A study into the relationship between dental development and cervical vertebral maturation in UK subjects

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Abstract

Aim:

To examine relationships between dental and skeletal maturity in White British and Asian UK subjects.

Methods:

Ninety subjects per ethnic group, with digital panoramic and lateral cephalometric radiographs, were selected from the records of Birmingham Dental Hospital. Dental maturity was assessed from the development stage of the left mandibular canine, first and second premolar, and second molar using the Demirjian Index (DI). Skeletal maturity was determined from cervical vertebral maturation (CVM) stage using the method of Baccetti. Spearman rank-order correlation coefficients were calculated to measure the association between DI and CVM.

Results:

Females reached each CVM stage at an earlier age than males. There was no statistically significant difference in the mean age of White British and Asian subjects at each CVM stage. The mandibular canine had the highest correlation with CVM stage in White British males (r = 0.568). The mandibular second molar demonstrated the highest correlation to CVM stage in White British females and in Asian males and females (r = 0.533; r = 0.752; r = 0.569 respectively).

Conclusion:

Moderate statistically significant correlations were observed between DI and CVM stages, suggesting that dental development stage can be considered as a method for determining skeletal maturity in UK subjects during orthodontic treatment planning.

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CVM	Cervical vertebral maturation
CVMI	Cervical vertebral maturational index
DI	Demirjian index
HWR	Hand wrist radiographs
MARA	Mandibular anterior repositioning appliance
PHV	Peak height velocity
QCVM	Quantitative cervical vertebral maturations system
RME	Rapid maxillary expansion
SMA	Skeletal maturation assessment
SMI	Skeletal maturation indicator
SROCC	Spearman rank order correlation coefficient
TFBC	Twin force bite corrector

Chapter 1

Literature review

Chapter 1 Literature Review

1.1 Introduction

When planning orthodontic treatment it is often important to determine whether an individual has reached or completed their pubertal growth spurt. The rate of mandibular growth peaks during puberty and it has been demonstrated that the greatest effects of functional orthodontic appliances occur when peak mandibular growth is included within the treatment period (Baccetti et al., 2000). The rate and timing of craniofacial growth can also affect orthodontic decision making with respect to the timing and use of interceptive treatments, extra-oral traction, the need for extractions, overbite control, retention regimes and the timing of orthognathic surgery (Björk, 1972; Houston, 1980; Kopecky and Fishman, 1993).

There is considerable variation between individuals concerning the onset, duration and intensity of the pubertal growth spurt. Several different measures have been used to assess maturation, including chronological age; increases in body height and weight; development of secondary sexual characteristics; skeletal maturity; and the stages of both dental calcification and eruption. These indicators have also been used to predict the timing of future pubertal growth and the amount of growth remaining.

The ability to identify an individual's stage of maturation is therefore an important concept in orthodontics due to the influence growth can have on treatment options and results. A simple and reliable method of determining maturation status would consequently be advantageous to clinicians.

1.2 Growth and maturation

The term growth, when used in relation to the human body, represents an increase in size or number whereas the term development signifies an increase in the degree of organisation and complexity (Proffit *et al*., 2012).

Rapid growth of the human body occurs during the foetal period and continues immediately after birth. The rate of growth then falls rapidly until a small and inconsistent spurt around 6 years of age, before levelling out to give a period of relatively steady increase in height and weight (Houston, 1980; Sullivan, 1983). When puberty commences, a rapid increase in height accompanies sexual development and progress towards maturity.

Growth is a differential process. Some parts of the human body enlarge more or less than others. Fifty percent of total body length is taken up by the head at the third month of intrauterine development. The ratio is 30 percent at birth and in adults it is 12 percent. This is due to faster growth of the limbs and trunk compared to the head and face (Proffit *et al*., 2012).

Scammon's curves (Scammon, 1930) are used to demonstrate how different tissue systems of the body vary in their rates of growth (Figure 1.1). Genital tissues and general body tissues such as bone, muscle and organs show an S-shaped pattern, with a slowing of the rate of growth during childhood before a rapid increase at the time of puberty.

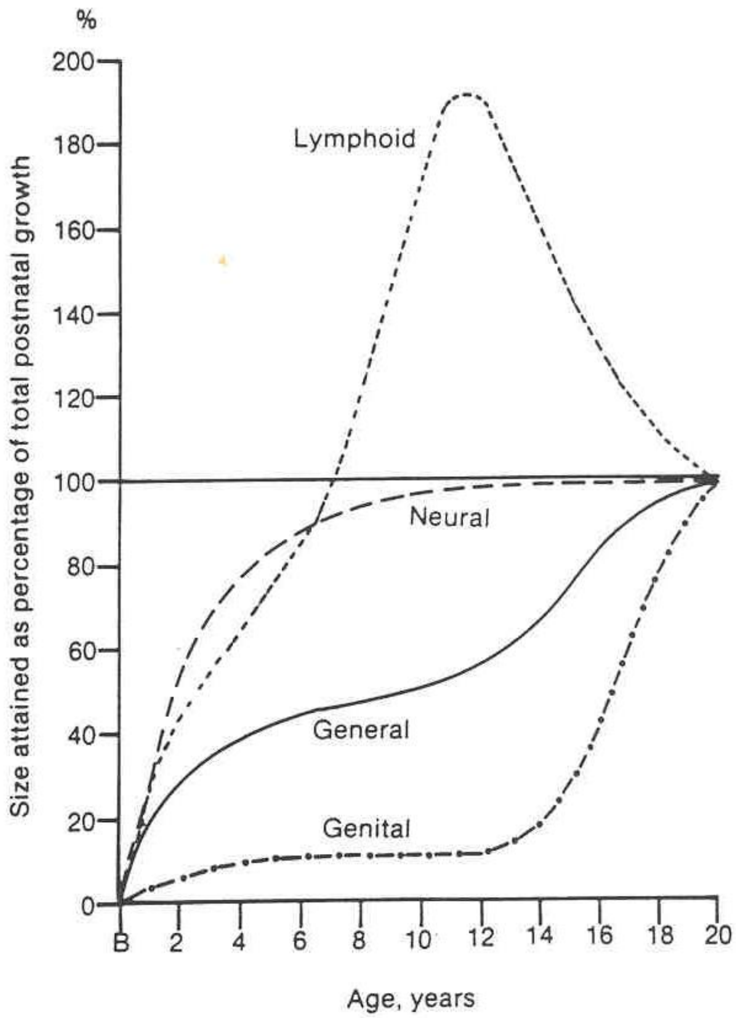

Figure 1.1 Scammon's curves of systemic growth (Scammon, 1930)

1.2.1 Facial growth

Information about the growth of the face and jaws has been gained through the examination of serial cephalometric radiographs taken of subjects recruited to longitudinal growth studies. Björk (1955) placed implants in the jaws of his subjects allowing the growth pattern of the facial skeleton to be analysed further.

Facial growth is closely related to growth of the body as a whole and also accelerates during adolescence (Bambha, 1961; Hunter, 1966; Bergersen, 1972). Growth of the face follows a similar curve to that of general skeletal growth (Nanda, 1955). However, there is significant individual variation in growth patterns (Nanda and Ghosh, 1995b) and some individuals, particularly females, demonstrate a juvenile spurt in jaw growth 1-2 years before the pubertal growth spurt.

Sexual dimorphism results in larger facial growth increments at a younger age in girls than boys (Nanda and Ghosh, 1995b). The male development period usually lasts 2 years longer than that for females and provides relatively more growth (Nanda and Ghosh, 1995a; Nanda and Ghosh, 1995b; Ochoa and Nanda, 2004). In males this has the effect of straightening the facial profile as the chin becomes more prominent. Female profiles remain convex due to less incremental growth and duration of growth of the mandible.

Different growth rates have been observed for different dentofacial structures, with the mandible growing twice as much in length as the maxilla from the age of 6 to 20 years (Nanda and Ghosh, 1995a; Ochoa and Nanda, 2004).

The face continues to grow after increases in body height have ceased (Nanda, 1955). In the past, growth of the face was thought to be complete by early adulthood but it has been shown to progress throughout life albeit at a much reduced rate (Behrents, 1984; Nanda and Ghosh, 1995b). Late facial growth follows the pattern seen in maturation with the most prominent changes occurring in the vertical dimension followed by antero-posterior changes. Transverse changes are least evident. Late growth changes can be substantial in some individuals. Even a small amount of growth between ages 18-24 years can have a significant impact for patients requiring orthognathic surgery (Nanda and Ghosh, 1995a).

1.2.2 Maturation

Age is measured chronologically as the amount of time since conception or birth (Proffit *et al.*, 2012). Maturation is the process of change from an immature state to a fully developed one over time.

There can be considerable difference in the degree of physical development and maturity of children of the same chronological age. This is due to a wide variation in the onset, intensity and duration of pubertal growth between individuals (Houston, 1980; Hägg and Taranger, 1982; Demirjian *et al.*, 1985).

1.2.3 Factors affecting growth and maturation

Multiple environmental, hormonal and genetic factors influence human growth and development and the onset of puberty (Wei and Gregory, 2009). Environmental factors include climate, urbanisation, socio-economic conditions, nutrition, level of physical activity and psychological state. Exposure to chemicals, such as through passive smoking, access to public health measures and general health and illness levels also have an effect. Differences in growth and maturation are found between ethnic groups and genders (Soegiharto *et al*., 2008a). Genetics plays a key role in growth and facial dimensions are largely inherited (Hunter *et al.*, 1970). Tooth formation is genetically determined (Garn *et al*., 1960), as is the timing of puberty (Palmert and Boepple, 2001).

The concept of physiological or developmental age was developed based upon the degree of maturation of different systems and tissues as a way of representing an individual's progress towards maturity. Different parameters can be used to evaluate the level of maturity of an individual, including somatic; sexual; skeletal and dental development and these can be applied separately or collectively.

1.3 Somatic maturity

Somatic growth is assessed by measuring increases in height or weight over time. Standard growth charts, based on large-scale studies of groups of children, allow the height and weight of a child to be compared to that which would be expected for their age and sex.

Tanner et al., (1966) produced the first UK standards. Examples of current UK growth charts are shown in Figure 1.2 (RCPCH, 2013). Serial recordings allow a child to be followed over time and growth abnormalities can be detected if a child changes their percentile position relative to their peer group. The growth of other body parts can also be plotted in this way.

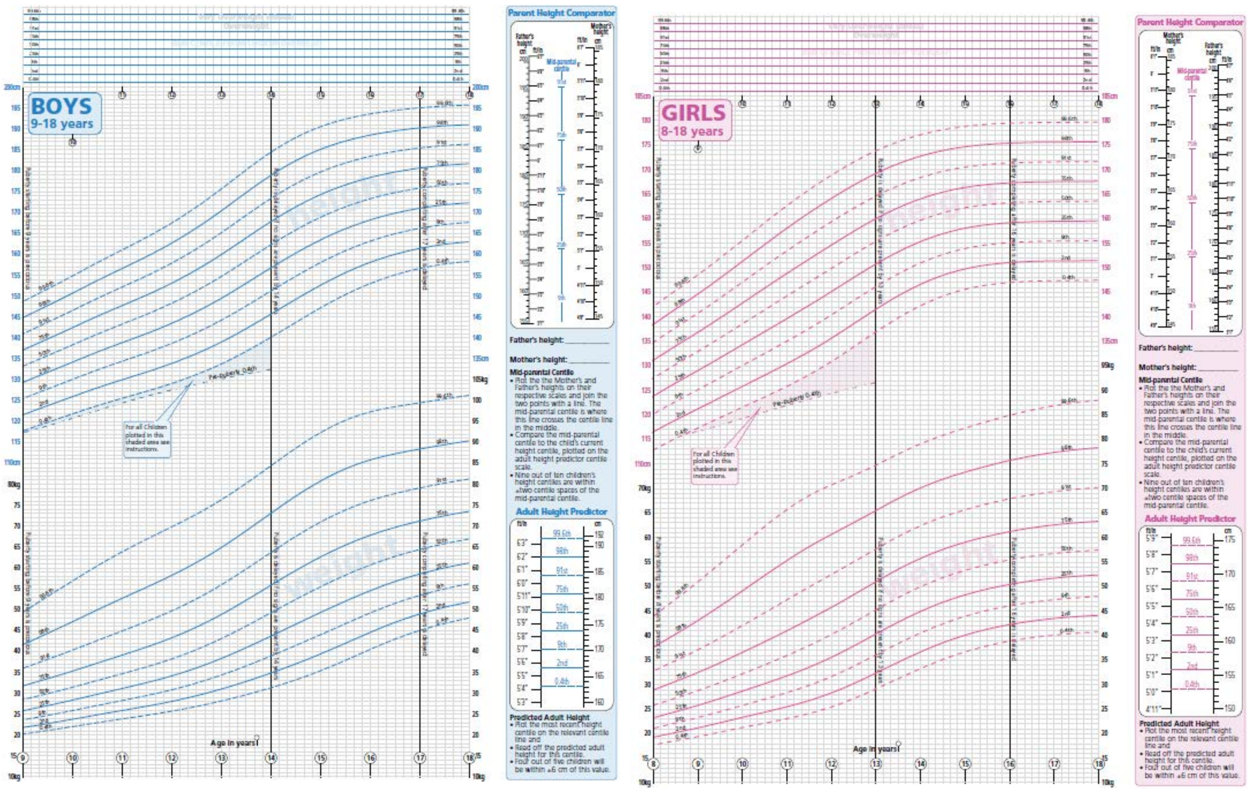

Figure 1.2 UK growth charts (Royal College of Paediatrics and Child Health, 2013)

1.3.1 Peak height velocity

Serial height increases can be plotted against age to assist identification of the adolescent growth spurt. However, this is a prolonged means of identifying this event and caries a risk that peak pubertal growth may not be identified until it is well underway or even complete (Houston, 1980). A height velocity graph plots height increments each year rather than the total height increase and allows a change in the rate of growth to be much more easily detected (Figure 1.3). The point where the highest rate of growth occurs is known as peak height velocity (PHV) represented by the peak on the graph. It is much easier to identify peak growth by plotting height velocity in cm/year rather than height increase in cm.

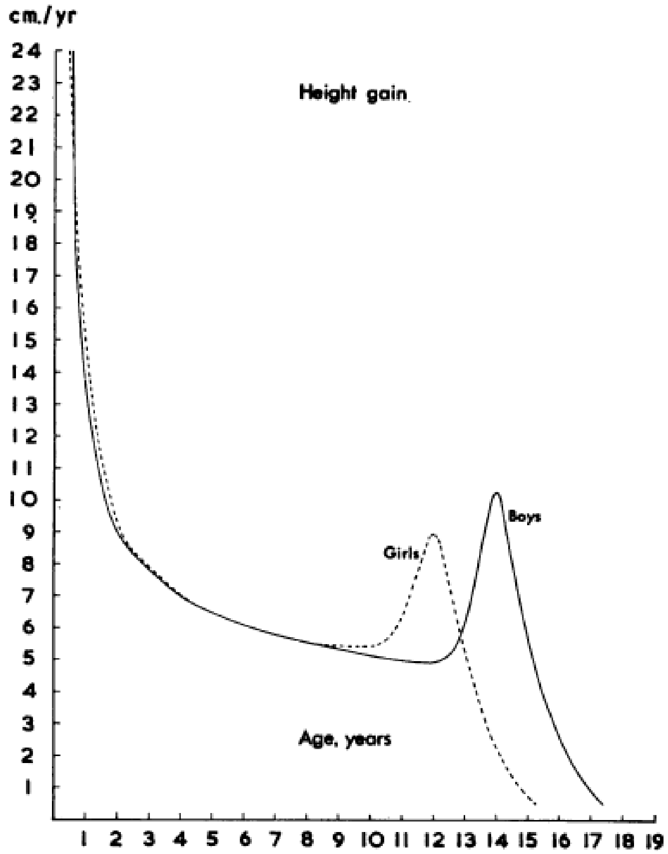

Figure 1.3 Height velocity graphs (Tanner *et al.*, 1966)

PHV was found to occur between 10-14 years in females and 12-16 years in males using longitudinal height records from the United Kingdom Harpenden growth study (Tanner *et al*., 1966; Sullivan, 1983). Wide individual variation was observed in both sexes. Sullivan (1983) used these data to establish a method for predicting the point approximately 1 year before PHV using serial height recordings and height velocity charts. The aim was to enable orthodontic treatment to be timed to begin at the onset of the pubertal growth spurt so it could be completed during the 2 year period of maximal skeletal growth.

In order to observe growth changes, serial height measurements taken with a stadiometer are required, ideally at no more than 3 monthly intervals. Some orthodontic practitioners do use this method to monitor growth, however longitudinal records of height are not that commonly used due to the associated time demands on both practitioners and patients (Hägg and Taranger, 1982; Franchi *et al*., 2000).

1.3.2 Relationship between facial growth and peak height velocity

Peak velocity of facial growth and peak velocity of stature are associated during adolescence (Bambha, 1961; Hunter, 1966; Bergersen, 1972). Bergersen, (1972) found a significant correlation between the onset of the male adolescent growth spurt for all facial dimensions and standing height. Successful prediction of the timing of peak height velocity would allow orthodontic treatment to be carried out during the period of peak facial growth. Maximal craniofacial growth, although closely associated with stature, has been reported to occur slightly later than maximal growth in height by some researchers (Nanda, 1955; Björk, 1972) and slightly earlier by others (Mellion *et al*., 2013). Bishara (1981) found that the growth profile of height was significantly different from that of mandibular length and relationship.

Summary – *Somatic maturity can be assessed by measuring height increases over time. Interpretation of a height velocity graph allows identification of PHV which is associated with peak velocity of facial growth. Its prediction is therefore important to orthodontic treatment planning.*

1.4 Sexual maturity

Adolescence is the period of life when sexual maturity is achieved. Its initiation is influenced by both endogenous and exogenous factors. Hormonal signals sent from the brain to the gonads control the process and lead to the release of sex hormones into the bloodstream. Accelerated general body growth, development of secondary sexual characteristics, maturation of sexual organs and attainment of fertility all occur as a result. Puberty is the process of physical changes that occur during adolescence. There has been a trend over recent decades for puberty to begin at an earlier age, however it is unclear if this trend is continuing or if it has halted. The most common changes occurring for males and females are listed in the table below.

Male	**Female**
Lowering of voice pitch	Development of the breasts
Enlargement of the larynx (Adam's apple)	Underarm and pubic hair
Facial, body, underarm and pubic hair	Enlargement of the genitalia
Enlargement of genitalia	Widening of hips and pelvis
Increase in stature	Change in fat distribution
Increased muscle mass and strength	Increase in stature
Increased secretions of oil and sweat glands	Commencement of menarche

Table 1.1 Physical changes during puberty

It would not be appropriate to ask questions regarding many of these changes in the context of an orthodontic clinic as they require a physical examination or questions of a sensitive nature. However some, such as the presence of facial hair in males, can be easily detected.

1.4.1 Relationship between voice changes and peak height velocity

During the pubertal growth spurt boys experience a complete change from the pre-pubertal to an adult male voice. Voice changes begin between 11.5 - 16.5 years with a mean age of 13.9 years and a duration varying from less than one year to greater than three years (Hägg and Taranger, 1980a). Growth is at its most intense when voice changes begin and has started to slow down when adult voice characteristics are observed. Hägg and Taranger (1982) found that the pubertal voice occurs near PHV with the male voice becoming established at or after PHV. Attainment of the male voice therefore suggests that a boy has reached or passed PHV. Boys can be questioned about their voice changes (Andersen, 1968) or differences can reliably be observed clinically in conversation (Hägg and Taranger, 1980a; Hägg and Taranger, 1982) or through measurement with audiological instruments (Hodges-Simeon *et al*., 2013).

1.4.2 Relationship between menarche and peak height velocity

In females the onset of menstruation can be used as an indicator of sexual maturity (Shuttleworth, 1938). The mean age of menarche was reported as 13 years and 11 months by Björk and Helm (1967) and 13.1 years by Hägg and Taranger (1980a). A trend for decreasing age of menarche has been reported (Herman-Giddens, 2006). Björk and Helm, (1967) reported that menarche took place 17 +/- 2.5 months after peak pubertal growth on average. Therefore menarche was an indication that maximum pubertal skeletal growth had been attained or passed. Other studies showed similar findings, with PHV generally occurring before menarche (Tanner *et al*., 1976; Hägg and Taranger, 1980a).

Orthodontists could consider finding out whether or not female patients have reached menarche in order to determine whether PHV has already passed. However it does require questions of a sensitive nature and it has been reported that girls sometimes give false responses to such questions, especially if they are developing before or after members of their peer group (Hägg and Taranger, 1982).

Summary – *Sexual maturity involves assessment of the physical changes that occur during puberty. Many of these changes are not suitable for assessment on an orthodontic clinic. Male voice change and onset of menarche are associated with PHV and may be useful indicators of maturity status.*

1.5 Skeletal maturity

The assessment of skeletal maturity is a further method for establishing physiological development. Ossification is the process of bone development and formation. During growth bones go through a series of changes in size and shape and these morphological changes can be identified and staged. Radiographs of developing bones are inspected to assess their initial appearance. Further radiographs taken at a later date allow ossification changes to be identified. Radiographs of a number of parts of the skeleton have been used for this purpose including the ankle; foot; hip; elbow; hand-wrist and cervical vertebrae (Krailassiri *et al*., 2002).

1.5.1 Hand-wrist maturation

Radiographs of the hand-wrist region have been used as a method of assessing the stage of skeletal maturity (Fig 1.4). Thirty small bones which undergo a predictable sequence of ossification changes can be identified (Flores-Mir *et al*., 2004). A number of different methods exist for assessing skeletal maturity from hand-wrist radiographs (HWR).

Figure 1.4 Hand-wrist radiograph

Greulich and Pyle (1959) published an atlas containing plates of typical hand-wrist radiographs taken at 6 monthly intervals as part of a longitudinal growth study. To determine skeletal age, a radiograph of the hand wrist region is compared with standards. Each bone is assigned an age in months and these are then averaged to give a mean skeletal age. This comparison is complex and time consuming so that a modified and more rapid version of the technique is often used, whereby the overall appearance of a radiograph is compared with reference radiographs and the closest match is chosen. This method is considerably faster than the original but may be less accurate.

Tanner et al., (1975) assessed hand-wrist radiographs by comparing individual examples with radiographic standards of the skeletal maturity of ‘normal’ children of similar sex and age. Phalangeal maturity stages and the appearance of the adductor sesamoid are described (Coutinho *et al*., 1993). In this analysis a biological weighted scoring system is used to rate individual bones and to assign an overall skeletal age.

Grave and Brown (1976) studied at 14 ossification events grouped into 2 categories; events in individual bones and epiphyseal changes in the first, second and third fingers and radius.

They noted that in the majority of individuals three stages occur:

1. **Accelerative phase** = events occurring before peak growth velocity

   Ossification events 1-5

2. **Peak phase** = events coincide with peak growth

   Ossification events 6-10

3. **Decelerative phase** = follows peak growth in most subjects

   Ossification events 11-14

Björk and Helm (1967) described how ossification of the ulnar sesamoid at the metacarpophalangeal joint of the thumb (S) occurs with close association to the age of maximum growth in body height. Ossification usually occurred one year before maximum pubertal skeletal growth and it never occurred after peak growth. Capping of the 3rd middle phalanx has also been reported to coincide with peak height velocity (Björk, 1972).

Uysal *et al*., (2004), in a study of skeletal maturity, used a scale which condensed the methods of Björk (1972) and Grave and Brown (1976) into a 9 stage system. This has since been used in other investigations (Gandini *et al*., 2006).

Fishman (1982) described a system of Skeletal Maturation Assessment (SMA). Four ossification stages are assigned to six anatomical sites on the thumb, third finger, fifth finger and radius. 11 ossification changes, known as Skeletal Maturation Indicators (SMIs) were described which occur in a stable sequence, for example:

- SMI 1-3: Accelerating growth velocity
- SMI 4-7: High growth velocity
- SMI 8-11: Decelerating growth velocity

Fishman's approach has been described as an 'organised and relatively simple' method for determining maturation level (Krailassiri *et al*., 2002), but these authors chose to use only 5 of the 11 SMIs (MP3, S stage, MP3cap, DP3u, MP3u) since they represent a meaningful interpretation of growth status.

Discrepancies exist between skeletal and chronological age when assessing skeletal maturation in hand-wrist radiographs. Cole *et al*., (1988) put this down to three possible reasons:

1. Differences in the rate of skeletal maturity between individuals
2. Systematic error in skeletal age assessment
3. Variation between different observers

It is likely that a combination of these reasons is responsible for the discrepancies.

1.5.2 Relationship between hand-wrist and other measures of maturation

Significant correlation has been found between maturation stages on hand-wrist radiographs and both pubertal height increases and facial growth (Hunter, 1966; Björk and Helm, 1967; Hägg and Taranger, 1980b). Hand-wrist radiographs have therefore been used as an accepted method for establishing whether an individual has reached the period of peak pubertal growth and as a method of determining the best time to start orthodontic treatment.

However the validity of hand-wrist radiographs for predicting skeletal age has been questioned (Smith, 1980). A study by Hunter *et al*., (2007) concluded that skeletal age is not a reliable predictor of the timing of peak mandibular growth velocity. Houston (1980) stated that information from hand-wrist radiographs is of only limited value for predicting the timing of PHV and that without frequent radiographs predictions are less accurate. These concerns, along with the risks associated with additional radiographic exposure, have led to a decline in the use of the technique. The British Orthodontic Society guidelines on radiographic selection criteria state that hand-wrist radiographs are not indicated to assess skeletal maturation (Isaacson and Thom, 2000).

Summary – *A relationship exists between skeletal maturity as assessed from hand-wrist radiographs and peak facial and statural growth. The accuracy of this assessment has been questioned and so has the justification for exposing a patient to additional radiation.*

1.5.3 Cervical vertebrae maturation

Lateral cephalometric radiographs are commonly used in orthodontics for imaging the facial skeleton and cranial vault. A cephalostat is used to position the head in a standardised and reproducible position so that valid comparisons can be made between members of the same population group or films of the same individual measured at different points in time (Proffit *et al.*, 2012).

Lateral cephalometric radiographs are taken as part of assessment and treatment planning to diagnose pathology, assess the aetiology of a malocclusion, including the anterio-posterior relationships of the jaws and the inclination of incisor teeth and for monitoring growth and treatment progress. The first seven vertebrae in the spinal column constitute the cervical spine (C1-C7) and these cervical vertebrae can also be visualised on cephalometric radiographs.

Figure 1.5 Lateral cephalometric radiograph

Changes in the morphology and dimensions of the cervical vertebrae during growth were first reported by Todd and Pyle (1928) and then by Lainer (1939). Many methods have been reported for evaluating and staging these developmental changes (Table 1.2). They range from simple evaluation of vertebral shape and size using qualitative criteria (Lamparski, 1972; Hassel and Farman, 1995), through quantitative analyses of vertebral shape, mainly changes in the height-width ratio of vertebral bodies and the depth of the inferior concavity (Baccetti *et al*., 2002; Baccetti *et al*., 2005), to more complex analyses involving geometric morphometrics (Chatzigianni and Halazonetis, 2009) and regression formulae (Caldas Mde *et al*., 2007). Studies have attempted to correlate these cervical vertebrae development stages with the peak of mandibular growth (Table 1.2).

Authors and year	Vertebrae examined (Number)	Stages	Population	Method	Results
Lamparski 1972	C2-C6 (5)	6 points	Patients of Orthodontic Department, University of Pittsburgh, USA	First developed scale	
O'Reilly and Yanniello 1988	C2-C6 (5)	6 stages 1-6	Bolton-Broadbent growth study, Cleveland, USA	Used Lamparski's standards	Stage 1-3 prior to peak velocity of mandibular growth Stage 2+3 in year immediately before peak growth velocity
Hassel and Farman 1995	C2-C4 (3)	6 stages CVMI 1-6	Bolton-Brush growth study, Cleveland, USA.	Devised CVMI index. Compared cervical vertebrae and hand wrist maturity	CVMI 2 corresponds to accelerating growth velocity
Franchi *et al*., 2000	C2-C6 (5)	6 stages Cvs 1-6	University of Michigan growth study, USA	Used modification to Lamparski's stages. Compared cervical vertebrae with stature height and mandibular length increases	Greatest increment in mandibular growth and peak in statural height during interval Cvs3-Cvs4
Baccetti *et al*., 2002	C2-C4 (3)	5 stages CVMS I-V	University of Michigan growth study, USA	Modification to Cvs scale	Peak mandibular growth occurs between CVMSII-III
Baccetti *et al*., 2005	C2-C4 (3)	6 stage CS1-CS6	University of Michigan growth study, USA	Modification to CVMS scale	Peak mandibular growth occurs between CS3-4

Table 1.2 Methods of staging cervical vertebrae maturation and its relation to peak mandibular growth

Lamparski (1972) created a six point system for staging the size and shape of the second to sixth cervical vertebrae. He described a predictable progression in their morphology with growth, the stages marking an annual change. The vertebral bodies show changes in both height and width and the lower borders demonstrate increasing concavity. O'Reilly and Yanniello (1988) used Lamparski's standards to stage the cervical vertebrae of female subjects from the Bolton-Broadbent growth study. The standards were then related to pubertal growth changes in the mandible. On average stages 1- 3 occurred prior to peak mandibular growth velocity and stages 2 and 3 were seen in the year immediately preceding peak growth velocity.

The Cervical Vertebral Maturational Index (CVMI) was devised by Hassel and Farman (1995) using data from the Bolton-Brush growth centre study to combine observed skeletal changes in the hand-wrist with changes in cervical vertebrae. Only the 2nd- 4th cervical vertebrae (C2,C3,C4) were assessed, as these can be still be seen when a lead collar is used during imaging. Six CVMI categories from initiation to completion were described and correlated with the 11 SMIs of Fishman (1982). CVMI 2 is associated with a period of accelerating growth velocity.

- CVMI 1- Initiation = SMI 1+2
- CVMI 2 – Acceleration = SMI 3+4
- CVMI 3 – Transition = SMI 5+6
- CVMI 4 – Deceleration = SMI 7+8
- CVMI 5 – Maturation = SMI 9+10
- CVMI 6 –Completion = SMI 11

Seedat and Forsberg (2005) used a simplified version of the method described by Hassel and Farman (1995), in that only the first cervical vertebrae (C3) was assessed. The study was carried out on a population of Black subjects in South Africa and skeletal maturational changes were observed.

Franchi et al., (2000) compared cervical vertebral changes with stature height and mandibular length increases for subjects in the University of Michigan growth study. A modified version of Lamparski's method with 6 stages (Cvs1 – Cvs6) was used to assess 5 cervical vertebrae (C2-C6). The greatest increment in mandibular growth and the peak in statural height were both found to occur during the interval from Cvs3- Cvs4. It was therefore suggested that inclusion of the growth interval Cvs3 to Cvs4 in the active treatment period could greatly benefit cases requiring functional appliance treatment. This method allows mandibular skeletal maturity to be appraised to assess maturation changes based on a single radiograph, without the need for an additional x-ray exposure.

An improved staging system was later published by the same team (Baccetti *et al*., 2002). Only 3 cervical vertebrae (C2 - C4) were examined. It was concluded that the first two stages of the previous version Cvs1 and Cvs2 could be merged to form a five stage system from CVMS I-V. Peak mandibular growth occurred between stages CVMSII and CVMSIII and CVMS V marked a time 2 years after the peak.

A further modification of the cervical vertebral maturation method was published three years later (Baccetti *et al*., 2005). 3 cervical vertebrae, CS2-CS4, are assessed on a 6 stage scale from CS1-CS6 (Figs 1.6 and 1.7). CS1 and CS2 are pre-peak stages; the peak in mandibular growth occurs between CS3 and CS4. CS6 is recorded at least 2 years after the peak.

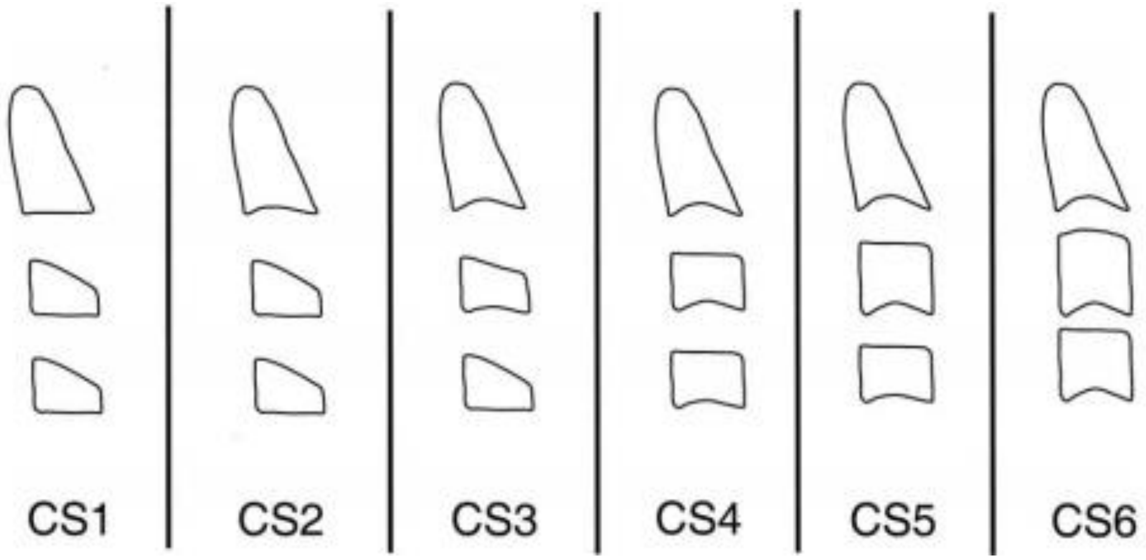

Figure 1.6 Cervical vertebrae stages – diagrammatic illustration (Baccetti *et al*., 2005)

	**Cervical stage 1 (CS1)** The lower borders of all three vertebrae (C2-C4) are flat. The bodies of both C3 and C4 are trapezoid in shape (the superior border of the vertebral body is tapered from posterior to anterior). The peak in mandibular growth will occur on average 2 years after this stage.
	**Cervical stage 2 (CS2)** A concavity is present at the lower border of C2 (in four of five cases, with the remaining subjects still showing a cervical stage 1). The bodies of both C3 and C4 are still trapezoid in shape. The peak in mandibular growth will occur on average 1 year after this stage
	**Cervical stage 3 (CS3)** Concavities at the lower border of both C2 and C3 are present. The bodies of C3 and C4 may be either trapezoid or rectangular horizontal in shape. The peak in mandibular growth will occur during the year after this stage.

Figure 1.7 Radiographic images of cervical vertebrae maturation stages with description (Baccetti *et al.*, 2005)

	**Cervical stage 4 (CS4)** Concavities at the lower borders of C2, C3 and C4 are now present. The bodies of both C3 and C4 are rectangular horizontal in shape. The peak in mandibular growth has occurred within 1 or 2 years before this stage.
	**Cervical stage 5 (CS5)** The concavities at the lower borders of C2, C3, and C4 still are present. At the least one of the bodies of C3 and C4 is squared in shape. If not squared, the body of the other cervical vertebra still is rectangular horizontal. The peak in mandibular growth has ended at least 1 year before this stage.
	**Cervical stage 6 (CS6)** The concavities at the lower borders of C2, C3, and c4 still are evident. At least one of the bodies of C3 and C4 is rectangular vertical in shape. If not rectangular vertical the body of the other cervical vertebra is squared. The peak in mandibular growth has ended at least 2 years before this stage.

Figure 1.7 (cont.) Radiographic images of cervical vertebrae maturation stages with description (Baccetti *et al.*, 2005)

Caladas Mde *et al*., (2007) used measurements of cervical vertebrae on lateral cephalometric radiographs of Brazilian children to produce new formulae for evaluating skeletal maturation. Regression formulae were developed to calculate cervical vertebral bone age and the results showed statistically significant correlations between bone age and chronological age, indicating the reliability of such formulae in this population.

Chen *et al*., (2008) used longitudinal records to develop the quantitative cervical vertebral maturations system (QCVM). Three morphologic parameters were determined and used in an equation to place patients into one of four QCVM stages. This staging system was used to investigate the relative growth rates of the maxilla and mandible and it was found that the growth of these two bones was not synchronous (Chen *et al*., 2010b). The greatest growth rate of maxillary length and height occurred in QCVM stage I, whereas the greatest rate of growth in mandibular length and height occurred at QCVM stage II.

Chatzigianni and Halazonetis (2009) used geometric morphometrics to determine cervical vertebral shape by marking fixed and sliding landmarks on tracings of the first four vertebrae. They found a strong correlation between vertebral shape and skeletal age.

Alhadlaq and Al-Shayea (2013) devised a method for assessing cervical vertebral maturation using radiographs of male subjects in Saudi Arabia. This involved calculating angular measurements of the lower borders of the bodies of C2 - C4. Significant correlations were found between the angular stages and skeletal age and maturity using hand-wrist radiographs of the same subjects, suggesting that this approach is a valid means for determining skeletal maturity.

The CVMS method of Baccetti *et al*., (2002) has been reported as being efficient and repeatable (Gandini *et al*., 2006). Jaqueira *et al*., (2010) compared three methods for the evaluation of cervical vertebrae in order to determine skeletal maturation stage and concluded that the method of Baccetti *et al*., (2002) had the best clinical applicability, followed by those of Hassel and Farman (1995) and Seedat and Forsberg (2005).

It has been suggested that, as cervical vertebral assessment is subjective, errors may occur in its application (Mito *et al*., 2002). Gabriel *et al*., (2009) reported poor inter-observer reproducibility of below 50 percent and intra-observer agreement only slightly better at 62 percent for the CVM method (Baccetti *et al*., 2005). In a letter, Baccetti *et al*., (2010) countered that inadequate practitioner training and interpretation of statistics may have accounted for the lower reproducibility found by Gabriel *et al*., (2009). Santiago (2012), in a systematic review of cervical vertebral maturation, suggested that Gabriel's statistical interpretation may be flawed. An alternative scale to score intra-examiner reproducibility would reclassify it from 'low' to 'moderate to substantial'. Nestman *et al*., (2011) suggested that the reason for poor reproducibility lay in the difficulty of distinguishing between the different shapes of the C2 and C3 vertebral bodies from rectangular horizontal through to rectangular vertical. Pasciuti *et al*., (2013) have since reported a high degree of repeatability and reproducibility in cervical vertebral maturation assessment. Substantial intra-observer and inter-observer agreements in CVM stages have been recently reported (Rainey, 2014).

Gabriel *et al*., (2009) also suggested that reproducibility results might often be overstated. This is due to authors often being the ones carrying out the observations and therefore having a much higher 'research-level' understanding of cervical vertebral maturation than the average clinician. This lead Santiago *et al*., (2012) to advise that studies should clearly report in both the discussion and conclusion sections whether or not the observers were experienced in the cervical vertebral method.

1.5.4 Relationship between cervical vertebrae development and other measures of maturation

A significant correlation has been reported between growth increases in the height and length of the cervical vertebrae and statural height increases during puberty (Hellsing, 1991). Increases in cervical vertebrae length have been shown to have a strong correlation with changes in mandibular length, body height and hand bones in a longitudinal study of females during puberty (Mitani and Sato, 1992). Bone age, assessed from cervical vertebrae, has also been reported to reflect skeletal maturity (Mito *et al*., 2002).

A number of studies have related cervical vertebral maturation stages with the period of peak mandibular growth (Table 1.2). O'Reilly and Yanniello (1988) found that Stages 1-3 of Lamparski's standards (1972) occurred prior to peak mandibular growth velocity with stage 2 and 3 in the year immediately before peak growth velocity. Franchi *et al*., (2000) reported that the greatest increases in statural height and mandibular length that occur during puberty, closely coincide with the transition between cervical vertebral development stages Cvs3-Cvs4. Baccetti (2002) observed peak mandibular growth to occur between CVMSII-III. This was supported by a study of Aboriginal Australian children, where peak growth also occurred between stages II and III (Grave and Townsend, 2003). Using a later modification to a 6 stage system, peak mandibular growth was reported to occur between stages C3-C4 (Baccetti *et al*., 2005).

Ball *et al*., (2011) studied serial cephalometric radiographs of 90 males from the Burlington growth study to assess the relationship between growth of the mandible, measured as mandibular length increases and maturation of the cervical vertebrae according to Baccetti's (2005) 6 stage system. Subjects were split into advanced, average and delayed groups of maturation for analysis, to allow for differences in the pattern of maturation. The peak of mandibular growth occurred, on average, at age 14.4 +/- 1.4 years. In all groups the peak growth velocity of the mandible occurred most frequently in cervical maturation stage 4. The largest amount of mandibular growth was observed during this stage with an average of 9.4mm over a period of 3.79 years. The time spent in each cervical maturation stage varied between groups from an average of 1.5 to 4.2 years with the most time being spent in stage 4 for all groups. This differed from the annual progression between stages described by Lamparski (1972). Ball *et al*., (2011) concluded that, due to the large variations observed, cervical vertebral maturation stages do not predict the commencement of peak mandibular growth accurately and that the method should be used alongside other means of determining maturity.

Summary - *It is clear that a relationship does exist between cervical vertebral development and other measures of maturity, including increases in statural height and mandibular length. However these relationships differ between ethnic groups and between the sexes. This can make it hard for clinicians to rely on cervical vertebral maturation as a way of predicting peak mandibular growth.*

1.5.5 Comparison of hand-wrist and cervical vertebral maturation

The validity of skeletal maturity assessment using cervical vertebral maturation has been compared with hand-wrist methods in studies in a variety of different population groups.

Kucukkeles (1999) found a significant relationship between maturation of the hand-wrist and the cervical vertebrae in a Turkish population. A statistically significant relationship was observed by Chang *et al*., (2001) who concluded that using cervical vertebrae to assess skeletal age was a reliable, reproducible and valid technique. Gandini (2006), also observed correlations between the two measures of skeletal maturation in Italian children, concluding that cervical vertebral analysis is as valid as analysis of hand-wrist bones.

Uysal *et al*., (2006) found high correlations between skeletal maturation stages of the hand-wrist and those of the cervical vertebrae in Turkish subjects. Correlations were higher in female subjects than males, a finding also observed by San Roman *et al*., (2002). Uysal *et* *al*., (2006) found similar correlations between chronological age and both methods of assessing skeletal maturation. The maturation stages of cervical vertebrae were felt to have a clinical use in indicating maturity and the timing of the peak pubertal growth.

Flores-Mir *et al*., (2006) examined this correlation using the methods of Fishman (1982) and Baccetti *et al*., (2002). Subjects were placed in three groups depending on their skeletal maturation level; advanced; average or delayed. A moderately high correlation was observed between the two methods for determining skeletal maturation. Skeletal maturation level influenced the correlation, leading the authors to advise that it should be taken into consideration where possible. They did however conclude that due to the high variability of mandibular growth correlations, skeletal maturation assessment has limited use in the clinical assessment of patients on an individual level and is better suited for research purposes.

Soegiharto *et al*., (2008b) studied radiographs of Indonesian and white children. Hand-wrist radiographs as assessed by SMI (Fishman, 1982) and lateral cephalometric radiographs assessed using the cervical vertebrae index of Baccetti *et al*., (2002) were used to discriminate between subjects who have reached or passed peak pubertal growth and those that have not yet attained it. Both methods had good discriminatory ability, there being only small differences between the two, so both methods are valid. Large variations were found in chronologic age for each skeletal maturity stage and observed differences in the timing of skeletal maturity between ethnic groups and sexes using both SMI and CVM methods (Soegiharto *et al*., 2008a).

Imanimoghaddam *et al*., (2008) examined the correlation between four different cervical vertebral maturation methods and one method of skeletal maturation assessment using hand-wrist radiographs. A range of correlation levels were observed between the methods, leading to the conclusion that accuracy, correlation and reproducibility may be influenced by the method of cervical vertebral maturation used (Santiago *et al*., 2012).

Wong *et al*., (2009) found a highly significant correlation between cervical vertebral maturation and maturation on hand-wrist radiographs, leading to the conclusion that cervical vertebral maturation is a valid indicator of skeletal growth. They also suggested that cervical vertebral maturation methods are only sensitive during the growth spurt period. Correlation coefficients may be affected by including subjects whose age lies well above or below the time when peak pubertal growth would be expected to occur.

Other studies have also found a high correlation between the two techniques, leading to the overall conclusion that cervical vertebrae can be used with the same degree of confidence as hand-wrist radiographs (Garcia-Fernandez *et al*., 1998; San Roman *et al*., 2002; Gandini *et al*., 2006; Kamal *et al*., 2006; Al Khal *et al*., 2008). This has led some authors to strongly question the justification for additional radiation exposure for a hand-wrist radiograph when skeletal maturation can be assessed by a lateral cephalometric radiograph that was taken for other diagnostic reasons (San Roman *et al*., 2002; Soegiharto *et al*., 2008b; Stiehl *et al*., 2009).

Santiago *et al*., (2012) carried out a systematic review to determine if cervical vertebrae maturation stages can determine peak pubertal growth reliably. 23 studies met the inclusion criteria including many of those discussed above. However the methods of only six studies were of sufficient quality to be included in the analysis. In those studies, the correlation between hand-wrist and cervical vertebral maturation methods was statistically significant. The reproducibility of the cervical vertebrae maturation method was moderate to high. The authors concluded that many studies showed serious failings in their methodology and that even those analysed were not good enough to determine the validity of cervical vertebrae maturation stages. Improvements that could be made in future studies were suggested, including better sample size calculations, randomisation and selection criteria. It was suggested that longitudinal rather than cross-sectional data should be used in studies of growth, ethical issues with raised over serial radiographic recordings and problems with access to the limited databases of existing growth studies.

Cericato *et al*., (2014) carried out a systematic review and meta-analysis on the validity of skeletal maturation assessment by cervical vertebral analysis in order to evaluate whether the technique can replace the use of hand-wrist radiographs to determine peak pubertal growth. The review included nineteen articles comparing radiographs of the hand-wrist and cervical vertebral regions. Positive correlations were observed in all articles. The meta-analysis found a higher correlation in females. The authors concluded that cervical vertebrae maturation indexes show good reliability and can replace hand-wrist radiographs to determine peak pubertal growth.

Summary – *Every study found by the author reported close associations between assessment of skeletal maturity made from hand-wrist radiographs and cervical vertebral maturation. This supports the view that hand-wrist radiographs are not justified for this use.*

1.6 Dental maturity

Dental development has been used as a way for determining progress towards maturity. It can be assessed by staging tooth formation and by tooth emergence or eruption. An overall estimate of dental age can also be made. This is useful in forensic dentistry and legal cases for age determination of subjects of unknown birth date.

1.6.1 Tooth eruption/emergence

Dental eruption is a continuous process beginning with a tooth moving from its developmental position in the jaw, emerging through the gingivae into the oral cavity and clinically reaching its functional position at the occlusal level. Tooth emergence is a brief event in the process and may be easily missed, making it difficult to use it as a measure of dental development. The process of tooth eruption is susceptible to environmental influences (Demirjian *et al*., 1973) including malnutrition, crowding, ankylosis, premature or delayed loss of primary teeth and decay (Moorrees *et al*., 1963; Fanning and Brown, 1971; Alvarez and Navia, 1989). Wide individual variation exists but average tooth eruption times have been published (Table 1.3). It has been suggested that dental emergence stage should not be used as an indicator of the pubertal growth spurt due to a very low correlation between dental emergence and pubertal height increases (Hägg and Taranger, 1981; Hägg and Taranger, 1982).

Deciduous Teeth				Permanent Teeth		
	Eruption Time (Months)				Eruption Time (Years)	
Tooth	Maxillary	Mandibular		**Tooth**	Maxillary	Mandibular
A	7	6.5		1	7-8	6-7
B	8	7		2	8-9	7-8
C	16-20	16-20		3	11-12	9-10
D	12-16	12-16		4	10-11	10-12
E	21-30	21-30		5	10-12	11-12
				6	6-7	6-7
				7	12-13	12-13
				8	17-21	17-21

Table 1.3 Average tooth eruption times adapted from Berkovitz, Holland and Moxham, (2002).

1.6.2 Tooth formation

Tooth formation or calcification is thought to be a more reliable method for determining dental maturation as it is less variable than tooth eruption (Nolla, 1960; Fanning, 1962; Moorrees *et al*., 1963). The rate of permanent tooth formation is not affected by premature loss of the deciduous teeth (Fanning, 1962). Tooth formation (Garn *et al*., 1960) and root development is under genetic control (Pelsmaekers *et al*., 1997).

A number of different systems have been proposed for determining dental calcification stage from radiographs (Nolla, 1960; Fanning, 1961; Haavikko, 1970; Gustafson and Koch, 1974). The most commonly used method is the Demirjian Index (Demirjian *et al*., (1973) which estimates dental maturity by assessment of seven left permanent mandibular teeth (third molar excluded). This method was based on a study of panoramic radiographs of 1446 boys and 1482 girls of French Canadian origin. A scale of 8 tooth developmental stages from A to H was devised (Fig 1.8, Table 1.4). Each stage has one to three written criteria and a pictorial chart to illustrate the appearance. The first four stages describe development of the crown and the second four describe the root. Root development is assessed through changes in the shape of the pulp chamber, the amount of dentine deposited and the root length relative to crown height. The method offers the advantage of increased reliability compared with taking measurements of actual root length since radiographic images may be elongated or foreshortened.

The stage of development of each tooth can be converted into a score using tables published for boys and girls (Demirjian *et al*., 1973). Individual tooth scores are then summed to give a maturity score. The maturity score may then in turn be converted directly into a dental age using a centile chart. Dental age and chronological age are then correlated.

Third molar development is sometimes used to assess dental development since this tooth continues to develop once the other teeth are completely formed.

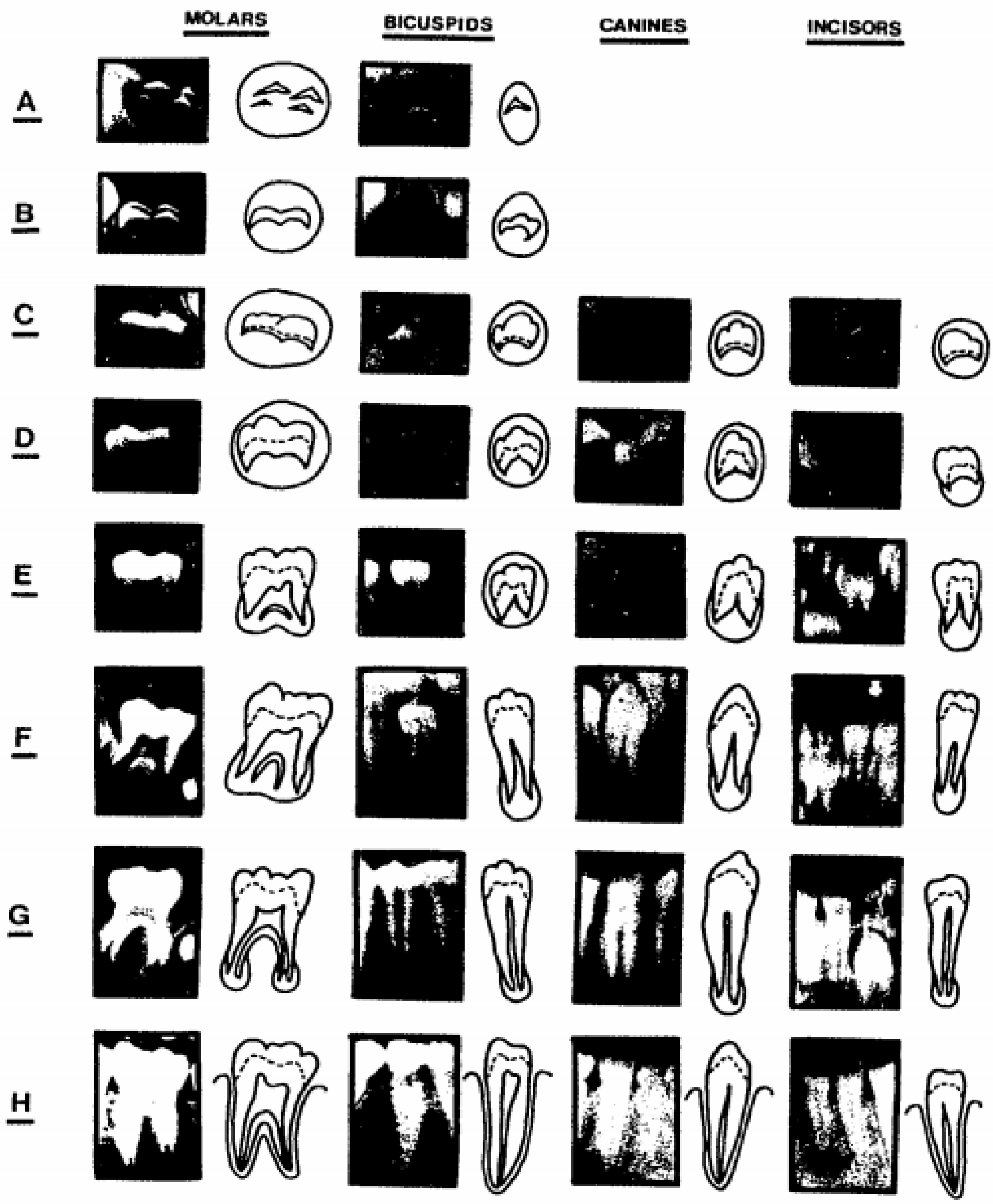

Figure 1.8 Development stages of the permanent dentition (Demirjian *et al.*, 1973)

Stage	Description
A	In both uniradicular and multiradicular teeth, a beginning of calcification is seen at the superior level of the crypt in the form of an inverted cone or cones. There is no fusion of these calcified points.
B	Fusion of the calcified points forms one or several cusps which unite to give a regularly outline occlusal surface.
C	a. Enamel formation is complete at the occlusal surface. Its extension and convergence towards the cervical region is seen
	b. The beginning of a dentinal deposit is seen
	c. The outline of the pulp chamber has a curved shape a the occlusal border
D	a. The crown formation is completed down to the cement-enamel junction
	b. The superior border of the pulp chamber in the uniradicular teeth has a definite curved form, being concave towards the cervical region. The projection of the pulp horns if present, gives an outline shaped like an umbrella top. In molars the pulp chamber has a trapezoidal form.
E	Uniradicular teeth:
	a. The walls of the pulp chamber now form straight lines whose continuity is broken by the presence of the pulp horn, which is larger than in the previous stage.
	b. The root length is less than the crown height
	Molars:
	a. Initial formation of the radicular bifurcation is seen in the form of either a calcified point or a semi-lunar shape
	b. The root length is still less than the crown height
F	Uniradicular teeth:
	a. The walls of the pulp chamber now form a more or less isosceles triangle. The apex ends in a funnel shape
	b. The root length is equal to or greater than the crown height
	Molars:
	a. The calcified region of the bifurcation has developed further down from its semi-lunar stage to give the roots a more definite and distinct outline with funnel shaped endings
	b. The root length is equal to or greater than the crown height
G	a. The walls of the root canal are now parallel and its apical end is still partially open (Distal root in molars)
H	a. The apical end of the root canal is completely closed (Distal root in molars)
	b. The periodontal membrane has a uniform width around the root and the apex

Table 1.4 Development stages of the permanent dentition (Demirjian *et al.*, 1973)

Individual variation occurs in dental maturity but differences have also been reported in the timing of dental maturation between populations and racial groups (Demirjian *et al*., 1973; Chaillet *et al*., 2005; Liversidge, 2008). In a South African study, Chertkow (1980) found marked racial differences with dental development being earlier in black children than white children. Marked differences have been found in the time that subjects from two different areas of the USA reached dental mineralisation stages (Mappes *et al*., 1992). Those in the Midwest achieved dental mineralisation stages at least 1.5 years earlier on average than those in the Midsouth. Some studies have found a delay in dental age compared with chronological age and others have found the opposite. Peiris *et al*., (2009) reported a delay in the dental age of Australian subjects compared to UK subjects, along with a significant difference between chronological and dental age.

1.6.3 Relationship between dental and skeletal maturity

Controversy exists over the relationship between dental and skeletal maturity (Flores-Mir *et al*., 2006; Uysal *et al*., 2006; Chen *et al*., 2010a). A low correlation between dental maturity and other measures of development has been reported (Lewis and Garn, 1960; Anderson *et al*., 1975). It is suggested that this poor relationship occurs due to dental and skeletal development being distinct processes (Lewis, 1991). Low or insignificant correlations have been found between dental and skeletal ages (Lewis and Garn, 1960; Garn *et al*., 1962), particularly when the dentition is looked at as a whole. Kataja *et al*., (1989) suggested that examining the relationship between the calcification stages of key individual teeth and skeletal maturity may reduce accidental errors. Several investigators have studied this relationship and some of the methods and key results reported are summarised in Table 1.6. Higher correlations have been observed when individual teeth are assessed although the findings are inconsistent. A high correlation between dental and skeletal development could allow dental calcification stage to be used as a means of estimating the period of peak pubertal growth, without the need for a hand-wrist or cephalometric radiograph (Coutinho *et al*., 1993; Krailassiri *et al*., 2002; Rozylo-Kalinowska *et al*., 2011).

All the studies included in Table 1.5 had a similar methodology but were carried out in different populations and with varying subject numbers and age ranges. A variety of methods were used for skeletal maturation assessment, including hand-wrist methods and cervical vertebral maturation. The results for males and females were separated in the majority of studies, due to the reported differences in the timing of maturation between the sexes. Most studies reported their findings as a Spearman Rank Order correlation coefficient between dental and skeletal development for each of the teeth studied. Others used Pearson correlation. A range of conclusions were drawn by the authors from the results obtained.

Authors	**Country**	**Number of subjects** M=Male F=Female	**Age range (yrs)**	**Dental maturity method + Teeth included**	**Skeletal maturity method**	**Correlation between dental and skeletal maturity (Highest-lowest tooth)**	**Highest correlation – tooth left mandibular quadrant**	**Lowest correlation – tooth left mandibular quadrant**
Krailassiri *et al*., 2002	Thailand	361 M = 139 F = 222	7-19	Demirjian's Index (DI) Mandibular 3,4,5,7,8	**HWR** Fishman (1982)	M = 5,4,7,3,8 F = 5,7,3/4,8	**5** M r = 0.66 F r = 0.69 SROCC	**8** M r = 0.47 F r = 0.31
Uysal *et al*., 2004	Turkey	500 M = 215 F = 285	7-20	DI Mandibular 3,4,5,7,8	**HWR** Björk (1972) and Grave and Brown (1976)	M = 7,5,4,3,8 F = 7,5,4,3,8	**7** M r = 0.706 F r = 0.826 SROCC	**8** M r = 0.414 F r = 0.490
Rai *et al*., 2008	India	66 M = 34 F = 32	9-21	DI Mandibular 3,4,5,7	**CVM** Hassel and Farman (1995)	M+F = 7,4,3,5	**7** M r = 0.73 F r = 0.69 SROCC	**5** M r = 0.42 F r = 0.43
Chen *et al*., 2010	China	302 M = 134 F = 168	8-16	DI Mandibular 3,4,5,7	**CVM** Baccetti et al., (2005)	M = 3,5,7,4 F = 7,4,5,3	**3** M r = 0.496 **7** F r = 0.528 SROCC	**4** M r = 0.464 **3** F r = 0.391
Rozylo-Kalinowska *et al*., 2011	Poland	718 M = 283 F = 431	6-17	DI Mandibular 1,2,3,4,5,6,7	**CVM** Baccetti et al., (2005)	M=3,5,4,7,6,2,1 F = 5,7,4,3,6,2,1	**3** M r = 0.5213 **5** F r = 0.5849	**1** M r = 0.1827 F r = 0.1439
Khan and Ijaz, 2011	Pakistan	200 M = 100 F = 100	8-16 Into 3 groups	DI Mandibular 3 only	**HWR** Fishman (1982) (Used 5/11 stages)	N/A	**3** 0.858 SROCC	N/A
Mittal *et al*., 2011	India	100 M = 46 F = 54	9-18	DI Mandibular 3,4,5,7,8	**CVM** Hassel and Farman (1995)	M+F = 7,5,4,3,8	**7** M r = 0.758 F r = 0.811 SROCC	**8** M r = 0.403 F r = 0.419
Kumar *et al*., 2012	India	300 M = 137 F = 163	9-18	DI Mandibular 7 only	**CVM** Hassel and Farman (1995)	N/A	**7** M C = 0.854 F C = 0.866 Pearson	N/A
Perinetti *et al*., 2012	Italy	354 M = 146 F = 208	6-17	DI Mandibular 3,4,5,7	**CVM** Baccetti et al., (2005) (Grouped into 3 growth phases)	M+F = 7,5,4,3 (Results not separated by gender)	**7** r = 0.77 S rho CC	**3** r = 0.71

Table 1.5 Studies investigating the relationship between skeletal and dental maturity

Demirjian's Index is used to determine the dental development stage from panoramic radiographs. Usually teeth on only one side of the mouth are examined, as tooth calcification of homologous teeth is symmetrical (Demisch and Wartmann, 1956; Nolla, 1960; Demirjian *et al*., 1973). Maxillary teeth are usually excluded as there is often superimposition of calcified structures in the area of the maxillary posterior teeth (Krailassiri *et al*., 2002; Uysal *et al*., 2004). Teeth that are likely to have completed root formation and achieved apical closure at the age of examination are also excluded, this usually includes mandibular incisors and first permanent molars. Mandibular third molars are often excluded as they are the most common missing teeth and because their development can be so varied. However inclusion of third molars gives the advantage that this tooth continues to develop once all other teeth are complete and can no longer provide useful information. Some investigators have studied the relationship between skeletal maturation and just one key tooth for example the mandibular canine (Khan and Ijaz, 2011) or the mandibular second molar (Kumar *et al*., 2012). Others have included up to seven different teeth (Rozylo-Kalinowska *et al*., 2011).

Skeletal maturity stage is assessed in the studies from hand-wrist radiographs (Table 1.6) (Krailassiri *et al*., 2002; Uysal *et al*., 2004; Khan and Ijaz, 2011) or by determining cervical vertebral maturation stage using the method of Hassel and Farman (Rai, 2008; Mittal *et al*., 2011; Kumar *et al*., 2012) or Baccetti (Chen *et al*., 2010a; Perinetti *et al*., 2011; Rozylo-Kalinowska *et al*., 2011).

The dental development stage of the mandibular canine has been shown to have a high correlation with skeletal development in a number of studies. A close relationship has been found between development stage G of the mandibular canine, the stage just before apical closure, and calcification of the adductor metacarpophalangeal sesamoid of the thumb on hand-wrist radiographs (Chertkow and Fatti, 1979; Chertkow, 1980). Ossification commences in this area during the year prior or at the time of commencement of the pubertal growth spurt. The authors therefore suggested that the mineralisation stage of the mandibular canine root could be used as a maturity indicator. The correlations between other teeth and skeletal maturity were low, with significant differences between the sexes. Sierra (1987) examined the correlation between dental and skeletal maturity in 8-12 years olds and also found the mandibular canine to show the strongest correlation.

Due to these positive findings, a number of investigators have focussed their studies on the mandibular canine alone (Coutinho *et al*., 1993; Flores-Mir *et al*., 2005; Khan and Ijaz, 2011). Coutinho *et al*., (1993) investigated the correlations between dental and skeletal maturity, as assessed on panoramic and hand-wrist radiographs, of 415 children aged between 7-16 years. 81% of the children who had attained canine stage G showed presence of an adductor sesamoid, 77% had capping of the diaphysis of the 3rd middle phalanx and 87% had capping of the fifth proximal phalanx on hand-wrist radiographs. Capping of the 3rd middle phalanx coincides with peak height velocity (Björk, 1972). Through comparison with growth reference data of American children Coutinho *et al*., (1993) suggested that stage G occurs approximately 0.4yrs before peak height velocity in females and 1.3yrs before in males. They therefore suggested that the intermediate stage between canine development stages F and G marks the early part of the pubertal growth spurt.

Flores-Mir *et al*., (2005) found Spearman correlations greater than r = 0.80 between the mandibular canine dental development stages and skeletal maturation of the medial phalanx of the third finger of the hand. Khan and Ijaz (2011) reported a Spearman rank order correlation coefficient of 0.858 between the mandibular canine and skeletal development of the hand-wrist. 83.8% of children at MP3cap show stage G of canine root calcification, again indicating that mandibular canine stage G could be used identify peak pubertal growth velocity.

Others studies have observed a poor relationship between skeletal maturity assessed on hand-wrist radiographs and calcification of the mandibular canine. So (1997) reported the lack of a close relationship between root development and the adductor sesamoid of the hand. Krailassiri *et al*., (2002) and Uysal *et al*., (2004) also observed lower correlations between skeletal maturity and mandibular canine development than with the other teeth.

A correlation has also been reported between development of the mandibular canine and skeletal development assessed by the cervical vertebral maturation method Baccetti et al., (2005). Chen *et al*., (2010a) found a low but statistically significant Spearman rank order correlation coefficient (SROCC) of r = 0.496 in their Chinese male subjects while Rozylo-Kalinowska *et al*., (2011) reported a moderate and statistically significant SROCC of r = 0.5213 in Polish males. Correlations between cervical vertebral maturation and canine development stages were lower in the females in these two studies. The mandibular second molar (r = 0.528) and the mandibular second premolar (r = 0.5849) were the highest correlations for female subjects in these two studies.

The mandibular first premolar had the highest correlation with skeletal maturity in only one study (Sukhia and Fida, 2010). The second premolar had the highest correlation to skeletal maturation determined from hand-wrist radiographs in both male (r = 0.66) and female (r = 0.69) Thai subjects (Krailassiri *et al*., 2002). Development of the mandibular second premolar also had the strongest correlation with skeletal maturation determined by cervical vertebral maturation in Polish females (r = 0.5849) and the second strongest in males (r = 0.4864) (Rozylo-Kalinowska *et al*., 2011). Conversely this tooth demonstrated the lowest correlation of the four mandibular teeth studied in India for both males and females (Rai, 2008).

The mandibular second molar has been identified as the tooth with the highest correlation to skeletal maturity in a number of studies in different populations. This correlation was highest for both Turkish males (r = 0.706) and females (r = 0.826) using the hand-wrist method (Uysal *et al*., 2004). In Indian subjects the correlation between second molar development and skeletal maturity using the cervical vertebral method was r = 0.73 for males and r = 0.69 for females (Rai *et al*., 2008). The second molar was also the tooth most highly correlated to skeletal maturity assessed by cervical vertebral maturation in Chinese females (r = 0.528) (Chen *et al*., 2010a). Males and females were grouped together in an Italian study using the cervical vertebral maturation method in which this tooth also showed the highest correlation (r = 0.77) (Perinetti *et al*., 2012). Kumar *et al*., (2012) found highly significant correlations using the Pearson correlation in both males (C = 0.854) and females (C= 0.866) for the relationship between the mandibular second molar alone and cervical vertebral maturation.

Development of the lower third molar has a poor relationship with skeletal maturity (Garn *et al*., 1962; Demirjian and Levesque, 1980; Kullman, 1995). Studies that included third molars all found it to have the lowest correlation (Table 1.6) (Krailassiri *et al*., 2002; Uysal *et al*., 2004; Mittal *et al*., 2011). The poor correlation has been attributed to the large variation in third molar development. However, a strong correlation between tooth development and skeletal development based upon fewer tooth development stages has been reported (Engstrom *et al*., 1983). Only one study in Table 1.6 included the lower incisors and these demonstrated low correlation to skeletal maturity (Rozylo-Kalinowska *et al*., 2011)). This is most likely due to the fact that the development of these teeth will already have been complete for the majority of the subjects in the study.

It is clear that different geographical areas and ethnic groups show varying associations between dental and skeletal maturity (Chertkow, 1980; Uysal *et al*., 2004; Chen *et al*., 2010a; Rozylo-Kalinowska *et al*., 2011). Discrepancies between studies could also be attributed to the use of different methods of evaluating dental and skeletal maturity (Uysal *et al*., 2006; Chen *et al*., 2010a; Rozylo-Kalinowska *et al*., 2011).

Female skeletal development is more advanced than for males of similar age, with the mean chronologic age for each skeletal stage being consistently lower in females (Coutinho *et al*., 1993; Chen *et al*., 2010a; Rozyl-Kalinowska *et al*., 2011). Male subjects however, display more advanced dental development stages than females at the same skeletal development stages (Chertkow, 1980; Krailassiri *et al*., 2002; Uysal *et al*., 2006).

Due to the correlations established between dental development and skeletal development on hand-wrist radiographs, dental calcification stage has been suggested as a simple method for estimating the period of peak pubertal growth (Coutinho *et al*., 1993). The mp3cap stage on hand–wrist radiographs bears a close relationship to maximum pubertal growth. Krailissiri *et al*., (2002) found that the canine stage F to correlated closely with mp3 stage in both males and females. They suggested that the timing of peak pubertal growth may therefore be identified simply by examining dental development on a panoramic radiograph. Other researchers have come to the same conclusion (Uysal *et al*., 2004). Further studies identified statistically significant correlations between dental development stage and cervical vertebrae maturation (Chen *et al*., 2010a; Rozylo-Kalinowska *et al*., 2011) . These studies indicated the validity of using dental maturity for assessing skeletal maturity and in turn, the timing of peak pubertal growth. This method has the benefit of requiring only a panoramic radiograph, which is commonly taken by dentists and orthodontists to assess the developing dentition. The need for a hand-wrist or lateral cephalometric radiograph to determine cervical vertebrae maturation stage would therefore be negated. A panoramic radiograph would provide a simple means for using tooth calcification stages to indicate the pubertal growth period as an initial diagnostic tool.

Summary – *Dental maturity can be assessed through radiographic examination of the development of tooth crowns and roots. There are marked individual and racial variations in dental maturity. Relationships have been reported between dental and skeletal maturity, although these are inconsistent. A positive correlation would be beneficial in orthodontics as it would allow the use of tooth calcification stage to identify the period of peak growth.*

1.7 Optimal timing of orthodontic treatment

Many factors affect the optimal timing of orthodontic treatment, but two key elements are the stage of development of the dentition and the possibility of remaining facial growth. Growth impacts on orthodontic treatment planning decisions regarding interceptive measures, use of functional appliances and the timing of orthognathic surgery. Certain treatments are reported to be more successful when carried out before the period of peak pubertal growth whereas others achieve better results if peak growth is included in the treatment time. It has been suggested that the timing of the onset of treatment is as important as the choice of appliance and treatment provided (Baccetti *et al*., 2005). Successful identification of an individuals' peak pubertal and mandibular growth is therefore an important concept in orthodontic treatment planning.

Treatment of Class II malocclusions is thought to be most effective when the period of peak mandibular growth is included within the treatment time. Several studies involving functional appliances have identified larger mandibular length increases in subjects treated during puberty than in those treated before or after this time. Larger increases in mandibular length have been found when treatment with Frankel's functional regulator was carried out in an age group close to puberty (average start age 11.6 years) than with a group started pre-puberty (average 8.8 years) (McNamara *et al*., 1985).

The optimal timing for treatment with a Twin-block appliance is during or slightly after peak pubertal growth (Baccetti *et al*., 2000). More favourable skeletal changes were observed in subjects treated at cervical vertebral maturation stages 3-5 than stages 1-2, using the staging method of O'Reilly and Yanniello (1988). Baccetti *et al*., (2005) suggest that the ideal time to start functional appliance treatment is at CVM stage CS3, as peak mandibular growth will occur within the next year. The mandible was shown to undergo an average increase in length of 5.4mm between stages C3 – C4. This was much larger than the increases seen between the pre-peak and post-peak stages (CS1-2=2.5mm, CS2-3=2.5mm, CS4-5=1.6mm, CS5-6=2.1mm).

The effects of the Herbst appliance have been studied and related to increases in standing height during puberty and ossification changes on hand-wrist radiographs (Pancherz and Hägg, 1985; Hägg and Pancherz, 1988). Sagittal condylar growth was found to be more pronounced in the period of peak pubertal standing height increase, leading the authors to conclude that Herbst therapy should be commenced close to peak height velocity. Treatment with a modified activator with high pull headgear should also be initiated at a similar time as the skeletal effects produced are greater then (Malmgren *et al*., 1987).

Treatment of Class II division 1 malocclusions with the Herbst appliance, followed by fixed appliances is more efficient in adolescents or adults (von Bremen *et al*., 2009). Reductions in Peer Assessment Rating (PAR) scores for completed cases were studied for both adolescent and adult groups according to skeletal maturity on hand-wrist radiographs. Good occlusal treatment results were seen in both groups, with similar reductions in PAR scores, suggesting that combined treatment with Herbst and fixed appliances is equally efficient in adolescents and adults. However the pre-treatment age ranges of the groups were large and had considerable overlap (adolescent group mean age 13.5 years range 10.5-17.5 years, adult group mean age 20.7 years range 15.1-43.8 years).

Baccetti *et al*., (2009) studied the cephalometric radiographs of Class II patients who underwent non-extraction treatment involving headgear, fixed appliances and Class II elastics. Subjects were split into three groups according to their cervical vertebral maturation stage; pre-pubertal; pubertal and post-pubertal. Those treated before or during the pubertal growth spurt demonstrated favourable skeletal changes whilst patients treated after this time showed only significant dentoalveolar changes. The type of skeletal effects differed with pre-pubertal patients demonstrating restricted maxillary advancement and pubertal patients having enhanced mandibular growth. The greatest amount of dentoskeletal correction occurred in patients treated during the pubertal growth spurt.

A study comparing Class II patients treated with the Twin Force Bite Corrector (TFBC), a fixed functional appliance, classified subjects into prepubertal and postpubertal groups (Chhibber *et al*., 2013). The 5 stage cervical vertebral maturation stage (CVMS) method was used to determine whether patients had started treatment before or after the pubertal growth spurt (Baccetti *et al*., 2002). In this staging system peak mandibular growth is thought to occur between CVMS II-III. The prepubertal group were in CVMS stages I and II and the postpubertal group were at CVMS III to V at treatment start. The prepubertal group had significant skeletal correction during treatment whilst the postpubertal group demonstrated more dentalalveolar effects. However no differences were found between the two groups at the end of treatment when growth was complete. The overall treatment time for the prepubertal group was significantly longer and it was concluded that it was more efficient to commence treatment after puberty.

Ghislanzoni *et al*., (2013) suggested that the pubertal growth spurt is the optimal timing for treatment of Class II malocclusions with a Mandibular Anterior Repositioning Appliance (MARA) as larger mandibular skeletal changes were observed along with minimal dentoalveolar compensations.

A study of Class II patients treated with the Forsus appliance demonstrated more effective and efficient correction of Class II molar relationships when treatment occurred between CVM stages CS 3-4, compared to CS 5-6 (Servello *et al*., 2015).

A study relating Bionator treatment to cervical vertebral maturation status suggested that CVMS II, when there is a concavity on the lower border of C2 and C3, was the ideal time to start treatment (Faltin *et al*., 2003). The authors reported a 5.1mm long-term supplementary elongation of the mandible compared with controls. Franchi *et al*., (2013) studied Class II patients treated with either a Bionator or Activator followed by fixed appliances on a non-extraction basis. Significantly greater increases were observed in total mandibular length in those treated at puberty than in those treated before leading the authors to conclude that treatment was more effective at puberty.

Class III malocclusions may be more effectively treated at an early age however. Treatment with maxillary expansion and protraction is more effective in the early than the late mixed dentition (Baccetti *et al*., 1998; Franchi *et al*., 1998). Patients treated with rapid maxillary expansion and protraction face masks before the pubertal growth spurt (CS1) showed changes in both the maxilla and mandible (Franchi *et al*., 2004). Approximately 2mm of supplemental growth of the maxilla and 3.5mm mandibular growth restriction was observed, compared with untreated Class III controls. Treatment at the peak of mandibular growth (CS3) was only effective in the mandible where growth was restricted by approximately 4.5mm. These differences can be explained by growth maturation changes of the circum-maxillary sutures. The maxilla is more amenable to early orthopaedic intervention since the sutures begin to close during puberty (Melsen and Melsen, 1982). The maxillary mid-palatal suture also undergoes maturation changes becoming wavier and more interdigitated during adolescence (Melsen, 1975). This affects correction of transverse maxillary deficiencies.

A study of patients treated with rapid maxillary expansion (RME) examined the effects achieved at different stages of cervical vertebral maturation compared with untreated controls (Baccetti *et al*., 2001). Subjects treated early, before peak pubertal growth (CS1-3), had more pronounced transverse skeletal changes and those treated during or slightly after the peak (CS4-6) experienced more dentoalveolar changes.

Summary – *Correction of Class II malocclusions with functional appliances is most effective when the period of peak mandibular growth is included in the treatment time.*

1.8 Aims of the present study

The aim of the present study was to determine the relationship between dental development stage using the Demirjian Index and skeletal maturity using the cervical vertebral maturation method of Baccetti *et al*., (2005) in white British and Asian UK subjects.

The null hypothesis is that there is no statistically significant relationship between dental and skeletal maturity in UK subjects.

Chapter 2

Materials and Methods

Chapter 2 Materials and Methods

2.1 Introduction

The study was designed as a retrospective, cross-sectional study. Subjects were drawn from patient records in the Orthodontic department at Birmingham Dental Hospital, UK. Patients referred for routine orthodontic assessment or treatment who had both digital panoramic and lateral cephalometric radiographs taken as part of their initial examination were considered for inclusion. Successive subjects were identified from the radiography log book between September 2012 – June 2013. The radiographs were examined so that dental development stages could be determined from the panoramic radiographs and cervical vertebral maturation stages established from the lateral cephalometric radiographs.

2.2 Ethical approval

An application for ethical approval was made for the research to be carried out at Birmingham Dental Hospital, part of Birmingham Community Healthcare NHS Trust. Ethical approval was gained via proportionate review from NRES (National Research Ethics Service) Committee North East - Newcastle and North Tyneside 1. Reference number: 13/NE/0221

Local NHS Research and Development approval for the research was also gained from Birmingham and Black Country CLRN Consortium Office. Consortium ref: BCHCDent335.111340.

2.3 Sample size

The number of subjects to be included in the study so that clinically valuable results could be reported was calculated using Altman's nomogram (Altman, 1991). This calculation involves the use of four measures:

- The standard deviation of the variable (s) – Chen *et al*., (2010) reported a standard deviation of 15 months between CVM stages.
- Clinically relevant difference (crd) – This was set at 12 months
- Significance level – In order to give a high probability that the findings would be valid a 1% significance level was chosen.
- Power – To give a high probability of detecting differences the power was set at 0.9 (90%).

The ratio of crd/s gives the standardised difference (sd), in this case 12/15 months = 0.8.

Application of an sd of 0.8 and power of 0.9 to the nomogram produces a minimum total sample size of 90 subjects, 45 in each group. The decision was taken to double the sample size in order to permit the possible analysis of data from subgroups according to sex and ethnicity.

2.4 Selection criteria

Subjects were drawn from patients who attended the Orthodontic department at Birmingham Dental Hospital, UK for initial examination between September 2012 and June 2013. Successive patients that had both digital panoramic and lateral cephalometric radiographs taken as part of their routine orthodontic assessment were identified from the hospitals radiography log book. The following inclusion and exclusion criteria were used:

Inclusion criteria

- Males and females aged from 10 to 18 years old
- Caucasian or Asian ethnicity
- Medically fit and well, no general developmental impairments to craniofacial structures
- No previous orthodontic treatment
- All permanent teeth present in the lower left quadrant (excluding third molars)
- Panoramic and lateral cephalometric radiographs had been taken as part of orthodontic assessment

Exclusion criteria

- Dental anomalies – hypodontia, impactions, delayed dental development
- Previous orthodontic treatment
- Permanent teeth missing in the lower left quadrant
- Radiographic image distortion affecting estimation of tooth development stage/CVM

Patient demographics were determined from iPM, the hospitals patient administration software. Gender was recorded for each subject. This allowed results for males and females to be considered separately and to be compared.

Patient date of birth was recorded along with the date the radiographs were taken. This allowed the patients age at the time of the radiograph to be calculated. Patient age was rounded up or down to the nearest full year, for example:

Subject age 11 years and 5 months = 11 years

Subject age 11 years and 7 months = 12 years

The age range of the subjects reflected the population of patients who attend the department for orthodontic assessment and matched that used in previous studies with a similar methodology (Table 1.5). The age range covered the pubertal growth period, allowing data to be collected for subjects undergoing skeletal maturation from CVM stage 1 through to stage 6. The upper age limit was set as 18 years of age when dental development of the teeth to be studied is expected to be complete.

Ethnic group was recorded for each subject since differences have been found between the maturation patterns of individuals in different populations. Two ethnic groups were chosen for inclusion, Caucasian and Asian. Caucasian subjects were identified as being of 'White British' origin on IPM. Four IPM ethnic groups were combined for the Asian group; Asian/Asian British – Pakistani; Asian/Asian British – Indian; Asian/Asian British – any other; Asian/Asian British – Bangladeshi.

Only teeth in the lower left quadrant were examined. Those who had had previous orthodontic treatment were excluded as this could affect the appearance and grading of the root development if any root resorption had taken place.

Radiographic images were examined and subjects were excluded if there was any radiographic image distortion which could affect estimation of tooth development or CVM stage.

Overall 545 records were examined of which 180 satisfied the inclusion criteria.

365 records were excluded for the following reasons:

- Age outside prescribed range: 158
- Ethnic origin outside the study group: 77
- Medical history: 2
- Previous orthodontic treatment: 43
- Dental anomalies including missing teeth: 62
- Digital panoramic and lateral cephalometric radiograph unavailable: 9
- Radiographic image deformity: 14

2.5 Radiographic grade allocation

Digital radiographic images were viewed and graded under identical conditions by the principal investigator. They were viewed in a darkened room on a computer screen using the Sidexis software programme (Sirona Dental Systems) which allowed image manipulation, including magnification and changes in brightness and contrast, if required, to aid radiographic grading. The investigator was blinded to the subjects' gender, age and ethnic group. All the panoramic radiographs were viewed and graded first followed by the lateral cephalometric radiographs. This was to prevent the operator making assumptions about the patients' stage of development on one of their radiographs and thereby affecting the grade allocated on the second radiograph.

Dental development was assessed from the panoramic radiograph using the Demirjian Index (Demirjian *et al*., 1973) (Fig 1.8, Table 1.4). The following permanent left mandibular teeth were graded; canine (FDI notation 33), first premolar (FDI notation 34), second premolar (FDI notation 35) and second molar (FDI notation 37). Only teeth on the left side were selected as tooth calcification of homologous teeth is symmetrical (Demisch and Wartmann, 1956; Nolla, 1960; Demirjian *et al*., 1973). The maxillary teeth were excluded as there can be superimposition of calcified structures in the area of the maxillary posterior teeth (Krailassiri *et al*., 2002; Uysal *et al*., 2004). Apical closure of mandibular incisors and first permanent molars would already be complete in the age group selected so these teeth were also excluded. The third molar was not included for rating as it is often missing and its development is unpredictable. Each of the four teeth selected were assigned a grade from A – H that most closely matched those described by Demirjian according to the development stage of the root (Fig 2.1). Due to the age of the subjects selected only grades E – H were required. If a tooth fell between two grades, the earlier grade was selected.

Dental development stage F = 35 and 37, stage G = 33 and 34

Dental development stage H = 33,34,35,37

Fig 2.1 Examples of panoramic radiographs used in the study, with relevant dental development stages

Skeletal maturity was assessed from the lateral cephalometric radiograph using the latest modification of the cervical vertebral maturation method (Baccetti *et al*., 2005) (Figs 1.6 and 1.7). The bodies of the second (C2), third (C3), and fourth (C4) cervical vertebrae were studied and assigned a stage from CS1 to CS6 (Fig 2.2). If a subject fell between two grades, the lower grade was selected.

CS1

CS6

Fig 2.2 Examples of cervical vertebral maturity stages (Baccetti *et al*., 2005)

2.6 Pilot study

A pilot study was carried out over a period of one month. The aims of the pilot were to determine the ease of subject identification and to assess the numbers meeting the inclusion criteria. The pilot was also used to validate a data collection spreadsheet and standardise the grading of the radiographs. 63 patients were identified from the radiography logbook as having had digital panoramic and lateral cephalometric radiographs taken in the one month period between 21.08.12 and 21.09.12. Of these, 16 met the criteria for inclusion. With a sample size totalling 180 subjects it was estimated that it would require approximately one year of patient records to reach this.

2.7 Reproducibility study

30 subjects out of the total sample of 180 were selected using an on-line randomisation table (www.randomizer.org) and their panoramic and lateral cephalometric radiographs were graded on two separate occasions 4 weeks apart by the principal investigator to assess intra-examiner reproducibility. A second reviewer, a Consultant Orthodontist, graded the same 30 subjects radiographs to assess inter-examiner reproducibility.

2.8 Data recording and analysis

Data were recorded on to a Microsoft Excel (2010) spreadsheet. Each subject was allocated a study number and personal details such as name and hospital number were removed to preserve anonymity.

Statistical analysis of the data was performed using the IBM SPSS Statistics statistical package (version 22). The following analyses were carried out:

- Kappa values were used to evaluate intra and inter-observer agreement.
- Descriptive statistics were obtained by calculating mean and standard deviations for the chronological ages for the 6 stages of CVM.
- Spearman Rank Order Correlation Coefficient (SROCC) was used to measure associations between skeletal maturational indicators and dental calcification stage of individual teeth.
- The relationships between the stage of calcification of the teeth and the stage of skeletal maturation was studied by calculating the percentage distribution of the stages of calcification for each tooth.

Chapter 3

Results

Chapter 3 Results

3.1 Intra-examiner agreement

3.1.1 Cervical vertebral maturation stage

Measurements were taken from 30 lateral cephalometric radiographs (Measurement 1). The radiographs were re-graded one month later by the principal investigator to assess intra-examiner agreement (Measurement 2). The cross-tabulation of results in shown in Table 3.1. The Kappa value for intra-examiner agreement for CVM stages was 0.708 (Table 3.2).

Measurement1 * Measurement2 Cross-tabulation

Count

		Measurement2						Total
		1	2	3	4	5	6	
Measurement1	1	2	1	0	0	0	0	3
	2	0	2	1	0	0	0	3
	3	0	0	4	0	0	0	4
	4	0	0	0	2	2	0	4
	5	0	0	0	1	6	2	9
	6	0	0	0	0	0	7	7
Total		2	3	5	3	8	9	30

Table 3.1 Cross-tabulation of cervical vertebral maturation stage intra-examiner agreement

Symmetric Measures

		Value	Asymp. Std. Error[a]	Approx. T[b]	Approx. Sig.
Measure of Agreement	Kappa	.708	.096	8.048	.000
N of Valid Cases		30			

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

Table 3.2 Kappa value for cervical vertebral maturation stage intra-examiner agreement

3.1.2 Dental development stage

Dental development stages were assessed for 30 panoramic radiographs (Measurement 1). The radiographs were re-graded one month later by the principal investigator to assess intra-examiner agreement (Measurement 2). The cross-tabulation of results in shown in Table 3.3. The Kappa value for intra-examiner agreement for dental development stages was 0.811 (Table 3.4).

Measurement1 * Measurement2 Cross-tabulation

Count

		Measurement2				
		1	2	3	4	Total
Measurement1	2	1	9	0	0	10
	3	0	3	29	2	34
	4	0	0	6	70	76
Total		1	12	35	72	120

Table 3.3 Cross-tabulation of dental development stage intra-examiner agreement

Symmetric Measures

		Value	Asymp. Std. Error[a]	Approx. T[b]	Approx. Sig.
Measure of Agreement	Kappa	.811	.051	11.232	.000
N of Valid Cases		120			

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

Table 3.4 Kappa value for dental development stage intra-examiner agreement

3.2 Inter-examiner agreement

3.2.1 Cervical vertebral maturation stage

30 lateral cephalometric radiographs were graded by the principal investigator (Examiner 1) and then independently by a second investigator (Examiner 2) to assess inter-examiner agreement. The cross-tabulation of results in shown in Table 3.5. The Kappa value for inter-examiner agreement for CVM stages was 0.664 (Table 3.6).

Examiner1 * Examiner2 Cross-tabulation

Count

		Examiner2						Total
		1	2	3	4	5	6	
Examiner1	1	1	1	0	0	0	0	2
	2	0	3	0	0	0	0	3
	3	0	1	4	0	0	0	5
	4	0	0	0	3	0	0	3
	5	0	0	0	1	5	2	8
	6	0	0	0	0	3	6	9
Total		1	5	4	4	8	8	30

Table 3.5 Cross-tabulation of cervical vertebral maturation stage inter-examiner agreement

Symmetric Measures

		Value	Asymp. Std. Error[a]	Approx. T[b]	Approx. Sig.
Measure of Agreement	Kappa	.664	.103	7.461	.000
N of Valid Cases		30			

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

Table 3.6 Kappa value for cervical vertebral maturation stage inter-examiner agreement

3.2.2 Dental development stage

30 panoramic radiographs were graded by the principal investigator (Examiner 1) and then independently by a second investigator (Examiner 2) to assess inter-examiner agreement. The cross-tabulation of results in shown in Table 3.7. The Kappa value for inter-examiner agreement for dental development stages was 0.880 (Table 3.8).

Examiner1 * Examiner2 Cross-tabulation

Count

		Examiner2				Total
		1	2	3	4	
Examiner1	1	1	0	0	0	1
	2	0	11	1	0	12
	3	0	0	34	1	35
	4	0	0	6	66	72
Total		1	11	41	67	120

Table 3.7 Cross-tabulation of dental development stage inter-examiner agreement

Symmetric Measures

		Value	Asymp. Std. Error[a]	Approx. T[b]	Approx. Sig.
Measure of Agreement	Kappa	.880	.041	12.365	.000
N of Valid Cases		120			

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

Table 3.8 Kappa value for dental development stage inter-examiner agreement

3.3 Distribution of chronological age grouped by cervical vertebral maturation stage

3.3.1 All subjects

Data were collected for a total of 180 subjects, 82 males and 98 females ranging in age from 10 to 18 years. The distribution of chronological ages for all subjects, grouped by cervical vertebral maturation stage is shown in Table 3.9. The appearance of each CVM stage is slightly earlier in female subjects than male subjects, except for CVM stage 6. There was a statistically significant difference between the ages of the males and females at CVM stages 3 and 4 (p=0.006, p=0.036).

CVM Stage	Gender	Number of Subjects	Chronological Age (yrs)		P-value
			Mean	SD	
1	Male	8	11.73	1.10	0.118
	Female	4	10.76	0.29	
2	Male	11	12.61	1.37	0.053
	Female	8	11.51	0.72	
3	Male	9	13.47	1.21	**0.006**
	Female	7	11.80	0.76	
4	Male	17	14.91	1.38	**0.036**
	Female	21	13.87	1.53	
5	Male	19	15.67	2.14	0.467
	Female	24	15.23	1.84	
6	Male	18	16.20	1.04	0.876
	Female	34	16.26	8.77	
		Total 180			

Table 3.9 Distribution of chronological ages for all subjects grouped by cervical vertebral maturation stage

3.3.2 White British subjects

90 subjects were identified as White British, 42 males and 48 females. The distribution of chronological ages for the White British subjects, grouped by cervical maturation stage is shown in Table 3.10. The appearance of each CVM stage is slightly earlier in White British female subjects than White British male subjects in CVM stages 1-4. The difference between the ages of the males and females at CVM stages 3 and 4 was statistically significant (p=0.040, p=0.037).

CVM Stage	Gender	Number of Subjects	Chronological Age (yrs)		P-value
			Mean	SD	
1	Male	7	11.98	0.92	0.122
	Female	2	10.76	0.33	
2	Male	4	13.34	1.94	0.182
	Female	3	11.38	1.10	
3	Male	4	13.60	1.24	**0.040**
	Female	4	11.69	0.77	
4	Male	10	14.81	1.48	**0.037**
	Female	8	13.16	1.58	
5	Male	8	15.02	2.52	0.818
	Female	12	15.24	1.70	
6	Male	9	16.53	1.10	0.434
	Female	19	16.13	1.32	
		Total 90			

Table 3.10 Distribution of chronological ages for White British subjects according to cervical vertebral maturation stage

3.3.3 Asian subjects

90 subjects were identified as Asian, 40 males and 50 females. The distribution of chronological ages for the Asian subjects, grouped by cervical maturation stage is shown in Table 3.11. The appearance of each CVM stage is consistently earlier in Asian female subjects than Asian male subjects in CVM stages 2-5. However the differences between the ages of the males and females were not statistically significant at any of the CVM stages.

CVM Stage	Gender	Number of Subjects	Chronological Age (yrs)		P-value
			Mean	SD	
1	Male	1	10.02	0	
	Female	2	10.75	0.39	
2	Male	7	12.20	0.82	0.176
	Female	5	11.59	0.52	
3	Male	5	13.37	1.32	0.151
	Female	3	11.94	0.87	
4	Male	7	15.06	1.33	0.257
	Female	13	14.31	1.38	
5	Male	11	16.15	1.78	0.258
	Female	12	15.22	2.04	
6	Male	9	15.88	0.93	0.294
	Female	15	16.43	1.35	
		Total 90			

Table 3.11 Distribution of chronological ages for Asian subjects according to cervical vertebral maturation stage

3.3.4 Comparison of groups

The mean chronological age for each CVM stage is shown for all subjects, White British subjects and Asian subjects for males (Table 3.12) and females (Table 3.13). There were no statistically significant differences between the ages of White British and Asian males and females at any CVM stage.

CVM Stage	Mean Chronological Age (yrs)			P-value
	All subjects	White British	Asian	
1	11.73	11.98	10.02	0.094
2	12.61	13.34	12.20	0.195
3	13.47	13.60	13.37	0.796
4	14.91	14.81	15.06	0.733
5	15.67	15.02	16.15	0.264
6	16.20	16.53	15.88	0.196

Table 3.12 Mean chronological age of male subjects according to cervical vertebral maturation stage

CVM Stage	Mean Chronological Age (yrs)			P-value
	All subjects	White British	Asian	
1	10.76	10.76	10.75	0.981
2	11.51	11.38	11.59	0.727
3	11.80	11.69	11.94	0.702
4	13.87	13.16	14.31	0.095
5	15.23	15.24	15.22	0.984
6	16.26	16.13	16.43	0.512

Table 3.13 Mean chronological age of female subjects according to cervical vertebral maturation stage

3.4 Correlation between dental development stage and cervical vertebral maturation stage

3.4.1 All subjects

Spearman Rank Order Correlation Coefficients (r) between dental development stages of the four mandibular teeth and cervical vertebral maturation stage are shown in Table 3.14 for all subjects (n=180) separated by gender.

All associations were statistically significant and ranged from 0.526 to 0.625 for male subjects and 0.409 to 0.593 for females. The sequence of teeth from highest to lowest correlation with CVM was 35,33,37,34 in males and 37,35,33,34 in females.

In males the second premolar had the highest correlation with CVM (r = 0.625) whereas in females the second molar had the highest correlation (r = 0.593). The first premolar showed the lowest correlation for both sexes (r = 0.526 in males, r = 0.409 in females). The lowest correlation in males was only 10 percent less than that of the highest correlation in females.

Tooth (FDI notation)	Male (n=82)		Female (n=98)	
	r	P-value	r	P-value
Canine (33)	0.619	< 0.01	0.449	< 0.01
First Premolar (34)	0.526	< 0.01	0.409	< 0.01
Second Premolar (35)	**0.625**	< 0.01	0.539	< 0.01
Second Molar (37)	0.602	< 0.01	**0.593**	< 0.01

Table 3.14 Correlation between dental development stage and cervical vertebral maturation stage for all subjects

3.4.2 White British subjects

Spearman Rank Order Correlation Coefficients between dental development stage of each of the mandibular teeth and cervical vertebral maturation stage are shown in Table 3.15 for White British subjects (n=90) separated by gender.

All associations were statistically significant and ranged from 0.392 to 0.568 for male subjects and 0.291 to 0.533 for females. The sequence of teeth from highest to lowest correlation with CVM was 33,35,37,34 in males and 37,35,33,34 in females.

In males the canine had the highest correlation with CVM (r = 0.568) whereas in females the second molar demonstrated the highest correlation (r = 0.533). The first premolar showed the lowest correlation for both sexes (r = 0.392 in males, r = 0.291) in females.

Tooth (FDI notation)	Male (n=42)		Female (n=48)	
	r	P-value	r	P-value
Canine (33)	**0.568**	< 0.01	0.329	< 0.01
First Premolar (34)	0.392	< 0.01	0.291	< 0.01
Second Premolar (35)	0.565	< 0.01	0.469	< 0.01
Second Molar (37)	0.474	< 0.01	**0.533**	< 0.01

Table 3.15 Correlation between dental development stage and cervical vertebral maturation stage in White British subjects

3.4.3 Asian subjects

Spearman Rank Order Correlation Coefficients between dental development stage of each of the mandibular teeth and associated cervical vertebral maturation stage are shown in Table 3.16 for Asian subjects (n=90) separated by gender.

All associations were statistically significant and ranged from 0.669 to 0.752 for male subjects and 0.479 to 0.569 for females. The sequence of teeth from highest to lowest correlation with CVM was 37,35,34,33 in males and 37,35,33,34 in females.

The second molar had the highest correlation with CVM in both males (r = 0.752) and females (r = 0.569). The canine showed the lowest correlation in males (r=0.669) and the first premolar did for females (r = 0.479)

Tooth (FDI notation)	Male (n=40)		Female (n=50)	
	r	P-value	r	P-value
Canine (33)	0.669	< 0.01	0.489	< 0.01
First Premolar (34)	0.687	< 0.01	0.479	< 0.01
Second Premolar (35)	0.696	< 0.01	0.526	< 0.01
Second Molar (37)	**0.752**	< 0.01	**0.569**	< 0.01

Table 3.16 Correlation between dental development stage and cervical vertebral maturation stage in Asian subjects

3.4.4 Comparison of groups

The teeth with the highest Spearman Rank Order Correlation Coefficients between dental development stage and CVM stage are shown in Table 3.17 for all groups studied.

In males, when all subjects are combined the tooth showing the highest correlation was the left mandibular second premolar (r = 0.625). The tooth with the highest correlation in White British Males was the left mandibular canine (r = 0.568) where as in Asian males it was the left mandibular second molar (r = 0.752). Correlations between dental development stages for all the teeth studied and CVM scores were lower in the White British group (Table 3.15) than the Asian group (Table 3.16).

In females, the left mandibular second molar had the highest correlation with CVM in White British subjects (r = 0.533), Asian subjects (r = 0.569) and when all subjects were considered together (r = 0.593). Correlations were similar between the two ethnic groups.

Correlations were generally higher in males than females.

Ethnic Group	Male		Female	
	Tooth (FDI notation)	r	Tooth (FDI notation)	r
All subjects	Second Premolar (35)	0.625	Second Molar (37)	0.593
White British	Canine (33)	0.568	Second Molar (37)	0.533
Asian	Second Molar (37)	0.752	Second Molar (37)	0.569

Table 3.17 Teeth with highest correlation between dental development stage and cervical vertebral maturation stage in all ethnic groups

3.5 Percentage distributions of the relationship between dental development stages and cervical vertebral maturation stages

3.5.1 All subjects

Percentage distributions for the relationship between dental development stages of the four left mandibular teeth and CVM stage for all subjects are shown in Tables 3.18 to 3.23. There were 12 subjects at CVM stage 1, 8 males and 4 females (Table 3.18). The second molar stage G showed the highest percentage distribution in both males (62.5%) and females (75%). No second molars had reached stage H in both males and females. All the remaining teeth had a scattered distribution.

	Canine				First Premolar				Second Premolar				Second Molar			
DI Stage	**Male**		**Female**		**Male**		**Female**		**Male**		**Female**		**Male**		**Female**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	25
E	0	0	0	0	1	12.5	0	0	1	12.5	0	0	2	25	0	0
F	3	37.5	1	25	2	25	1	25	4	50	1	25	1	12.5	0	0
G	4	50	1	25	3	37.5	1	25	3	37.5	2	50	5	62.5	3	75
H	1	12.5	2	50	2	25	2	50	0	0	1	25	0	0	0	0
Total	8	100	4	100	8	100	4	100	8	100	4	100	8	100	4	100

Table 3.18 Percentage distribution of dental development stages of individual teeth at cervical vertebral maturation stage 1 for all subjects

There were 19 subjects at CVM stage 2, 11 males and 8 females (Table 3.19). All the examined teeth showed wide variation in tooth calcification stage from stage F to stage H. The second molar stage G showed the highest percentage distribution in males (63.64%). In females, no tooth development stages had a percentage distribution greater than 50%, although this figure was seen for a number of different tooth development stages.

	Canine				**First Premolar**				**Second Premolar**				**Second Molar**			
DI Stage	**Male**		**Female**		**Male**		**Female**		**Male**		**Female**		**Male**		**Female**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F	2	18.18	0	0	2	18.18	0	0	3	27.27	2	25	3	27.27	3	37.5
G	6	54.55	4	50	6	54.55	4	50	5	45.45	4	50	7	63.64	4	50
H	3	27.27	4	50	3	27.27	4	50	3	27.27	2	25	1	9.09	1	12.5
Total	11	100	8	100	11	100	8	100	11	100	8	100	11	100	8	100

Table 3.19 Percentage distribution of dental development stages of individual teeth at cervical vertebral maturation stage 2 for all subjects

There were 16 subjects at CVM stage 3, 9 males and 7 females (Table 3.20). The second premolar and second molar showed scattered distribution between dental development stages F to H. The second molar stage G showed the highest percentage distribution in males (66.67%). In females, the canine stage G showed the highest percentage distribution (57.14%).

	Canine				First Premolar				Second Premolar				Second Molar			
DI Stage	**Male**		**Female**		**Male**		**Female**		**Male**		**Female**		**Male**		**Female**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F	0	0	0	0	0	0	1	14.29	2	22.22	3	42.86	1	11.11	3	42.86
G	4	44.44	4	57.14	4	44.44	3	42.86	3	33.33	2	28.57	6	66.67	3	42.86
H	5	55.56	3	42.86	5	55.56	3	42.86	4	44.44	2	28.57	2	22.22	1	14.29
Total	9	100	7	100	9	100	7	100	9	100	7	100	9	100	7	100

Table 3.20 Percentage distribution of dental development stages of individual teeth at cervical vertebral maturation stage 3 for all subjects

There were 38 subjects at CVM stage 4, 17 males and 21 females (Table 3.21). For male subjects, root formation of the canine as well as the first and second premolars was completed (stage H) in the majority of subjects (88.24%, 82.35% and 82.35% respectively). Root development was also mostly complete for the canine and first premolar in females (85.71% and 85.71% respectively).

	Canine				First Premolar				Second Premolar				Second Molar			
DI Stage	**Male**		**Female**		**Male**		**Female**		**Male**		**Female**		**Male**		**Female**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F	0	0	0	0	0	0	0	0	0	0	2	9.52	0	0	1	4.76
G	2	11.76	3	14.29	3	17.65	3	14.29	3	17.65	8	38.1	8	47.06	14	66.67
H	15	88.24	18	85.71	14	82.35	18	85.71	14	82.35	11	52.38	9	52.94	6	28.57
Total	17	100	21	100	17	100	21	100	17	100	21	100	17	100	21	100

Table 3.21 Percentage distribution of dental development stages of individual teeth at cervical vertebral maturation stage 4 for all subjects

There were 43 subjects at CVM stage 5, 19 males and 24 females (Table 3.22). By CVM stage 5 the root development of the second molar was complete in the majority of males (68.42%) and females (62.5%).

DI Stage	Canine				First Premolar				Second Premolar				Second Molar			
	Male		Female		Male		Female		Male		Female		Male		Female	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E	0	0	0	0	0	0	0	0	0	0	0	0	1	5.26	0	0
F	1	5.26	0	0	1	5.26	0	0	2	10.53	1	4.17	2	10.53	1	4.17
G	1	5.26	3	12.5	2	10.53	3	12.5	2	10.53	6	25	3	15.79	8	33.33
H	17	89.47	21	87.5	16	84.21	21	87.5	15	78.95	17	70.83	13	68.42	15	62.5
Total	19	100	24	100	19	100	24	100	19	100	24	100	19	100	24	100

Table 3.22 Percentage distribution of dental development stages of individual teeth at cervical vertebral maturation stage 5 for all subjects

There were 52 subjects at CVM stage 6, 18 males and 34 females (Table 3.23). By CVM stage 6 in males, the root development was complete (Stage H) for all canines and second premolars and the vast majority of first premolars (94.44%) and second molars (88.89%). In females, all canines had reached stage H of development and most first premolars, second premolars and second molars were fully developed (97.06%, 94.12% and 82.35 respectively).

	Canine				**First Premolar**				**Second Premolar**				**Second Molar**			
DI Stage	**Male**		**Female**		**Male**		**Female**		**Male**		**Female**		**Male**		**Female**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
G	0	0	0	0	1	5.56	1	2.94	0	0	2	5.88	2	11.11	6	17.65
H	18	100	34	100	17	94.44	33	97.06	18	100	32	94.12	16	88.89	28	82.35
Total	18	100	34	100	18	100	34	100	18	100	34	100	18	100	34	100

Table 3.23 Percentage distribution of dental development stages of individual teeth at cervical vertebral maturation stage 6 for all subjects

Chapter 4

Discussion and Conclusions

Chapter 4 Discussion and Conclusions

4.1 Reproducibility

The Kappa value for reproducibility of the assessment of CVM stage was 0.708 for intra-examiner measurements and 0.664 for inter-examiner measurements. These values represent ‘substantial agreement’ according to a widely accepted method of classification (Table 4.1, Landis and Koch, 1977). The Kappa value for the assessment of dental development stage was 0.811 for intra-examiner measurements and 0.880 for inter-examiner measurements. These values represent ‘almost perfect agreement’. The assessment of dental development stage was more reliable than that of CVM stage. A recent study of cervical vertebrae maturation stage reliability also reported substantial agreement in intra-observer and inter-observer measurements (Rainey, 2014). Chen *et al*., (2010a) found almost perfect agreement for the reproducibility of CVM stages. Although CVM staging systems have been reported to be repeatable and highly reproducible (Gandini *et al*., 2006; Pasciuti *et al*., 2013), authors have suggested that errors may occur as assessment is subjective (Mito *et al*., 2002) or because changes in the vertebral body shapes can be difficult to distinguish (Nestman *et al*., 2011).

Value of K	**Interpretation**
< 0	Poor agreement
0.01 – 0.20	Slight agreement
0.21 – 0.40	Fair agreement
0.41 – 0.60	Moderate agreement
0.61 – 0.80	Substantial agreement
0.81 – 1.00	Almost perfect agreement

Table 4.1 Interpretation of Kappa values (Landis and Koch, 1977)

4.2 Relationship between chronological age and cervical vertebral maturation stage

Chronological age alone is a poor predictor of maturity due to wide individual variation in the onset and duration of puberty (Houston, 1980; Hägg and Taranger, 1982; Demirjian *et al.*, 1985). This was demonstrated in the present study by the relatively large standard deviations obtained for the mean age at each CVM stage (Table 3.9). The results clearly show that female subjects mature earlier than male subjects in both ethnic groups. Females were generally younger than males at each CVM stage, when all subjects were grouped together and also when the two ethnic groups were considered separately (Tables 3.12 - 3.13). This finding is consistent with studies carried out in different populations using similar methodologies to the present study (Chen *et al.*, 2010a; Rozylo-Kalinowska *et al.*, 2011). This is also in agreement with studies using hand-wrist radiographs to assess skeletal maturity stage, in which maturity was found to occur at a younger mean age in females (Krailassiri *et al.*, 2002; Uysal *et al.*, 2004). This finding also supports work in which other measures of maturation including height increases or sexual development were examined, and in which females were found to mature earlier than males (Prahl-Andersen *et al.*, 1979; Spencer, 2002).

Peak growth is likely to take place at CVM stages 3 – 4 (Baccetti *et al.*, 2005). At CVM stage 3, the difference in mean age between males (13.47 years, sd 1.21 years) and females (11.80 years, sd 0.76 years) was statistically significant. It was also statistically significant at CVM stage 4 for all subjects and for the White British ethnic group at CVM stages 3 and 4. The differences were not statistically significant in the Asian group. Functional appliance treatment is most effective if it coincides with peak growth (Baccetti *et al.*, 2005; Chhibber *et* *al*., 2013; Franchi *et al*., 2013; Servello *et al*., 2015). Since girls reach this stage at a significantly younger age than boys they need to be referred earlier and start treatment earlier in order to try to gain the maximum benefit from functional appliance treatment. Conversely, if boys start treatment with functional appliances at too young an age before peak growth is occurring, it may be less effective.

No significant differences were found in the mean ages of males and females in the White British and Asian ethnic groups at each CVM stage (Tables 3.12 - 3.13). The two ethnic groups can therefore be considered as one group. The mean age of the UK females in the present study at CVM stage 3 (11.80 years, sd 0.76 years) is consistent with the results of similar studies carried out in China (11.60 years, sd 1.44 years) (Chen *et al*., 2010a) and in Poland (11.85 years, sd 1.24 years) (Rozylo-Kalinowska *et al*., 2011). In UK males, the mean age at CVM stage 3 (13.47 years, sd 1.21 years) was slightly higher than that of Chinese individuals (12.73 years, sd 11.60 years) (Chen *et al*., 2010a) and Polish subjects (12.35 years, sd 1.44 years) (Rozylo-Kalinowska *et al*., 2011). Differences have been reported between the age at which individuals in different populations or racial groups reach their pubertal growth spurt (Soegiharto *et al*., 2008a). These have been attributed to reasons such as ethnicity or genetics and also environmental factors such as nutrition, socio-economic status, climate, and exposure to chemicals (Wei and Gregory, 2009). The fact that there was no significant difference in age found between the White British and Asian ethnic groups in the present study may be due to there being no true differences between the two ethnic groups or that, as the subjects all live in the same geographic area, they are subject to a similar range of environmental influences.

4.3 Correlation between dental development stage and cervical vertebral maturation stage

The relationship between dental and skeletal maturity is still not clear. Some authors have reported low correlations (Lewis and Garn, 1960; Anderson *et al*., 1975) and argued that dental and skeletal development are distinct processes (Lewis, 1991). Others have suggested that better correlations are achieved when key individual teeth are studied rather than the dentition as a whole (Kataja *et al*., 1989). However the results are not always consistent (Table1.5).

In the present study, the tooth with the highest correlation to CVM stage was the left mandibular canine in White British Males (r = 0.568) (Table 3.17). In White British females and both male and female Asian subjects, the highest correlation was found for the left mandibular second molar (r = 0.533; r = 0.752; r = 0.569 respectively) (Table 3.17). Whilst there is no standard interpretation of Spearman Rank Order Correlation Coefficients, correlations between 0.50 - 0.70 can be considered as ‘moderate’ and those 0.70 – 0.90 as ‘high’. The best correlations found in the present study can generally be considered only as moderate. Only the correlation between the left mandibular second molar in Asian male subjects and CVM stage could be interpreted as a high correlation (r = 0.752). It is surprising that all the correlations found were statistically significant as some were as low as r = 0.291 (Table 3.15). However these correlation results were taken direct from an SPSS analysis and are typical of non-parametric tests.

Table 4.2 allows comparisons between the results found in the present study and studies with similar methodologies but carried out in different populations. There is a common theme, with the mandibular canine in males and the second molar in both males and females demonstrating the highest correlation with skeletal maturity.

Author	Country	Gender	Tooth with highest correlation	Spearman Rank Order Correlation Coefficient (r)
Rai *et al.*, 2008	India	Male	7	0.73
		Female	7	0.69
Chen *et al.*, 2010	China	Male	3	0.496
		Female	7	0.528
Rozylo-Kalinowska *et al.*, 2011	Poland	Male	3	0.521
		Female	5	0.584
Mittal *et al.*, 2011	India	Male	7	0.758
		Female	7	0.811
Kumar *et al.*, 2012	India	Male	7	0.854
		Female	7	0.866
Perinetti *et al.*, 2012	Italy	Male + Female combined	7	0.77
Howell, 2015 (unpublished data)	**UK - White British**	Male	**3**	**0.568**
		Female	**7**	**0.533**
	UK - Asian	Male	**7**	**0.752**
		Female	**7**	**0.569**

Table 4.2 Teeth demonstrating the highest correlation to cervical vertebral maturation stage

The left mandibular canine tooth had the highest correlation in Chinese males (r = 0.496) (Chen *et al*., 2010a) and also in a Polish study (r = 0.521) (Rozylo-Kalinowska *et al*., 2011). These results are similar to that of the present study for White British males (r = 0.568). Chen *et al*., (2010a) described their correlation as low but statistically significant and suggested that stage G of the mandibular canine in males marks the beginning of the growth spurt. Coutinho *et al*., (1993) examined the correlation between skeletal maturity assessed from hand-wrist radiographs and dental maturity and found the mandibular canine had the highest correlation. They suggested that the canine dental development stage G occurs approximately 0.4yrs before peak height velocity in females and 1.3yrs before in males and that the intermediate stage between canine development stages F and G marks the early part of the pubertal growth spurt. Krailassiri *et al*., (2002) also studied the correlation with hand-wrist radiographs and suggested that the canine stage F may represent mp3 stage of the hand-wrist radiograph; which is when peak growth is most likely to occur. For male subjects in the present study at CVM stage 3, the pre-peak pubertal stage, the percentage distribution of stage G in the mandibular canine was 44% and stage H was 56% (Table 3.20). By CVM stage 4 only 12% demonstrated stage G and the vast majority of canine teeth were fully formed at stage H, 88% (Table 3.21). These results suggest that stages F, G and H could be considered respectively as the stages before, during and after peak growth.

The left mandibular second molar had the highest correlation in the majority of studies in Table 4.2, especially in females. The best correlations ranged from r = 0.528 in females in China (Chen *et al*., 2010a) to r = 0.866 in females in India (Kumar *et al*., 2012) which represents moderate to high correlation. Chen *et al*., (2010a) suggested that dental development stage F of the second molar marked the beginning of the growth spurt in females. Krailassiri *et al*., (2002) suggested that stage E of the second molar in females and stage G in males could be used as a simple way of determining the start of a period of accelerating growth. For female subjects in the present study, the percentage distribution of both stages F and G in the left mandibular second molar was 43% at CVM stage 3, the pre-peak pubertal stage (Table 3.20). By CVM stage 4, only 5% were at stage F, 67% were stage G and 29% stage H (Table 3.21). By CVM stage 5, a post peak growth stage, 63% of second molars were at the fully developed stage H (Table 3.22). Based on these results, it could be concluded that the transition from stages F - G in the mandibular second molar of females marks the start of a period of peak growth and the transition from stages G - H marks the progression from peak to post peak growth.

The mandibular second molar tooth may be the most useful to examine on panoramic radiographs as it forms later than the other mandibular teeth and continues its development through the pubertal growth period. The first premolar, for example, is more likely to be at its later stages of development during the relevant age range. The mandibular second molar is also rarely missing, unlike the second premolar. The overall prevalence of hypodontia is 6.4%, with the mandibular second premolar accounting for 29.9% of missing teeth and the second molar only 1.8% (Khalaf *et al*., 2014).

Lack of concordance between the teeth with the highest correlations and the degree of correlation in Table 4.2 may be due to differences in study methodologies (Uysal *et al*., 2006; Chen *et al*., 2010a; Rozylo-Kalinowska *et al*., 2011). The impact of the number of subjects studied and the age ranges included should be considered. Different ethnic groups and environmental factors may also account for variations in results (Sierra *et al*., 1987; Mappes *et al*., 1992).

Gender differences have been reported for growth and maturation ages (Soegiharto *et al*., 2008a). In the present study, male dental development was more advanced in relation to skeletal maturity stages than that of females. For the left mandibular second molar, at CVM stage 3 only 11% of males were still at dental development stage F compared with 43% of females. By CVM stage 4, 53% of males demonstrated stage H compared with only 29% of females. This is in agreement with other studies (Chertkow, 1980; Krailassiri *et al*., 2002; Uysal *et al*., 2006). It may be explained by dental and skeletal maturation being two distinct processes so that dental development of females is later at each CVM stage than in males whilst females reach each CVM stage at a younger age. The relationship between dental development and age is therefore closer between the sexes.

The teeth demonstrating the highest correlations have been discussed, however the correlations between many of the teeth are similar (Table 3.14). The number of subjects in the key CVM stages of 3 and 4 are relatively low when broken down (Table 3.9). In order to be able to draw more accurate conclusions on the relationship between dental development and these stages, in would be beneficial to repeat this study focusing only on subjects at CVM stage 3 and 4 in order to observe whether any differences exist.

4.4 Age prediction based upon dental development

A breakdown of dental development stage by age for the second molar tooth is shown in Table 4.3. The second molar was used because it was the tooth that generally demonstrated the highest correlation with skeletal maturation. If these results were to be applied as a method of predicting age from a panoramic radiograph, then it could be reasonable to assume that if the second molar dental development stage of a male was stage G then he would be at least 12 years old and if it was stage H he would be at least 13 years old. If the second molar dental development stage of a female was stage G then she would be at least 11 years old and if it was stage H she would be at least 13 years old.

This is presented as a discussion table since interpretation is somewhat speculative and more concrete conclusions would require greater numbers. However it appears that the transition from second molar dental development stage F to G occurs in males aged 12-13 years, which corresponds with pre-peak CVM stages. In females this occurs slightly earlier at ages 11-12 years which again corresponds with pre-peak CVM stages. The transition from second molar dental development stage F – G therefore seems to mark the beginning of the period of peak pubertal growth.

Age	Male						Female					
	Development stage					Total	Development stage					Total
	D	E	F	G	H		D	E	F	G	H	
10	0	2	0	0	0	2	0	0	1	1	0	2
11	0	0	4	1	0	5	1	0	3	5	1	10
12	0	0	2	7	0	9	0	0	3	7	0	10
13	0	0	0	10	2	12	0	0	1	10	3	14
14	0	0	1	5	3	9	0	0	0	6	6	12
15	0	0	0	6	8	14	0	0	0	6	5	11
16	0	0	0	2	12	14	0	0	0	3	12	15
17	0	1	0	0	11	12	0	0	0	0	16	16
18	0	0	0	0	5	5	0	0	0	0	8	8
Total	0	3	7	31	41	82	1	0	8	38	51	98

Table 4.3 Dental development stage of the second molar at each age.

4.5 Conclusions

Females were found to mature earlier than males in the present study, reaching each CVM stage at a younger age. This is consistent with studies with similar methodologies in different populations (Chen *et al*., 2010a; Rozylo-Kalinowska *et al*., 2011), and also with studies comparing different measures of maturation such as serial height increases (Prahl-Andersen *et al*., 1979; Spencer, 2002). This is important clinically as if growth is to be utilised to help correct a malocclusion, then functional appliance therapy needs to be initiated earlier in females than males.

There was no statistically significant difference in the mean age of White British and Asian males and females at each CVM stage. This suggests that either there is no inherited difference in the rate of skeletal maturation between these two groups or that the impact of exposure to similar environmental factors negates this.

The mandibular canine was found to have the highest correlation with skeletal development in White British males. The mandibular second molar demonstrated the highest correlation to skeletal development stage in White British females and in Asian males and females. These results were consistent with the findings of studies with similar methodologies carried out in other populations (Table 4.2). The correlations were statistically significant but can only really be interpreted as moderate. The null hypothesis that there is no statistically significant relationship between dental and skeletal maturity in UK subjects is therefore disproved. Males were found to be at a more advanced dental development stage than females at each

CVM stage. This is in agreement with other studies (Chertkow, 1980; Krailassiri *et al*., 2002; Uysal *et al*., 2006).

In order for these findings to be clinically useful, it would be necessary to assess the dental development stage of an individual tooth on a panoramic radiograph and use it as a guide to skeletal maturation. The results suggest that the transition from dental development stage F-G in the mandibular second molar marks the onset of a period of peak growth and that the transition from stage G-H indicates that peak growth has most likely been passed. This points to the fact that a simple assessment of skeletal maturation can be made from panoramic radiographs as a first level diagnostic tool without the need for a lateral cephalometric radiograph. However as the correlations observed were only moderate, it would be best considered as part of an overall picture of maturity stage alongside other maturity indicators such as age, height increases and secondary sexual characteristics to give a more accurate assessment of when to commence functional appliance treatment.

4.6 Further research

A more accurate measure of the relationship between dental development and the pubertal growth spurt could be gained by including other measures of maturation such as serial height increases or development of secondary sexual characteristics. Studies into the effectiveness of functional appliance treatment in relation to dental development stage would ultimately determine whether assessing dental development stage has clinical benefit as a tool for predicting when to begin treatment.

Chapter 5

Appendices and References

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Appendices

References

Appendix 1. Raw data

Subject number	Date of birth	Radiograph date	Age (years)	Age (nearest full year)	Gender	Ethnic Group	33	34	35	37	CS
1	13/10/2000	26/06/2013	12.71	13	0	0	7	7	6	7	3
2	12/01/2000	26/06/2013	13.46	13	0	1	8	8	7	7	3
3	27/06/1995	19/09/2012	17.24	17	1	0	8	8	8	8	6
4	22/08/1997	26/06/2013	15.86	16	0	0	8	8	8	7	6
5	14/07/1997	25/06/2013	15.96	16	0	0	8	8	8	8	6
6	27/12/1996	25/06/2013	16.51	16	0	1	8	8	8	8	6
7	10/12/2002	29/04/2013	10.39	10	0	0	6	5	6	5	1
8	03/04/1998	24/06/2013	15.24	15	1	1	8	8	8	8	4
9	23/12/1996	24/06/2013	15.82	17	1	1	8	8	8	8	4
10	09/04/1997	20/06/2013	16.21	16	1	1	8	8	8	7	5
11	25/08/1998	12/06/2013	14.81	15	0	1	8	8	8	8	6
12	24/05/1997	07/06/2013	16.05	16	0	1	8	8	8	8	6
13	24/06/1999	06/06/2013	13.96	14	1	1	8	8	7	7	4
14	17/09/1996	29/01/2013	16.38	16	1	1	8	8	8	8	6
15	03/11/1997	29/05/2013	15.58	16	1	1	8	8	8	7	5
16	01/01/2001	29/05/2013	12.42	12	0	0	8	8	7	7	1
17	05/11/2001	22/05/2013	11.55	12	0	1	7	8	7	7	3
18	07/04/1997	16/05/2013	16.12	16	1	1	8	8	8	8	6
19	23/09/1996	16/05/2013	16.66	17	1	1	8	8	8	8	6
20	22/02/1998	16/05/2013	15.24	15	1	0	8	8	8	7	4
21	18/12/2001	15/05/2013	11.42	11	0	0	7	7	7	7	1
22	13/10/2000	24/04/2013	12.54	13	1	0	7	8	8	7	2
23	09/08/1997	04/02/2013	15.5	15	1	1	8	8	8	7	4
24	17/02/2001	14/05/2013	12.24	12	0	0	7	8	7	7	1
25	16/12/1994	13/05/2013	18.42	18	0	1	8	8	8	8	5
26	17/03/1996	13/05/2013	17.17	17	0	1	8	7	8	8	5
27	27/12/1999	13/05/2013	13.39	13	0	0	7	7	6	7	1
28	18/11/1999	09/05/2013	13.48	13	1	1	8	8	8	7	4
29	01/09/1995	08/05/2013	17.7	18	0	1	8	8	8	8	5
30	12/10/2000	08/05/2013	12.58	13	0	1	8	7	6	7	2
31	14/06/1997	08/05/2013	15.91	16	0	1	8	8	8	7	4
32	03/05/1997	08/05/2013	16.03	16	1	0	8	8	8	8	6
33	23/07/2001	15/04/2013	11.74	12	1	1	7	7	6	6	2
34	08/11/2001	08/05/2013	11.5	11	1	0	8	7	7	7	4
35	14/10/1998	08/05/2013	14.58	15	0	1	8	8	8	7	4
36	05/05/1996	07/05/2013	17.02	17	1	0	8	8	8	8	6
37	27/10/1995	03/05/2013	17.53	18	1	1	8	8	8	8	6
38	22/03/2002	02/05/2013	11.12	11	1	1	7	7	6	6	3
39	06/09/1998	17/10/2012	14.12	14	1	0	8	8	8	7	6

40	31/08/1997	01/05/2013	15.68	16	1	0	8	8	8	8	5
41	04/09/1998	01/05/2013	14.67	15	1	0	8	8	8	7	6
42	19/08/1997	01/05/2013	15.71	16	1	1	8	8	8	7	6
43	09/09/1997	01/05/2013	15.65	16	0	1	8	8	8	8	6
44	15/06/1999	29/04/2013	13.88	14	1	1	8	8	8	8	6
45	25/07/1997	29/04/2013	15.77	16	0	1	8	8	8	8	5
46	03/05/1996	14/05/2013	17.04	17	1	0	8	7	8	8	6
47	24/05/1997	26/04/2013	15.94	16	0	1	8	8	8	8	6
48	13/02/1998	24/06/2013	15.37	15	0	0	8	8	8	8	4
49	10/12/1995	24/04/2013	17.39	17	0	0	8	8	8	8	6
50	20/01/2000	02/10/2012	12.71	13	1	0	8	8	6	7	4
51	18/02/1999	18/04/2013	14.18	14	1	0	8	8	8	7	6
52	14/10/1996	17/04/2013	16.52	17	1	0	8	8	8	8	5
53	08/10/1998	17/04/2013	14.51	15	0	1	8	8	8	8	6
54	24/09/2001	17/04/2013	11.57	12	0	0	7	7	7	6	2
55	26/11/1995	17/04/2013	17.41	17	0	0	8	8	8	8	6
56	16/01/2001	17/04/2013	12.26	12	1	1	8	8	7	7	5
57	22/06/2001	14/11/2012	11.41	11	0	0	6	6	6	6	5
58	05/10/1995	04/03/2013	17.42	17	1	1	8	8	8	8	6
59	26/01/2001	15/04/2013	12.22	12	1	0	8	8	8	7	3
60	10/01/2001	10/04/2013	12.25	12	1	0	8	8	7	7	4
61	22/04/2000	10/04/2013	12.98	13	1	0	7	7	6	7	4
62	28/12/1997	10/04/2013	15.3	15	0	1	8	8	8	8	6
63	11/03/1998	08/04/2013	15.09	15	0	0	8	8	8	8	3
64	21/12/1994	14/11/2012	17.92	18	1	1	8	8	8	8	5
65	04/12/2002	04/04/2013	10.34	10	1	0	8	8	7	6	2
66	09/09/1998	04/04/2013	14.58	15	0	0	8	8	8	7	4
67	07/06/2001	03/04/2013	11.83	12	1	0	8	8	7	7	3
68	19/04/1998	01/05/2013	15.04	15	1	1	8	8	8	7	4
69	05/08/1995	26/03/2013	17.21	18	0	0	8	8	8	8	6
70	25/01/1996	26/03/2013	17.18	17	0	0	8	8	8	8	6
71	08/07/1996	28/01/2013	16.57	17	1	1	8	8	8	8	6
72	05/06/2002	04/06/2013	11.01	11	0	1	6	6	6	6	2
73	12/12/1994	13/03/2013	18.26	18	1	0	8	8	8	8	5
74	09/05/2000	13/03/2013	12.85	13	1	1	8	8	8	8	3
75	16/11/1999	11/03/2013	13.33	13	1	0	7	7	6	6	5
76	25/02/2000	11/03/2013	13.05	13	0	1	7	7	7	7	2
77	26/06/1996	11/03/2013	16.72	17	0	1	8	8	8	8	6
78	07/07/2000	07/03/2013	12.67	13	0	1	7	7	6	7	3
79	18/08/1999	06/03/2013	13.56	14	0	0	8	8	8	8	4
80	07/07/1998	05/03/2013	14.67	15	0	0	8	8	7	7	5
81	05/07/1995	07/11/2012	17.36	17	1	1	8	8	8	8	6
82	18/04/1999	04/03/2013	13.89	14	0	1	8	8	8	7	4
83	23/08/2000	04/03/2013	12.54	13	0	1	8	8	8	7	2

84	26/07/2000	28/02/2013	12.6	13	1	1	8	8	7	7	4
85	09/09/1998	26/02/2013	14.48	14	1	1	8	8	8	8	5
86	05/08/1999	25/02/2013	13.57	14	1	1	7	8	7	7	5
87	24/04/1999	21/02/2013	13.84	14	1	1	8	8	7	8	6
88	15/11/1995	21/02/2013	17.28	17	1	0	8	8	8	8	5
89	18/11/1999	20/02/2013	13.48	13	1	1	7	8	7	7	4
90	12/12/1995	20/02/2013	17.21	17	1	1	8	8	8	8	5
91	18/04/2001	20/02/2013	11.85	12	1	1	7	7	7	6	3
92	22/02/1999	19/02/2013	14	14	1	0	8	8	7	7	6
93	27/09/1997	19/02/2013	15.41	15	0	1	8	8	8	8	5
94	20/12/1996	19/02/2013	16.18	16	0	1	8	8	8	8	4
95	06/10/1995	19/02/2013	17.39	17	0	0	8	8	8	8	5
96	06/10/1995	19/02/2013	17.39	17	0	0	8	8	8	8	4
97	14/11/1996	18/02/2013	16.27	16	1	1	8	8	8	8	6
98	27/08/1998	08/05/2013	14.71	15	1	0	8	8	8	7	6
99	16/02/2002	11/02/2013	10.99	11	1	0	8	8	8	7	1
100	20/02/1998	11/02/2013	14.99	15	0	0	8	7	8	7	6
101	18/12/2001	07/02/2013	11.15	11	1	0	8	8	7	6	4
102	18/10/1996	07/02/2013	16.32	16	1	0	8	8	8	8	6
103	17/04/2002	08/04/2013	10.98	11	1	1	7	7	7	7	2
104	26/10/1995	06/02/2013	17.3	17	1	1	8	8	7	8	5
105	05/10/1999	06/02/2013	13.35	13	0	0	8	7	7	7	4
106	15/07/1998	03/01/2013	14.48	14	1	0	8	8	8	8	5
107	07/01/1996	06/02/2013	17.1	17	0	1	8	8	8	8	4
108	20/03/1999	04/02/2013	13.89	14	1	1	8	8	8	8	5
109	06/01/2000	06/11/2012	12.84	13	0	1	6	6	6	7	2
110	24/09/2000	14/11/2012	12.15	12	1	0	7	6	6	6	3
111	23/09/2000	06/02/2013	12.38	12	1	1	8	7	7	7	2
112	16/09/1995	28/01/2013	17.38	17	0	1	8	8	6	5	5
113	20/11/1996	15/05/2013	16.49	16	0	0	8	8	8	8	4
114	22/03/2002	10/09/2012	10.48	10	1	1	8	7	7	7	1
115	25/11/1996	27/03/2013	16.35	16	0	0	8	8	8	8	5
116	12/03/1995	15/01/2013	17.86	18	1	0	8	8	8	8	6
117	01/08/2000	14/01/2013	12.46	12	0	0	8	8	8	7	3
118	02/11/1999	09/01/2013	13.2	13	1	1	8	7	7	7	5
119	10/03/1995	09/01/2013	17.85	18	0	1	8	8	8	8	5
120	09/08/1995	08/01/2013	17.43	17	0	1	8	8	8	8	6
121	19/07/1996	29/10/2012	16.29	16	1	0	8	8	8	8	6
122	25/06/2002	02/01/2013	10.53	11	1	0	6	6	6	4	1
123	14/04/2000	14/11/2012	12.59	13	0	0	8	8	8	8	4
124	30/10/1999	23/01/2013	13.24	13	0	0	7	7	7	7	2
125	13/09/2001	19/12/2012	11.27	11	1	0	8	7	6	6	2
126	22/01/1998	19/12/2012	14.92	15	0	1	8	7	8	7	3
127	30/04/1996	12/12/2012	16.63	17	0	1	8	8	8	8	5

128	18/07/1995	12/12/2012	17.42	17	0	0	8	8	8	8	6
129	25/01/1997	11/12/2012	15.89	16	1	1	8	8	8	8	6
130	18/09/1998	11/12/2012	14.14	14	0	1	7	7	7	6	3
131	07/09/2000	10/12/2012	12.27	12	0	1	7	7	7	7	2
132	25/10/1999	28/12/2012	13.19	13	1	1	8	8	8	7	5
133	01/01/1997	05/12/2012	15.94	16	1	1	8	8	8	8	6
134	17/10/1997	04/12/2012	15.14	15	1	0	8	8	8	8	4
135	10/01/2000	29/11/2012	12.25	13	1	1	8	8	8	7	4
136	01/07/1999	28/11/2012	13.42	13	1	0	8	8	7	7	5
137	09/08/1998	28/11/2012	14.32	14	1	0	8	8	8	7	4
138	03/01/1997	28/11/2012	15.91	16	0	0	8	8	8	8	5
139	10/11/1996	21/11/2012	16.04	16	1	1	8	8	8	8	4
140	06/12/2000	21/11/2012	11.97	12	0	0	6	6	6	7	1
141	27/10/1996	20/11/2012	16.08	16	1	0	8	8	8	8	6
142	13/10/2001	19/11/2012	11.11	11	0	1	7	7	7	6	2
143	27/11/1994	19/11/2012	17.99	18	0	0	8	8	8	8	5
144	01/07/2002	17/01/2013	10.56	11	1	0	7	7	6	7	3
145	02/12/1995	15/04/2013	17.38	17	1	0	8	8	8	8	6
146	06/01/2002	25/03/2013	11.22	11	0	0	7	7	7	6	5
147	21/11/1998	14/11/2012	13.99	14	0	1	7	7	7	7	4
148	24/01/1995	05/12/2012	17.88	18	1	1	8	8	8	8	5
149	28/07/1997	14/11/2012	15.31	15	1	1	8	8	8	8	4
150	21/06/1994	14/11/2012	18.41	18	1	1	8	8	8	8	6
151	18/06/2002	25/06/2013	11.03	11	1	1	7	8	7	7	1
152	01/08/2000	12/11/2012	12.29	12	1	1	7	8	7	7	4
153	02/11/2002	07/11/2012	10.02	10	0	1	6	6	5	5	1
154	18/10/1996	07/11/2012	16.07	16	0	0	8	8	8	8	2
155	21/10/1994	14/11/2012	18.08	18	1	0	8	8	8	8	6
156	29/09/1999	06/11/2012	13.12	13	0	1	8	8	8	8	5
157	02/02/1998	28/12/2012	14.91	15	0	0	8	8	8	8	6
158	18/09/1998	05/11/2012	14.24	14	0	0	8	8	8	8	3
159	03/08/1996	30/10/2012	16.25	16	1	0	8	8	8	8	6
160	06/01/2000	26/06/2013	13.48	13	1	0	8	8	8	8	5
161	23/02/1998	24/10/2012	14.68	15	0	0	7	7	7	7	4
162	04/11/1995	24/10/2012	16.98	17	1	0	8	8	8	8	6
163	18/08/1997	24/10/2012	15.19	15	0	0	8	8	8	8	5
164	23/11/1997	24/10/2012	14.93	15	1	0	8	8	8	8	6
165	05/07/2001	22/10/2012	11.31	11	1	1	8	8	8	8	2
166	08/06/1998	22/10/2012	14.39	14	0	1	8	8	8	7	5
167	13/05/1999	06/02/2013	13.75	14	0	1	8	8	8	8	4
168	13/10/2000	17/10/2012	12.02	12	0	0	7	7	6	6	1
169	06/10/1997	17/10/2012	15.04	15	1	0	7	7	7	7	5
170	23/12/1996	15/10/2012	15.82	16	0	0	8	8	8	8	4
171	05/08/1995	15/10/2012	17.21	17	1	0	8	8	8	8	6

172	15/12/1995	12/10/2012	16.84	17	1	0	8	8	8	8	5
173	02/07/1998	09/10/2012	14.28	14	0	0	8	8	8	7	4
174	29/12/1997	14/02/2013	15.14	15	1	0	8	8	8	8	5
175	20/03/1999	17/01/2013	13.84	14	0	1	8	8	8	7	5
176	25/03/2000	18/09/2012	12.49	12	0	0	7	8	8	7	2
177	08/05/1999	12/09/2012	13.36	13	1	0	8	8	8	8	5
178	27/09/1994	14/03/2013	18.47	18	1	1	8	8	8	8	6
179	23/02/2001	03/09/2012	11.53	12	1	1	7	8	7	7	2
180	02/11/1998	07/09/2012	13.86	14	1	1	8	7	7	8	4

Data codes

Gender	**Ethnic group**	**Dental development stage**
0 = Male	0 = White British	1 = A
1 = Female	1 = Asian	2 = B
		3 = C
		4 = D
		5 = E
		6 = F
		7 = G
		8 = H

Appendix 2. Raw data for reproducibility measurements

Random subject number	33		34		35		37		CS	
	Examiner		Examiner		Examiner		Examiner		Examiner	
	1	2	1	2	1	2	1	2	1	2
40	8	7	8	8	8	8	8	8	5	6
20	8	7	7	7	8	8	7	7	5	5
56	8	8	8	8	7	7	7	7	4	4
28	8	8	8	8	8	8	7	7	5	5
77	8	8	8	8	8	8	8	8	6	6
21	7	7	7	7	6	7	7	7	1	1
38	7	7	7	7	6	6	7	7	3	2
55	8	8	8	8	8	8	8	8	6	6
10	8	8	8	8	8	8	7	7	5	5
75	7	7	7	7	6	6	6	6	5	5
72	6	6	6	6	6	6	5	5	2	2
115	8	8	8	8	8	8	8	8	4	4
60	8	8	7	7	6	6	7	7	3	3
67	8	8	8	8	7	7	7	7	3	3
59	8	8	8	8	8	8	7	7	3	3
65	8	8	8	8	7	7	6	6	2	2
9	8	8	8	8	8	8	8	8	5	4
76	7	7	7	7	7	7	7	7	2	2
42	8	8	8	8	8	8	7	7	6	6
35	8	8	8	8	8	8	7	7	4	4
18	8	8	8	8	8	8	8	8	5	6
58	8	8	8	8	8	8	8	7	6	6
47	8	8	8	8	8	8	8	8	6	5
62	8	8	8	7	8	7	7	7	6	5
32	8	8	8	8	8	8	8	8	6	6
52	8	8	8	8	8	8	8	7	5	5
27	6	6	7	7	6	6	7	7	1	2
26	7	7	7	7	7	8	8	8	6	6
78	7	7	7	7	6	6	7	7	3	3
46	8	8	8	8	8	8	8	8	6	5

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