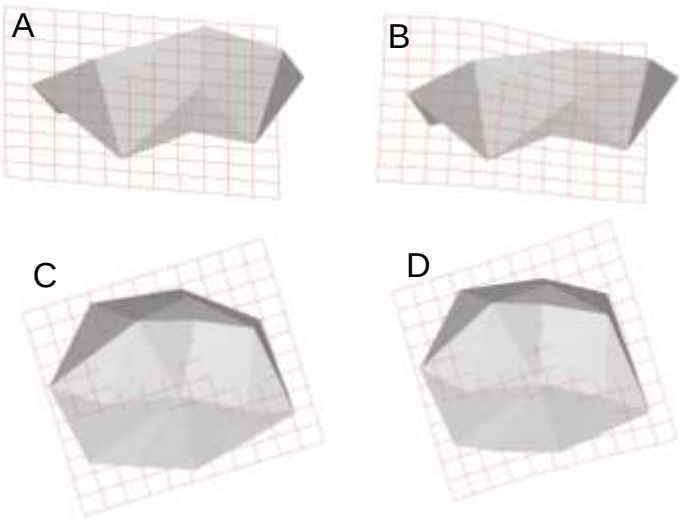

Figure 4.24 **Upper right first molar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Upper right second premolar

Twelve landmarks were selected on the upper right second premolar (Figure 4.25).

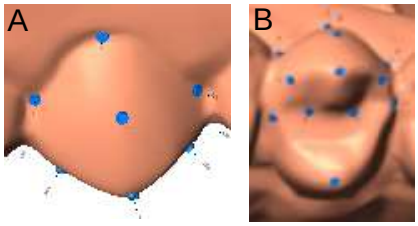

Figure 4.25 **Landmarks of upper right second premolar (scanned image). A, Buccal view; B, Occlusal view.**

Buccal view:

The upper second premolar in the severe hypodontia group had a more parallel proximal surface when compared to that in the control subjects, which had divergent proximal surfaces towards the occlusal surfaces of the upper second premolars. In addition, the teeth of the severe hypodontia group had a flatter gingival outline (Figure 4.26, A & B).

Occlusal view:

The occlusal outline was slightly more tapered towards the palatal surface in the severe hypodontia group in comparison to the occusal surface of the control subjects. The outline of the palatal aspect was less prominent in the severe hypodontia group than in the control (Figure 4.26, C & D).

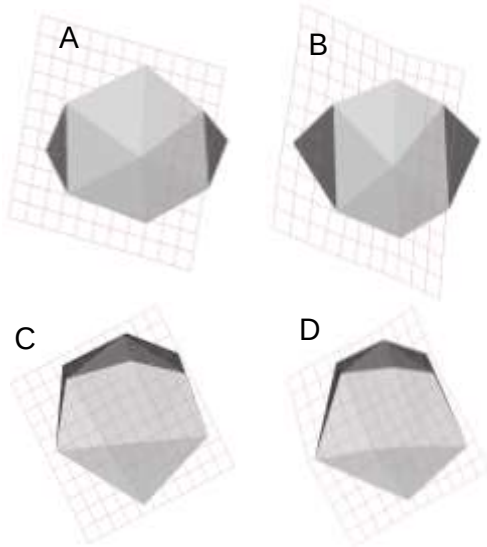

Figure 4.26 **Upper right second premolar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Upper right first premolar

Twelve landmarks were selected on the upper right first premolar (Figure 4.27)

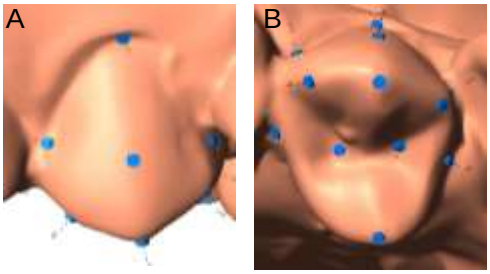

Figure 4.27 **Landmarks of upper right first premolar (scanned image). A, Buccal view; B, Occlusal view.**

Buccal view:

The teeth of the severe hypodontia group had more parallel proximal surfaces when compared to those of the control subjects, which had divergent proximal surfaces towards the occlusal surface. In addition, the severe hypodontia teeth had a flatter gingival outline than the controls (Figure 4.28, A & B).

Occlusal view:

The teeth of severe hypodontia subjects had a slightly more tapered (towards the palatal surface) proximal surface than those of control subjects. In addition, both buccal and lingual aspects were flatter in the severe hypodontia than in the control group (Figure 4.28, C & D).

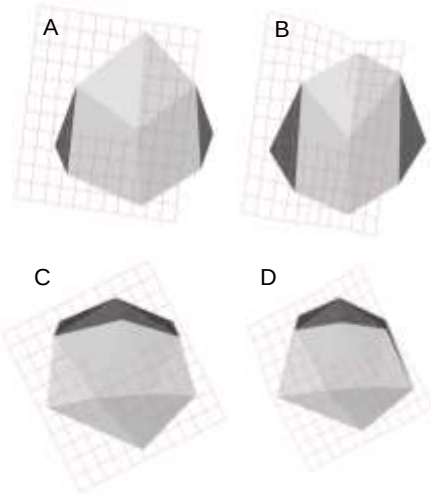

Figure 4.28 **Upper right first premolar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Upper right canine

Nine landmarks were selected on the upper right canine (Figure 4.29).

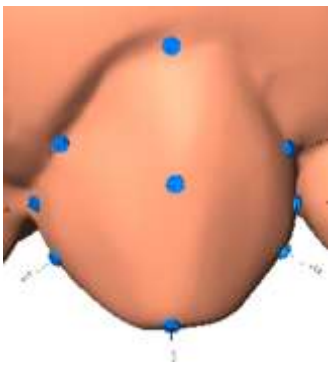

Figure 4.29 Landmarks of upper right canine (scanned image), Buccal view.

Buccal view:

The severe hypodontia teeth had a flatter gingival outline compared to the controls. In the severe hypodontia teeth the incisal edge was more tapered (more prominent cusp) than that of the control, and also had more tapered (towards the incisal edge) proximal surfaces (Figure 4.30, A & B).

Lateral view:

The teeth of the severe hypodontia group had a less bulbous labial surface when compared to the control subjects when viewed laterally (Figure 4.30, C & D).

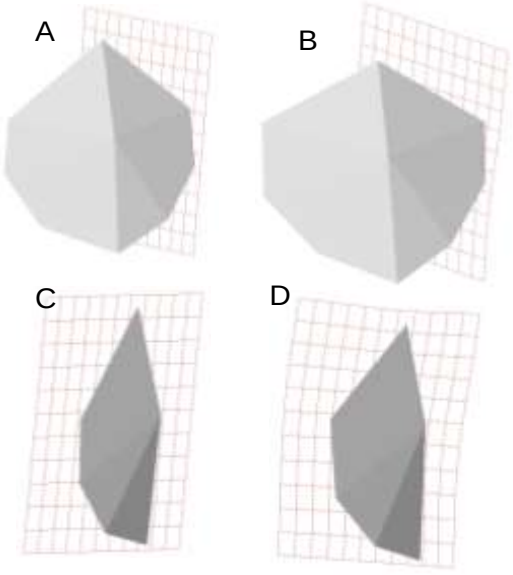

Figure 4.30 Upper right canine, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).

Upper right lateral incisor

Nine landmarks were selected on the upper right lateral incisor (Figure 4.31).

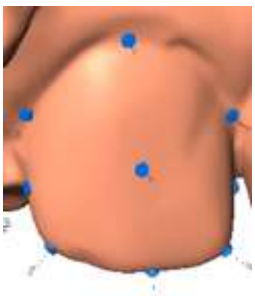

Figure 4.31 **Landmarks of upper right lateral incisor (scanned image), Buccal view.**

Buccal view:

The mean shape of the severe hypodontia teeth showed a flatter gingival outline when compared to that of the control subjects. In addition, the proximal surfaces in the severe hypodontia group were more tapered toward the incisal edge than those in the control group (Figure 4.32, A & B).

Lateral view:

The severe hypodontia teeth had a less bulbous/prominent labial surface when compared to the controls (Figure 4.32, C & D).

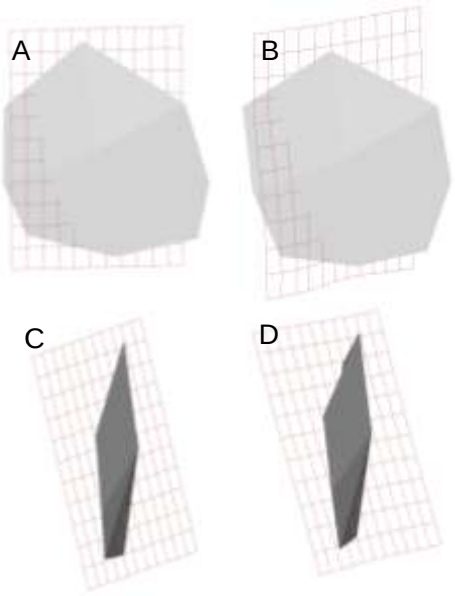

Figure 4.32 **Upper right lateral incisor, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Upper right central incisor

Nine landmarks were selected on the upper right central incisor (Figure 4.33).

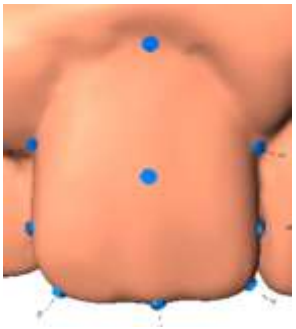

Figure 4.33 **Landmarks of upper right central incisor (scanned image), Buccal view.**

Buccal view:

The teeth of the severe hypodontia group had a flatter gingival outline and more parallel proximal surfaces when compared to those of the control subjects (Figure 4.34, A & B).

Lateral view:

The severe hypodontia teeth had a less prominent labial surface in comparison to the controls (Figure 4.34, C & D).

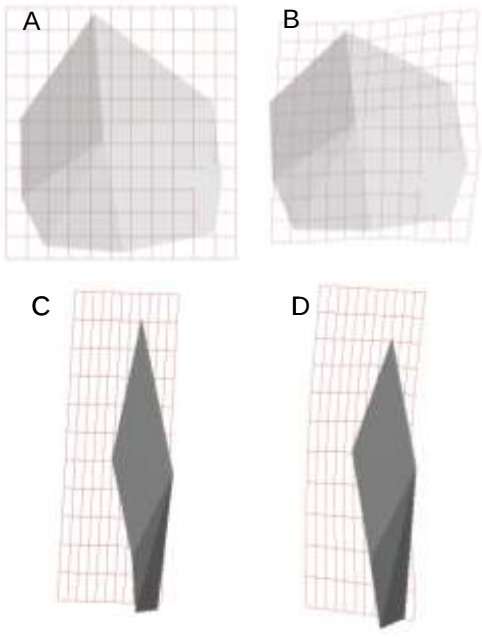

Figure 4.34 **Upper right central incisor, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Lower right central incisor

Nine landmarks were selected on the lower right central incisor (Figure 4.35).

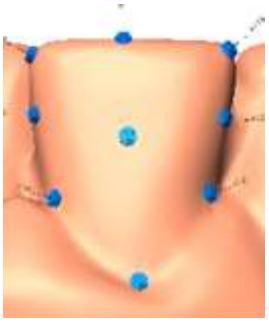

Figure 4.35 **Landmarks of lower right central incisor (scanned image), Buccal view.**

Buccal view:

In females the teeth of the severe hypodontia group had more tapered proximal surfaces toward the incisal edge and a flatter gingival margin when compared to control subjects (Figure 4.36, A & B). A similar pattern was found for differences between the groups of male subjects.

Lateral view:

The labial surface of the teeth of female severe hypodontia subjects was slightly flatter than that of the female control subjects (Figure 4.36, C & D). A similar pattern was found for differences between these groups for the male subjects.

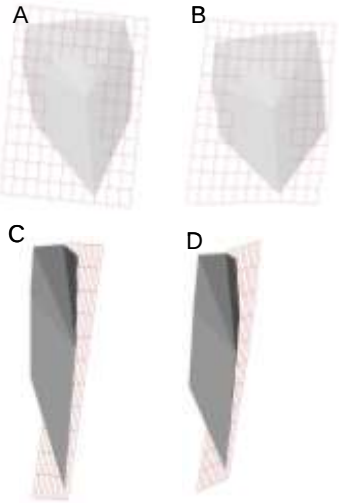

Figure 4.36 **Lower right central incisor, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Lower right lateral incisor

Nine landmarks were selected on the lower right lateral incisor (Figure 4.37).

Figure 4.37 **Landmarks of lower right lateral incisor (scanned image), Buccal view.**

Buccal view:

The mean shape of the teeth of female severe hypodontia subjects showed more tapered proximal surfaces toward the incisal edge and a flatter gingival margin when compared to the female control subjects (Figure 4.38, A & B). A similar pattern was found for differences between the groups for the male subjects.

Lateral view:

The labial surface of the teeth of the female severe hypodontia group was slightly less prominent than that of the female control subjects (Figure 4.38, C & D). A similar pattern was found for differences between the groups of male subjects.

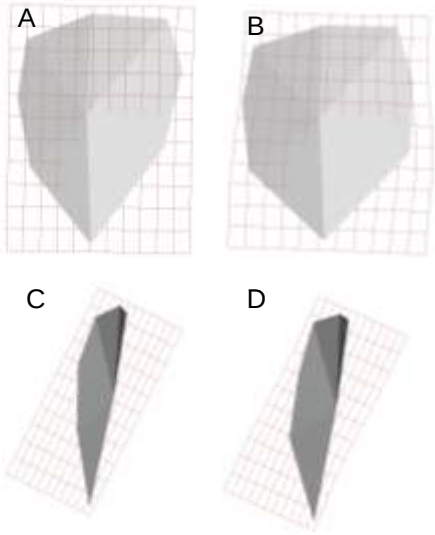

Figure 4.38 **Lower right lateral incisor, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Lower right canine

Nine landmarks were selected on the lower right canine (Figure 4.39).

Figure 4.39 Landmarks of lower right canine (scanned image), Buccal view.

Buccal view:

The teeth of the female severe hypodontia group had more tapered proximal surfaces toward the incisal edge and a flatter gingival margin when compared to the female control subjects (Figure 4.40, A & B). A similar pattern was found for differences between the groups for the male subjects.

Lateral view:

The labial surface in the teeth of the female severe hypodontia group was less bulbous/prominent than that in the female control subjects (Figure 4.40, C & D). A similar pattern was found for differences between the groups of male subjects.

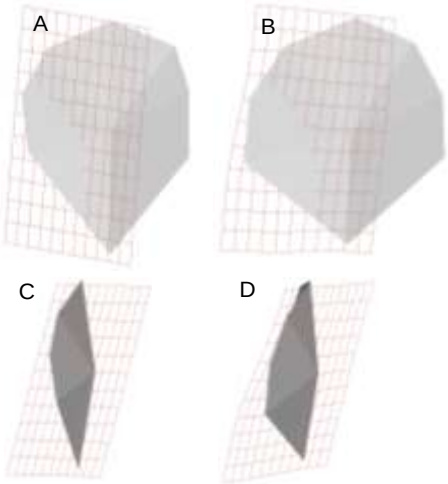

Figure 4.40 Lower right canine, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).

Lower right first premolar

Twelve landmarks were selected on the lower right first premolar (Figure 4.41).

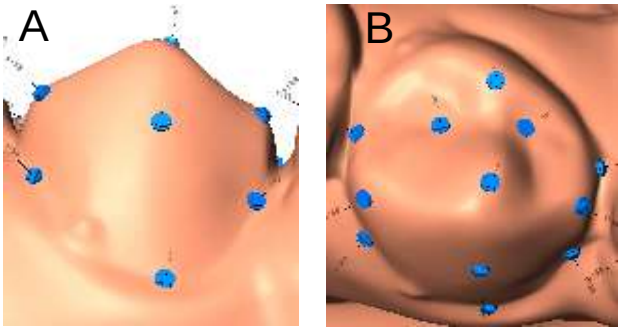

Figure 4.41 **Landmarks of lower right first premolar (scanned image). A, Buccal view; B, Occlusal view.**

Buccal view:

The proximal surface of teeth in the severe hypodontia group was more tapered toward the occlusal surface when compared to the control subjects (Figure 4.42, A & B).

Occlusal view:

The severe hypodontia teeth had less prominent cusp heights and more obtuse proximal surfaces than those of the control subjects (Figure 4.42, C & D).

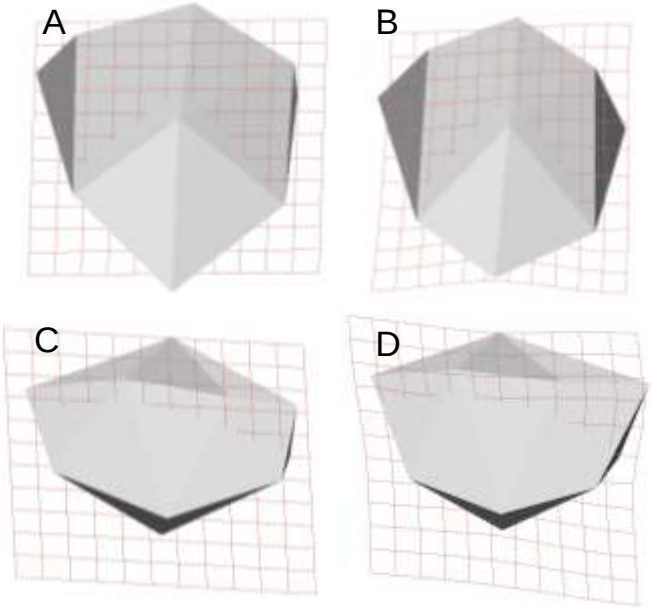

Figure 4.42 **Lower right first premolar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Lower right second premolar

Twelve landmarks were selected on the lower right second premolar (Figure 4.43).

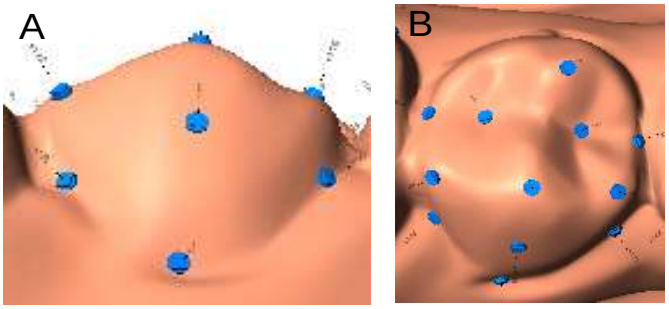

Figure 4.43 **Landmarks of lower right second premolar (scanned image). A, Buccal view; B, Occlusal view.**

Buccal view:

The proximal surface in the severe hypodontia teeth was more tapered toward the occlusal surface when compared to the control. In addition, the severe hypodontia teeth had less prominent cusp heights with a flatter occlusal plane (Figure 4.44, A & B).

Occlusal view:

The mean shape of the severe hypodontia teeth showed less prominent cusp heights and more obtuse proximal surfaces when compared to the controls (Figure 4.44, C & D).

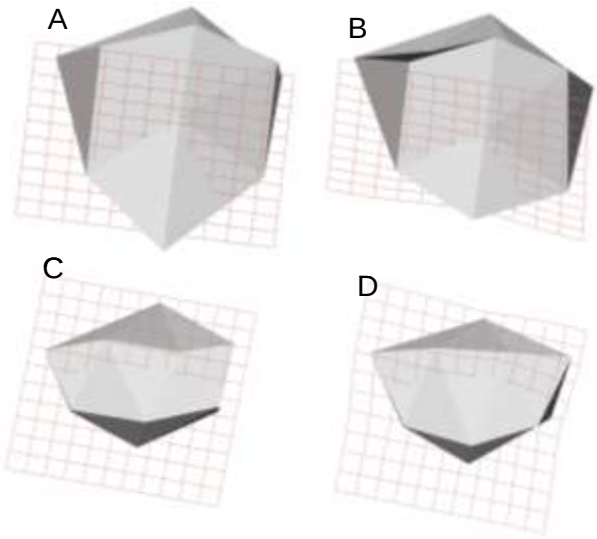

Figure 4.44 **Lower right second premolar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Lower right first molar

Eighteen landmarks were selected on the lower right first molar (Figure 4.45).

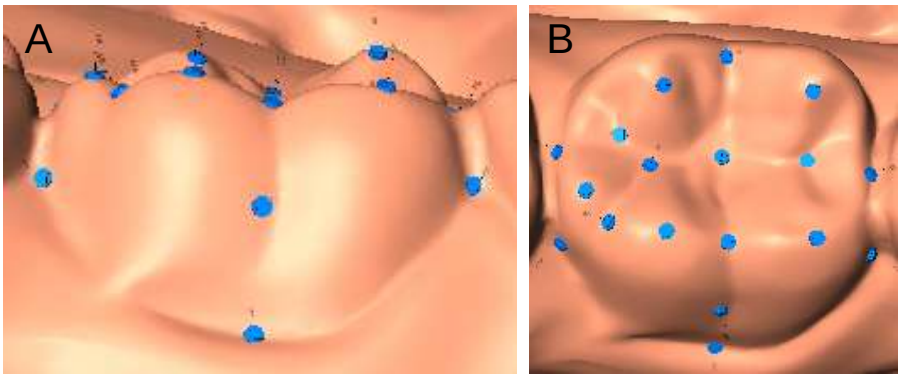

Figure 4.45 **Landmarks of lower right first molar (scanned image). A, Buccal view; B, Occlusal view.**

Buccal view:

The cusp tips on the teeth of the female severe hypodontia group were less prominent when compared to those of the female control subjects. In addition, the severe hypodontia teeth had a flatter gingival outline and. the proximal surfaces were more tapered towards the gingival margin than in the controls (Figure 4.46, A, B, C &D). A similar pattern was found for differences between the groups for the male subjects.

Occlusal view:

The teeth of the female severe hypodontia subjects had a less prominent buccal aspect when compared to those of the female controls from the occlusal view. The severe hypodontia teeth were also more bulbous at the proximal surfaces and had less prominent cusp tips in comparison to the controls (Figure 4.46, D & F). A similar pattern was found for differences between the groups of male subjects.

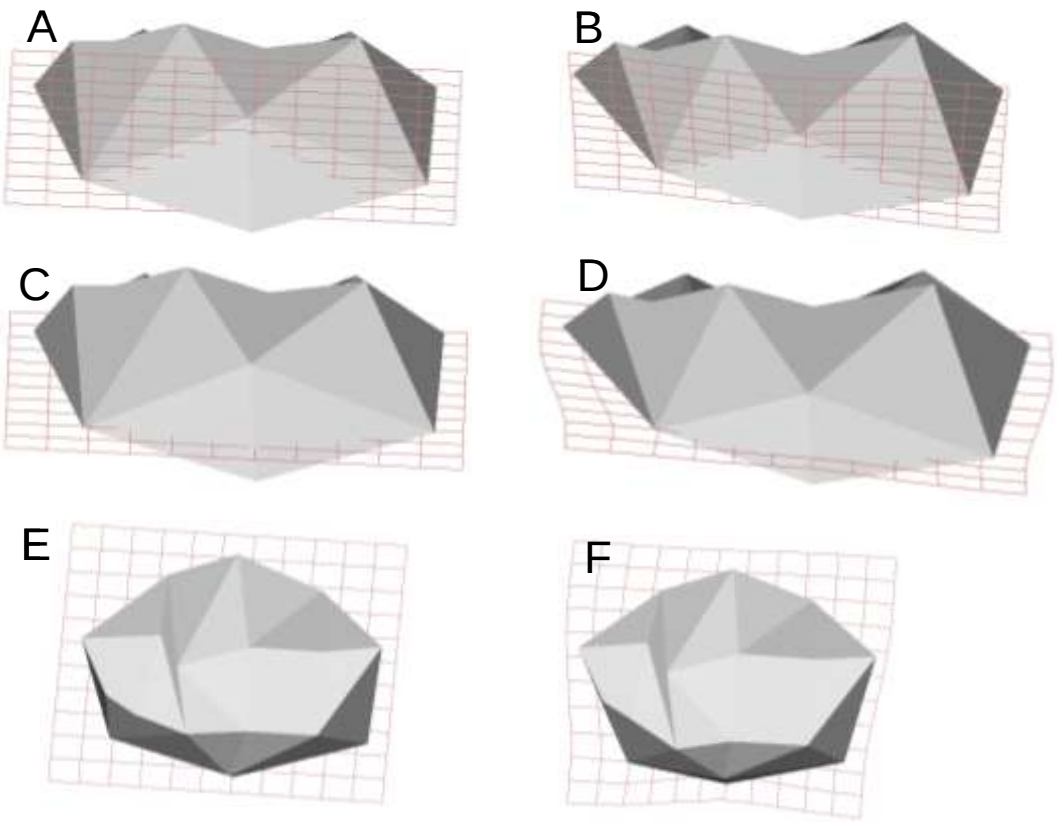

Figure 4.46 **Lower right first molar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Lower right second molar

Fifteen landmarks were selected on the lower right second molar (Figure 4.47).

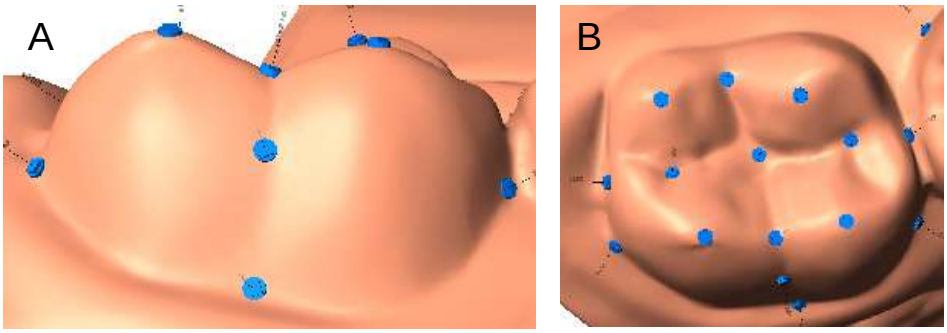

Figure 4.47 **Landmarks of lower right second molar (scanned image). A, Buccal view; B, Occlusal view.**

Buccal view:

The teeth of the severe hypodontia group had a flatter gingival outline when compared to those of the control subjects. The mesial cusp tips in the severe hypodontia teeth were less prominent than in the controls. The mesial surface in the severe hypodontia teeth was less bulbous while the distal surface was found to be more bulbous than in the controls (Figure 4.48, A & B).

Occlusal view:

The mean shape of the severe hypodontia teeth showed less prominent cusp tips when compared to the control subjects. The mesial surface was less bulbous while the distal wall was more bulbous in the severe hypodontia group than in the control subjects (Figure 4.48, C & D).

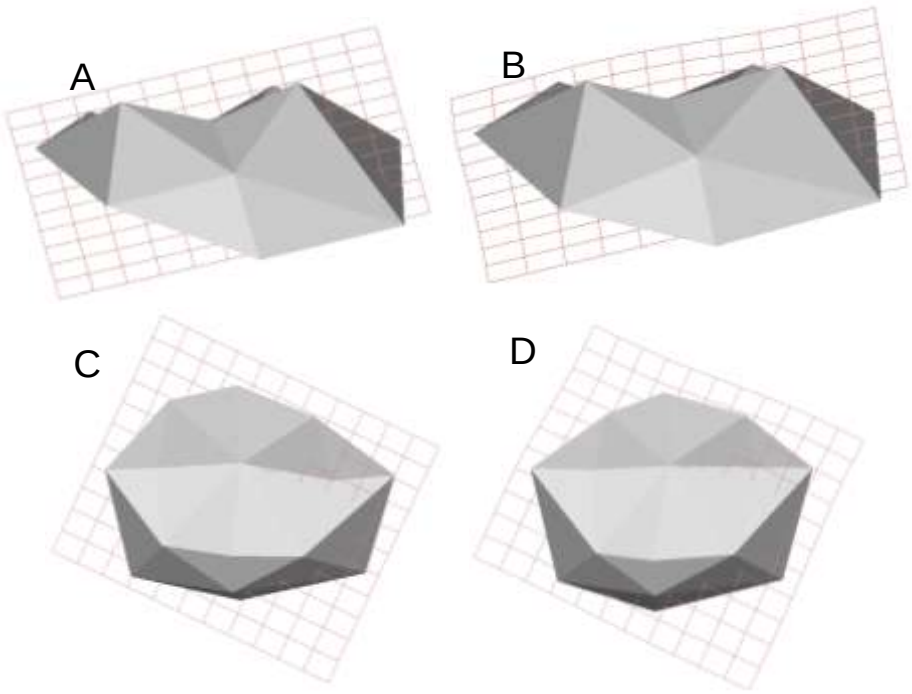

Figure 4.48 **Lower right second molar, Shape variation along PC1 visualized with a transformation grid using thin-plate splines derived from the difference between reference form (control subject - A: Buccal view, C: Occlusal view) and target form (severe hypodontia - B: Buccal view, D: Occlusal view).**

Chapter 5 Discussion

This is the largest and most comprehensive 3D morphometric study on tooth shape that has concentrated on subjects with hypodontia. In a recent review of the multivariate statistical approach to measuring teeth, Townsend et al. (2009a) point out that previous researchers have all used the traditional method of measuring crown diameters, and suggest that new measurement techniques that provide more information about tooth form should be adopted. This is the first study of modern human dentitions to implement a comprehensive multivariate statistical analysis of tooth size and shape. Three main variation factors have been considered in this project: size, shape and allometric variation. These factors were tested in comparisons between control subjects and hypodontia groups and between hypodontia groups themselves. Separate statistical models were built for each factor.

This chapter consists of seven parts: in the first part the application of geometric morphometric methods in the dental field is discussed; in the second part, a discussion of the study design and the main population. The discussion of the main findings is presented in the third and the fourth parts. The findings are divided into tooth variation (size, shape and allometric variations) and sexual dimorphism (sexual dimorphism in size and shape); part five describes the clinical relevance of this study, and in the last two parts conclusions and recommendations are drawn from the study according to each of the stated aims.

5.1 The geometric morphometric method

Landmark-based geometric morphometric methods (GMM) (Rohlf and Marcus, 1993; Adams *et al.*, 2004; Zelditch *et al.*, 2004; Baab and McNulty, 2009) capture the form of a structure, providing information about the geometry of the tooth; this geometry is difficult to quantify using traditional methods. Landmark methods offer advantages over traditional methods, particularly whenever landmarks represent well defined, biologically homologous points (Jensen, 2003). Furthermore, the use of the 3D scanning imaging system enabled the researcher to capture detailed information within all coordinates. The choice of landmarks is a crucial step in the analysis (Robinson *et al.*, 2002). The use of outline methods, in which landmarks are equally spaced points on the object's contour

and do not depend on the explicit identification of anatomical landmarks (Adams *et al.*, 2004), does result in a large amount of information about surfaces; however, it presents problems in terms of biological meaningfulness and the large number of variables produced (Viscosi and Cardini, 2011). In order to quantify size and shape, GMM analyse the relative positions of anatomical landmarks used to approximate the outlines and surfaces of the tested object. The geometric information about shape variation is retained and statistical power is increased. A variety of diagrams are available for use in GMM, which make it possible to visualize shape patterns. Furthermore, an increasing number of published biological studies and other studies in different fields have been demonstrating and confirming the efficacy of this set of methods (Viscosi and Cardini, 2011).

In this study the number of anatomical points was identified for each tooth type to enable the researcher to capture the maximum amount of information about the crown morphology (e.g., molars have a large number of landmarks, whereas incisors and canines have a small number because they are less complex), while taking care to obtain the optimal number of landmarks. The landmarks consist of features such as cusp-tips and fissure junctions that are usually used in clinical measurements. Increasing the number of points used to describe a structure quantitatively may also lead to problems in parametric statistical testing, as the number of variables easily becomes larger than the sample size and tests may not always be possible; assumptions are more difficult to test and estimates of parameters (e.g., means and variances) could be problematic. Further care is addressed to allow a successful implementation of landmarks which depend on the accuracy and reliability of the landmarks identification. The findings of this study, however, indicate a negligible error on both main levels of error (scanning and digitization).

Bernal (2007) obtained more information about molar contour when he used a landmark-based method, rather than measuring crown diameters. According to Bailey (2004), information that is obtained from measuring the mesiodistal (MD) and buccolingual (BL) dimensions as well as the crown indices (i.e., (MD/BL) ratio), is insufficient to describe tooth shape. This reflects the serious limitation of traditional methods to describe the shape of irregular objects, in that no information about the geometry of the tooth in inter-landmark areas is retained. GMM preserve information about the geometry of the structure described by a specific landmark configuration: i.e., the pattern of the relative positions of anatomical points and changes in these positions across individuals and between groups (Monteiro *et al.*, 2002; Adams *et al.*, 2004; Zelditch *et al.*, 2004). In

Procrustes-based GMM, size and shape are explicitly and rigorously defined and produce a set of morphometric descriptors with desirable statistical properties (Rohlf, 2003). The traditional methods succeed in measuring size but can only inaccurately estimate shape. Bernal (2007) claimed that both traditional methods and GMM have a comparable accuracy in estimating size. However, 2D GMM does not show as much about the contour and fine details of the tooth shapes as do 3D methods. 3D is more accurate and does not squeeze the third dimension, whereas 2D methods poorly approximate 3D structures. 3D GMM overcome any difficulties the researcher may have in orientating to the imaged object if working on 2D projections of 3D objects (Gómez-Robles *et al.*, 2007). Various studies have indicated the differences between the traditional and landmark-based methods (Dos Reis *et al.*, 2002; Monteiro *et al.*, 2002; Perez *et al.*, 2006), and it has been suggested that the use of GMM increases power and accuracy (Rohlf and Marcus, 1993). Thus, GMM might provide data that are biologically more meaningful than conventional measures of crown morphology, thereby potentially advancing our knowledge of dental morphological variability from a clinical perspective. Besides, no traditional morphometric method allows for the effective visualization achieved by GMM using shape diagrams (e.g., Thin-Plate Spline) and image/surface rendering. Shape variation interpretation in traditional morphometrics is done by looking at the PC loadings, but in GMM this cannot be done based on PC loadings. Instead, diagrams are used to visualize shape differences between two groups (Viscosi and Cardini, 2011). The thin-plate spline interpolation enables investigators to explore variations in the space whose boundaries are defined by the landmarks, and to visualize shape differences between a reference and a target regardless of the superimposition used to compute the shape coordinates. It also allows clinicians to explore shape variation among different groups in greater detail, especially if it is performed in 3D. Additionally, 3D GMM may provide additional insights into the role played by the highly complex and interrelated factors (genetic, epigenetic and environmental factors) in influencing the long process of dental development (Townsend *et al.*, 2011).

The theory of statistical shape analysis is complex and requires a strong background in mathematics to be fully understood. However, the methods are now well established. Also, the software for the application of a variety of GMM techniques now includes a wide range of user-friendly and mostly freeware programs. Multivariate statistics is necessary in order to perform shape analysis correctly, because shape is inherently

multivariate, and this is reflected in the 'nature' of Procrustes shape data (Zelditch *et al.*, 2004; Viscosi and Cardini, 2011). However, the principle of most multivariate methods is the same as that of their univariate equivalent and the range of programs available for their application is even broader than for GMM. Often, GMM programs will include routines for multivariate statistics. The option of performing a series of univariate tests on single shape variables is rarely, if ever, adequate, as discussed in a number of studies (Rohlf, 1998; Adams *et al.*, 2004; Zelditch *et al.*, 2004; Viscosi and Cardini, 2011).

5.2 Study design and population

Four groups were analysed, control subjects and three hypodontia groups. The hypodontia groups were classified according to the number of missing teeth into three groups. The hypodontia groups have drawn from the hypodontia database in Newcastle Dental Hospital in the north east of England. This group of non-syndromic untreated patients is considered as a representative group of the wider population of hypodontia. The patients were untreated as teeth may be altered by orthodontic or prosthodontic mechanics. The syndromic cases were excluded from the study since it has different aetiological casuses. Teeth affected by wear and attrition are also excluded as they may affect the size and shape measurements.

The control group in this study included subjects attending orthodontic clinic in Newcastle Dental Hospital from the same demographic area and the same ethnicity of the hypodontia groups to rule out influencing factors such as ethnicity differences or environmental factors. In addition, the control subjects were age and sex-matched to the hypodontia groups. Groups were distributed equally within the sample. The sample age group was 12 – 18 years to avoid any measurement bias and to avoid any other factors such as high age range that might affect enamel of the teeth such as enamel wear or attrition or gingival recession. The study design matches what has been presented in many previous studies that have investigated size differences in hypodontia (Brook *et al.*, 2002; McKeown *et al.*, 2002; Brook *et al.*, 2009b).

5.3 Tooth variation in hypodontia

5.3.1 Size

In general, it was found that the hypodontia subjects had a smaller tooth size than the control group. The more severe the hypodontia, the more marked was the reduction in tooth size with the mean size values decreasing progressively from the control subjects through mild, moderate and then severe hypodontia. This finding concerning centroid size, obtained using GMM, is consistent with those of previous studies that have employed traditional measurement techniques that have also demonstrated this trend and shown that tooth size reduction is associated with hypodontia (Garn and Lewis, 1970; Baum and Cohen, 1971c; Rune and Sarnas, 1974; Brook, 1984; Ooshima *et al.*, 1996; Schalk-van der Weide and Bosman, 1996; Brook *et al.*, 2002; McKeown *et al.*, 2002; Brook *et al.*, 2009b). Also, many other researchers have reported that the degree of size reduction was associated with the degree of the severity of the hypodontia (Rantanen, 1956; Alvesalo and Portin, 1969; Garn and Lewis, 1970; Lavelle, 1970; Rune and Sarnas, 1974; Brook, 1984; Brook *et al.*, 2009c; Mirabella *et al.*, 2011; Yaqoob *et al.*, 2011). This may indicate that part of the cause lies in genetic components. It has also been noted that dental agenesis is genetically heterogeneous, which indicates that more than one gene or different mutations in the same gene contribute to its clinical variations (Vastardis, 2000). Furthermore, other groups of researchers claim that different independent genes can act alone or in combination with other genes, leading to different patterns of agenesis (Tan *et al.*, 2011). This leads us to say that in hypodontia subjects different genes are responsible for the anomalies. In fact, this correlation between the findings obtained using this novel 3D GM methodology and those obtained using the old traditional morphometrics will help to fill the gap in our understanding of the aetiological factors that lie behind the dental developmental process and allow new researchers to establish a proper link between the early molecular events and the present variations within the human dentition. For example, the limited knowledge of shape that has been obtained by the metric and non-metric dental variables should be overcome by the use of GMM in corporation with multivariate shape statistics. This knowledge will indeed greatly improve clinical practice in both diagnosis and treatment planning and counselling and usher in a new era in methods of investigating the causes of and the relationships between different types of dental anomaly: i.e., tooth number, size and shape.

The moderate and severe hypodontia groups showed reductions in tooth size when compared with the controls across the whole dentition. The mild hypodontia group when compared with the controls, on the other hand, showed a significant reduction in tooth size for premolar and anterior teeth only and not in the molar teeth for both males and females (Figures 4.11 and 4.12). Bearing in mind the fact that the number of missing teeth in the anterior region was larger in the mild hypodontia group than in the other hypodontia subgroups, the above finding may be explained by a local effect of the location of the hypodontia: in other words, the nearer the tooth to the location of the missing tooth the more affected it was by size reduction. This is consistent with the "Local Field Effect Theory" suggested by Khalaf et al. (2009c) , applied to the presence of supernumerary teeth. This trend may suggest also that the influence of the degree of severity of the hypodontia on the size of remaining teeth is variable. This could be explained by the differential impact of the environmental conditions on each type of hypodontia in relation to the degree of reaction of the individuals to adverse environmental conditions.

The degree of variation in size within the dentition was found to be more pronounced in the anterior than in the posterior region for all hypodontia groups when compared to the controls. Baum and Cohen's (1971a) findings also suggested a greater variation in the anterior than in the posterior region. Brook et al. (2009b) found a trend for the anterior teeth to be more affected and to show a greater reduction in size when compared to control subjects. Potter et al. (1976) also reported that genetic factors control whole regions of the dentition rather than specific teeth. This trend will further explain the complex aetiology of anomalies in tooth number and size, which is in agreement with the multifactorial model of tooth development proposed by Brook (1984; 2009). The model suggests an association between different types of anomaly and proposes that they be considered in one single model. The model also proposes a complex process of developmental interaction between genetic, epigenetic and environmental factors. This is a multilevel process, taking place at molecular and cellular levels, which interact to produce a clinical outcome. It is also a multidimensional process, as it grows and develops on three axes: x, y and z, and in the fourth dimension of time. It is also a long-term process and might be affected by various factors: genetic, epigenetic or environmental. This has been readdressed recently in a study carried out by Brook and his colleagues (2009b), in which size variation within the dentition was found to be affected

by the degree of anomaly in tooth number, and there were more variations close to the area of the anomaly.

In the comparisons within the hypodontia subgroups the only differences found were between the mild and severe hypodontia groups, and these were more pronounced in males. This trend is congruent with Baum and Cohen's (1971b) finding of greater size reduction in males than in females. Brook has described this in a single multifactorial model (1984; 2009). The model suggests that male hypodontia subjects deviate further from the mean tooth size of male control subjects than female hypodontia subjects from the mean tooth size of female control subjects. In other words, male hypodontia subjects deviate further from their normal mean than female hypodontia subjects, while the converse is true for subjects with supernumerary teeth. However, this might also be explained by a lack of power in small samples, when group differences are expected to be smaller (e.g., mild vs. moderate and moderate vs. severe).

According to Butler's morphogenetic theory (1939), within each field, one "key" tooth is presumed to be stable; flanking teeth within the field become progressively less stable. Dahlberg (1945) updated this concept for the human dentition and suggested a field for each of the four classes: incisors, canines, premolars and molars. The suggested key teeth are central incisor, canine, first premolar and first molar. The concept is that the most distal tooth is the tooth which varies most within the class. In this project, all teeth showed differences in crown size with different percentages of variation. The average variance differed according to the position of the tooth type within its region. The pattern here supports morphogenetic field theory most of the time for both sexes, but some of the teeth show a reversed pattern. In female subjects, for example, the upper first premolars were found to be more varied in size than the upper second premolars, and the lower left lateral incisors had a greater size variation than the central incisors (see Table 5.1). On the other hand, in male subjects, upper left first premolars had a greater size variation than upper left second premolars, and lower lateral incisors were more varied in size than the corresponding central incisors (see Table 5.1). The reverse trend in female lower incisors was also reported recently by Brook et al. (2009b). The multifactorial model including genetic, epigenetic and environmental factors may help to explain the differences in the expression of size variation in hypodontia patients. This may suggest that different genetic components are involved in the developmental process, with some variations in the local epigenetic events in the odontogenesis phase. This explanation is supported by Kangas et

al. (2004), who showed that the factors that cause the congenital absence of teeth are not independent of one another but are all interlinked. The fact that the size and shape of teeth in hypodontia subjects as well as morphogenetic traits are intercorrelated within and among tooth types is further addressed by Townsend et al. (2009b) in their twin studies who proposed viewing this opinion clinically using findings on dental patterning in individuals with missing and extra teeth .

		Female subjects		Male subjects	
Tooth class	**Tooth #**	**Average Variance (%)**	**Variance diff**	**Average Variance (%)**	**Variance diff**
Molar region	**16**	27.25	17 > 16	17.57	17 > 16
	17	30.21		20.11	
	26	14.18 (P)	27 > 26	14.18 (P)	27 > 26
	27	18.36		19.18	
	36	19.67	37 > 36	15.86	37 > 36
	37	22.36		20.34	
	46	21.17	47 > 46	19.11	47 > 46
	47	27.39		25.15	
Premolar region	**14**	45.97	**14 > 15**	24.35	15 > 14
	15	25.39 (P)		25.39 (P)	
	24	33.17 (P)	**24 > 25**	33.17 (P)	**24 > 25**
	25	25.84		22.61	
	34	26.93 (P)	35 > 34	26.93 (P)	35 > 34
	35	29.67 (P)		29.67 (P)	
	44	24.19 (P)	45 > 44	24.19 (P)	45 > 44
	45	33.13 (P)		33.13 (P)	
Incisor region	**11**	19.79	12 > 11	36.41	12 > 11
	12	42.65		42.78	
	21	21.06	22 > 21	33.58	22 > 21
	22	33.64		40.51	
	32	32.32 (P)	**32 > 31**	32.32 (P)	**32 > 31**
	31	27.06 (P)		27.06 (P)	
	42	29.32	41 > 42	46.74	**42 > 41**
	41	31.14 (P)		31.14 (P)	

Table 5.1 **Variations in size between tooth types in the same region in both sexes. Right-hand table shows size variations in female subjects; left-hand table shows size variations in male subjects; (P) pooled sexes.**

Harris (1988; 2003) demonstrated that most of the variation is related to the type, rather than the position of the tooth, as no evidence of negative correlation was found between pairs of teeth within the same field. In this study, however, although there did appear to be a general trend of size variation according to tooth type between the hypodontia groups and control subjects, there was a noticeable difference between the anterior and posterior regions in this respect, with anterior teeth showing a greater variation than posterior teeth. In addition, it was found that the pattern of variation in the upper jaw was different from that in the lower jaw, which is in agreement with the review of McCollum and Sharpe (2001), who reported differences in morphogenesis between upper teeth and lower teeth. This may demonstrate the complexity of the underlying morphogenesis, which is under the control of different genetic programmes. After conducting a series of studies, Gomez-Robles (2007; 2008) reported that the evolution of the human dentition is monitored by a complex mixed pattern rather than a simple explanation.

The complexity of the aetiology and interlink between genetic, epigenetic and environmental factors (Brook, 2009) and also the lack of a quantitative method such as a 3D method to quantify tooth form accurately and extensively may partly explain why different authors have reached different conclusions as to the cause of changes in tooth shape and size (Townsend *et al.*, 2009a). Thus, Brook (2009b) points out that clinical practice needs a knowledge of tooth shape as well as size, and recommends using data from 3D imaging techniques to acquire more information about tooth form, since all previous studies have tended to use a traditional morphometric technique based on linear tools only. Furthermore, a very recent review recommends the use of GMM and multivariate shape statistics to quantify the crown morphology (Townsend *et al.*, 2011). The methodology of the present study was based on the use of GMM in conjunction with multivariate statistical analysis. This method may help to enhance our knowledge and open up a clear future line of research that will assist in understanding the underlying aetiological factors of the dental developmental process and that will add more value to clinical based research.

Sofaer and colleagues (1971) reported in their study that teeth on the left side were more affected than those on the right side. There is no evidence to support this statement in the findings of the present study, and in fact there seemed to be a propensity for there to be slightly larger differences on the right side compared to the left, although this finding was not consistent. A recent study on tooth dimensions in hypodontia patients with PAX9

mutation showed the same trend but with different percentages of variation (Brook *et al.*, 2009a). However, other researchers have reported no significant asymmetry in either the control (Khalaf *et al.*, 2009b) or the hypodontia groups (Brook *et al.*, 2009a). Testing asymmetries, however, was not one of the aims of the current research, and larger samples would be required to detect the presumably small right to left differences.

5.3.2 Shape

It was found that the hypodontia groups had different tooth shapes from the control group. Generally, the more severe the hypodontia, the higher the degree of tooth shape differences. The variation in shape within hypodontia subgroups was found to affect the whole dentition but was manifested mainly in the posterior dentition (Figures 4.15 and 4.16). This trend does not completely support the findings of Axelsson and Kirveskari (1983), who reported that the lateral incisor showed the greatest variability of crown shape in the maxilla, and the central incisor in the mandible. First molars showed the greatest stability in crown form. This contradiction might be owing to differences between the populations (Northeast Iceland vs. Northeast UK), differences in methodology (linear morphometrics: i.e., crown indices, vs. geometric morphometrics: i.e., GMM), or they might have been related to differences in genetic and environmental components or might be due to the limitations of their sample.

In the current research, the shape of the teeth in the hypodontia subgroups showed a progressive shortening of the clinical crown at the gingival margin. In addition, the gingival margin became flatter with a less bulbous labial surface as the shape warped from the control towards the hypodontia subjects. Furthermore, the buccal cusp tips of hypodontia subjects were less prominent than those of the control subjects for posterior teeth. The proximal surfaces were less tapered towards the occlusal surface in hypodontia when compared to control subjects.

According to Kondo and Townsend (2006), shape variation in teeth is related more to genetic and environmental than to other factors; however, they also state that these changes are expressed more in the crown development stage, which is congruent with the findings in Brook's review (2009). The stage of tooth morphogenesis within the development process controls the presence or absence and the size and shape of the individual tooth (Brook, 2009). Larger upper first molars tend to display Carabelli cusps,

while smaller molars tend to have no or less developed Carabelli cusps (Kondo and Townsend, 2006). This is consistent with our finding suggesting that hypodontia patients, with their generally smaller teeth, tend to have flatter occlusal surfaces with less prominent cusps in all molar teeth. Other researchers who have measured crown height (Miyabara, 1915; Bolton, 1958; Lavelle, 1968; Volchansky *et al.*, 1981) or the crown shape index (Garn *et al.*, 1967; Lavelle, 1968; Lavelle, 1970) found shorter crowns and smaller crown indices among hypodontia subjects. However, the nature of the measurements they used inevitably limited the amount of information they were able to capture concerning the morphology of the teeth. Robinson and colleagues (2001) applied Procrustes methods to images using the image-analysis system developed by Brook et al. (1998) to explore differences in the buccal surface of the upper central incisors. The results of their study indicated that the teeth of hypodontia patients were different in shape at the incisal corners, such that the incisors were more tapered towards the incisal edge than those of control subjects. Again their investigation was limited to only one surface, which was based on a 2D imaging system. The 3D GM method of analysing and describing tooth shape variation used in the current study produces far more descriptive results than any of the methods employed in previous research in this area. This result enables clinicians to see visually the degree of tooth shape variation between hypodontia groups and control subjects.

In the current research it was also found that shape variation was not localized to a particular tooth but generalized among all teeth (Figures 4.15 and 4.16), with a consistent noticeable pattern of the degree of shape variation being higher in the distal tooth in each class (see Table 5.2 below), which completely supports the morphogenetic field theory. Although shape variations with this specific pattern were found in both the hypodontia groups and the control group, the percentages of explained variance in tooth shape are lower than for tooth size. This is a common finding in shape analysis and it is likely to be related to the multifactorial nature of shape variation, which makes it more resilient to strong changes in response to a single specific factor.

Tooth type	Tooth number	Sex	Average variance (%)	Variance difference
Molar region	16	P	6.94	17 > 16
	17	P	**8.14**	
	26	P	4.07	27 > 26
	27	P	**6.15**	
	36	F	8.49	37 > 36
		M	7.57	
	37	P	**9.22**	
	46	F	9.63	47 > 46
		M	7.63	
	47	P	**10.11**	
Premolar region	14	P	8.1	15 > 14
	15	P	**9.02**	
	24	P	5.98	25 > 24
	25	P	**6.26**	
	34	P	7.15	35 >34
	35	P	**7.67**	
	44	P	6.82	45 > 44
	45	P	**7.84**	
Incisor region	11	P	0.063	12 > 11
	12	P	**3.77**	
	21	P	4.83	22 > 21
	22	P	**6.56**	
	32	P	6.79	31 > 32
	31	F	**7.92**	
		M	**12.42**	
	42	F	7.01	41 > 42
		M	9.22	
	41	F	**8.15**	
		M	**11.21**	

Table 5.2 **Differences in shape variation among tooth types in the same region. (P) pooled sexes, (F) females and (M) males.**

5.3.3 Allometric effects

Shape differences were assessed while controlling for allometry (the relation between size and shape when both are calculated separately) in order to determine whether these were related solely to shape or were simply the result of size differences. Generally, the geometric morphometric method (GMM) efficiently separates size from shape but they do not remove any covariation between these two factors.

Allometric variation was found to be expressed more obviously in control subjects than in all the hypodontia groups. In addition, the more severe the hypodontia the less allometric variation was found. The characteristics of the form of each individual tooth became clearer as we moved from severe to moderate followed by mild hypodontia and finally to the control subjects. This may be explained by the complex nature of the tooth shape of the control subjects. The tooth forms in the control subjects were well developed, and all features (namely, grooves, fissures and cusp tips, which support the complexity of these teeth) were all well defined. The more severe the hypodontia, the less complex in shape were the teeth and the greater variability they showed. The allometric variance across all the eight groups was in the same range as reported by previous studies (Martinón-Torres *et al.*, 2006; Gómez-Robles *et al.*, 2007).

Variations found in centroid size indicated that the effect of allometry was significant in each group for most of the teeth. However, the differences were not simply allometric in nature, because even after controlling for the effect of allometry in a MANCOVA, group differences were significant: for example, among the male moderate hypodontia subjects, the lower left first molar showed an allometric variation; however, the 'size-corrected' shape analyses were virtually identical to those for the actual shape without size correction, which would be expected if the effect of size on shape were negligible. This means that shape variation across groups is not simply a 'side-effect' of size differences, which were large for most teeth. In conclusion, the allometric effect was found to be very small, which means that it cannot be considered to be a factor in causing the variations in crown morphology.

5.4 Sexual dimorphism

An analytical design was built to test each sex separately when there is sexual dimorphism. Bearing in mind the fact that the more you increase the number of tests, the more you increase the rate of Type I error, which means that the null hypothesis may be rejected when it should not be. The female and male data were pooled where no significant sexual dimorphism was evident. This choice may help to increase the statistical power and help to reduce the errors in all parameter estimates (means, variances etc.) as the sample size is increased.

5.4.1 Size

The mean centroid size (CS) was found to be significantly greater in males than in females for most of the teeth. The results revealed a non-significant interaction between groups and sexes for all teeth except the lower right canine. This indicates that the pattern of sexual dimorphism in tooth size was similar across groups. Tooth size reduction was seen in both sexes but was more pronounced in males with hypodontia, who had more teeth reduced in size than females with hypodontia when compared to male and female controls respectively. Previous studies have demonstrated sexual dimorphism in size, reporting that the teeth of females are smaller than those of males, but with differences in the frequency of occurrence and degree of expression. (Miyabara, 1915; Baum and Cohen, 1971b; Lavelle, 1972; Richardson and Malhotra, 1975; Perzigian, 1976; Potter *et al.*, 1981; Axelsson and Kirveskari, 1983; Kieser *et al.*, 1985; Townsend and Martin, 1992; Yuen *et al.*, 1997; Pinkerton *et al.*, 1999). Others have found no differences between the sexes (Grahnen, 1956; Rune and Sarnas, 1974).

The findings of the present study revealed that the explained variance within the male hypodontia groups, when present, was higher than that in female hypodontia groups when compared to their corresponding control subjects (Figures 4.11 and 4.12). Similarly, a recent study conducted by Brook et al. (2009b) found that, on average, the percentage reductions in the tooth dimensions for MD and BL measurements were higher in males than in females, which indicates that the degree of tooth size variation was higher in the male subjects. This could be explained by Brook's model (1984; 2009) that suggests that the teeth of male hypodontia subjects deviate further from the normal mean than those of females. The expression of tooth size reduction in hypodontia subjects is greater in males than in females.

Brook and his colleagues (2009b) reported that in general males had a greater size reduction than females in the posterior BL dimensions and the anterior MD dimensions, with no clear explanation for this occurrence. The finding of such differences between the anterior and posterior regions could be explained by the serious limitations imposed by the use of traditional morphometrics: that is, their inability to capture the whole geometry of the tooth in the way the 3D landmark-configuration GMM used in the current research do. The main shortcoming of traditional morphometrics is that it treats each landmark separately, which may compromise measurement findings. The findings of the current study revealed general reduction on teeth size but more obvious in the anterior than posterior regions.

In the lower dentition, there was no sexual dimorphism found within any of the groups for the lower incisors or for the lower premolars, with the exception of the lower right lateral incisor. If this were to be confirmed on larger samples, this would suggest that sexual differences do not affect the whole dentition equally. In the upper dentition, however, the whole dentition showed sexual dimorphism, with the exception of three teeth: the upper right second premolar, upper left first premolar and upper left first molar. This may rule out the exclusive effect of a single gene and support the interaction of several different genes in certain environments, that may result in different variations in hypodontia, as reported by Parkin et al. (2009).

5.4.2 Shape

Differences in tooth shape between the sexes were only found in the lower first molar on both sides. This may be explained by the complexity of the shape of this tooth type and by the fact that congenital absence and/or microdontia may have a different aetiology from that of lower first molars. It may due the fact that molars are only rarely missing in hypodontia as in this study only seven lower first molars were missing.

The percentage of shape differences varied between the sexes: greater differences were found between the female hypodontia groups and female control subjects than between the male hypodontia groups and male controls; however, the same pattern of shape variation was found when using the thin-plate spline visualization technique for, e.g., lower first molars, lower central incisors and the lower right canine. This may suggest

that, as with size variation, shape variation is expressed more in female than in male subjects.

In summary, sexual dimorphism of tooth size was found to be more pronounced across the whole dentition than that of tooth shape. This is to be expected because sex-related differences (5%) in the size of human teeth have been reported in the literature (Scott and Turner, 2000). The same small percentage of differences between the sexes was also found in this study within each group for each tooth, with an average difference between the sexes of 4.92%. This appears to suggest that there are no significant differences between the sexes with regard to shape, since even if there were an effect of allometry it would not have been large enough to have a measurable effect on the small samples used in this study.

5.5 Relevance of study findings

Size and shape of teeth have been described using traditional tools limited to selected dental variables or very simple indices. The collected information is limited and does not describe dental variation visually. With the development in the imaging field (i.e., 3D scanner) and the increased knowledge in the multivariate shape statistics (i.e., GMM), it has been possible to overcome such limitations and describe dental variation clinically with a high degree of accuracy and precision. This gained knowledge not only provides improved clinical discrimination but it also explores new lines of research to obtain better understanding of the underlying developmental process that occurs during odontogenesis. Besides helping to differentiate between different groups it may also be able to investigate the contributions of different aetiological factors such as genetic, epigenetic and environmental factors to observed variation (Townsend *et al.*, 2011).

A knowledge of the complexity of the interrelated factors that might create dental anomalies when linked to the morphogenetic field may help to give an idea about which teeth are the most affected: i.e., third molars, second premolars and lateral incisors (Townsend *et al.*, 2009a), and, furthermore, give an idea about the variability within the dentition. Such knowledge will also help the multidisciplinary team with diagnosis and with drawing up treatment plans.

The consequences of the congenital absence of teeth may be both physical and emotional, especially if the missing teeth are located in the anterior region (Hobkirk *et al.*, 2011).

The congenital absence of teeth requires extensive care by a multidisciplinary team. The multidisciplinary team works together to devise the best treatment plan and delivery of care for the management of patients. The role of the dental team is to maintain the remaining dentition, improve aesthetics, improve function, promote psychological and emotional well-being and to encourage the acceptance of such patients by their families and peers. However, what treatment is necessary depends on the pattern of tooth absence, the presence and severity of the microdontia and abnormal tooth shape, the amount of residual spacing, the presence of malocclusion and the attitude of the patient (Valle *et al.*, 2011). The initial steps, including a diagnostic wax-up with a good set of models and radiographs, will certainly lead to clear planning (McNamara *et al.*, 2006).

Clinically, a good knowledge of the size and shape of each tooth enables the clinician to form the provisional and future definitive treatment plans. Furthermore, quantifying tooth shape provides valuable information for evaluating the final tooth position and morphology. The presence of 3D imaging tools may, therefore, add value to the treatment plan presented to the patient.

The present findings have revealed a general trend for the anterior teeth of hypodontia subjects to have flatter labial surfaces and for the posterior teeth to have flatter buccal surfaces than the teeth of control subjects. At the moment, when orthodontic brackets are used for hypodontia patients the final tooth position is not optimal, since the built-in prescriptions are based on the tooth shape of control patients. Also, it would be useful for clinicians to have some knowledge of the consequences of dental anomalies, as many studies have demonstrated a correlation between congenitally missing teeth and delayed eruption, ectopic eruption, malposition, taurodontism, rotation of teeth, short teeth and arch length form alteration (Baccetti, 1998).

In general, from a clinical perspective, many clinicians have found insufficient space for an implant to replace a missing tooth or teeth after orthodontic treatment, even in the presence of good occlusion (Mirabella *et al.*, 2011). They have suggested that this is owing to a generalized size reduction in all teeth. For example, if you would replace a lateral incisor with an implant you need a minimum 6 mm of space to be opened up (Tarnow *et al.*, 2000). One would expect after orthodontic treatment a good posterior occlusion with an appropriate incisor relationship; however, patients with hypodontia have a smaller tooth size than average and anomalous tooth forms, which require careful attention to finishing, including composite build up and/or veneers. This leads us to the

importance of a full knowledge of each tooth shape at the stage of diagnosis and treatment planning to allow clinicians to draw up the right treatment plan before they begin, and then to discuss it with the patients and their parents.

5.6 Conclusions

In this section, the conclusions drawn from the study in relation to each of the research aims are presented.

First aim

To develop a new method based on geometric morphometric analysis to quantify the size and shape of teeth in three dimensions.

Null hypothesis

Geometric morphometric methods are neither applicable nor useful in quantifying tooth size and shape.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- A new, comprehensive 3D method based on landmark configuration is applicable and useful in the analysis of tooth shape and size.

Second aim

To determine whether there are significant differences in 3D tooth size between hypodontia patients and matched control subjects.

Null hypothesis

There are no significant differences in 3D tooth size between hypodontia and control subjects.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- There are significant differences in 3D tooth size between all hypodontia groups and control subjects. Hypodontia subjects have a smaller tooth size than the control subjects.

Third aim

To determine whether there are significant differences in 3D tooth size between mild, moderate and severe hypodontia subgroups.

Null hypothesis

There are no significant differences in 3D tooth size between mild, moderate and severe hypodontia subgroups.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- The more severe the hypodontia the greater the reduction in tooth size. The mean size values decrease progressively from the control subjects through mild, moderate and then severe hypodontia.

Fourth aim

To demonstrate the pattern of size differences between the teeth of hypodontia patients and those of control subjects.

Null hypothesis

There is no pattern of size differences between the teeth of hypodontia patients and those of control subjects.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- The explained variance among group membership is generally larger in the anterior than in the posterior region. Moreover, most of the time this pattern supports morphogenetic field theory. This is the same for both sexes. Within hypodontia groups themselves there is some evidence of a pattern whereby the front teeth and premolars seem to be more strongly affected by size differences. Differences in size variation between hypodontia subgroups are less significant than those between the controls on the one hand and all hypodontia patients on the other.

Fifth aim

To determine whether there are significant differences in 3D tooth shape between hypodontia patients and matched control subjects.

Null hypothesis

There are no significant differences in 3D tooth shape between hypodontia patients and controls.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- Hypodontia subjects have a different tooth shape from the control group. Hypodontia subgroups show a progressive shortening of the clinical crown at the gingival margin. In addition, the gingival margin becomes flatter with a less bulbous labial surface as the shape warps from the control towards the hypodontia subjects. Furthermore, the buccal cusp tips of the posterior teeth of hypodontia subjects are less prominent than those of control subjects. The proximal surfaces are less tapered towards the occlusal surface in hypodontia subjects when compared to control subjects.

Sixth aim

To determine whether there are significant differences in 3D tooth shape between mild, moderate and severe hypodontia subgroups.

Null hypothesis

There are no significant differences in 3D tooth shape between mild, moderate and severe hypodontia subgroups.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- Generally the more severe the hypodontia, the higher the degree of tooth shape differences. The shape variation between hypodontia subgroups seems to be located mostly in the posterior dentition.

Seventh aim

To demonstrate the pattern of shape differences between the teeth of hypodontia patients and control subjects.

Null hypothesis

There is no visible pattern of shape differences between the teeth of hypodontia patients and control subjects.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- There is shape variability in all teeth between and within all groups. There is an obvious pattern, which completely supports the morphogenetic field theory. Posterior teeth are the most affected when hypodontia subgroups are compared.

Eighth aim

To determine if there is a significant difference in 3D tooth allometry between hypodontia patients and control subjects.

Null hypothesis

There are no significant differences in 3D tooth allometry between hypodontia and control subjects.

The null hypothesis was rejected and the related conclusion drawn from the study was:

- The effect of tooth size on shape is significant for most teeth, but mainly in the anterior region, and shape differences are still significant after controlling, when possible, for allometry.

Ninth aim

To determine sexual dimorphism of tooth size and shape.

Null hypothesis

There is no sexual dimorphism of tooth size and shape.

The null hypothesis was rejected and the related conclusions drawn from the study were:

- The mean centroid size (CS) is significantly greater in males than in females for most of the teeth. Tooth size reduction is seen in both sexes, but is more pronounced in males, in that males with hypodontia have more teeth reduced in size than females with hypodontia when they are compared to male and female controls respectively.
- The percentage of shape differences varies between the sexes: females have higher percentages in shape differences than males but with the same pattern.

5.7 Recommendations

The current study raises interesting questions about the potential for future studies using more sophisticated analyses, such as the following:

- Correlations between hypodontia subgroups and genetic or other factors.
- Covariation between different types of hypodontia teeth with differing degrees of severity.
- Varying degrees of variation among tooth types.
- Patterns of asymmetry for both hypodontia groups and control subjects using three-dimensional imaging tools.

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Appendices

- Appendix I Data summary tables
- Appendix II Size analysis for all teeth
- Appendix III Shape analysis for all teeth
- Appendix IV Allometry analysis for all teeth
- Appendix V Shape transformation for all teeth
- Appendix VI Shape visualization for all teeth in 3D (CD attached)

Appendix I Data summary tables

Table 1: Size analysis; summary for upper anterior teeth

#	Groups	Mean (CS) *mm*		ANOVA			Split-sexes	Pairwise comparison					
								groups		P		%	
		Female	Male	Interaction Sex*Groups	Sex	Groups		F	M	F	M	F	M
11	**C**	12.48	13.19	×	0.005	0.001	✓	CM	CM	0.0075	0.0070	17.75	17.18
	M	12.15	12.58					CS	CD	0.0015	0.0006	21.83	29.90
	D	11.71	12.18						CS		0.0001		62.16
	S	11.46	11.40						MS		0.0001		39.40
									DS		0.0069		18.09
21	**C**	12.48	13.11	×	0.033	0.001	✓	CD	CD	0.0073	0.0002	17.14	25.39
	M	12.10	12.45					CS	CS	0.0010	0.0001	24.97	41.76
	D	11.68	11.91						MD		0.0006		24.96
	S	11.35	11.40										
12	**C**	9.60	9.76	×	0.026	0.001	✓	CD	CS	0.0001	0.0002	39.43	42.78
	M	8.60	8.86					CS		0.0001		45.86	
	D	8.16	9.38										
	S	7.62	8.25										
22	**C**	9.34	9.68	×	0.029	0.001	✓	CD	CD	0.0018	0.0039	29.02	31.84
	M	8.10	8.79					CS	CS	0.0001	0.0001	38.26	49.17
	D	8.18	8.62										
	S	7.54	8.08										
13	**C**	10.82	11.47	×	0.009	0.001	✓	CM	CD	0.0018	0.0023	23.28	24.80
	M	10.04	10.67					CS	CS	0.0023	0.0001	26.34	49.24
	D	10.15	10.43										
	S	9.82	9.84										
23	**C**	10.70	11.24	×	0.006	0.001	✓	CM	CS	0.0021	0.0001	24.20	43.74
	M	9.87	10.36					CD		0.0035		23.29	
	D	9.76	10.36					CS		0.0010		29.55	
	S	9.58	9.65										

Tooth number, **C** Control, **M** Mild Hypodontia, **D** Moderate Hypodontia, **S** Severe Hypodontia, **P** P value with a sequential Bonferroni correction, **%** percentage of variance explained by group membership, **x** No, ✓ **Yes, CM** control vs. mild, **CD** control vs. moderate, **CS** control vs. severe, **MS** mild vs. severe, **DS** moderate vs. severe.

Table 2: Size analysis; summary for lower anterior teeth

#	Groups	Mean (CS) *mm*		ANOVA			Split-sexes	Pairwise					
		Female	Male	Interaction Sex*Groups	Sex	Groups		Groups		P		%	
								F	M	F	M	F	M
31	**C**	9.24	9.55	×	×	0.001	×	CM		0.0001		18.22	
	M	8.62	8.36					CD		0.0001		23.59	
	D	8.42	8.27					CS		0.0001		39.38	
	S	8.12	7.82										
41	**C**	9.40	9.66	×	×	0.001	×	CM		0.0001		21.36	
	M	8.66	8.34					CD		0.0001		26.99	
	D	8.30	8.56					CS		0.0001		45.08	
	S	8.24	7.88										
32	**C**	9.47	9.74	×	×	0.001	×	CM		0.0001		24.19	
	M	8.82	9.20					CD		0.0001		32.35	
	D	8.51	8.72					CS		0.0001		40.15	
	S	8.39	8.15					MS		0.0015		22.30	
42	**C**	9.56	9.98	×	0.042	0.001	✓	CM	CD	0.0015	0.0001	24.16	45.05
	M	8.75	9.29					CD	CS	0.0001	0.0001	23.09	48.42
	D	8.56	8.68					CS	MS	0.0001	0.0015	40.71	23.34
	S	8.37	8.27										
33	**C**	10.43	10.91	×	0.034	0.001	✓	CD	CD	0.0017	0.0032	22.00	19.18
	M	9.81	10.39					CS	CS	0.0001	0.0001	34.86	39.04
	D	9.68	9.99						MS		0.0012		24.77
	S	9.20	9.10										
43	**C**	10.42	11.01	✓	×	0.001	✓	CM	CD	0.0035	0.0001	19.80	65.56
	M	9.70	10.33					CD	CS	0.0001	0.0001	32.00	34.58
	D	9.53	8.68					CS	MD	0.0001	0.0001	38.75	44.93
	S	9.05	9.13										

Table 3: Size analysis; summary for upper posterior teeth

#	Groups	Mean (CS) *mm*		ANOVA			Split-sexes	Pairwise					
								Groups		P		%	
		Female	Male	Interaction Sex*Groups	Sex	Groups		F	M	F	M	F	M
14	**C**	12.44	12.35	×	0.045	0.001	✓	CM	CM	0.0001	0.0017	51.17	23.83
	M	11.01	11.71					CD	CD	0.0003	0.0054	29.94	20.92
	D	11.37	11.47					CS	CS	0.0001	0.0026	56.80	28.31
	S	10.82	11.29										
24	**C**	12.27	12.52	×	×	0.001	×	CM		0.0001		27.10	
	M	11.35	11.74					CD		0.0001		28.09	
	D	11.33	11.43					CS		0.0001		44.31	
	S	10.78	10.86					MS		0.0015		16.59	
15	**C**	11.75	11.76	×	×	0.001	×	CM		0.0001		25.67	
	M	10.82	11.08					CD		0.0001		24.39	
	D	10.82	10.91					CS		0.0001		26.11	
	S	10.73	10.53										
25	**C**	11.76	11.92	×	0.032	0.001	✓	CM	CM	0.0028	0.0066	23.53	20.58
	M	11.00	11.34					CD	CD	0.0009	0.0029	27.54	24.18
	D	10.81	11.16					CS	CS	0.0059	0.0002	26.46	23.08
	S	10.70	11.06										
16	**C**	17.27	17.48	×	0.002	0.001	✓						
	M	16.54	17.16					CD	CS	0.0037	0.0062	21.53	17.57
	D	16.31	16.83					CS		0.0001		32.96	
	S	16.11	16.59										
26	**C**	16.99	17.15	×	×	0.004	×						
	M	16.69	17.05					CS		0.0010		14.18	
	D	16.44	16.77										
	S	16.14	16.44										

Table 4: Size analysis; summary for lower posterior teeth

#	Groups	Mean (CS) *mm*		ANOVA			Split-sexes	Pairwise					
		Female	Male	Interaction Sex*Groups	Sex	Groups		Groups		P		%	
								F	M	F	M	F	M
34	**C**	12.21	12.33	×	×	0.001	×	CM		0.0001		26.89	
	M	11.11	11.78					CD		0.0001		23.57	
	D	11.41	11.50					CS		0.0001		30.34	
	S	11.21	10.93										
44	**C**	11.98	12.10	×	×	0.001	×	CM		0.0001		19.70	
	M	11.14	11.72					CD		0.0001		22.41	
	D	11.26	11.30					CS		0.0001		30.47	
	S	11.16	11.13										
35	**C**	12.04	11.87	×	×	0.001	×	CM		0.0001		21.57	
	M	11.16	11.56					CD		0.0001		23.04	
	D	11.38	11.08					CS		0.0001		44.41	
	S	10.84	10.57					MS		0.0065		18.04	
								DS		0.0041		20.63	
45	**C**	12.07	12.11	×	×	0.001	×	CM		0.0001		31.92	
	M	11.02	11.52					CD		0.0001		23.44	
	D	11.12	11.12					CS		0.0001		44.03	
	S	10.63	10.61					MS		0.0020		19.52	
36	**C**	18.58	18.81	×	0.010	0.001	✓	CS	CS	0.0050	0.0081	19.67	15.86
	M	17.88	18.57										
	D	17.84	18.39										
	S	17.51	17.82										
46	**C**	18.29	18.72	×	0.003	0.030	✓	CS	CS	0.0043	0.0076	21.17	19.11
	M	17.89	18.65										
	D	17.98	18.53										
	S	17.65	17.90										

Table 5: Shape analysis; summary for upper anterior teeth

#	MANOVA			Split-sexes	Pairwise						DA					
	Interaction Sex*Groups	Sex	Groups		Groups		P		%		Analysis		X-val		P	
					F	M	F	M	F	M	F	M	F	M	F	M
11	×	0.083	0.001	×	CM CD CS MD		0.0001 0.0001 0.0001 0.0021		6.16 6.18 7.31 4.69		56.00		48.00		0.001	
21	×	0.155	0.001	×	CD CS		0.0023 0.0001		3.98 5.68		54.70		43.40		0.001	
12	×	0.117	0.001	×	CM CD CS		0.0010 0.0010 0.0010		4.01 3.36 3.93		52.00		40.00		0.001	
22	×	0.220	0.006	×	CM CD CS		0.0001 0.0023 0.0009		6.86 6.86 5.97		53.90		36.30		0.005	
13	×	0.001	0.002	✓	---	CM CD CS	---	0.0042 0.0038 0.0008	---	7.85 8.41 11.33	49.30	56.30	25.00	41.00	0.201	0.02
23	×	0.433	0.001	×	CM CD CS		0.0007 0.0018 0.0001		5.80 4.93 8.33		49.30		39.60		0.001	

Table 6: Allometry analysis; summary for upper anterior teeth

#	Groups	Regression				MANCOVA						DA					
		P		%		CS*Groups		CS		Groups		Analysis		X-val		P	
		F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
11	C	0.0486		4.90		x		0.009		0.001		56.00		47.80		0.0001	
	M	0.0343		5.69													
	D	0.3549		2.79													
	S	0.7614		1.72													
21	C	0.0124		6.46		✓		0.032		0.023		Stop here					
	M	0.0093		6.77													
	D	0.5118		2.29													
	S	0.0772		4.47													
12	C	0.1009		4.34		Stop here											
	M	0.1334		10.15													
	D	0.1864		6.18													
	S	0.7783		3.34													
22	C	0.1097		4.02		x		0.306		0.398		Stop here					
	M	0.0121		14.27													
	D	0.3291		5.56													
	S	0.1935		6.28													
13	C	0.0078	0.0370	13.55	10.20	0.017	0.066	0.001	0.022	0.118	0.499	Stop here					
	M	0.0131	0.0117	12.37	16.02												
	D	0.1428	0.0071	8.92	17.20												
	S	0.6569	0.1768	5.57	12.04												
23	C	0.0007		11.48		✓		0.001		0.042		Stop here					
	M	0.0001		11.56													
	D	0.0001		14.37													
	S	0.0621		6.49													

Table 7: Shape analysis; summary for lower anterior teeth

#	MANOVA			Split-sexes	Pairwise						DA					
	Interaction Sex*Groups	Sex	Groups		Groups		P		%		Analysis		X-val		P	
					F	M	F	M	F	M	F	M	F	M	F	M
31	✓	0.189	0.001	✓	CM	CM CD CS	0.0020	0.0025 0.0008 0.0001	7.92	10.19 12.19 14.88	57.70	64.80	42.30	45.10	0.009	0.001
41	✓	0.209	0.002	✓	CS	CS	0.0020	0.0002	8.15	11.21	54.90	59.20	32.40	39.40	0.014	0.008
32	×	0.349	0.001	×	CM CD CS		0.0042 0.0036 0.0025		6.10 5.27 9.01		56.00		47.30		0.001	
42	✓	0.009	0.001	✓	CM	CS	0.0003	0.0001	7.01	9.22	64.50	59.20	50.00	34.40	0.001	0.001
33	×	0.282	0.001	×	CM CD CS MS DS		0.0004 0.0001 0.0001 0.0053 0.0062		4.79 5.03 11.37 3.76 3.89		45.30		34.00		0.001	
43	✓	0.008	0.001	✓	CS	CD CS MD DS	0.0055	0.0001 0.0001 0.0001 0.0001	6.82	22.55 10.39 20.84 25.91	57.50	77.00	38.80	59.50	0.002	0.001

Table 8: Allometry analysis; summary for lower anterior teeth

#	Groups	Regression				MANCOVA						DA					
		P		%		CS*Groups		CS		Groups		Analysis		X-val		P	
		F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
31	C	0.0411	0.4852	11.03	4.92	X	X	0.034	0.001	0.061	0.077	Stop here					
	M	0.0676	0.0002	9.09	35.36												
	D	0.7134	0.0015	3.93	33.59												
	S	0.5579	0.0081	7.08	21.23												
41	C	0.0101	0.1180	13.13	8.12	X	X	0.001	0.001	0.064	0.084	Stop here					
	M	0.3643	0.0001	5.59	34.06												
	D	0.0910	0.0104	9.99	28.14												
	S	0.3796	0.0218	8.92	16.34												
32	C	0.0001		10.76		X		0.376		0.001		56.00		47.30		0.001	
	M	0.0013		8.08													
	D	0.0382		6.54													
	S	0.0216		7.65													
42	C	0.1194	0.0496	8.40	10.86	X	X	0.001	0.001	0.002	0.028	73.70	71.10	50.00	47.40	0.001	0.001
	M	0.0060	0.0403	13.37	10.52												
	D	0.5071	0.0160	4.72	14.71												
	S	0.6887	0.0131	4.18	18.16												
33	C	0.0004		9.00		X		0.094		0.114		Stop here					
	M	0.0001		11.39													
	D	0.0008		10.95													
	S	0.0001		15.24													
43	C	0.0446	0.0008	10.38	16.18	✓	✓	0.001	0.001	0.257	0.045	Stop here					
	M	0.0001	0.0002	15.64	22.92												
	D	0.2677	0.0153	6.37	14.71												
	S	0.0001	0.0030	17.50	19.11												

Table 9: Shape analysis; summary for upper posterior teeth

#	MANOVA			Split-sexes	Pairwise						DA					
	Interaction Sex*Groups	Sex	Groups		Groups		P		%		Analysis		X-val		P	
					F	M	F	M	F	M	F	M	F	M	F	M
14	×	0.308	0.001	×	CM CD CS MS DS		0.0001 0.0002 0.0001 0.0001 0.0002		9.43 5.31 9.56 15.76 8.63		74.80		63.40		0.001	
24	×	0.759	0.001	×	CM CD CS MS DS		0.0001 0.0007 0.0001 0.0001 0.0001		6.63 3.65 7.67 10.70 7.62		69.60		60.70		0.001	
15	×	0.427	0.001	×	CM CD CS MS DS		0.0001 0.0001 0.0001 0.0001 0.0001		8.46 7.51 11.08 16.80 12.36		78.70		68.00		0.001	
25	×	0.816	0.001	×	CM CD CS MS DS		0.0001 0.0001 0.0002 0.0001 0.0001		7.47 5.75 5.55 11.82 4.86		71.70		59.20		0.001	
16	×	0.299	0.001	×	CM CD CS MS DS		0.0001 0.0001 0.0001 0.0001 0.0001		6.09 6.98 7.74 10.06 5.99		71.20		56.40		0.001	
26	×	0.180	0.001	×	CM CD CS MS DS		0.0001 0.0004 0.0005 0.0003 0.0001		4.83 3.58 3.80 3.46 6.24		66.00		47.10		0.001	

Table 10: Allometry analysis; summary for upper posterior teeth

#	Groups	Regression				MANCOVA						DA					
		P		%		CS*Groups		CS		Groups		Analysis		X-val		P	
		F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
14	C	0.0012		7.74		X		0.002		0.064		Stop here					
	M	0.0228		4.82													
	D	0.0432		5.73													
	S	0.2366		6.79													
24	C	0.0046		5.81		X		0.001		0.362		Stop here					
	M	0.2273		3.17													
	D	0.0557		4.95													
	S	0.5297		4.34													
15	C	0.0023		7.34		X		0.026		0.131		Stop here					
	M	0.3931		3.07													
	D	0.1661		5.24													
	S	0.0813		8.11													
25	C	0.5810		2.27		Stop here											
	M	0.7175		2.21													
	D	0.1995		4.71													
	S	0.6271		5.03													
16	C	0.2451		3.03		X		0.012		0.126		Stop here					
	M	0.0022		6.18													
	D	0.1390		3.48													
	S	0.0648		4.25													
26	C	0.2474		3.03		X		0.016		0.053		Stop here					
	M	0.0437		3.98													
	D	0.4080		2.76													
	S	0.2121		3.61													

Table 11: Shape analysis; summary for lower posterior teeth

#	MANOVA			Split-sexes	Pairwise						DA					
	Interaction Sex*Groups	Sex	Groups		Groups		P		%		Analysis		X-val		P	
					F	M	F	M	F	M	F	M	F	M	F	M
34	×	0.312	0.001	×	CM CD CS MD MS DS		0.0001 0.0001 0.0001 0.0017 0.0001 0.0001		12.21 5.86 3.39 14.51 15.76 7.51		72.10		61.40		0.001	
44	×	0.405	0.001	×	CM CD CS MD MS DS		0.0001 0.0001 0.0001 0.0017 0.0001 0.0001		10.68 3.08 6.71 5.58 16.23 6.74		73.90		62.00		0.001	
35	×	0.312	0.001	×	CM CS MS DS		0.0001 0.0001 0.0001 0.0001		7.07 8.26 16.58 14.14		76.50		62.70		0.001	
45	×	0.459	0.001	×	CM CD CS MD MS		0.0001 0.0030 0.0001 0.0001 0.0001		13.72 3.72 6.05 7.29 11.17		77.60		67.30		0.001	
36	✓	0.002	0.001	✓	CM CD CS MD MS DS	CM CD CS MS DS	0.0001 0.0001 0.0001 0.0001 0.0001 0.0002	0.0022 0.0006 0.0001 0.0001 0.0036	11.20 6.61 7.65 18.57 18.27 6.65	6.03 5.82 10.86 10.68 6.95	89.90	79.70	65.80	55.40	0.001	0.001
46	✓	0.009	0.001	✓	CM CD CS MD MS DS	CD CS MD MS DS	0.0001 0.0001 0.0001 0.0001 0.0001 0.0011	0.0005 0.0001 0.0025 0.0001 0.0001	13.17 7.58 8.14 10.46 15.16 5.80	5.78 9.48 5.12 13.15 9.72	85.70	77.60	64.90	42.10	0.001	0.001

Table 12: Allometry analysis; summary for lower posterior teeth

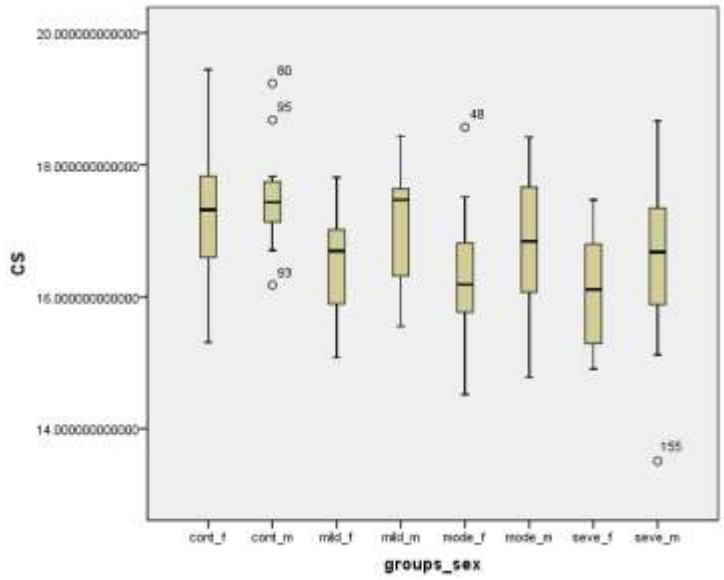
#	Groups	Regression				MANCOVA						DA					
		P		%		CS*Groups		CS		Groups		Analysis		X-val		P	
		F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
34	C	0.0001		8.95		✓		0.004		0.005		Stop here					
	M	0.0024		6.39													
	D	0.1559		4.17													
	S	0.0542		6.44													
44	C	0.0119		5.38		✓		0.002		0.369		Stop here					
	M	0.0728		4.06													
	D	0.4745		2.76													
	S	0.1387		5.12													
35	C	0.0887		4.23		Stop here											
	M	0.1512		4.75													
	D	0.6153		4.97													
	S	0.6322		6.81													
45	C	0.5938		2.32		Stop here											
	M	0.7108		2.52													
	D	0.0983		6.59													
	S	0.1541		12.33													
36	C	0.1171	0.2102	7.05	6.31	X	X	0.078	0.001	0.001	0.001	89.90	79.70	65.80	55.40	0.001	0.001
	M	0.2325	0.5855	6.20	4.72												
	D	0.0649	0.0255	7.48	8.81												
	S	0.4877	0.2569	5.37	8.51												
46	C	0.1849	0.8846	6.45	3.53	X	X	0.03	0.038	0.001	0.001	85.70	77.60	64.90	42.10	0.001	0.001
	M	0.0319	0.8286	8.78	3.77												
	D	0.6804	0.0436	4.79	7.77												
	S	0.5722	0.5073	5.40	6.29												

Appendix II Size analysis for all teeth

Upper right first molar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	17.27	0.90	20
	mild	16.54	0.80	20
	moderate	16.31	0.98	19
	severe	16.11	0.79	18
Male	**control**	17.48	0.65	20
	mild	17.16	0.84	20
	moderate	16.83	0.99	20
	severe	16.59	1.24	19



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	9.143	0.001
sex	1	9.689	0.002
groups * sex	3	0.385	0.764

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	9.248	0.001
sex	1	9.781	0.002

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	16.29%	21.53%	32.96%
mild	0.0093	-	1.70%	0.06%
moderate	0.0037	0.4287	-	1.32%
severe	0.0001	0.8823	0.4875	-

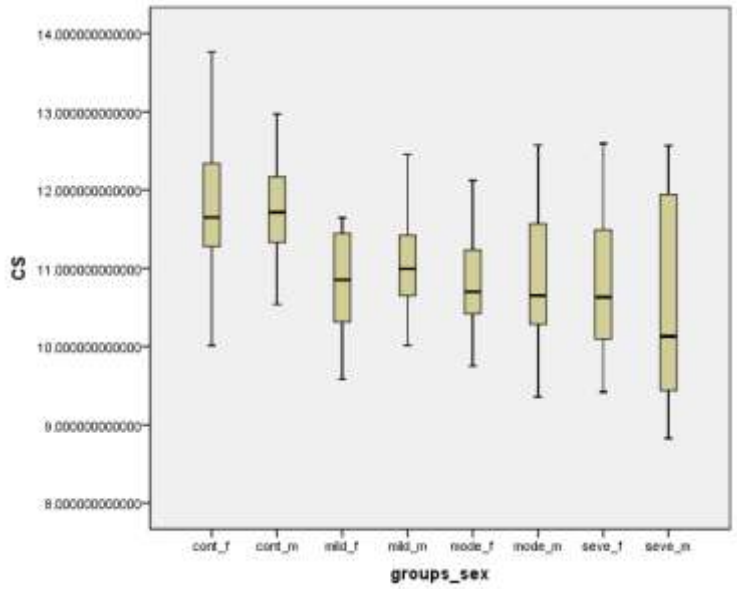
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	4.39%	13.58%	17.57%
mild	0.2007	-	3.39%	7.21%
moderate	0.0208	0.2608	-	1.18%
severe	0.0062	0.1013	0.5131	-

Upper right second premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	11.75	0.89	20
	mild	10.82	0.65	19
	moderate	10.82	0.71	13
	severe	10.73	1.04	9
Male	**control**	11.76	0.60	20
	mild	11.08	0.65	16
	moderate	10.91	0.97	13
	severe	10.53	1.34	12



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	11.099	0.001
sex	1	0.06	0.806
groups * sex	3	0.335	0.800

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	11.593	0.001
sex	1	0.17	0.681

Size variation between groups

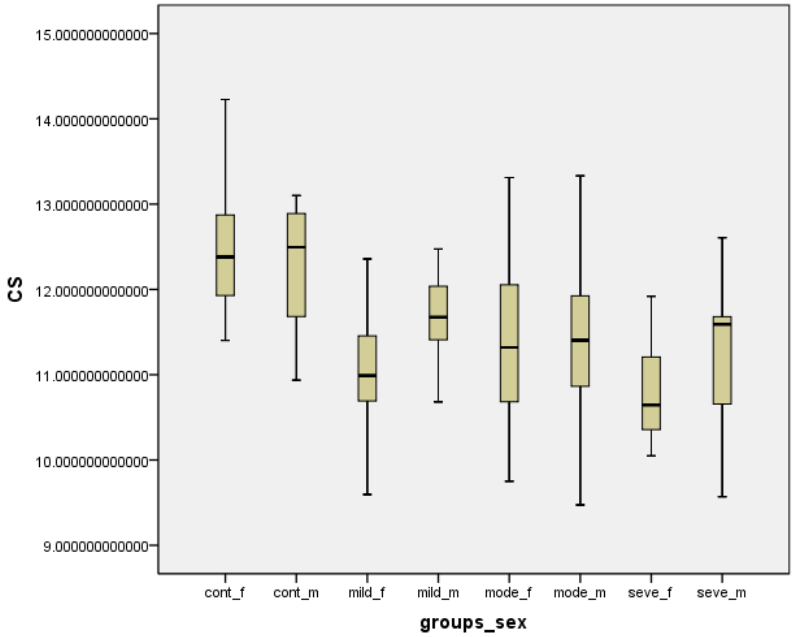
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	25.67%	24.39%	26.11%
mild	<.0001	-	0.26%	2.99%
moderate	<.0001	0.6891	-	1.48%
severe	<.0001	0.1998	0.4189	-

Upper right first premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	control	12.44	0.73	20
	mild	11.01	0.70	20
	moderate	11.37	0.96	15
	severe	10.82	0.59	10
Male	control	12.35	0.68	20
	mild	11.71	0.47	20
	moderate	11.47	1.06	17
	severe	11.29	1.06	9



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	18.468	0.001
sex	1	4.269	0.041
groups * sex	3	1.935	0.127

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	18.182	0.001
sex	1	4.09	0.045

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	51.17%	29.94%	56.80%
mild	<.0001	-	4.66%	2.04%
moderate	0.0003	0.2146	-	10.24%
severe	<.0001	0.4517	0.1194	-

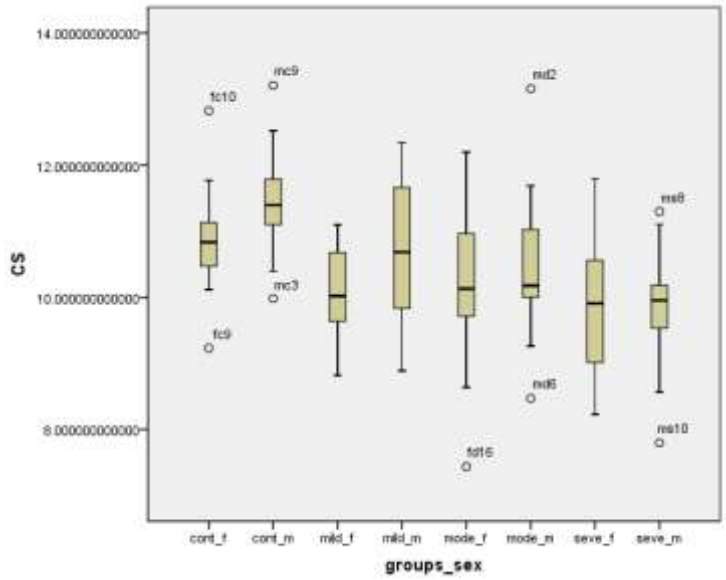
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	23.83%	20.92%	28.31%
mild	0.0017	-	2.35%	7.84%
moderate	0.0054	0.366	-	0.73%
severe	0.0026	0.1421	0.6729	-

Upper right canine

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	10.82	0.74	19
	mild	10.04	0.70	19
	moderate	10.15	1.16	17
	severe	9.82	0.98	14
Male	**control**	11.47	0.74	20
	mild	10.67	1.07	17
	moderate	10.43	1.13	15
	severe	9.84	0.96	12



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	11.354	0.001
sex	1	5.675	0.019
groups * sex	3	0.784	0.505

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	11.278	0.001
sex	1	7.014	0.009

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	23.28%	11.37%	26.34%
mild	0.0018	-	0.32%	1.90%
moderate	0.0408	0.746	-	2.41%
severe	0.0023	0.4389	0.4179	-

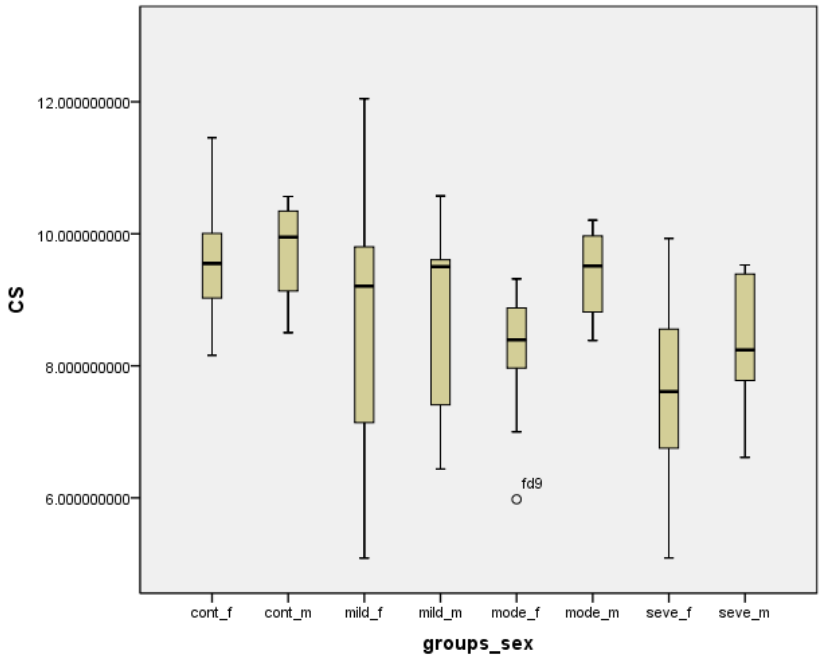
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	17.03%	24.80%	49.24%
mild	0.0112	-	1.25%	14.48%
moderate	0.0023	0.5392	-	7.66%
severe	<.0001	0.0388	0.1687	-

Upper right lateral incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	9.60	0.85	20
	mild	8.60	2.32	7
	moderate	8.16	0.97	13
	severe	7.62	1.37	11
Male	**control**	9.76	0.72	19
	mild	8.86	1.47	9
	moderate	9.38	0.65	10
	severe	8.25	1.08	9



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	10.984	0.001
sex	1	5.454	0.022
groups * sex	3	1.121	0.345

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	11.265	0.001
sex	1	5.1	0.026

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	9.96%	39.43%	45.86%
mild	0.1118	-	2.05%	7.44%
moderate	<.0001	0.5474	-	5.32%
severe	<.0001	0.2763	0.2822	-

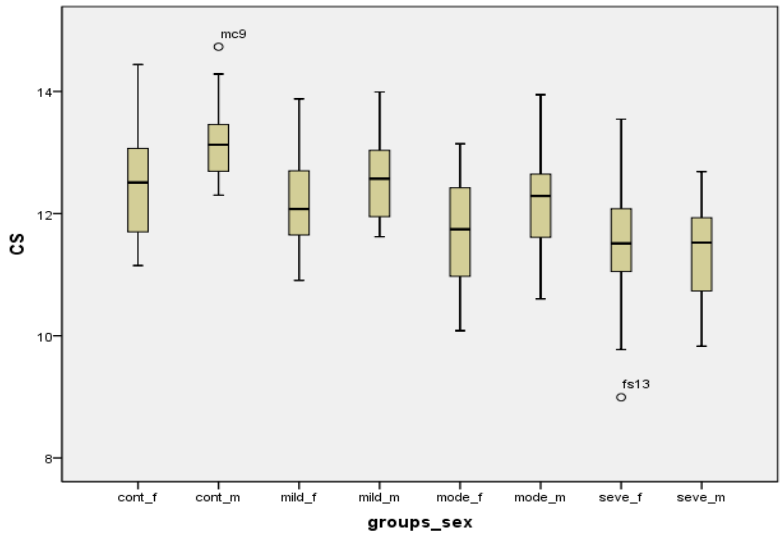
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	15.84%	6.92%	42.78%
mild	0.0317	-	5.70%	5.77%
moderate	0.1639	0.3325	-	31.18%
severe	0.0002	0.3415	0.0116	-

Upper right central incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	12.48	0.83	20
	mild	12.15	0.8	20
	moderate	11.71	0.86	20
	severe	11.46	1.12	20
Male	**control**	13.19	0.65	20
	mild	12.58	0.72	20
	moderate	12.18	0.92	19
	severe	11.4	1.01	20



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	19.946	0.001
sex	1	8.337	0.004
groups * sex	3	1.458	0.228

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	19.778	0.001
sex	1	8.243	0.005

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	4.15%	17.75%	21.83%
mild	0.2060	-	6.70%	11.50%
moderate	0.0057	0.1073	-	1.63%
severe	0.0017	0.0319	0.4379	-

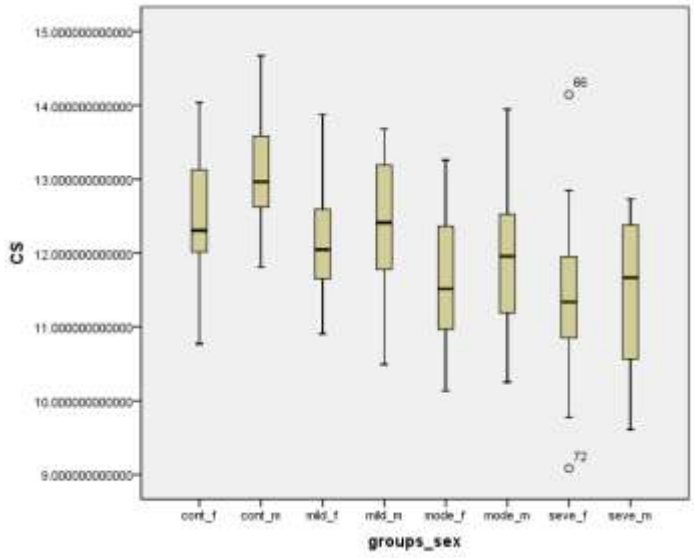
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	17.18%	29.90%	62.16%
mild	0.0070	-	5.83%	39.40%
moderate	0.0006	0.1408	-	18.09%
severe	<.0001	<.0001	0.0069	-

Upper left central incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	control	12.48	0.86	20
	mild	12.10	0.80	19
	moderate	11.68	0.96	20
	severe	11.35	1.14	20
Male	control	13.11	0.73	20
	mild	12.45	0.84	20
	moderate	11.91	1.04	20
	severe	11.40	1.02	20



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	17.236	0.001
sex	1	4.58	0.034
groups * sex	3	0.656	0.580

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	17.355	0.001
sex	1	4.604	0.033

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	5.51%	17.14%	24.97%
mild	0.1526	-	4.80%	11.85%
moderate	0.0073	0.1869	-	2.47%
severe	0.0010	0.0342	0.3356	-

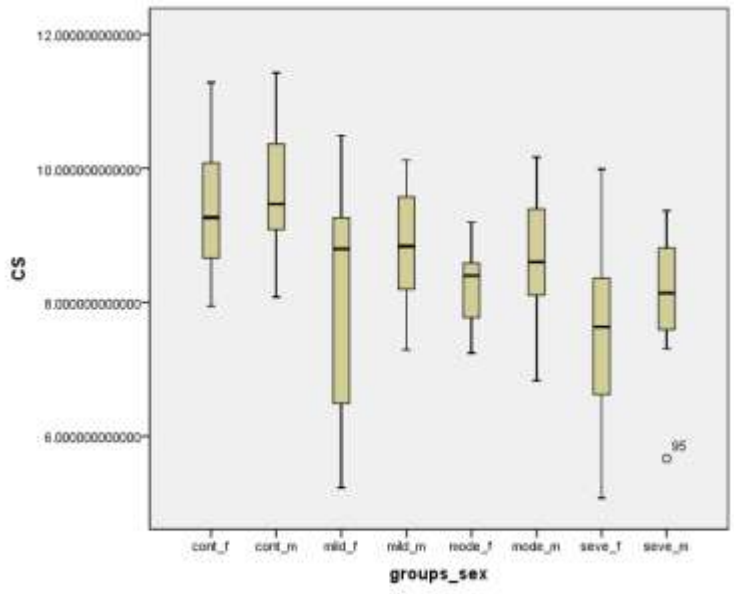
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	15.32%	25.39%	41.76%
mild	0.0125	-	7.98%	24.96%
moderate	0.0002	0.0006	-	6.10%
severe	<.0001	0.1259	0.1261	-

Upper left lateral incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	9.34	1.02	20
	mild	8.10	1.83	8
	moderate	8.18	0.62	11
	severe	7.54	1.34	12
Male	**control**	9.68	0.85	20
	mild	8.79	0.96	10
	moderate	8.62	0.96	10
	severe	8.08	1.07	11



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	13.746	0.001
sex	1	5.06	0.027
groups * sex	3	0.116	0.950

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	14.133	0.001
sex	1	4.937	0.029

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	16.92%	29.02%	38.26%
mild	0.0271	-	0.10%	3.43%
moderate	0.0018	0.9011	-	9.07%
severe	<.0001	0.4232	0.1636	-

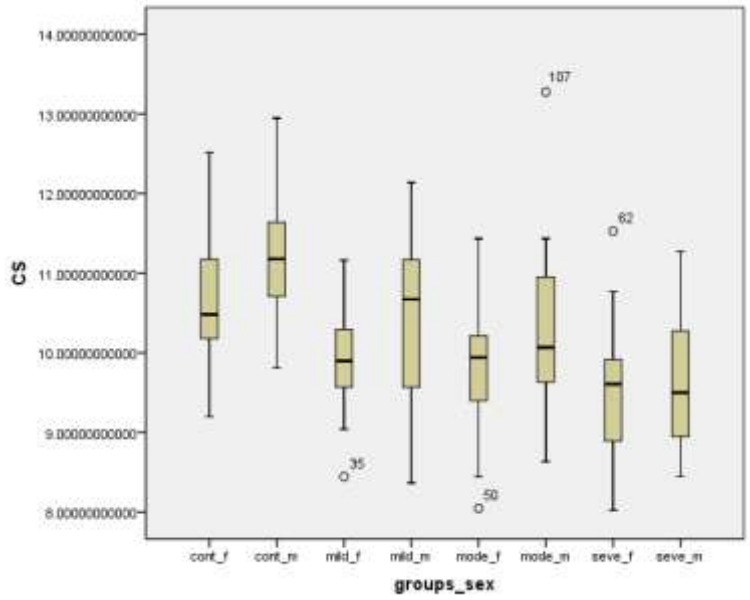
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	19.56%	31.84%	49.17%
mild	0.0147	-	0.83%	11.57%
moderate	0.0039	0.6953	-	7.06%
severe	<.0001	0.1296	0.2457	-

Upper left canine

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	10.70	0.84	20
	mild	9.87	0.64	19
	moderate	9.76	0.91	15
	severe	9.58	0.93	14
Male	**control**	11.24	0.95	20
	mild	10.36	1.08	17
	moderate	10.36	1.16	15
	severe	9.65	0.85	14



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	13.123	0.001
sex	1	6.904	0.010
groups * sex	3	0.492	0.689

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	13.286	0.001
sex	1	7.697	0.006

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	24.20%	23.29%	29.55%
mild	0.0021	-	0.60%	3.66%
moderate	0.0035	0.6584	-	1.00%
severe	0.0010	0.2863	0.6026	-

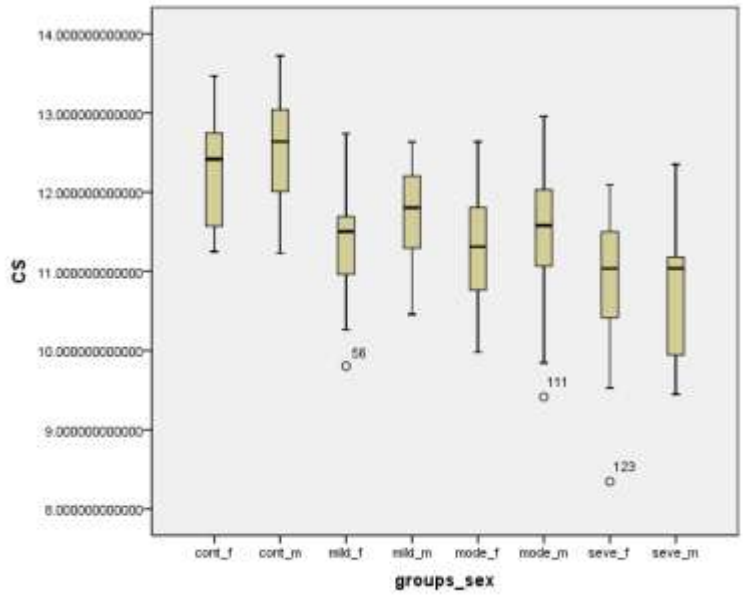
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	16.44%	15.50%	43.74%
mild	0.0100	-	0.00%	12.18%
moderate	0.0182	0.9936	-	11.33%
severe	<.0001	0.0562	0.0743	-

Upper left first premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	control	12.27	0.73	20
	mild	11.35	0.65	20
	moderate	11.33	0.78	16
	severe	10.78	1.09	11
Male	control	12.52	0.80	20
	mild	11.74	0.59	20
	moderate	11.43	0.97	18
	severe	10.86	0.95	10



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	20.399	0.001
sex	1	2.06	0.154
groups * sex	3	0.266	0.850

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	20.743	0.001
sex	1	2.763	0.099

Size variation between groups

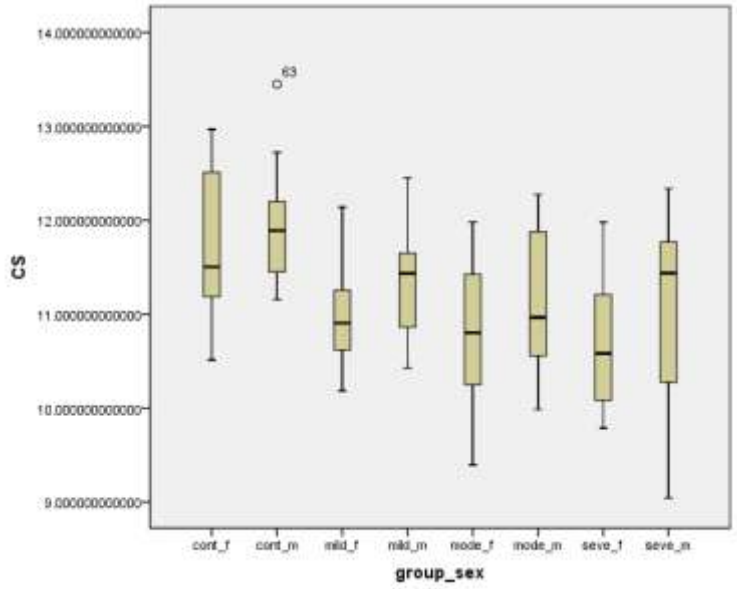
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	27.10%	28.09%	44.31%
mild	<.0001	-	1.10%	16.59%
moderate	<.0001	0.3713	-	8.41%
severe	<.0001	0.0015	0.0323	-

Upper left second premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	11.76	0.79	20
	mild	11.00	0.58	18
	moderate	10.81	0.77	15
	severe	10.70	0.82	7
Male	**control**	11.92	0.59	20
	mild	11.34	0.57	17
	moderate	11.16	0.79	13
	severe	11.06	1.05	10



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	11.23	0.001
sex	1	4.599	0.034
groups * sex	3	0.152	0.928

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	11.532	0.001
sex	1	4.686	0.032

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	23.53%	27.54%	26.46%
mild	0.0028	-	2.05%	4.35%
moderate	0.0009	0.4168	-	0.45%
severe	0.0059	0.3081	0.7674	-

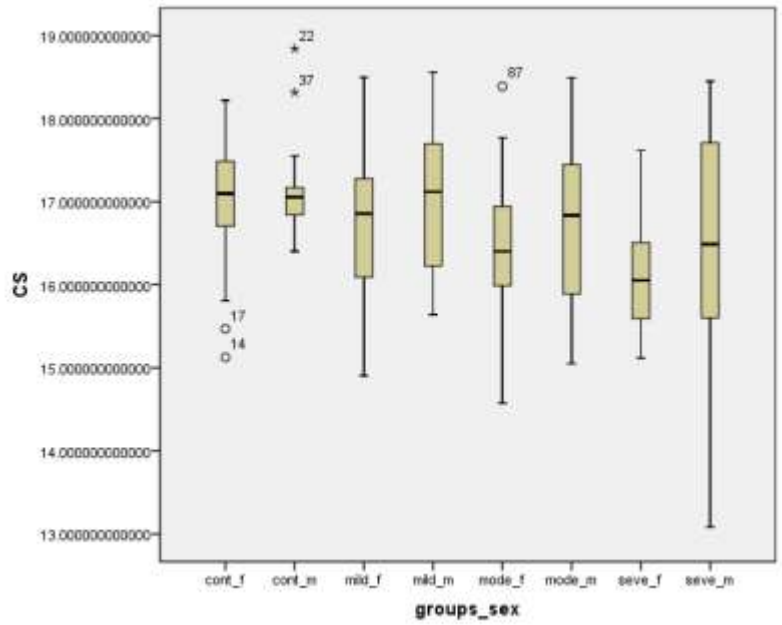
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	20.58%	24.18%	23.08%
mild	0.0066	-	1.83%	3.29%
moderate	0.0029	0.4695	-	0.37%
severe	0.0002	0.3709	0.7819	-

Upper left first molar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	16.99	0.82	20
	mild	16.69	0.90	20
	moderate	16.44	1.03	18
	severe	16.14	0.73	17
Male	**control**	17.15	0.57	20
	mild	17.05	0.84	20
	moderate	16.77	1.07	20
	severe	16.44	1.51	18



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	4.535	0.005
sex	1	3.332	0.070
groups * sex	3	0.082	0.970

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	4.616	0.004
sex	1	3.378	0.068

Size variation between groups

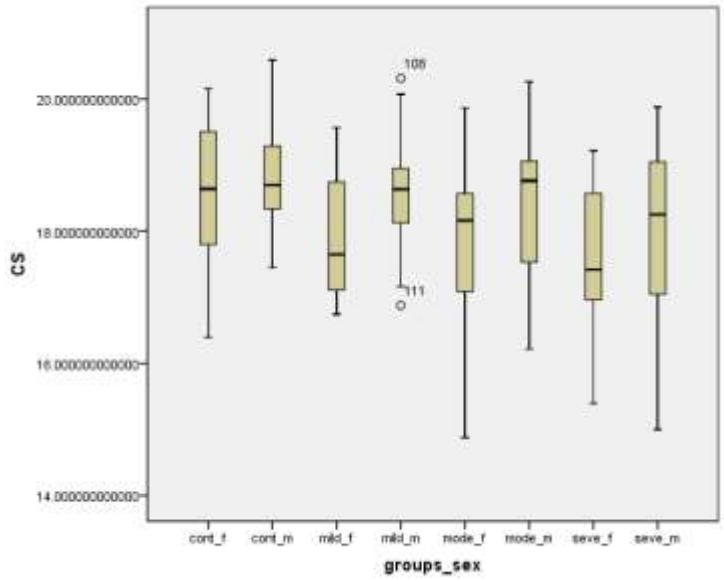
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	1.56%	6.30%	14.18%
mild	0.2692	-	1.79%	7.28%
moderate	0.0258	0.2445	-	2.02%
severe	0.0010	0.0171	0.2388	-

Lower left first molar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	control	18.58	1.04	20
	mild	17.88	0.90	20
	moderate	17.84	1.11	20
	severe	17.51	1.17	19
Male	control	18.81	0.79	20
	mild	18.57	0.84	20
	moderate	18.39	1.09	19
	severe	17.82	1.53	15



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	5.816	0.001
sex	1	6.621	0.011
groups * sex	3	0.4	0.753

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	5.829	0.001
sex	1	6.899	0.010

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	11.52%	11.09%	19.67%
mild	0.0358	-	3.21%	3.21%
moderate	0.0355	0.2664	-	2.11%
severe	0.0050	0.2764	0.3757	-

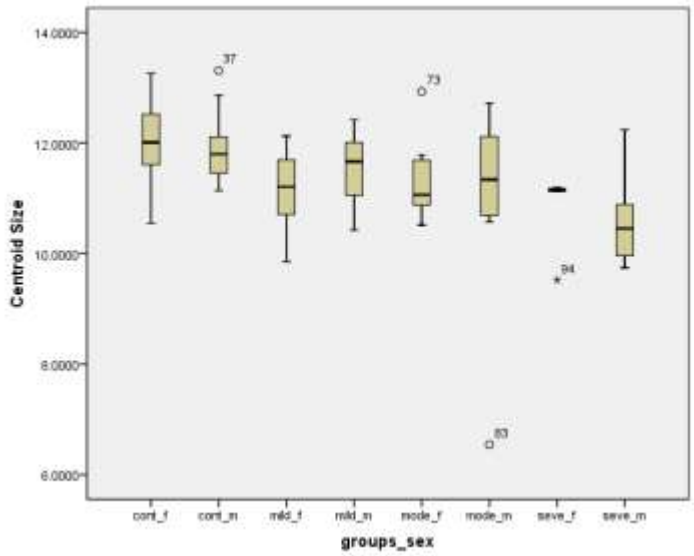
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	2.11%	4.87%	15.86%
mild	0.3688	-	0.96%	9.68%
moderate	0.1752	0.5562	-	4.83%
severe	0.0081	0.0693	0.2137	-

Lower left second premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	12.04	0.71	20
	mild	11.16	0.63	16
	moderate	11.38	0.82	7
	severe	10.84	0.73	5
Male	**control**	11.87	0.58	20
	mild	11.56	0.58	14
	moderate	11.08	1.61	12
	severe	10.57	0.82	8



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	8.568	0.001
sex	1	0.193	0.662
groups * sex	3	0.989	0.402

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	9.245	0.001
sex	1	0.034	0.853

Size variation between groups

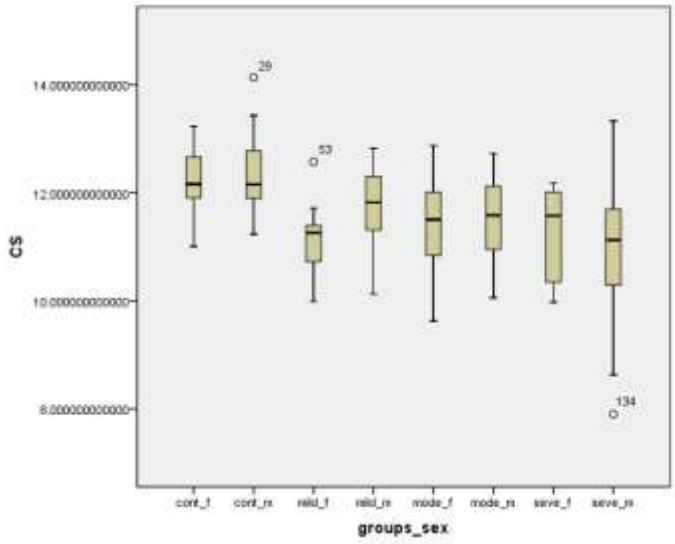
Pairwise comparison group averages

	control	mild	moderate	severe
control	-	21.57%	23.04%	44.41%
mild	<.0001	-	0.52%	18.04%
moderate	0.0065	0.6275	-	20.63%
severe	<.0001	0.0041	0.0090	-

Lower left first premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	12.21	0.60	20
	mild	11.11	0.58	20
	moderate	11.41	0.80	18
	severe	11.21	0.88	11
Male	**control**	12.33	0.76	20
	mild	11.78	0.65	20
	moderate	11.50	0.86	15
	severe	10.93	1.40	16



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	13.038	0.001
sex	1	1.09	0.298
groups * sex	3	1.882	0.136

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	13.516	0.001
sex	1	1.897	0.171

Size variation between groups

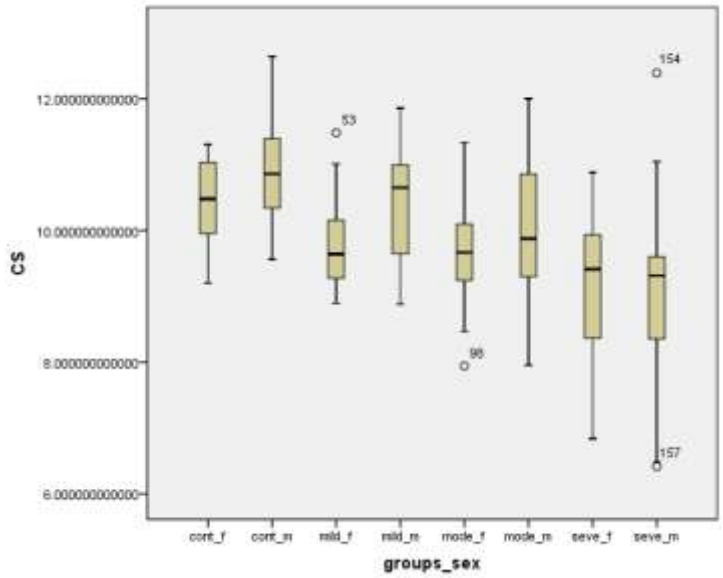
Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	26.89%	23.57%	30.34%
mild	<.0001	-	0.00%	4.45%
moderate	<.0001	0.9871	-	4.00%
severe	<.0001	0.0921	0.1266	-

Lower left canine

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	control	10.43	0.66	20
	mild	9.81	0.70	20
	moderate	9.68	0.79	20
	severe	9.20	1.03	20
Male	control	10.91	0.84	20
	mild	10.39	0.82	20
	moderate	9.99	1.07	20
	severe	9.10	1.42	19



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	17.7	0.001
sex	1	4.482	0.036
groups * sex	3	0.983	0.403

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	17.585	0.001
sex	1	4.56	0.034

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	17.78%	22.00%	34.86%
mild	0.0087	-	0.88%	11.35%
moderate	0.0017	0.5612	-	6.62%
severe	<.0001	0.0328	0.1093	-

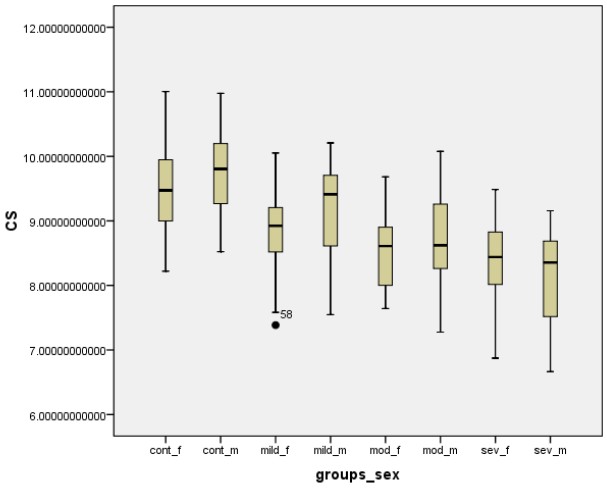
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	9.43%	19.18%	39.04%
mild	0.0503	-	4.29%	24.77%
moderate	0.0032	0.2052	-	11.80%
severe	0.0001	0.0012	0.0336	-

Lower left lateral incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	9.47	0.77	20
	mild	8.82	0.69	20
	moderate	8.51	0.59	19
	severe	8.39	0.71	17
Male	**control**	9.74	0.67	19
	mild	9.20	0.76	20
	moderate	8.72	0.79	19
	severe	8.15	0.71	16



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	23.541	0.001
sex	1	1.858	0.175
groups * sex	3	1.276	0.285

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	23.21	0.001
sex	1	2.276	0.134

Size variation between groups

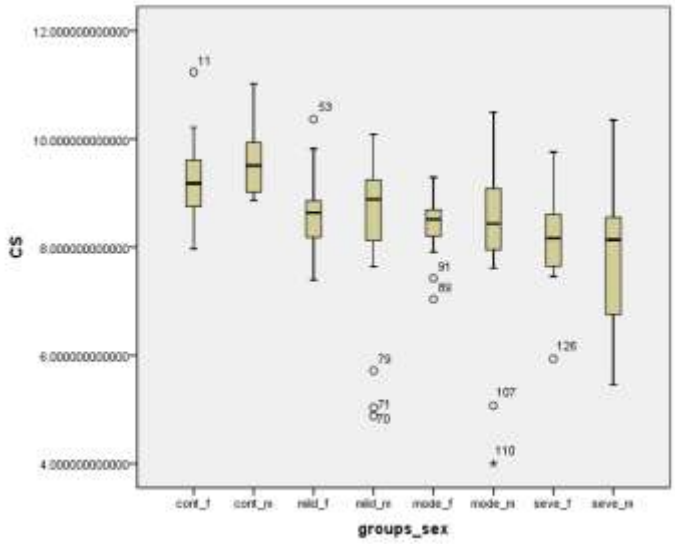
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	24.16%	32.09%	40.71%
mild	0.0001	-	2.28%	8.98%
moderate	0.0001	0.3465	-	2.26%
severe	<.0001	0.0015	0.3797	-

Lower left central incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	9.24	0.75	20
	mild	8.62	0.72	20
	moderate	8.42	0.56	18
	severe	8.12	0.96	13
Male	**control**	9.55	0.57	20
	mild	8.36	1.55	19
	moderate	8.27	1.68	16
	severe	7.82	1.27	16



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	11.493	0.001
sex	1	0.312	0.578
groups * sex	3	0.652	0.583

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	11.723	0.001
sex	1	0.21	0.648

Size variation between groups

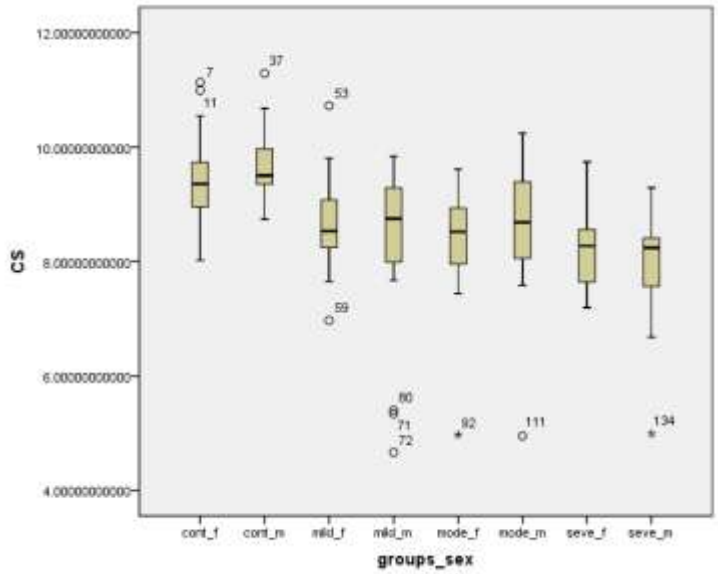
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	18.22%	23.59%	39.38%
mild	<.0001	-	0.39%	2.05%
moderate	<.0001	0.6122	-	2.78%
severe	<.0001	0.3147	0.1966	-

Lower right central incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	control	9.40	0.82	20
	mild	8.66	0.84	20
	moderate	8.30	1.01	18
	severe	8.24	0.73	13
Male	control	9.66	0.62	20
	mild	8.34	1.51	20
	moderate	8.56	1.23	16
	severe	7.88	1.07	15



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	13.808	0.001
sex	1	0.06	0.807
groups * sex	3	1.011	0.390

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	14.003	0.000
sex	1	0.027	0.870

Size variation between groups

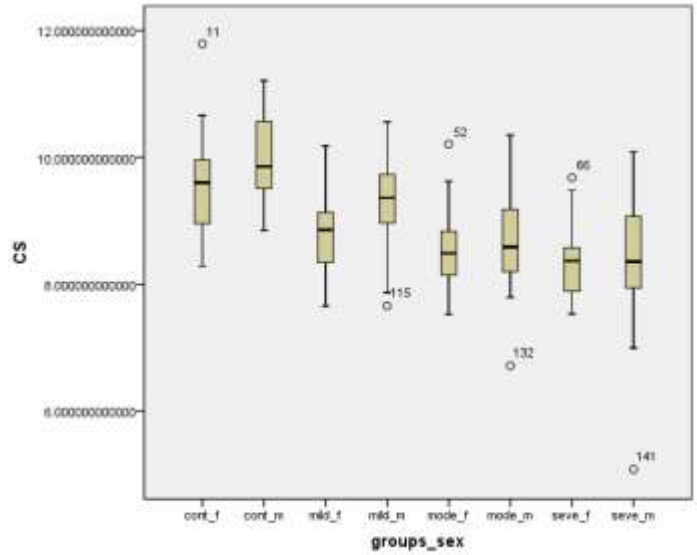
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	21.36%	26.99%	45.08%
mild	0.0001	-	0.11%	3.93%
moderate	<.0001	0.7801	-	3.20%
severe	<.0001	0.1051	0.1645	-

Lower right lateral incisor

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	9.56	0.84	19
	mild	8.75	0.62	20
	moderate	8.56	0.64	20
	severe	8.37	0.59	17
Male	**control**	9.98	0.63	20
	mild	9.29	0.74	20
	moderate	8.68	0.84	18
	severe	8.27	1.14	18



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	24.884	0.000
sex	1	3.82	0.053
groups * sex	3	1.353	0.260

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	24.879	0.000
sex	1	4.189	0.042

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	24.16%	23.09%	40.71%
mild	0.0015	-	2.28%	8.98%
moderate	0.0001	0.3465	-	2.26%
severe	<.0001	0.0714	0.3797	-

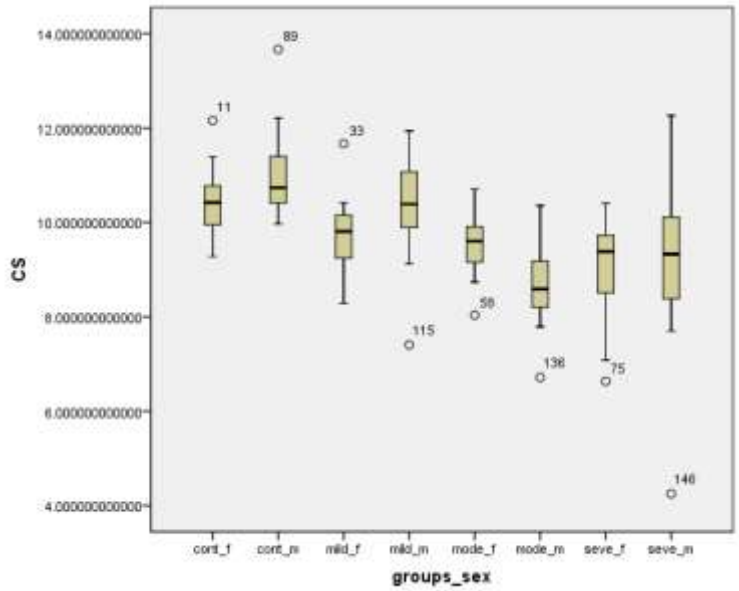
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	2.96%	45.05%	48.42%
mild	0.2951	-	13.59%	23.34%
moderate	<.0001	0.0201	-	4.27%
severe	<.0001	0.0015	0.2296	-

Lower right canine

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	10.42	0.72	20
	mild	9.70	0.75	20
	moderate	9.53	0.61	20
	severe	9.05	1.01	20
Male	**control**	11.01	0.89	20
	mild	10.33	1.02	20
	moderate	8.68	0.84	18
	severe	9.13	1.72	16



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	25.06	0.001
sex	1	0.507	0.478
groups * sex	3	4.81	0.003

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	19.80%	32.00%	38.75%
mild	0.0035	-	1.74%	12.19%
moderate	<.0001	0.4169	-	7.68%
severe	<.0001	0.0256	0.0797	-

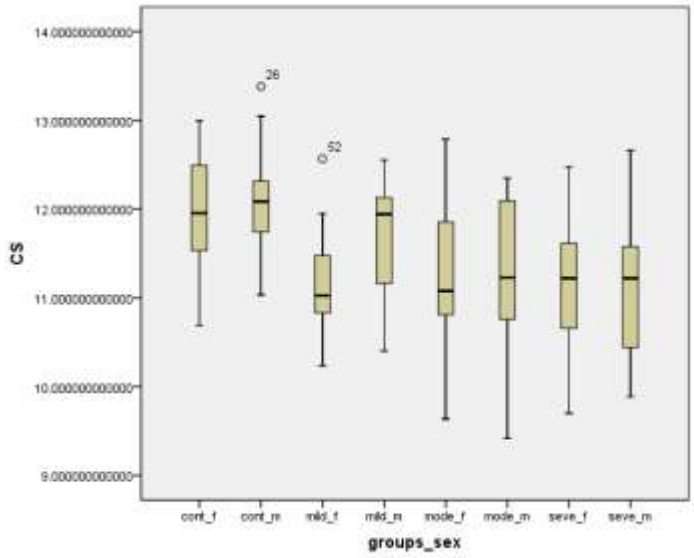
Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	11.75%	65.56%	34.58%
mild	0.0286	-	44.93%	16.66%
moderate	<.0001	<.0001	-	2.99%
severe	<.0001	0.0098	0.3442	-

Lower right first premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	control	11.98	0.64	20
	mild	11.14	0.55	20
	moderate	11.26	0.79	19
	severe	11.16	0.74	12
Male	control	12.10	0.61	19
	mild	11.72	0.61	19
	moderate	11.30	0.84	17
	severe	11.13	0.78	16



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	11.532	0.001
sex	1	2.187	0.142
groups * sex	3	1.444	0.233

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	11.697	0.001
sex	1	2.742	0.100

Size variation between groups

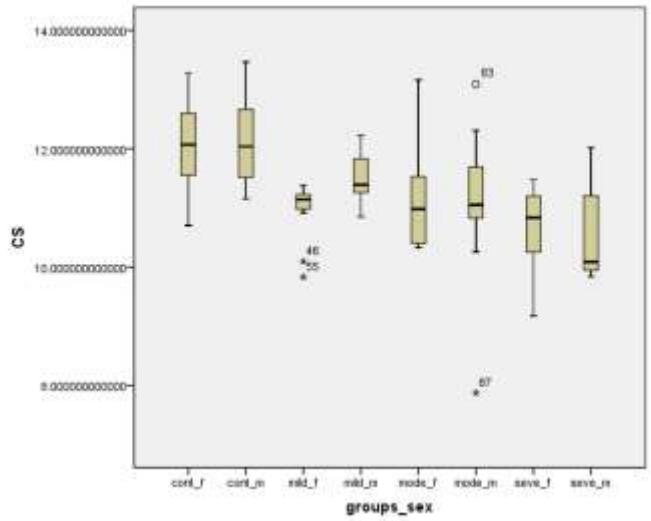
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	19.70%	22.41%	30.47%
mild	0.0001	-	0.94%	3.86%
moderate	<.0001	0.4049	-	0.78%
severe	<.0001	0.1112	0.4935	-

Lower right second premolar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	12.07	0.69	20
	mild	11.02	0.42	17
	moderate	11.12	0.85	10
	severe	10.63	0.85	6
Male	**control**	12.11	0.74	19
	mild	11.52	0.43	15
	moderate	11.12	1.24	13
	severe	10.61	0.86	7



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	16.294	0.001
sex	1	0.643	0.424
groups * sex	3	0.75	0.525

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	16.76	0.001
sex	1	1.213	0.273

Size variation between groups

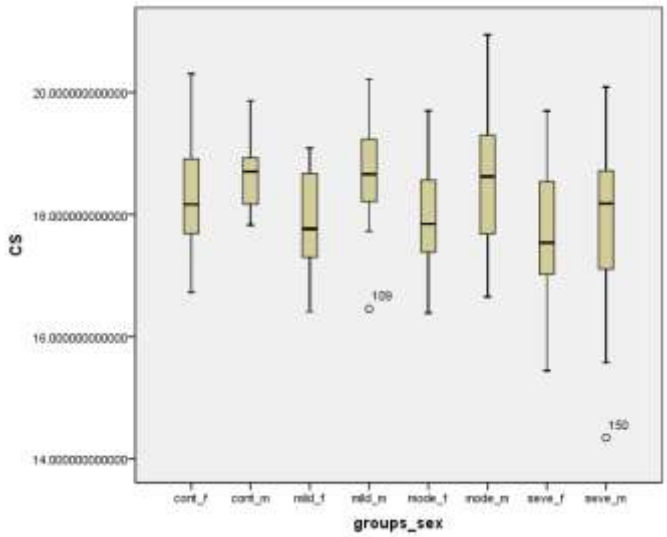
Pairwise comparison of group averages

	control	mild	moderate	severe
control	-	31.92%	23.44%	44.03%
mild	<.0001	-	0.67%	19.52%
moderate	<.0001	0.5635	-	6.08%
severe	<.0001	0.0020	0.1491	-

Lower right first molar

Descriptive Statistics for groups by Gender

Sex	Groups	Mean	SD	N
Female	**control**	18.29	0.90	20
	mild	17.89	0.87	20
	moderate	17.98	0.98	19
	severe	17.65	1.25	18
Male	**control**	18.72	0.58	20
	mild	18.65	0.84	20
	moderate	18.53	1.22	20
	severe	17.90	1.49	16



Boxplot of Groups by Gender

Size variation in groups and between sexes

ANOVA of Groups by Gender

Source	df	F	Sig.
groups	3	3.098	0.029
sex	1	8.812	0.004
groups * sex	3	0.404	0.750

ANOVA of Groups by Gender without the Interaction Term

Source	df	F	Sig.
groups	3	3.07	0.030
sex	1	9.311	0.003

Size variation between groups

Pairwise comparison of female group averages

	control	mild	moderate	severe
control	-	5.04%	2.82%	21.17%
mild	0.1646	-	0.22%	1.28%
moderate	0.3056	0.7742	-	2.13%
severe	0.0043	0.5022	0.387	-

Pairwise comparison of male group averages

	control	mild	moderate	severe
control	-	0.21%	1.00%	19.11%
mild	0.7887	-	0.36%	9.64%
moderate	0.5477	0.7118	-	5.37%
severe	0.0076	0.0631	0.1808	-

Appendix III Shape analysis for all teeth

Upper right first molar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.217	4.293	60	385.7	0.001
sex	0.842	1.213a	20	129	0.254
groups * sex	0.598	1.209	60	385.7	0.15

MANOVA of Groups by Gender without interaction

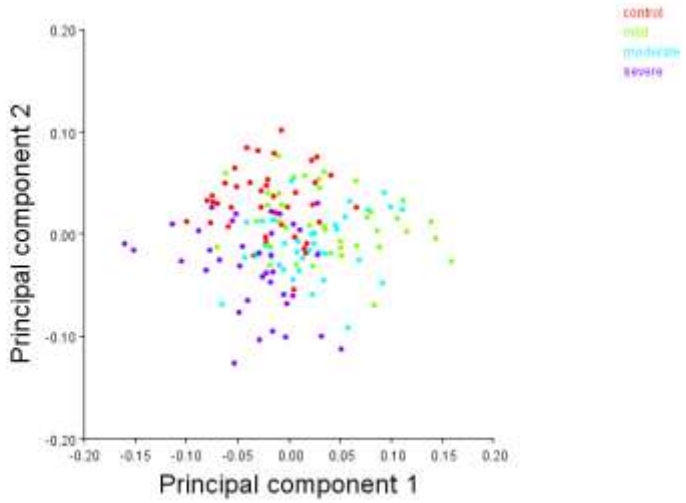
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.227	4.228	60	394.65	0.001
sex	0.85	1.160a	20	132	0.299

Group differences

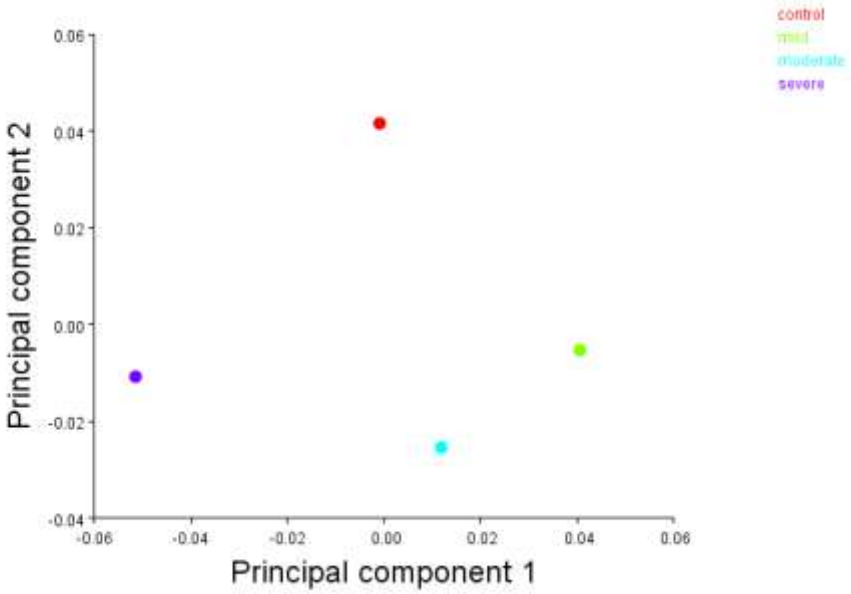
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	6.09%	6.98%	7.74%
mild	<.0001	-	2.63%	10.06%
moderate	<.0001	0.0086	-	5.99%
severe	<.0001	<.0001	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	77.5	65.0
Mild	67.5	42.5
Moderate	59.0	46.2
Severe	81.1	73.2

Upper right second premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.132	6.452	45	297.855	0.001
sex	0.854	1.138a	15	100	0.333
groups * sex	0.559	1.432	45	297.855	0.064

MANOVA of Groups by Gender without interaction

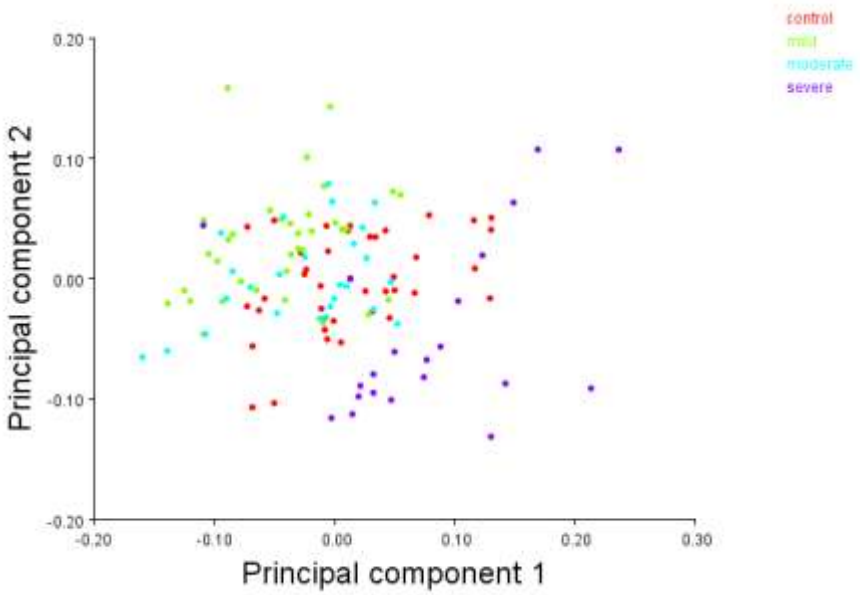
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.151	6.073	45	306.767	0.001
sex	0.869	1.035a	15	103	0.427

Group differences

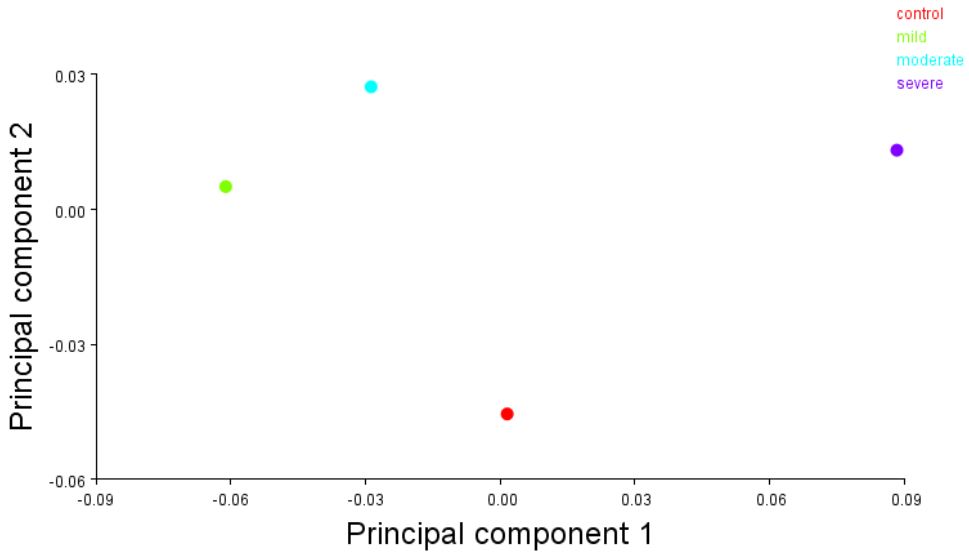
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	8.46%	7.51%	11.08%
mild	<.0001	-	3.29%	16.80%
moderate	<.0001	0.0113	-	12.36%
severe	<.0001	<.0001	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	Analysis	Jacknife
Control	90.0	85.0
Mild	71.4	57.1
Moderate	61.5	38.5
Severe	90.5	90.5

Upper right first premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.176	5.739	45	324.592	0.001
sex	0.874	1.051a	15	109	0.410
groups * sex	0.658	1.089	45	324.592	0.330

MANOVA of Groups by Gender without interaction

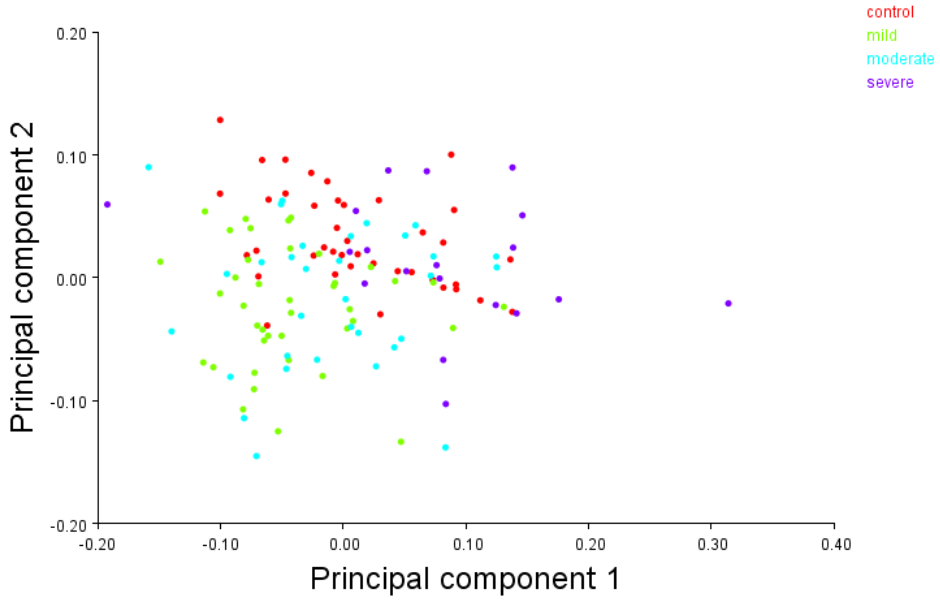
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.18	5.793	45	333.504	0.001
sex	0.865	1.166a	15	112	0.308

Group differences

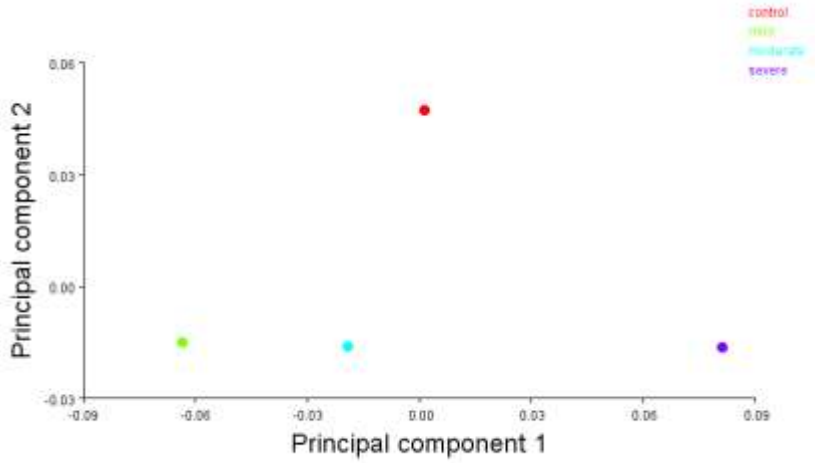
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	9.43%	5.31%	9.56%
mild	<.0001	-	3.09%	15.76%
moderate	0.0002	0.0097	-	8.63%
severe	<.0001	<.0001	0.0002	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	Analysis	Jacknife
Control	87.5	80.0
Mild	80.0	70.0
Moderate	50.0	31.3
Severe	78.9	68.4

Upper right canine

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.628	1.952	30	341.159	0.003
sex	0.796	2.971a	10	116	0.002
groups * sex	0.743	1.21	30	341.159	0.212

MANOVA of Groups by Gender without interaction

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.63	1.99	30	349.964	0.002
sex	0.789	3.189a	10	119	0.001

Group differences

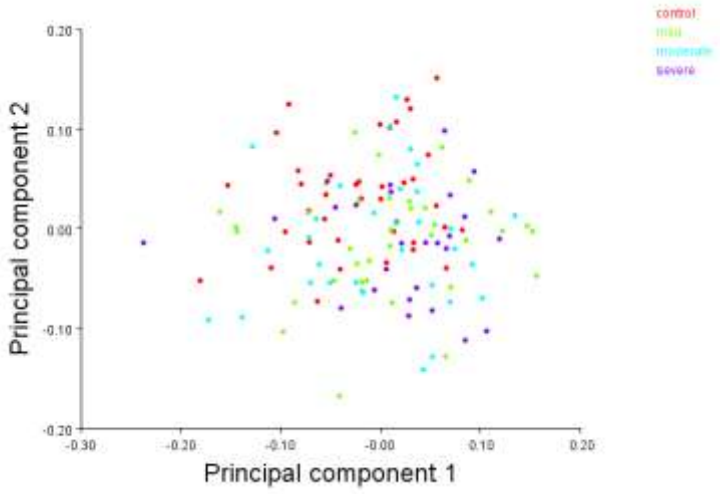
Pairwise test

Pairwise tests for mean shape differences between female groups

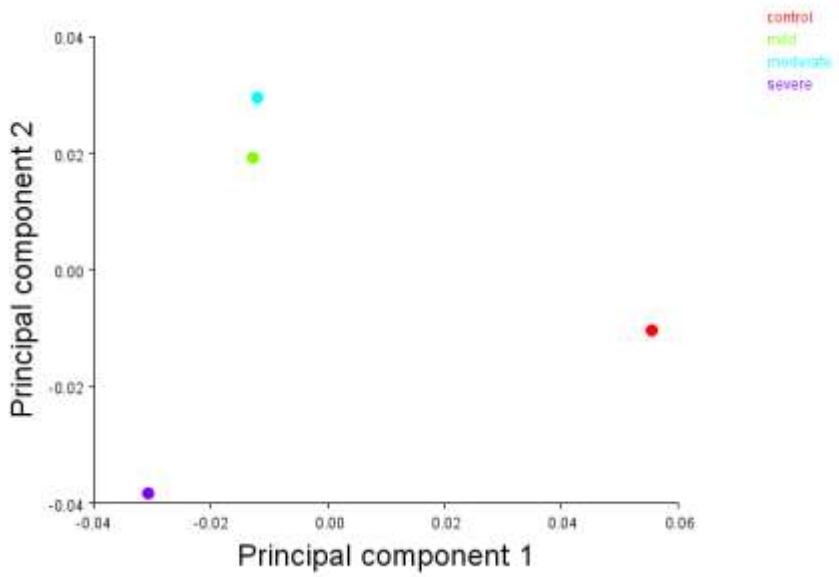
	control	mild	moderate	severe
control	-	5.69%	3.64%	6.08%
mild	0.0292	-	1.97%	2.99%
moderate	0.2154	0.7461	-	4.34%
severe	0.0503	0.4596	0.2075	-

Pairwise tests for mean shape differences between male groups

	control	mild	moderate	severe
control	-	7.85%	8.41%	11.33%
mild	0.0042	-	2.24%	5.12%
moderate	0.0038	0.6994	-	6.36%
severe	0.0008	0.157	0.0854	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender			
	Female (%)		Male (%)	
Groups	Analysis	Jacknife	Analysis	Jacknife
Control	47.4	21.1	75.0	55.0
Mild	52.6	21.1	52.9	29.4
Moderate	41.2	11.8	40.0	26.7
Severe	57.1	50.0	50.0	50.0

Upper right lateral incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.47	2.335	30	238.427	0.001
sex	0.848	1.457a	10	81	0.171
groups * sex	0.631	1.352	30	238.427	0.113

MANOVA of Groups by Gender without interaction

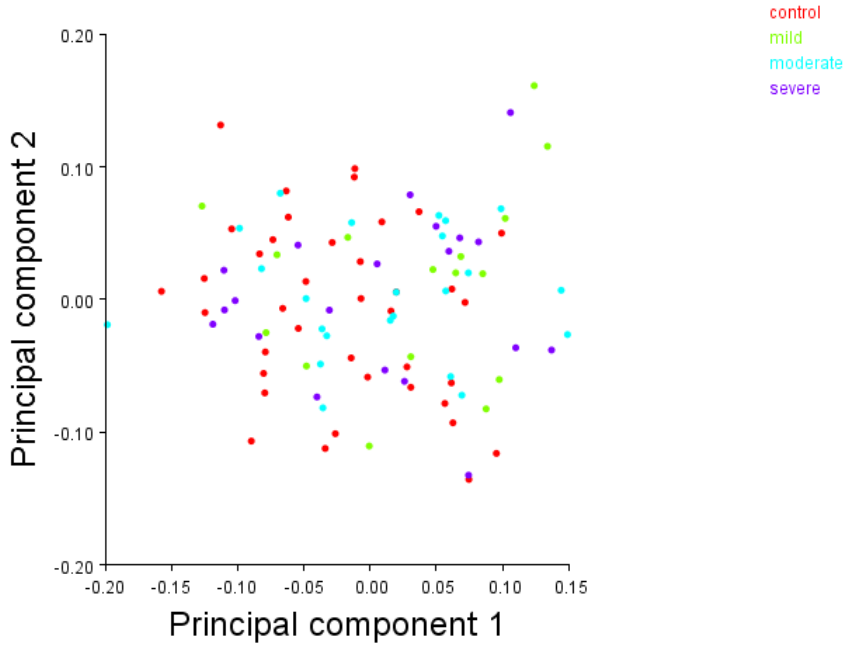
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.496	2.224	30	247.233	0.001
sex	0.839	1.611a	10	84	0.117

Group differences

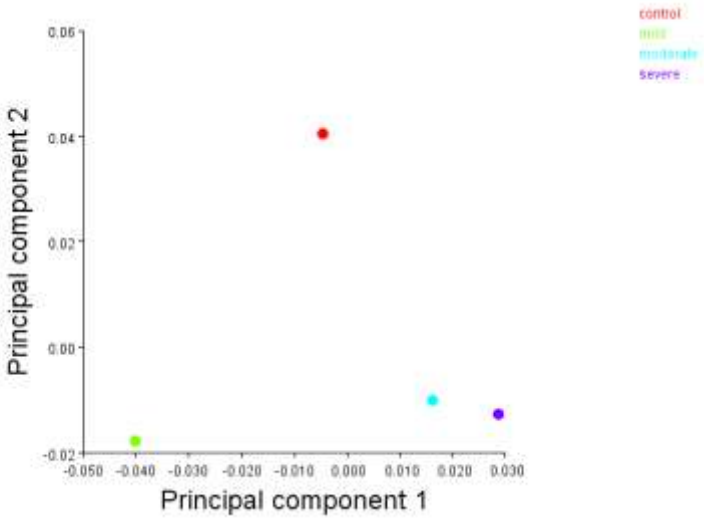
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	4.01%	3.36%	3.93%
mild	0.0010	-	3.58%	4.80%
moderate	0.0010	0.1720	-	1.21%
severe	0.0010	0.0827	0.8995	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	51.3	46.2
Mild	62.5	43.8
Moderate	47.8	34.8
Severe	50.0	30.0

Upper right central incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.49	3.823	30	417.474	0.001
sex	0.89	1.754a	10	142	0.074
groups * sex	0.778	1.242	30	417.474	0.181

MANOVA of Groups by Gender without interaction

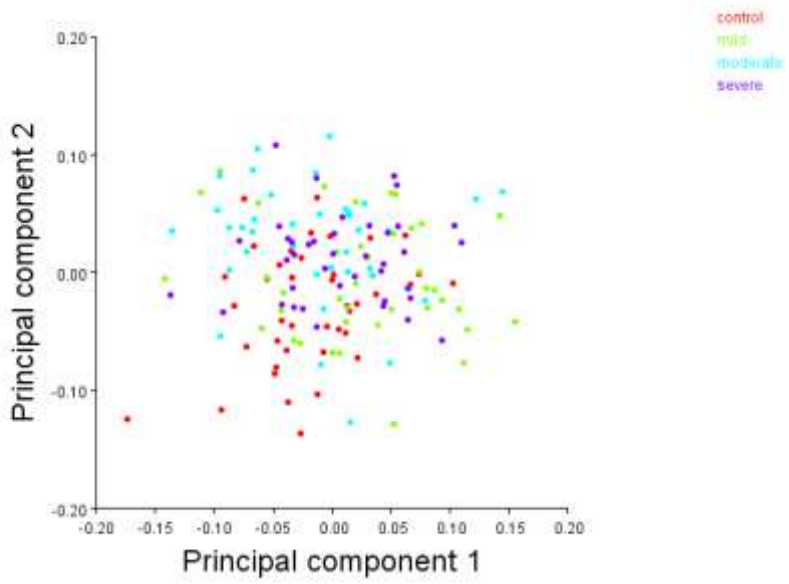
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.503	3.753	30	426.28	0.001
sex	0.894	1.711a	10	145	0.083

Group differences

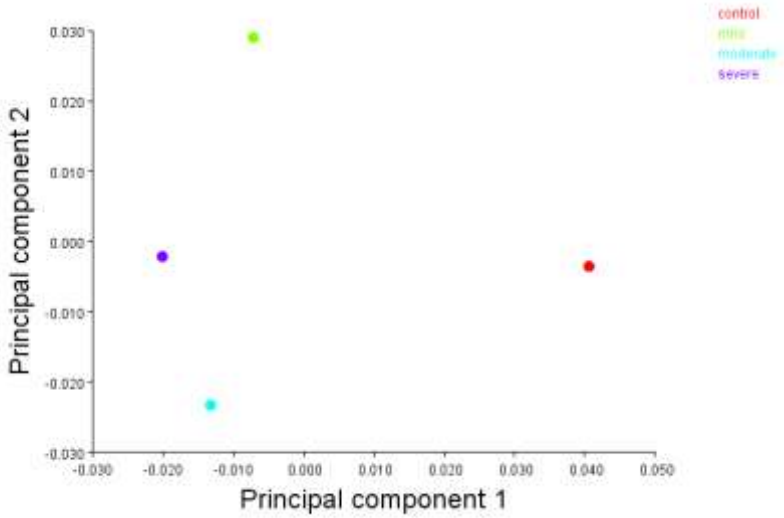
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	0.06%	0.06%	0.07%
mild	<.0001	-	0.05%	0.03%
moderate	0.0001	0.0021	-	0.02%
severe	<.0001	0.0100	0.0400	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	**Analysis**	**Jacknife**
Control	62.5	62.5
Mild	55	47.5
Moderate	46.2	30.8
Severe	60	50

Upper left central incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.548	3.162	30	417.474	0.001
sex	0.907	1.461a	10	142	0.160
groups * sex	0.847	0.809	30	417.474	0.754

MANOVA of Groups by Gender without interaction

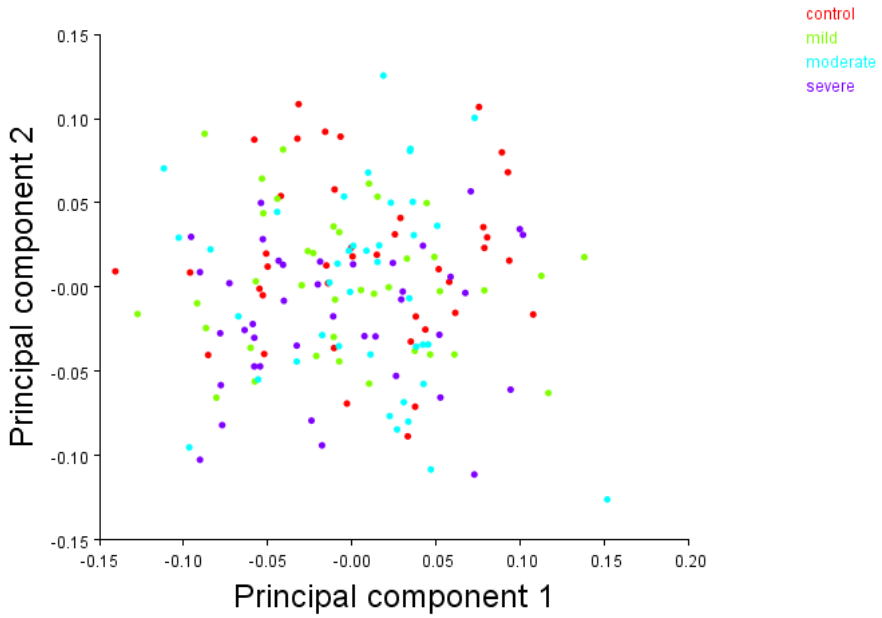
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.554	3.171	30	426.28	0.001
sex	0.908	1.473a	10	145	0.155

Group differences

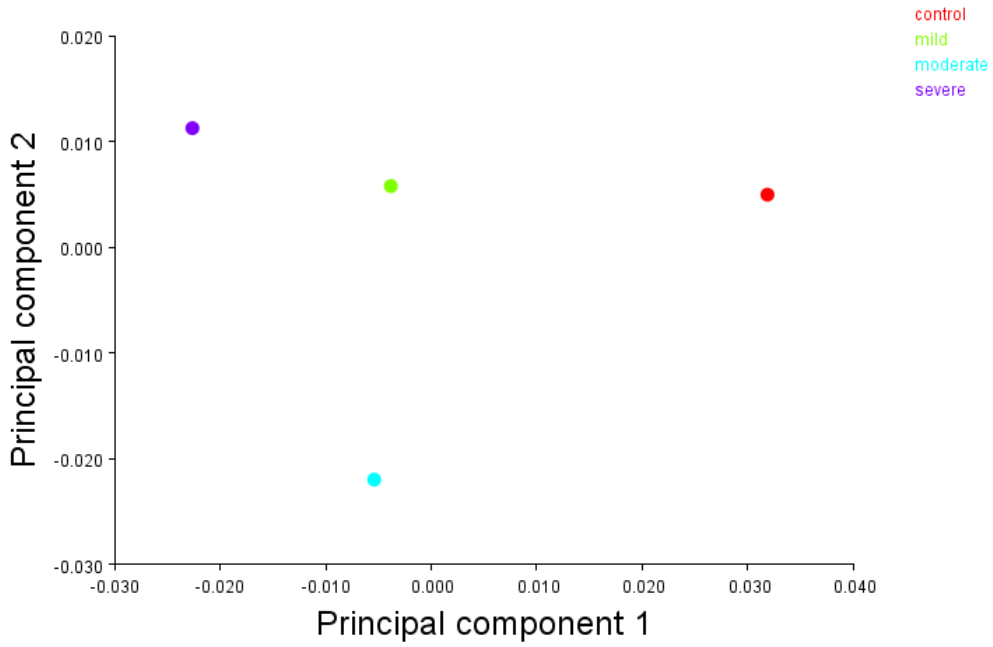
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	2.99%	3.98%	5.68%
mild	0.0115	-	1.89%	1.89%
moderate	0.0023	0.1273	-	2.75%
severe	0.0001	0.1259	0.0256	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	60.0	55.0
Mild	51.3	35.9
Moderate	52.5	40.0
Severe	55.0	42.5

Upper left lateral incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.535	1.979	30	250.168	0.003
sex	0.863	1.347a	10	85	0.219
groups * sex	0.672	1.207	30	250.168	0.219

MANOVA of Groups by Gender without interaction

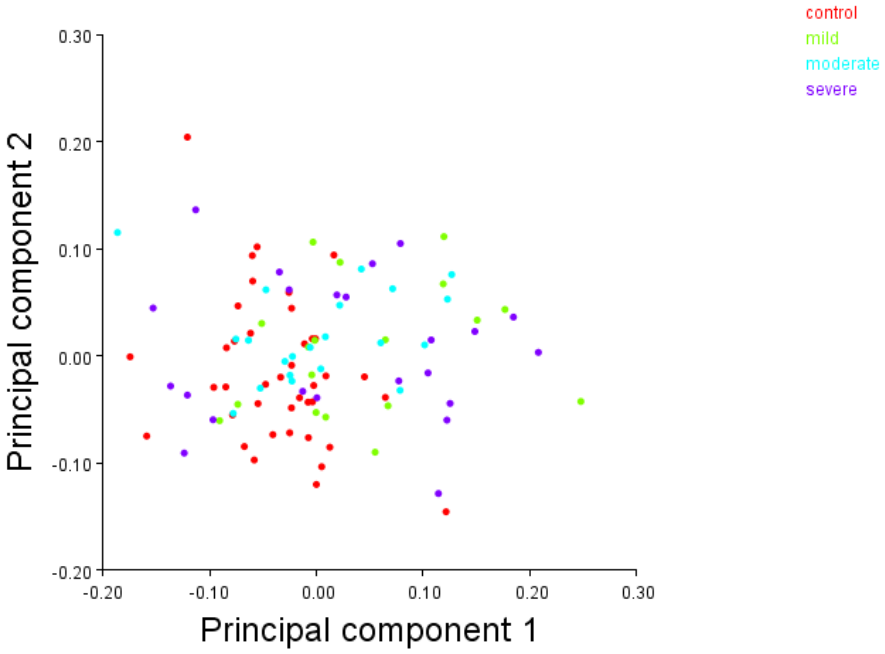
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.564	1.86	30	258.973	0.006
sex	0.867	1.345a	10	88	0.220

Group differences

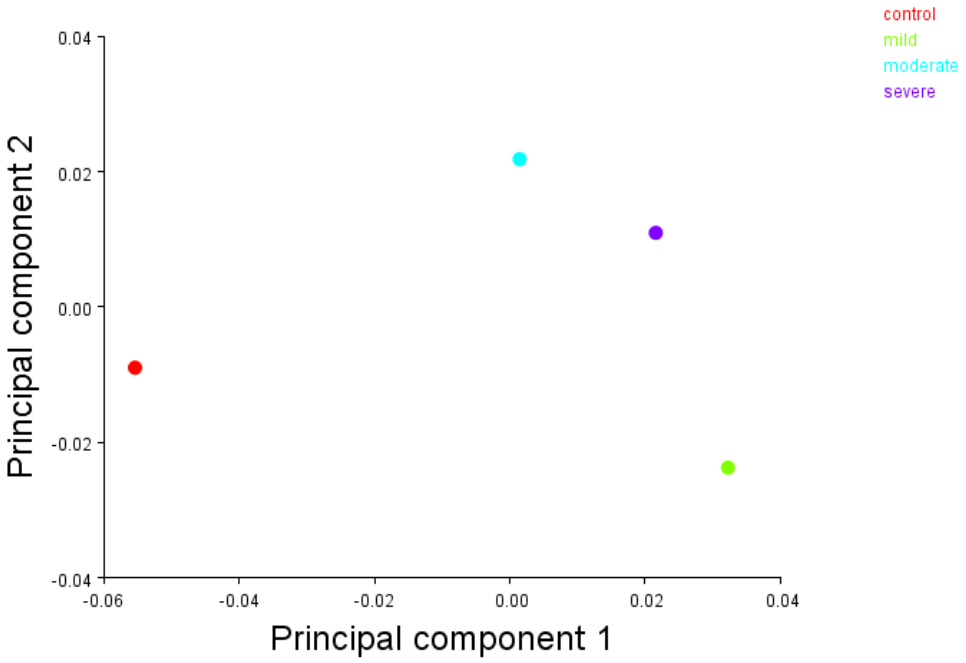
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	6.86%	6.86%	5.97%
mild	0.0001	-	3.07%	1.46%
moderate	0.0023	0.2921	-	1.40%
severe	0.0009	0.7878	0.7832	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	72.5	62.5
Mild	50.0	16.7
Moderate	38.1	19.0
Severe	39.1	21.7

Upper left canine

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.539	2.69	30	344.094	0.001
sex	0.918	1.040a	10	117	0.414
groups * sex	0.85	0.652	30	344.094	0.922

MANOVA of Groups by Gender without interaction

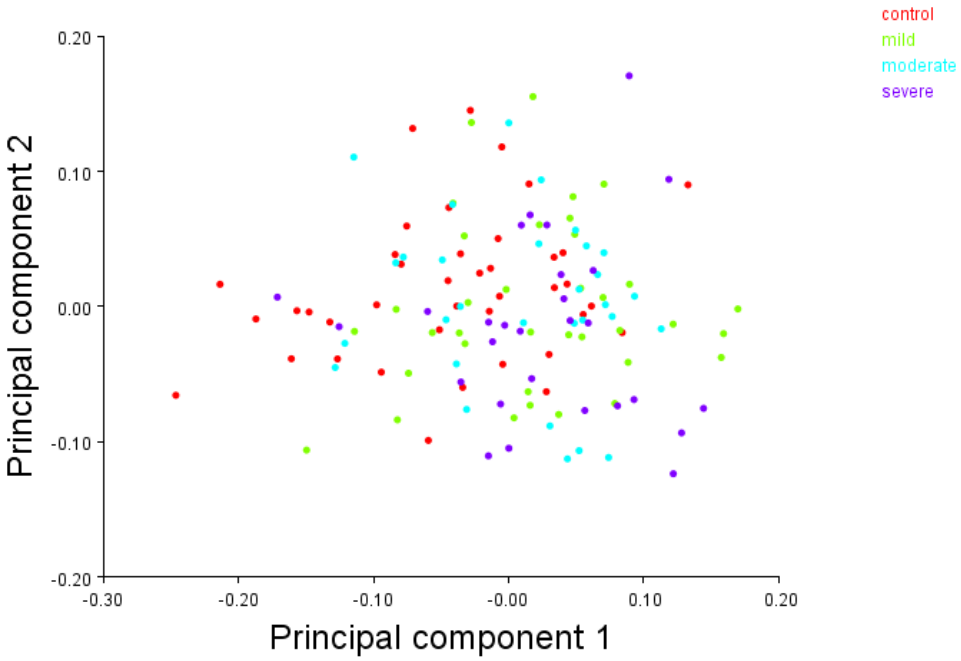
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.547	2.687	30	352.9	0.001
sex	0.922	1.017a	10	120	0.433

Group differences

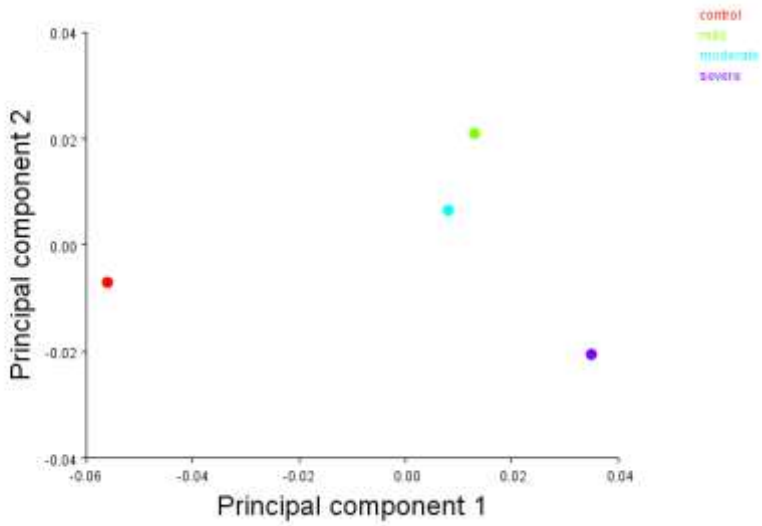
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	5.80%	4.93%	8.33%
mild	0.0007	-	0.99%	2.17%
moderate	0.0018	0.7894	-	1.93%
severe	<.0001	0.1739	0.3399	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	70.0	65.0
Mild	47.2	38.9
Moderate	26.7	16.7
Severe	46.4	28.6

Upper left first premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.202	5.324	45	336.475	0.001
sex	0.906	.780a	15	113	0.697
groups * sex	0.628	1.267	45	336.475	0.127

MANOVA of Groups by Gender without interaction

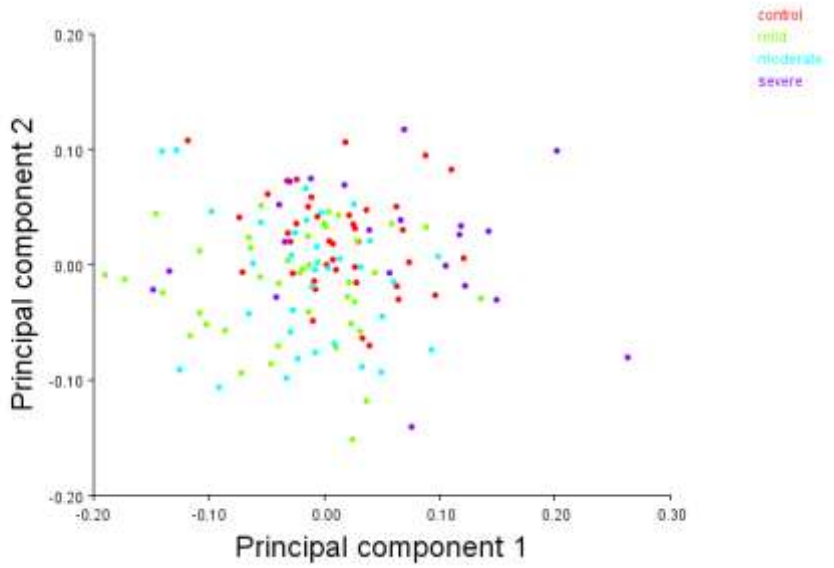
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.215	5.201	45	345.387	0.001
sex	0.915	.721a	15	116	0.759

Group differences

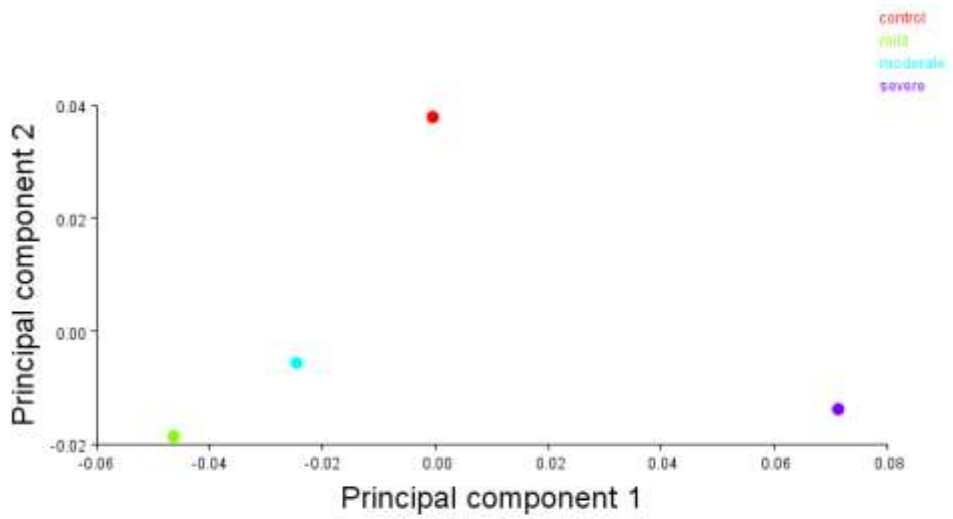
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	6.63%	3.65%	7.67%
mild	<.0001	-	1.67%	10.70%
moderate	0.0007	0.2331	-	7.62%
severe	<.0001	<.0001	0.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	72.5	67.5
Mild	72.5	62.5
Moderate	47.1	38.2
Severe	95.2	81.0

Upper left second premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.23	4.149	45	291.914	0.001
sex	0.879	.899a	15	98	0.567
groups * sex	0.641	1.049	45	291.914	0.395

MANOVA of Groups by Gender without interaction

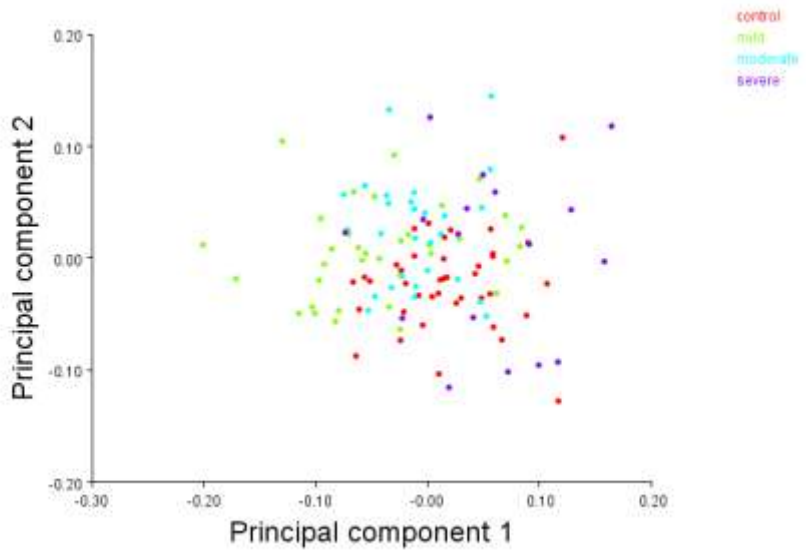
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.24	4.117	45	300.826	0.001
sex	0.911	.661a	15	101	0.816

Group differences

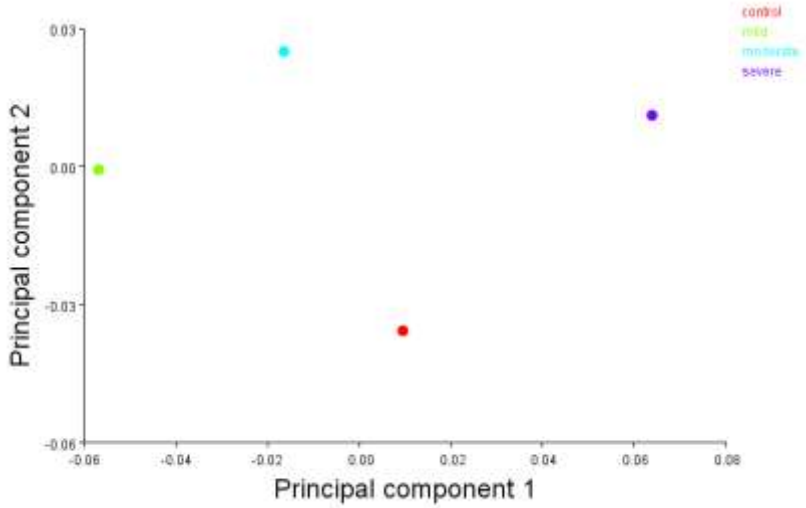
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	7.47%	5.75%	5.55%
mild	<.0001	-	3.89%	11.82%
moderate	<.0001	0.0092	-	4.86%
severe	0.0002	<.0001	0.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	**Analysis**	**Jacknife**
Control	72.5	67.5
Mild	77.1	65.7
Moderate	64.3	50.0
Severe	70.5	41.2

Upper left first molar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.332	2.811	60	376.75	0.001
sex	0.821	1.374a	20	126	0.147
groups * sex	0.595	1.192	60	376.75	0.169

MANOVA of Groups by Gender without interaction

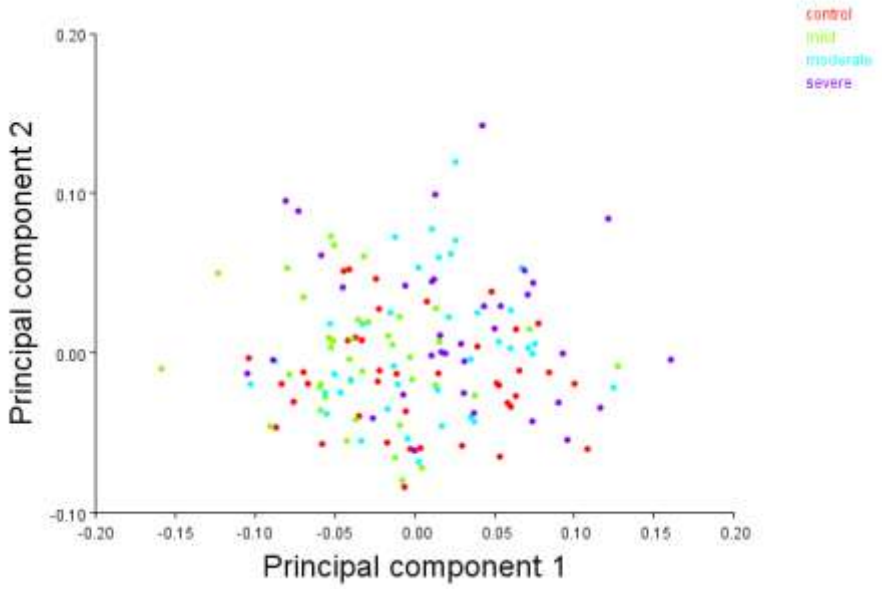
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.338	2.822	60	385.7	0.001
sex	0.831	1.316a	20	129	0.180

Group differences

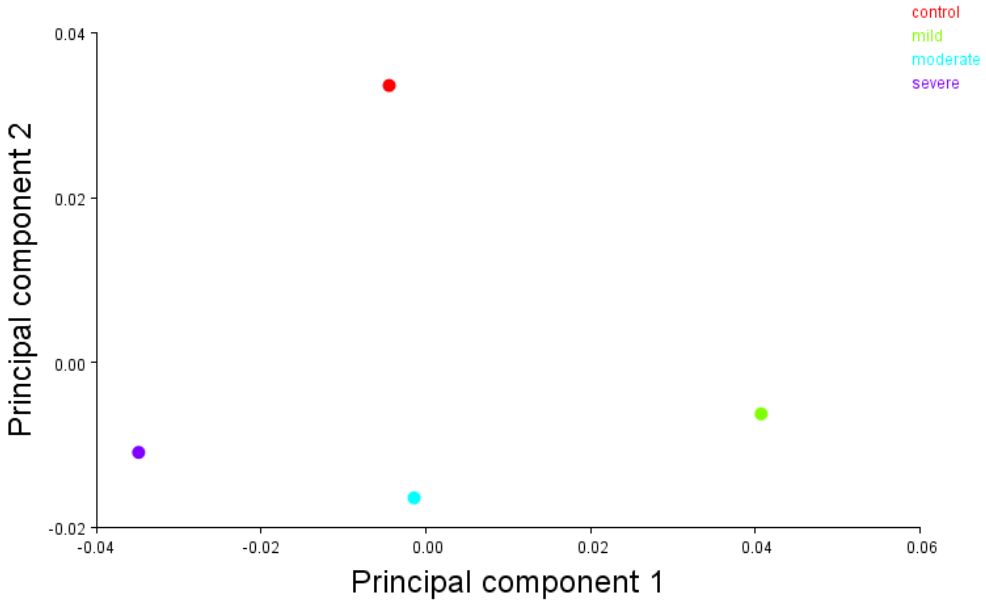
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	4.83%	3.58%	3.80%
mild	<.0001	-	2.66%	3.46%
moderate	0.0004	0.0124	-	6.24%
severe	0.0005	0.0003	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	72.5	55.0
Mild	70.0	50.0
Moderate	60.5	42.1
Severe	60.0	40.0

Lower left first molar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.143	5.762	60	376.75	0.001
sex	0.698	2.723a	20	126	0.001
groups * sex	0.491	1.69	60	376.75	0.002

Group differences

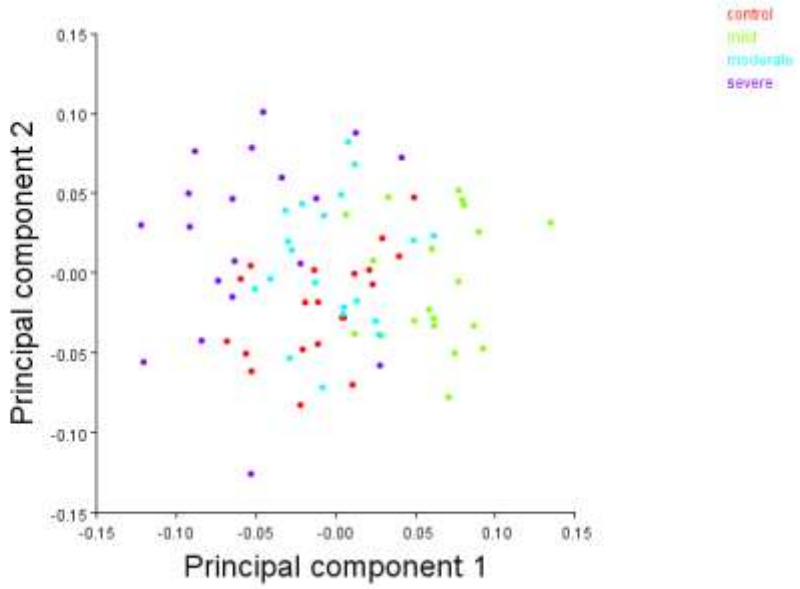
Pairwise test

Pairwise tests for mean shape differences between female groups

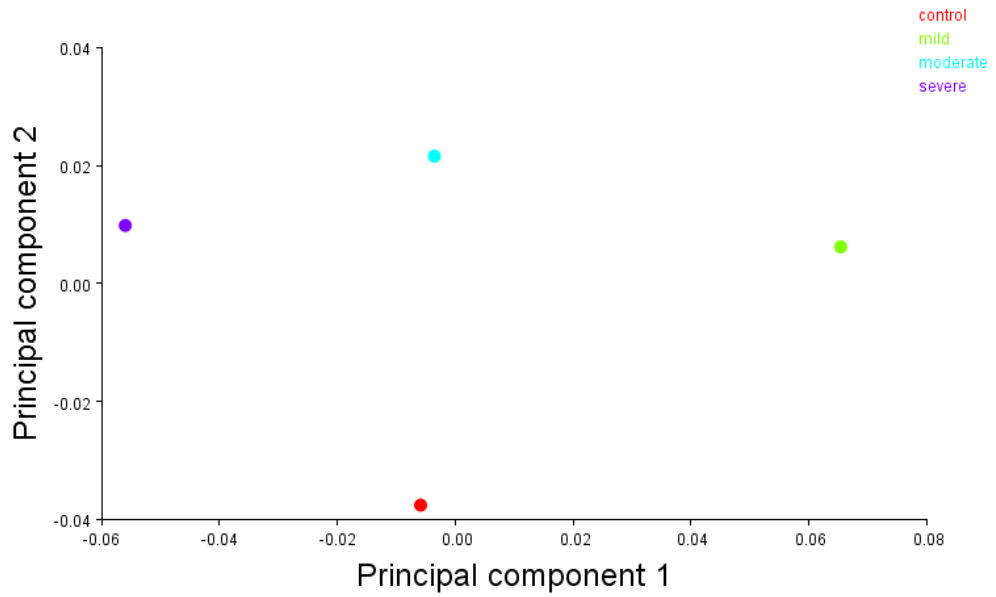
	control	mild	moderate	severe
control	-	11.20%	6.61%	7.65%
mild	<.0001	-	18.27%	18.27%
moderate	<.0001	<.0001	-	6.65%
severe	<.0001	<.0001	0.0002	-

Pairwise tests for mean shape differences between male groups

	control	mild	moderate	severe
control	-	6.03%	5.82%	10.86%
mild	0.0022	-	4.11%	10.68%
moderate	0.0006	0.0370	-	6.95%
severe	<.0001	<.0001	0.0036	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender			
	Female (%)		Male (%)	
Groups	Analysis	Jacknife	Analysis	Jacknife
Control	90.0	70.0	95.0	80.0
Mild	100.0	70.0	75.0	65.0
Moderate	90.0	65.0	73.7	21.1
Severe	78.9	57.9	73.3	53.3

Lower left second premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.221	4.565	36	245.96	0.001
sex	0.885	.898a	12	83	0.552
groups * sex	0.711	0.836	36	245.96	0.736

MANOVA of Groups by Gender without interaction

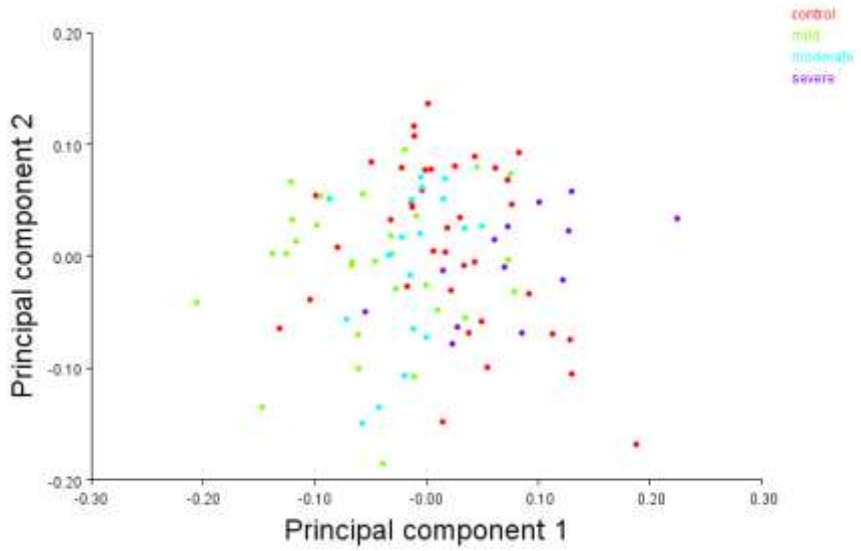
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.220	4.746	36	254.824	0.001
sex	0.888	.902a	12	86	0.549

Group differences

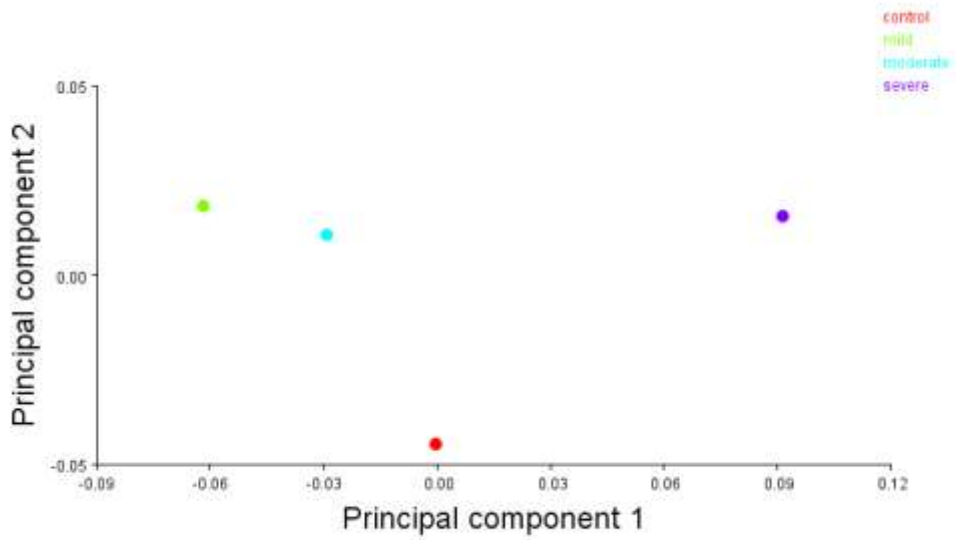
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	7.07%	3.98%	8.26%
mild	<.0001	-	3.00%	16.58%
moderate	0.0115	0.1307	-	14.14%
severe	<.0001	<.0001	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	72.5	57.5
Mild	76.7	70.0
Moderate	73.7	47.4
Severe	92.3	84.6

Lower left first premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.169	6.399	45	351.329	0.001
sex	0.861	1.271a	15	118	0.231
groups * sex	0.627	1.33	45	351.329	0.084

MANOVA of Groups by Gender without interaction

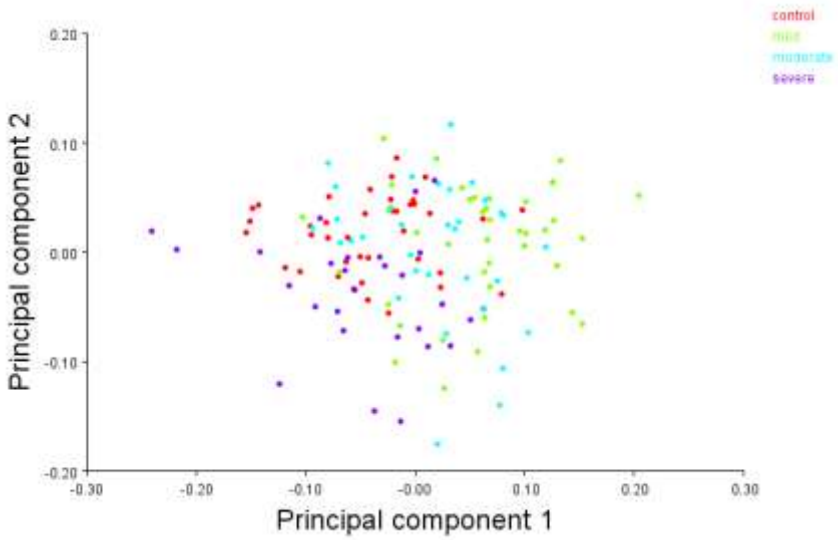
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.176	6.367	45	360.241	0.001
sex	0.874	1.160a	15	121	0.312

Group differences

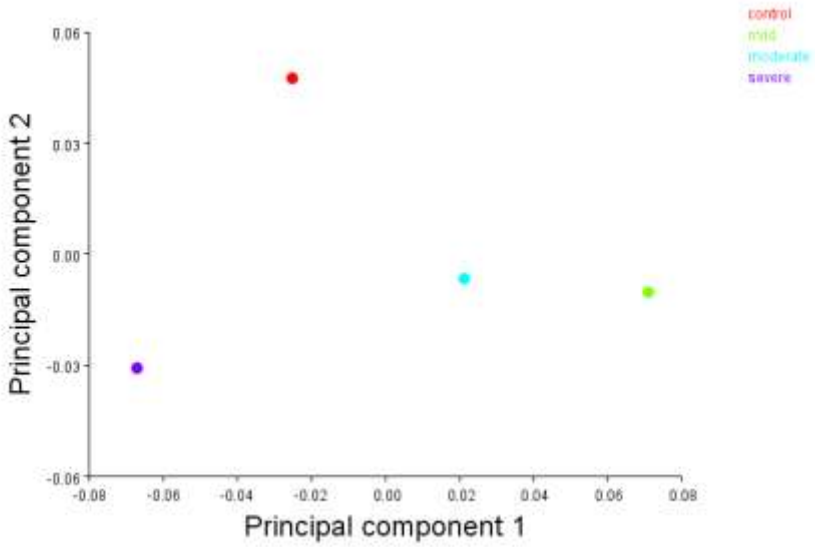
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	12.21%	5.86%	3.39%
mild	<.0001	-	14.51%	15.76%
moderate	<.0001	0.0017	-	7.51%
severe	<.0001	<.0001	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	**Analysis**	**Jacknife**
Control	85.0	75.0
Mild	77.5	62.5
Moderate	42.4	33.3
Severe	81.5	74.1

Lower left canine

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.617	2.487	30	417.474	0.000
sex	0.922	1.206a	10	142	0.292
groups * sex	0.805	1.066	30	417.474	0.376

MANOVA of Groups by Gender without interaction

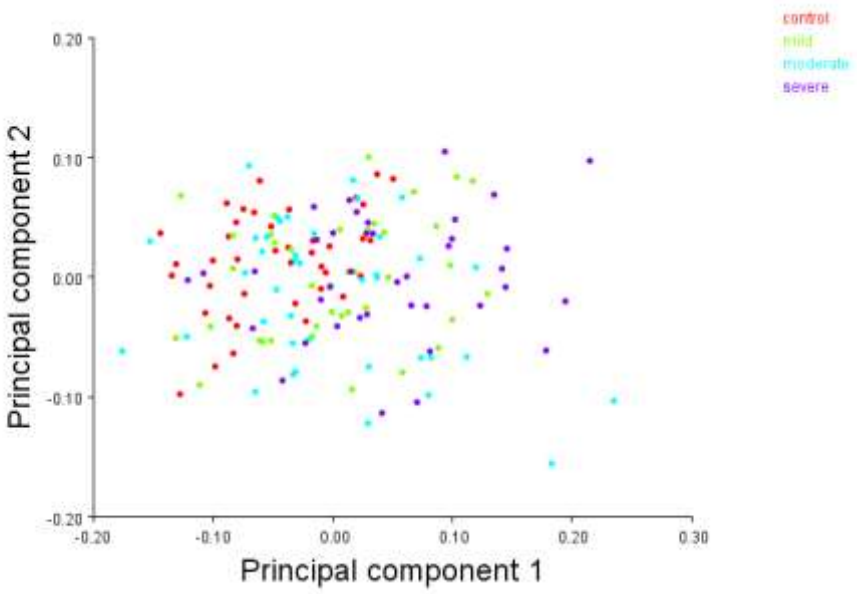
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.621	2.508	30	426.28	0.001
sex	0.922	1.222a	10	145	0.282

Group differences

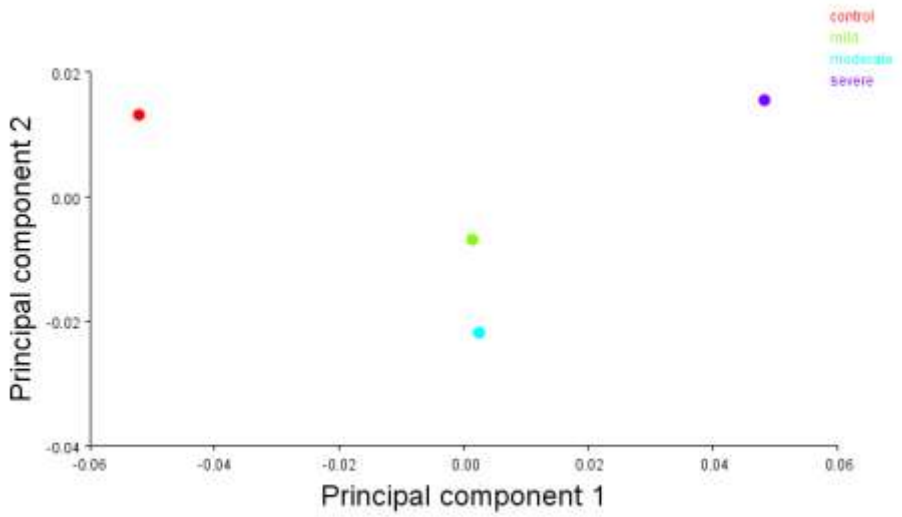
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	4.79%	5.03%	11.37%
mild	0.0004	-	1.16%	3.76%
moderate	<.0001	0.4959	-	3.89%
severe	<.0001	0.0053	0.0062	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	Analysis	Jacknife
Control	62.5	50.0
Mild	27.5	22.5
Moderate	40.0	25.0
Severe	51.3	38.5

Lower left lateral incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.436	4.262	30	391.057	0.000
sex	0.927	1.055a	10	133	0.402
groups * sex	0.795	1.059	30	391.057	0.386

MANOVA of Groups by Gender without interaction

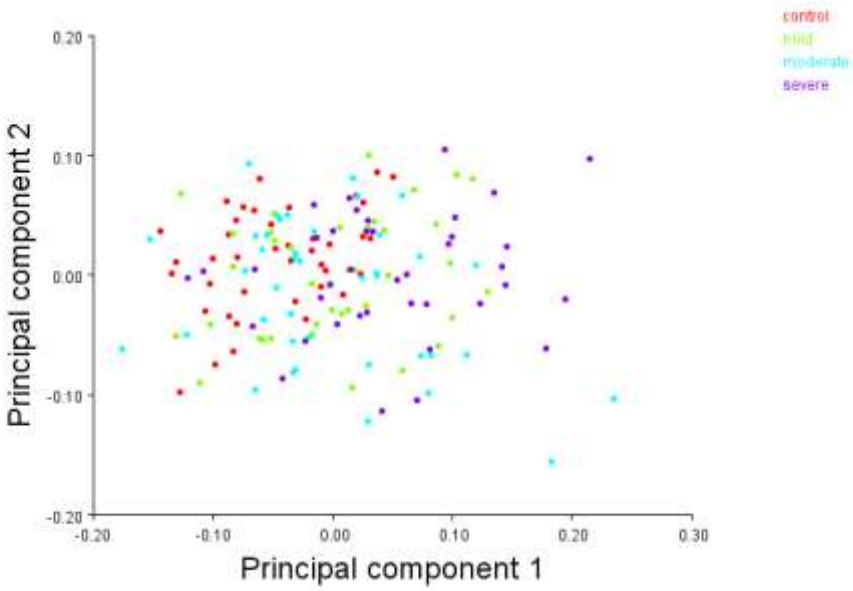
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.444	4.241	30	399.863	0.001
sex	0.924	1.124a	10	136	0.349

Group differences

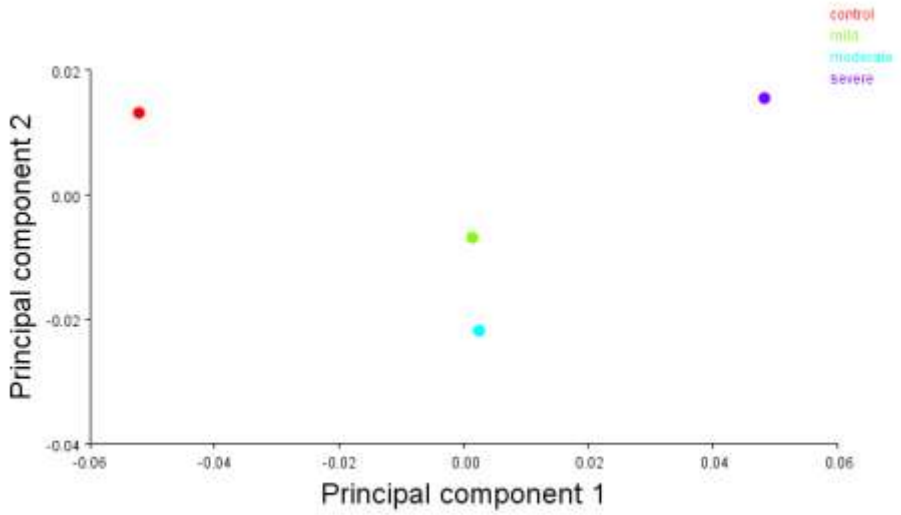
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	6.10%	5.27%	9.01%
mild	0.0042	-	2.21%	2.87%
moderate	0.0036	0.0368	-	2.33%
severe	0.0025	0.0444	0.0403	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

Groups	Gender (%)	
	Analysis	Jacknife
Control	64.1	59.0
Mild	57.5	52.5
Moderate	44.7	34.2
Severe	57.6	42.2

Lower left central incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.563	2.651	30	367.576	0.000
sex	0.899	1.398a	10	125	0.189
groups * sex	0.698	1.594	30	367.576	0.027

Group differences

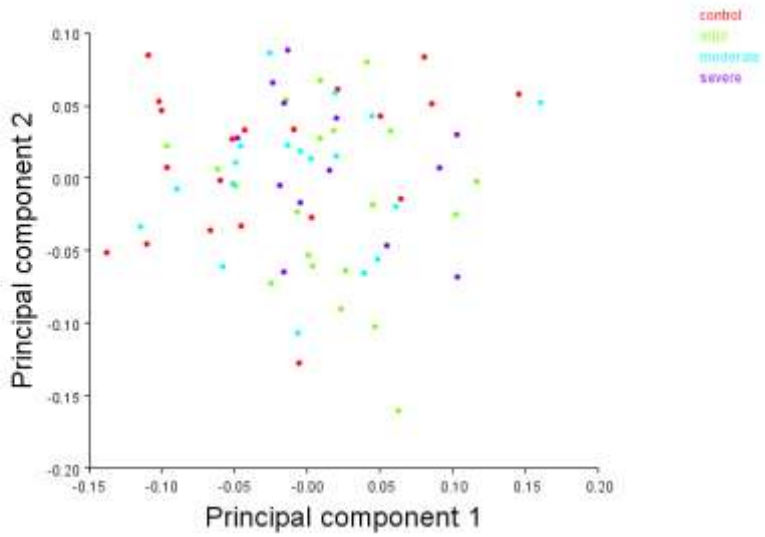
Pairwise test

Pairwise tests for mean shape differences between female groups

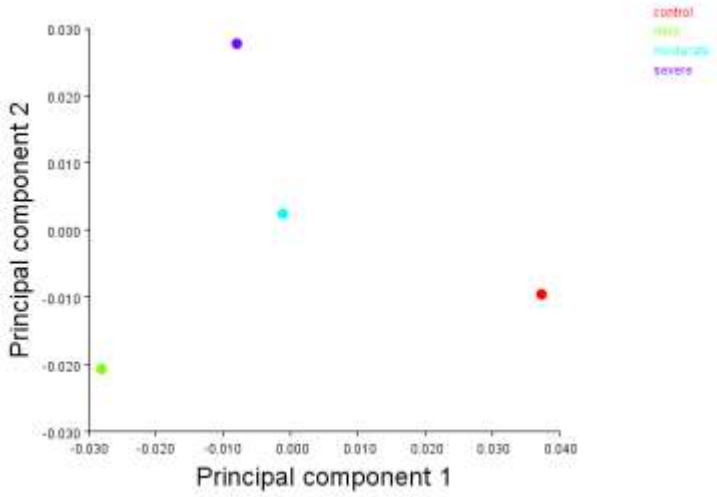
	control	mild	moderate	severe
control	-	7.92%	3.83%	4.75%
mild	0.0020	-	3.87%	4.52%
moderate	0.1569	0.1592	-	3.40%
severe	0.1242	0.1400	0.3779	-

Pairwise tests for mean shape differences between male groups

	control	mild	moderate	severe
control	-	10.19%	12.19%	14.88%
mild	0.0025	-	3.42%	1.70%
moderate	0.0008	0.2881	-	4.93%
severe	<.0001	0.7650	0.1430	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender			
	Female (%)		Male (%)	
Groups	Analysis	Jacknife	Analysis	Jacknife
Control	55.0	50.0	80.0	55.0
Mild	65.0	50.0	36.8	21.1
Moderate	55.6	38.9	68.8	56.3
Severe	53.8	23.1	75.0	50.0

Lower right central incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.642	1.997	30	367.576	0.002
sex	0.902	1.355a	10	125	0.209
groups * sex	0.675	1.758	30	367.576	0.009

Group differences

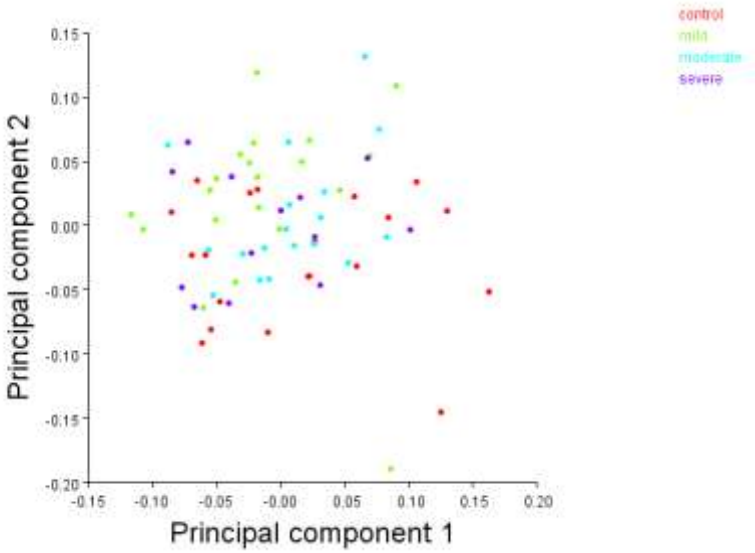
Pairwise test

Pairwise tests for mean shape differences between female groups

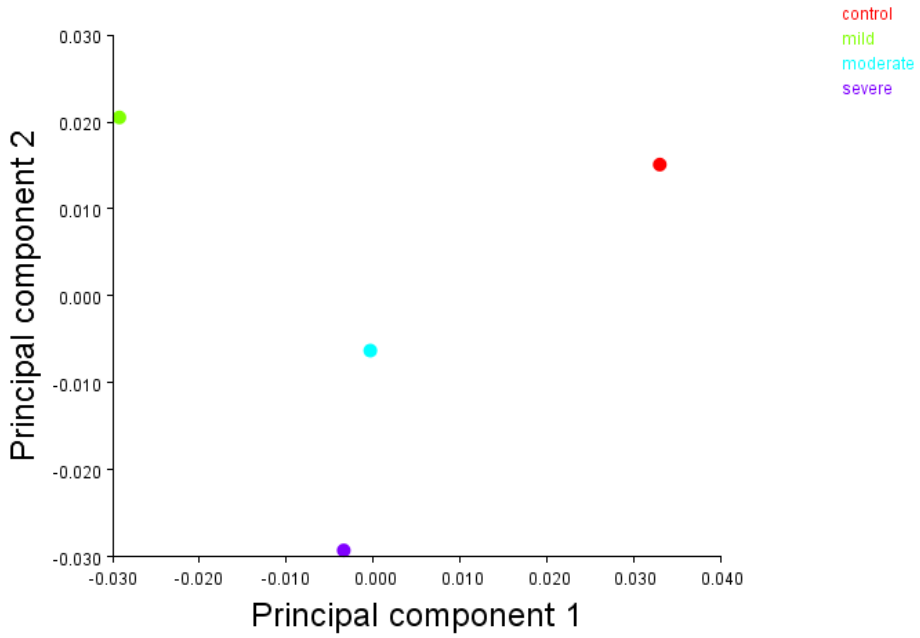
	control	mild	moderate	severe
control	-	5.56%	3.25%	8.15%
mild	0.0288	-	3.68%	5.26%
moderate	0.2664	0.1871	-	2.40%
severe	0.0020	0.0878	0.7085	-

Pairwise tests for mean shape differences between male groups

	control	mild	moderate	severe
control	-	5.05%	5.32%	11.21%
mild	0.0625	-	2.34%	3.73%
moderate	0.0652	0.5091	-	2.45%
severe	0.0002	0.2352	0.6333	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender			
	Female (%)		Male (%)	
Groups	Analysis	Jacknife	Analysis	Jacknife
Control	50.0	30.0	60.0	35.0
Mild	65.0	50.0	60.0	45.0
Moderate	38.9	16.7	56.3	37.5
Severe	69.2	30.8	60.0	40.0

Lower right lateral incisor

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.583	2.673	30	396.928	0.001
sex	0.845	2.482a	10	135	0.009
groups * sex	0.677	1.879	30	396.928	0.004

Group differences

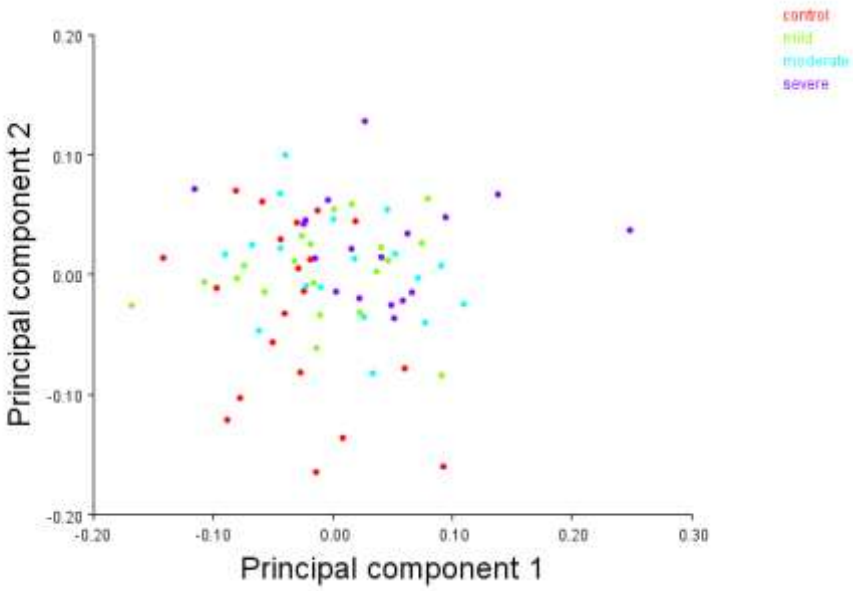
Pairwise test

Pairwise tests for mean shape differences between female groups

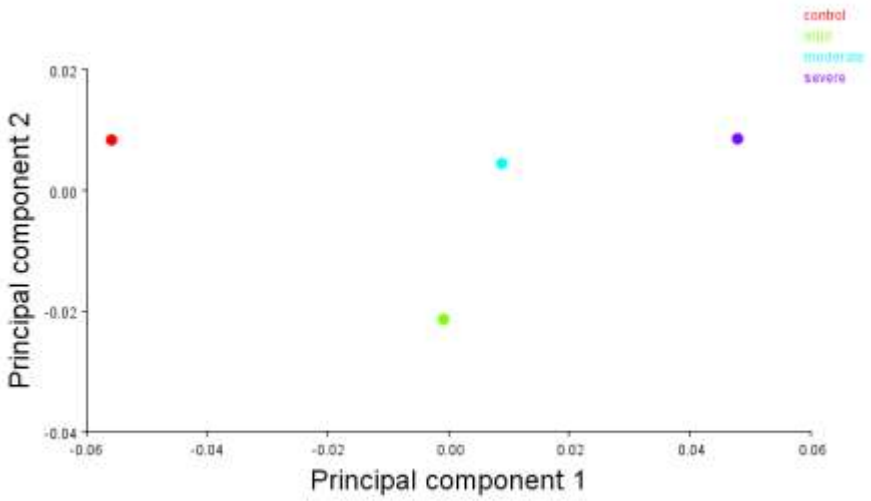
	control	mild	moderate	severe
control	-	7.01%	3.98%	4.84%
mild	0.0003	-	11.06%	2.89%
moderate	0.1056	<.0001	-	4.09%
severe	0.0809	0.3833	0.1245	-

Pairwise tests for mean shape differences between male groups

	control	mild	moderate	severe
control	-	4.45%	7.04%	9.22%
mild	0.0242	-	2.01%	4.89%
moderate	0.0092	0.6608	-	3.72%
severe	<.0001	0.0717	0.2113	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender			
	Female (%)		Male (%)	
Groups	Analysis	Jacknife	Analysis	Jacknife
Control	52.6	36.8	75.0	70.0
Mild	85.0	80.0	45.0	15.0
Moderate	70.0	45	44.4	33.3
Severe	47.1	35.3	72.2	55.6

Lower right canine

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.315	6.466	30	402.798	0.001
sex	0.844	2.530a	10	137	0.008
groups * sex	0.577	2.77	30	402.798	0.001

Group differences

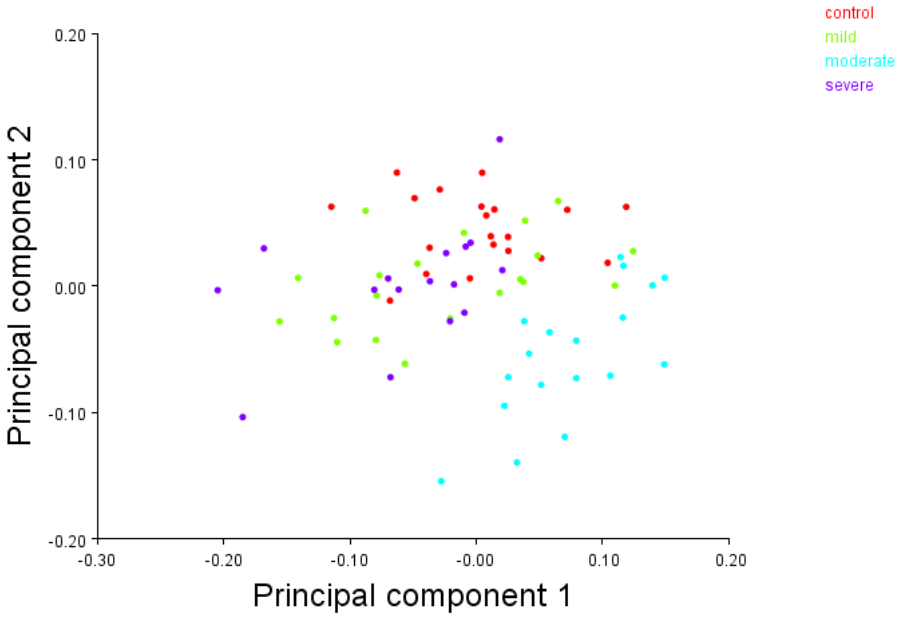
Pairwise test

Pairwise tests for mean shape differences between female groups

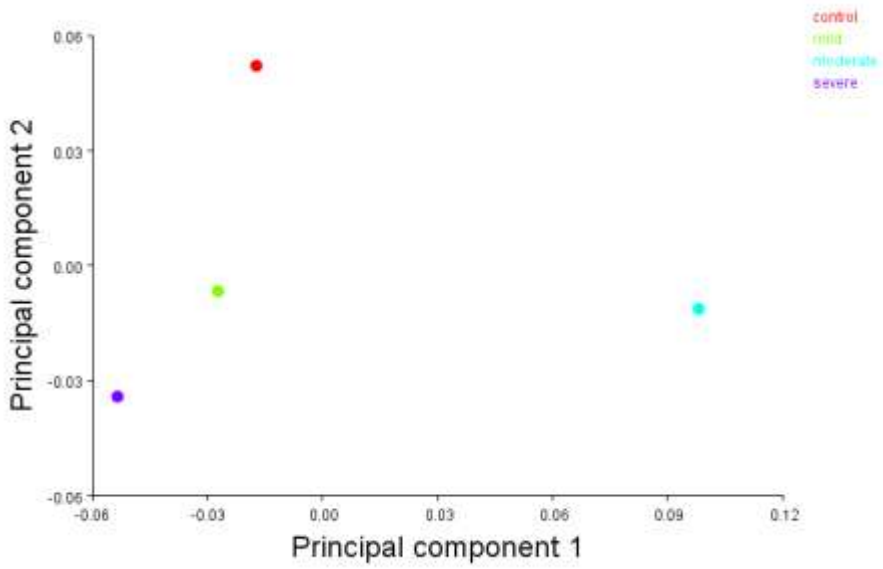
	control	mild	moderate	severe
control	-	4.71%	4.21%	6.82%
mild	0.0427	-	5.48%	4.38%
moderate	0.0798	0.0176	-	2.66%
severe	0.0055	0.0697	0.3926	-

Pairwise tests for mean shape differences between male groups

	control	mild	moderate	severe
control	-	6.53%	22.55%	10.39%
mild	0.0120	-	20.84%	4.27%
moderate	<.0001	<.0001	-	25.91%
severe	0.0001	0.1296	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender			
	Female (%)		Male (%)	
Groups	Analysis	Jacknife	Analysis	Jacknife
Control	50.0	45.0	80.0	65.0
Mild	80.0	60.0	60.0	45.0
Moderate	55.0	25.0	100.0	88.9
Severe	45.0	25.0	68.8	37.5

Lower right first premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.207	5.541	45	357.27	0.001
sex	0.892	.964a	15	120	0.497
groups * sex	0.766	0.747	45	357.27	0.884

MANOVA of Groups by Gender without interaction

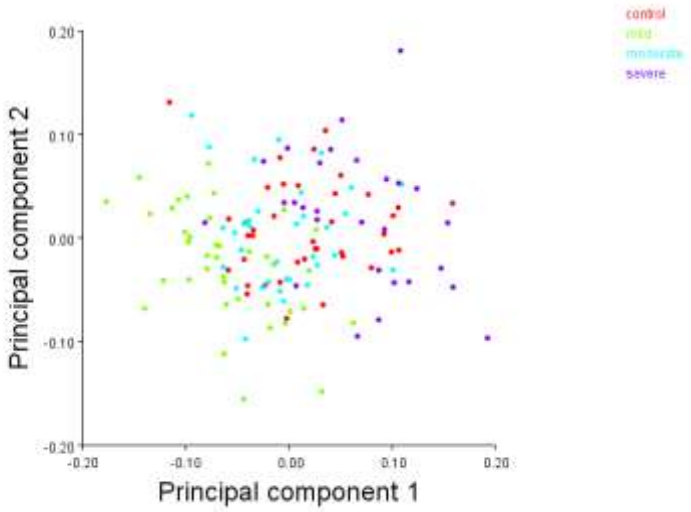
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.206	5.717	45	366.182	0.001
sex	0.886	1.056a	15	123	0.405

Group differences

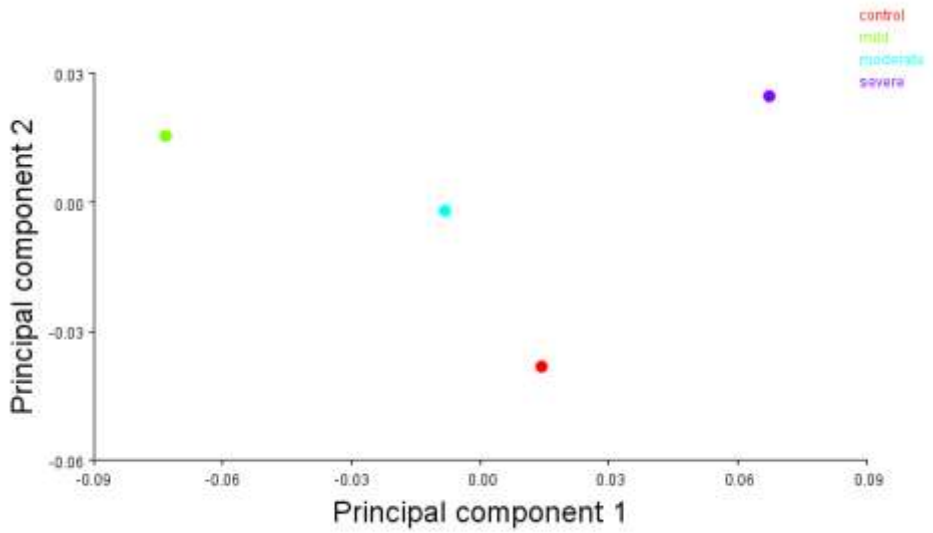
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	10.68%	3.08%	6.71%
mild	<.0001	-	5.58%	16.23%
moderate	0.0001	0.0017	-	6.74%
severe	<.0001	<.0001	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	Analysis	Jacknife
Control	71.8	61.5
Mild	82.1	74.4
Moderate	69.4	47.2
Severe	71.4	64.3

Lower right second premolar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.164	4.712	45	253.294	0.001
sex	0.89	.703a	15	85	0.775
groups * sex	0.612	1.013	45	253.294	0.457

MANOVA of Groups by Gender without interaction

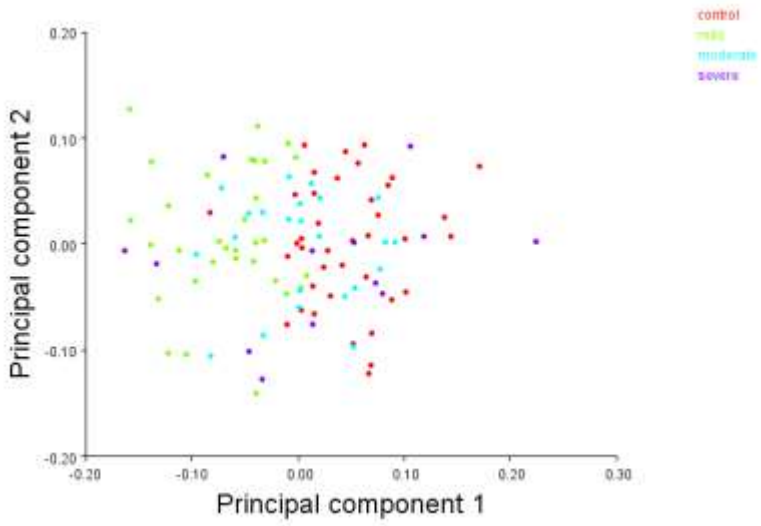
Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.169	4.784	45	262.206	0.001
sex	0.854	1.003a	15	88	0.459

Group differences

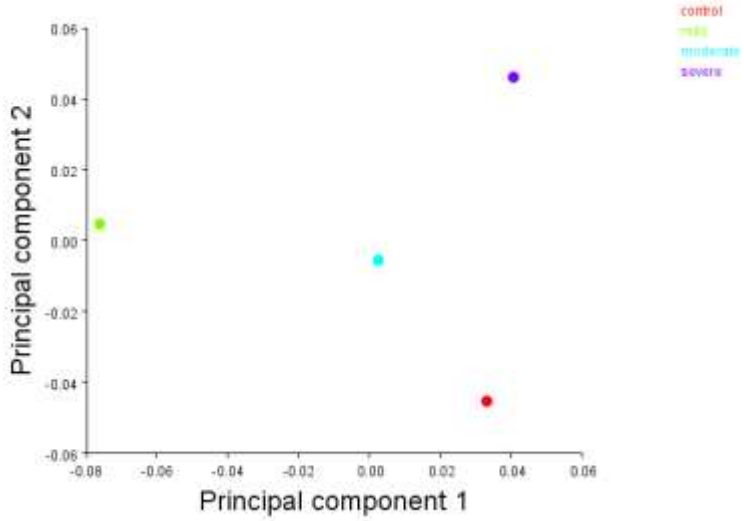
Pairwise test

Pairwise tests for mean shape differences between groups

	control	mild	moderate	severe
control	-	13.75%	3.72%	6.05%
mild	<.0001	-	7.29%	11.17%
moderate	0.0030	<.0001	-	4.46%
severe	0.0001	<.0001	0.0964	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender (%)	
Groups	Analysis	Jacknife
Control	82.1	74.4
Mild	84.4	75.0
Moderate	65.2	43.5
Severe	69.2	69.2

Lower right first molar

Differences in Shape

MANOVA of Groups by Gender

Effect	Wilks' Lambda	F	Hypothesis df	Error df	Sig.
groups	0.14	5.869	60	376.75	0.001
sex	0.754	2.054a	20	126	0.009
groups * sex	0.375	2.441	60	376.75	0.001

Group differences

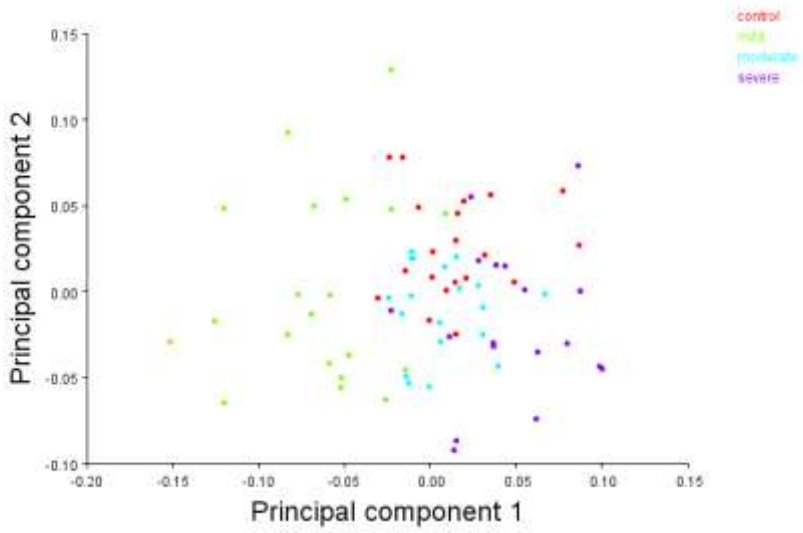
Pairwise test

Pairwise tests for mean shape differences between female groups

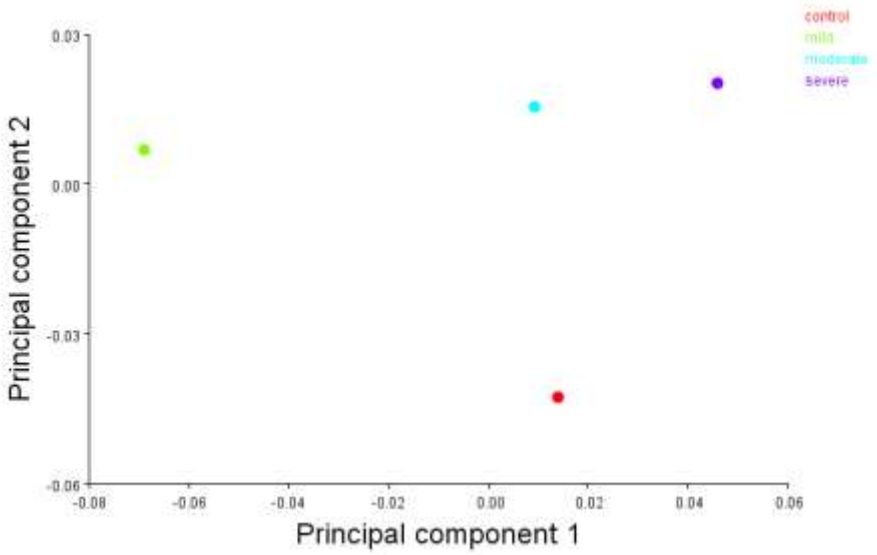
	control	mild	moderate	severe
control	-	13.17%	7.58%	8.14%
mild	<.0001	-	10.46%	15.16%
moderate	<.0001	<.0001	-	5.80%
severe	<.0001	<.0001	0.0011	-

Pairwise tests for mean shape differences between male groups

	control	mild	moderate	severe
control	-	4.59%	5.78%	9.48%
mild	0.0154	-	5.12%	13.15%
moderate	0.0005	0.0025	-	9.72%
severe	<.0001	<.0001	<.0001	-



Groups overall shapes. Scatter plots of the first two principal components (PCs) of shape variables



Groups mean shapes. Scatter plots of the first principal components (PCs) of shape variables

Discriminant analysis

Percentages of correctly classified specimens in discriminant analyses

	Gender			
	Female (%)		Male (%)	
Groups	Analysis	Jacknife	Analysis	Jacknife
Control	90.0	85.0	75.0	30.0
Mild	85.0	70.0	80.0	45.0
Moderate	78.9	52.6	75.0	40.0
Severe	88.9	50.0	81.3	56.3

Appendix IV Allometry analysis for all teeth

Upper right first molar

Group regression onto size

Groups	%	P value
control	3.03%	0.2451
mild	6.18%	0.0022
moderate	3.48%	0.1390
severe	4.25%	0.0648

Upper right second premolar

Group regression onto size

Groups	%	P value
control	7.34%	0.0023
mild	3.07%	0.3931
moderate	5.24%	0.1661
severe	8.11%	0.0813

Upper right first premolar

Group regression onto size

Groups	%	P value
control	7.74%	0.0012
mild	4.82%	0.0228
moderate	5.73%	0.0432
severe	6.79%	0.2366

Upper right canine

Group regression onto size

Gender	Groups	%	P value
Female	control	13.55%	0.0078
	mild	12.37%	0.0131
	moderate	8.92%	0.1428
	severe	5.57%	0.6569
Male	control	10.20%	0.0370
	mild	16.02%	0.0117
	moderate	17.20%	0.0071
	severe	12.04%	0.1768

Upper right lateral incisor

Group regression onto size

Groups	%	P value
control	4.34%	0.1009
mild	10.15%	0.1344
moderate	6.18%	0.1864
severe	3.34%	0.7783

Upper right central incisor

Group regression onto size

Groups	%	P value
control	4.90%	0.0486
mild	5.69%	0.0343
moderate	2.79%	0.3549
severe	1.72%	0.7614

Upper left central incisor

Group regression onto size

Groups	%	P value
control	6.46%	0.0124
mild	6.77%	0.0093
moderate	2.29%	0.5118
severe	4.47%	0.0772

Upper left lateral incisor

Group regression onto size

Groups	%	P value
control	4.02%	0.1097
mild	14.27%	0.0121
moderate	5.56%	0.3291
severe	6.28%	0.1935

Upper left canine

Group regression onto size

Groups	%	P value
control	11.48%	0.0007
mild	11.56%	0.0001
moderate	14.37%	<.0001
severe	6.49%	0.0621

Upper left first premolar

Group regression onto size

Groups	%	P value
control	5.81%	0.0046
mild	3.17%	0.2273
moderate	4.95%	0.0557
severe	4.34%	0.5297

Upper left second premolar

Group regression onto size

Groups	%	P value
control	2.27%	0.5810
mild	2.21%	0.7175
moderate	4.71%	0.1995
severe	5.03%	0.6271

Upper left first molar

Group regression onto size

Groups	%	P value
control	3.03%	0.2474
mild	3.98%	0.0437
moderate	2.76%	0.4080
severe	3.61%	0.2121

Lower left first molar

Group regression onto size

Gender	Groups	%	P value
Female	control	7.05%	0.1171
	mild	6.20%	0.2325
	moderate	7.48%	0.0649
	severe	5.37%	0.4877
Male	control	6.31%	0.2102
	mild	4.72%	0.5855
	moderate	8.81%	0.0255
	severe	8.51%	0.2569

Lower left second premolar

Group regression onto size

Groups	%	P value
control	4.23%	0.0887
mild	4.75%	0.1512
moderate	4.97%	0.6153
severe	6.81%	0.6322

Lower left first premolar

Group regression onto size

Groups	%	P value
control	8.95%	0.0001
mild	6.39%	0.0024
moderate	4.17%	0.1559
severe	6.44%	0.0542

Lower left canine

Group regression onto size

Groups	%	P value
control	9.00%	0.0004
mild	11.39%	0.0001
moderate	10.95%	0.0008
severe	15.24%	<.0001

Lower left lateral incisor

Group regression onto size

Groups	%	P value
control	10.76%	0.0001
mild	8.08%	0.0013
moderate	6.54%	0.0382
severe	7.65%	0.0216

Lower left central incisor

Group regression onto size

Gender	Groups	%	P value
Female	control	11.03%	0.0411
	mild	9.09%	0.0676
	moderate	3.93%	0.7134
	severe	7.08%	0.5579
Male	control	4.92%	0.4852
	mild	35.36%	0.0002
	moderate	33.59%	0.0015
	severe	21.23%	0.0081

Lower right central incisor

Group regression onto size

Gender	Groups	%	P value
Female	control	13.13%	0.0101
	mild	5.59%	0.3643
	moderate	9.99%	0.0910
	severe	8.92%	0.3796
Male	control	8.12%	0.1180
	mild	34.06%	<.0001
	moderate	28.14%	0.0104
	severe	16.34%	0.0218

Lower right lateral incisor

Group regression onto size

Gender	Groups	%	P value
Female	control	8.40%	0.1194
	mild	13.37%	0.0060
	moderate	4.72%	0.5071
	severe	4.18%	0.6887
Male	control	10.86%	0.0496
	mild	10.52%	0.0403
	moderate	14.71%	0.0160
	severe	18.16%	0.0131

Lower right canine

Group regression onto size

Gender	Groups	%	P value
Female	control	10.38%	0.0446
	mild	15.64%	<.0001
	moderate	6.37%	0.2677
	severe	17.50%	<.0001
Male	control	16.18%	0.0008
	mild	22.92%	0.0002
	moderate	14.71%	0.0153
	severe	19.11%	0.0030

Lower right first premolar

Group regression onto size

Groups	%	P value
control	5.38%	0.0119
mild	4.06%	0.0728
moderate	2.76%	0.4745
severe	5.12%	0.1387

Lower right second premolar

Group regression onto size

Groups	%	P value
control	2.32%	0.5938
mild	2.52%	0.7108
moderate	6.59%	0.0983
severe	12.33%	0.1541

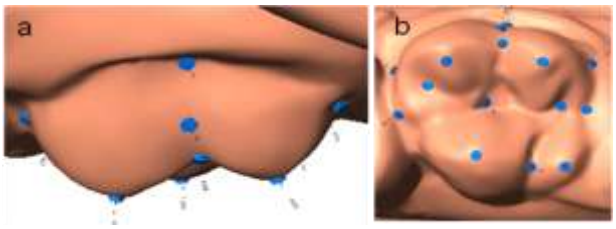
Lower right first molar

Group regression onto size

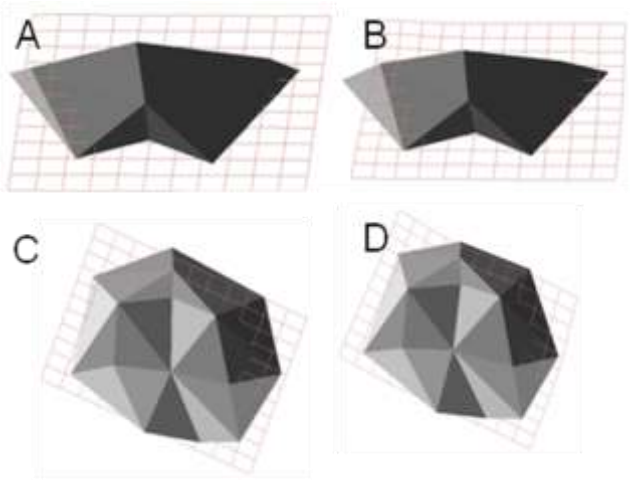
Gender	Groups	%	P value
Female	control	6.45%	0.1849
	mild	8.78%	0.0319
	moderate	4.79%	0.6804
	severe	5.40%	0.5722
Male	control	3.53%	0.8846
	mild	3.77%	0.8286
	moderate	7.77%	0.0436
	severe	6.29%	0.5073

Appendix V Shape transformation for all teeth

Upper left second molar

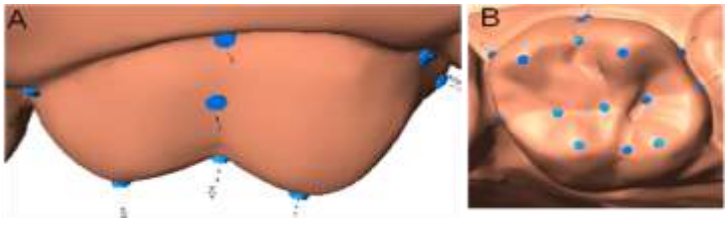


Upper left second molar's landmarks (scanned image). A, buccal view. B, occlusal view.

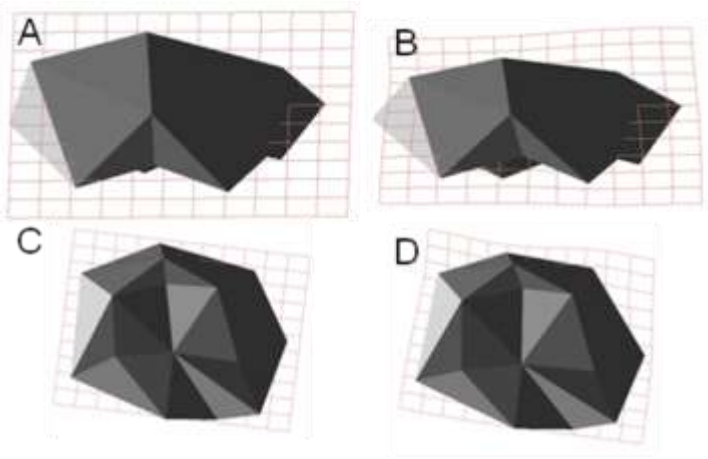


Upper left second molar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Occlusal view, and target form (severe hypodontia) - B: Buccal view, D: Occlusal view.

Upper left first molar

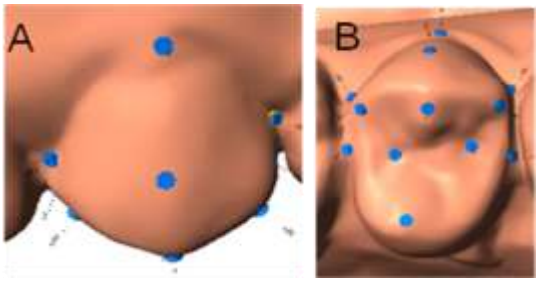


Upper left first molar's landmarks (scanned image). A, buccal view. B, occlusal view.

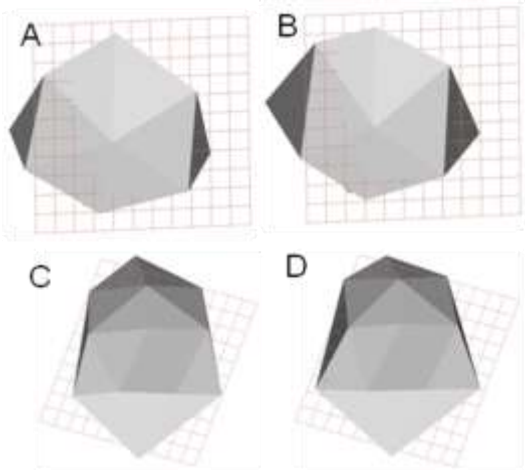


Upper left first molar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Occlusal view, and target form (severe hypodontia) - B: Buccal view, D: Occlusal view.

Upper left second premolar

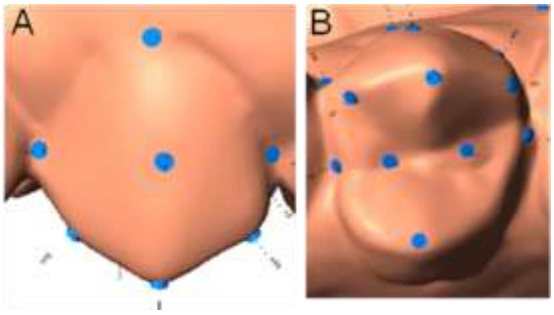


Upper left second premolar's landmarks (scanned image). A, buccal view. B, occlusal view.

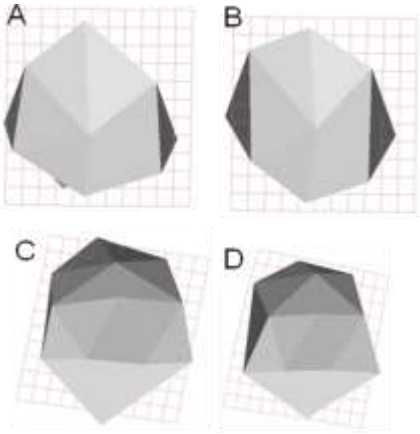


Upper left second premolar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Occlusal view, and target form (severe hypodontia) - B: Buccal view, D: Occlusal view.

Upper left first premolar

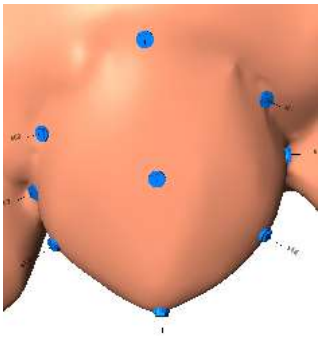


Upper left first premolar's landmarks (scanned image). A, buccal view. B, occlusal view.

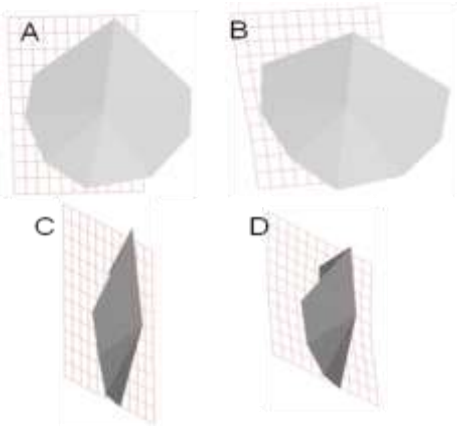


Upper left first premolar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Occlusal view, and target form (severe hypodontia) - B: Buccal view, D: Occlusal view.

Upper left canine

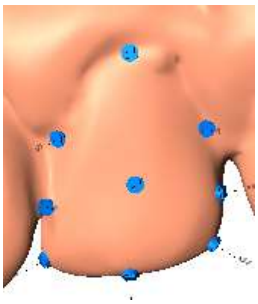


Upper right canine's landmarks (scanned image), buccal view.

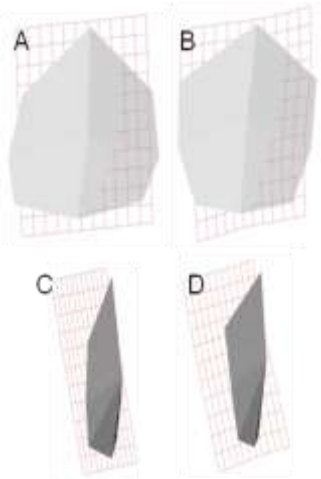


Upper left canine, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Lateral view, and target form (severe hypodontia) - B: Buccal view, D: Lateral view.

Upper right lateral incisor

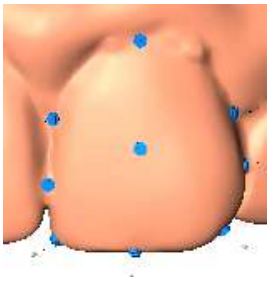


Upper left lateral incisor's landmarks (scanned image), buccal view.

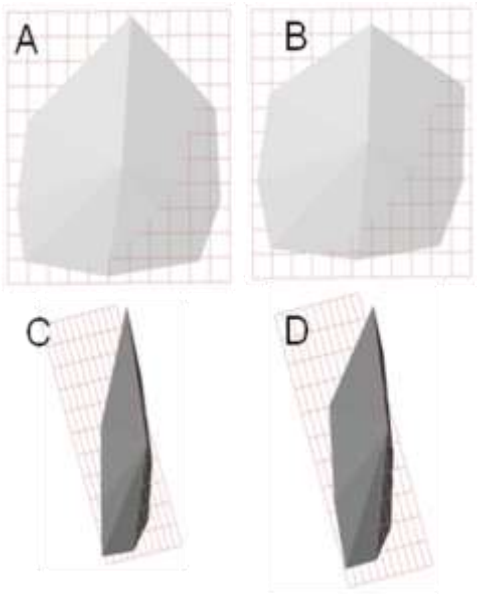


Upper left lateral incisor, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Lateral view, and target form (severe hypodontia) - B: Buccal view, D: Lateral view.

Upper left central incisor

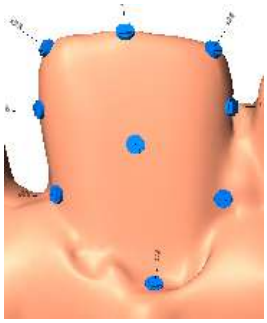


Upper left central incisor's landmarks (scanned image), buccal view.

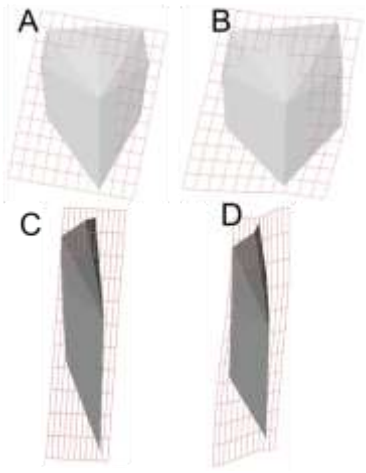


Upper left central incisor, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Lateral view, and target form (severe hypodontia) - B: Buccal view, D: Lateral view.

Lower left central incisor

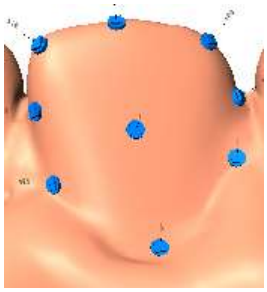


Lower left central incisor's landmarks (scanned image), buccal view.

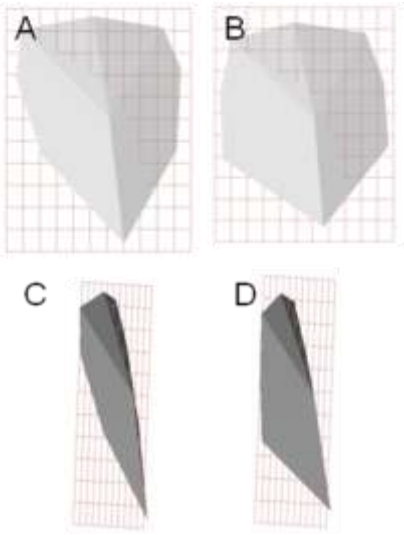


Lower left central incisor, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Lateral view, and target form (severe hypodontia) - B: Buccal view, D: Lateral view.

Lower left lateral incisor

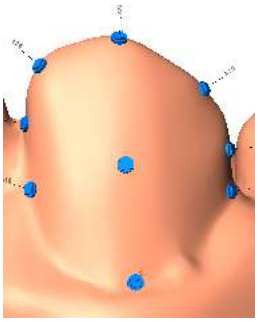


Lower left lateral incisor's landmarks (scanned image), buccal view.

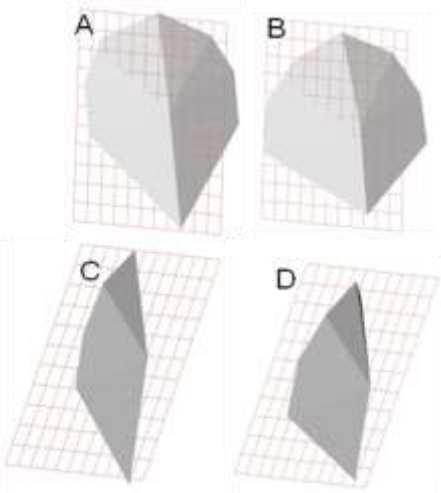


Lower left lateral incisor, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Lateral view, and target form (severe hypodontia) - B: Buccal view, D: Lateral view.

Lower left canine

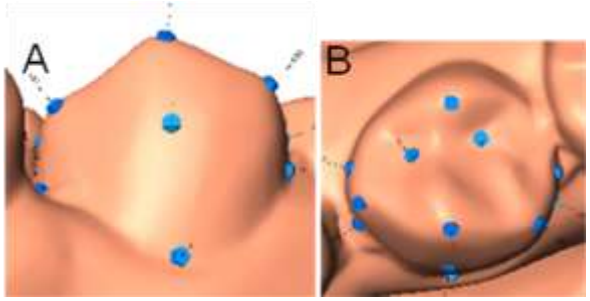


Lower lefet canine's landmarks (scanned image), buccal view.

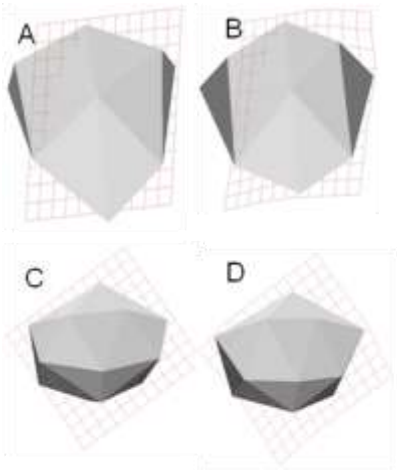


Lower left canine, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Lateral view, and target form (severe hypodontia) - B: Buccal view, D: Lateral view.

Lower left first premolar

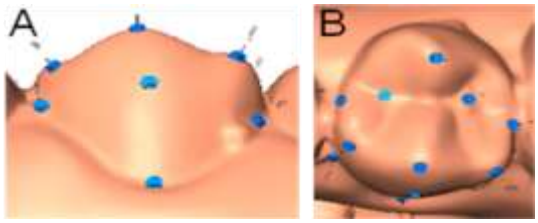


Lower left first premolar's landmarks (scanned image). A, buccal view. B, occlusal view.

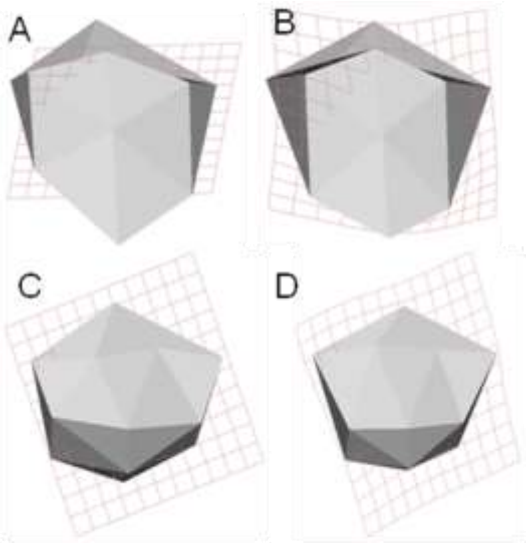


Lower left first premolar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Occlusal view, and target form (severe hypodontia) - B: Buccal view, D: Occlusal view.

Lower left second premolar

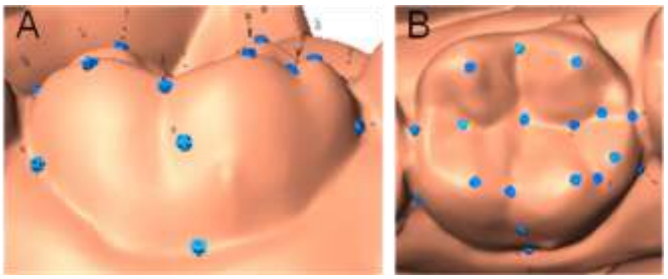


Lower left second premolar's landmarks (scanned image). A, buccal view. B, occlusal view.

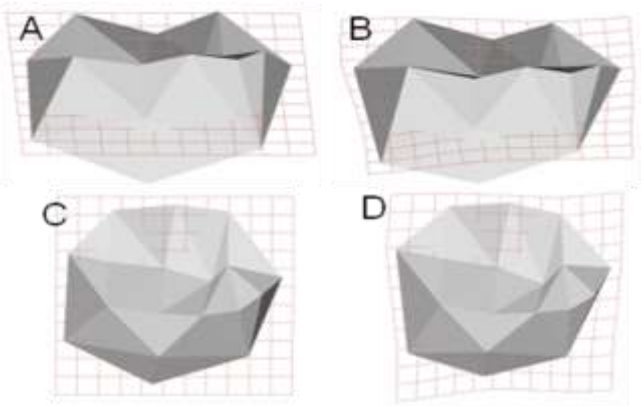


Lower left second premolar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Occlusal view, and target form (severe hypodontia) - B: Buccal view, D: Occlusal view.

Lower left first molar

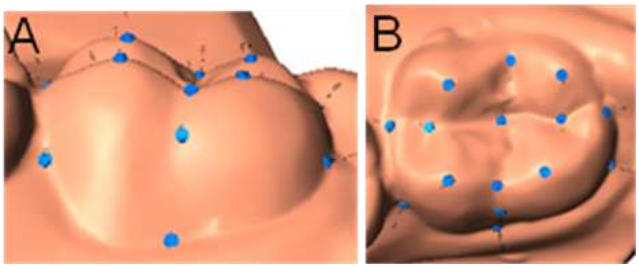


Lower left first molar's landmarks (scanned image). A, buccal view. B, occlusal view.

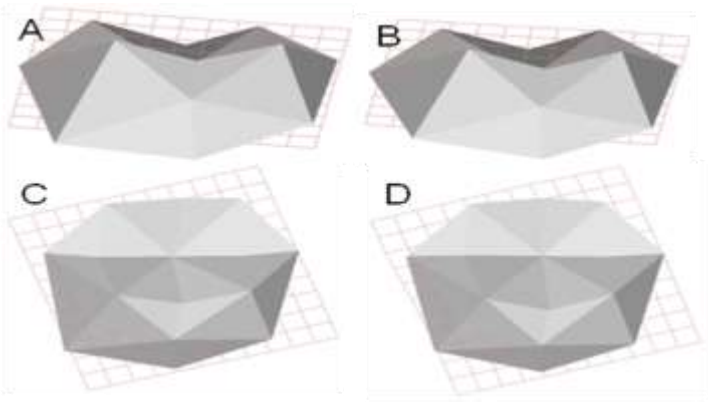


Lower left first molar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) – A: Buccal view, C: Occlusal view, and target form (severe hypodontia) – B: Buccal view, D: Occlusal view.

Lower left second molar



Lower left second molar's landmarks (scanned image). A, buccal view. B, occlusal view.



Lower left second molar, Shape variation along PC1 visualized with a transformation grid using thin plate splines derived from the difference between reference form (control subject) - A: Buccal view, C: Occlusal view, and target form (severe hypodontia) - B: Buccal view, D: Occlusal view.