Linking Malocclusion, Diet, and Body Mass via Genetic Variants Within the Hippo Signaling Pathway

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THESIS

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This thesis is dedicated to my fiancé, Kelsey, for always supporting me, and for loving me and inspiring me every day. This thesis is also dedicated to my parents for always pushing me to be the best version of myself.

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LIST OF ABBREVIATIONS

BFFQ	Block Food Frequency Questionnaire
BMI	Body Mass Index
CAV	Canonical Variate Analysis
CDC	Centers for Disease Control and Prevention
CV	Canonical Variate
DLW	Doubly Labeled Water
EFD	Estimated Food Diary
FFQ	Food Frequency Questionnaire
FMA	Frankfurt Mandibular Plane Angle
HIPAA	Health Insurance Portability and Accountability Act
PC	Principal Component
PCA	Principal Component Analysis
PNS	Posterior Nasal Spine
SNP	Single Nucleotide Polymorphism
SWH	Salvador-Warts-Hippo
TEE	Total Energy Expenditure

SUMMARY

Body Mass Index (BMI) has a profound effect on the body's growth and development. Since the mid-20th century, the number of obese individuals, especially in the young population, has been growing. According to the Centers for Disease Control and prevention, in 2019, obesity effected 18.5% of children between the ages of 2 and 19 which comes out to roughly 13.7 million children and adolescents (Defining Childhood Obesity | Overweight & Obesity | CDC 2019). With an increase in childhood obesity comes new health challenges to face. A growing number of orthodontic patients are obese, and it is important to understand the role BMI can play in orthodontic treatment. High BMI is known to have an effect on the growth and development of adolescents (Shalitin and Kiess 2017).

The purpose of this study is to evaluate how BMI relates to craniofacial morphology by looking at the Hippo Signaling Pathway as well as diet as potential influences on mandibular form. The Hippo Signaling Pathway is a central regulator of both tissue homeostasis and organ size development (Maugeri-Saccà and De Maria 2018).

At the initial appointment patients were screened for eligibility and enrollment into the study by one of the University of Illinois at Chicago, College of Dentistry, Department of Orthodontics' residents. At the records appointment initial information was acquired from the subject including medical history, height, weight, saliva sample, and pre-treatment cephalometric radiograph. Subjects were excluded from the study if they had craniofacial anomalies, cleft lip and/or palate, and/or any syndromes or disorders that potentially affect growth and development.

Subjects were also eliminated if they had a history of any significant endocrine disorder, were taking any medications that affect growth, or if they were under the age of 7 or over the age of 17.

For each cephalometric radiograph, 45 unique landmarks were identified (Table 1). These points are a combination of soft and hard tissue landmarks to create a measurable representation of the face. All cephalometric images were uploaded to a TpsDig2 Version 2.31 software (Copyright 2017 F. James Rohlf, Ecology and Anthropology, Stony Brook University). This software was used to capture the coordinates of landmarks in a wide variety of 2D image formats (Rohlf 2015). Landmark data was uploaded to MorphoJ for further analysis (Klingenberg, C. P. 2011). MorphoJ is an integrated software package for geometric morphometrics. After adjusting for age and sex, the samples were then pooled by race for comparison. A linear regression analysis was completed for this sample. The linear regression directly measured how the facial shape varies as a function of BMI. Next, a principal component analysis (PCA) was completed for the groups. A PCA is a way to measure the overall variation of a dataset. The last set of phenotypic analysis completed was a canonical variate analysis (CVA).

Next, genotype-phenotype analysis was completed to look for a potential association between the facial shape and the single nucleotide polymorphisms (SNPs) along the Hippo Signaling Pathway. For the first analysis the mean of the BMI regression was compared to the SNPs on genes along the Hippo Signaling Pathway. Previously it was determined that PC8 and PC32 showed a significant difference between the normal weight and the obese subjects. Next, these two principal components were analyzed to see if there was a difference in genetic composition between the obese and overweight subjects within each principal component. Lastly, we looked at the canonical variate analysis in comparison with our genetic data.

After looking at the 32 hard tissue landmarks for the female sample there was a significant correlation between facial shape and BMI percentage ($p=0.0386$). When looking at the mandible, the obese group appears to have a steeper FMA as well as clockwise rotation of the mandible. The normal BMI group has markedly more downward and forward growth of the maxilla. The cranial base angle appears more obtuse in the obese group. In comparing the two groups, the obese group appears more class III both dentally and skeletally. PC8 accounts for 2.81 percent of the variation and PC32 accounts for 0.171 percent of the variation in this sample. When looking at PC8, the obese group again has a more obtuse cranial base, and there appears to be deficient growth of the maxilla. When looking at PC32, the obese group has a slight clockwise rotation of the mandible. The cranial base is also slightly more obtuse in the obese group. Because we had three groups (normal BMI, overweight BMI, and obese BMI), there were two components identified from the CVA. When looking at CV1 one can see similar trends as the other analysis when comparing obese and normal weight individuals. There is a reduction in the growth of the maxilla. The cranial base angle is more obtuse and there is more vertical and clockwise growth of the mandible. Looking at CV2 there is also an increase in the cranial base angle, maxillary size is deficient, and there is a proclination of the lower incisors.

Variations in FOXO6, TEAD3, TEAD4, MST1, LATS2 and RUNX2 genes show significant phenotypic differences in obese and normal weight subjects. Amongst these genes, higher BMI individuals show an increase in vertical growth of the mandible when compared to normal weight subjects. Higher BMI individuals also show a restriction in the downward and forward growth of the maxilla, and an increased Frankfurt Mandibular Plane Angle (FMA) and gonial angle when compared to normal weight subjects. Higher BMI individuals also show a more class III dental and skeletal relationship when compared to normal weight subjects.

1. INTRODUCTION

1.1 Background

Body Mass Index (BMI) is argued to have an effect on the body's growth and development, and recent research has suggested that obesity may even affect facial growth (Ohrn et al. 2002, Sadeghazerani et al. 2005, Gordon et al. 2021). Malocclusion is also a problematic health condition seen throughout pediatric populations. Malocclusion has multiple etiologies, with differential growth of the mandible contributing to some cases. This study investigates the association between BMI and facial morphology. This study applies a multidisciplinary approach to examine the interaction between genetics (specifically, the Hippo Signaling Pathway), body mass, diet, and craniofacial morphology. The Hippo Signaling pathway is involved in the growth of organs and other tissues. Genes found in the Hippo Pathway are also involved in adipocyte proliferation, a potential factor in some cases of obesity. The Hippo Signaling pathway also has a role in the regulation of craniofacial morphogenesis and craniofacial development. When examining BMI it is important to evaluate diet as a potential confounding factor. In this study we use a food frequency questionnaire to control for the effect of diet.

1.2 Objective

The purpose of this study is to evaluate how BMI relates to craniofacial morphology by looking at the Hippo signaling pathway, as well as diet, as potential influences on mandibular morphology. Craniofacial morphology was assessed using geometric morphometric analysis of traditional coordinate landmarks. Correlations between high BMI and longer mandibular length have been seen in the past (Ohrn et al. 2002, Sadeghianrizi et al. 2005), but our study is the first to also include genetic data. There is currently minimal data on the association between BMI and mandibular size and shape. In this study, we not only evaluate diet, but look at a number of

markers along the Hippo signaling pathway to better understand the relationship between BMI and craniofacial morphology.

1.3 **Null Hypotheses**

- There is no correlation between genetic variation in the Hippo signaling pathway and craniofacial morphology.
- There is no correlation between BMI, diet, and craniofacial morphology.

2. BACKGROUND

2.1 Childhood Obesity Trends

Childhood obesity is quickly becoming an area of interest because of the prevalence of child obesity in both developed and developing countries. According to the Centers for Disease Control, in 2019, obesity affected 18.5% of children between the ages of 2 and 19 which comes out to roughly 13.7 million children and adolescents (Defining Childhood Obesity | Overweight & Obesity | CDC 2019). Between 1970 and 2000 the rate of childhood obesity tripled, and it has mostly continued to increase (Yanovski 2015). Childhood obesity can lead to a number of psychological and medical abnormalities. Obesity related diseases that were previously seldom seen in children include obesity-associated sleep apnea, type II diabetes, and non- alcoholic fatty liver disease with resultant cirrhosis (Yanovski 2015). A positive association between childhood and adolescent obesity and depression has been shown, as well as more severe depressive symptoms (Quek et al. 2017).

2.2 Effects of Obesity on Growth

Body Mass Index (BMI) is the most commonly used method for evaluation of obesity in children, but also has its limitations (Krebs et al. 2007). BMI establishes a ratio between the weight and height of a person. BMI is equal to mass (in kilograms) divided by the height (in meters) squared. It is often used because it is easily obtained, correlated highly with body fat percentage, and accurately identifies individuals with the greatest level of obesity. Other measures of body composition include skin fold thickness and waste circumference. Skin fold thickness accuracy is similar to BMI findings, but there is a considerable possibility of measurement errors which can lead to the inaccuracy of reading. Without added accuracy, it is not recommended to use this sensitive technique for determining body mass. Waist circumference can relay valuable

information regarding health risks for adolescents. The problem with utilizing waist circumference as a measure for body mass is the lack of cut off points to identify children at the highest risk for problems. Waist circumference can however be used as an adjunct measurement to evaluate risk at the 90th to 95th percentile patients (Krebs et al. 2007). Although BMI is universally used, that does not mean it is a perfect technique. BMI has been criticized because of the inability to discriminate between muscle, fat, bone and vital organs when looking at the numerator (weight). Individuals with high mass that is not due to free fat may have high BMI values but not be obese (Hedayati and Khalafinejad 2014).

High BMI is known to have an effect on the growth and development of adolescents (Shalitin and Kiess 2017). Children with high BMI often see an acceleration of velocity in growth in height as well as accelerated epiphysial growth plate maturation (Shalitin and Kiess 2017). Obese adolescents are argued to also go through pubertal development before their peers (Shalitin and Kiess 2017). Early pubertal development may also be associated with a loss of the pubertal growth spurt and lead to not reaching peak height potential in adulthood (Shalitin and Kiess 2017). Studies also show that females with higher BMI develop breasts and reach their menarche at an earlier age (Shalitin and Kiess 2017). Because orthodontists are treating children during the growth phase, it is important to understand the effects of BMI on growth and development.

Childhood obesity not only affects general growth of the body but can also have an effect on dental maturation. Children with a higher BMI percentage showed an acceleration in dental development (e.g., Hilgers et al. 3005, Must et al. 2012, Mack et al. 2013, Hedayati and Khalafinejad 2014; Nicholas et al. 2018). A higher BMI appears to be associated with not only

dental development but facial skeletal development as well (Ohrn et al. 2002, Gordon et al. 2021). According to recent data from the CDC, 18.4% of 6 to 11 year olds and 20.6% of 12-20 year old Americans were found to be obese (Defining Childhood Obesity | Overweight & Obesity | CDC 2019). These are the ages that the majority of orthodontic patients receive orthodontic treatment. An increased number of orthodontic patients are obese, and the practitioner should understand these effects on orthodontic care as well as the long-term health of the patient. (Mack et al. 2013)

In orthodontics, growth is important to understand in order to evaluate, diagnose and treat pre-adolescent and adolescent patients. Children with high BMI are more likely to be skeletally mature compared to normal weight children, and this may lead practitioners to need to render treatment earlier (Giuca et al. 2012). Changes to craniofacial growth and development have been seen in patients with high BMI. In one study, both males and females exhibited significantly greater mandibular and maxillary dimensions than controls (Sadeghianrizi et al. 2005). In another study, many linear cephalometric differences were seen between obese children and their peers. The most notable difference was in the length of the mandible with obese females showing an increase in length of 6.0mm and an increase in 8.7mm in obese males. A significant elongation of the anterior cranial base was also seen in both sexes (Ohrn et al. 2002). A subsequent study by Gordon et al. (2021) found an association between high BMI and mandibular length (condylion – pogonion), but only in females. In this study, the authors also found that as BMI increased, so too did the centroid size of the facial skeleton when controlling for age. They posited that this indicates that high BMI children may experience accelerated development of the facial skeleton (Gordon et al. 2021).

2.3 Measuring Dietary Intake

When investigating BMI, diet should be considered as a potential confounding or contributory factor. Many studies have investigated dietary intake in children and adolescents because of its importance in growth and development. In order to be effective, a dietary assessment technique must be inexpensive, concise, reproducible and reliable and accurate enough to be used in a wide range of demographics (Matthys et al. 2007). The difficulty lies in the ability of the child to accurately recall the intake and portion size of what they consume. (Hunsberger et al. 2015). Doubly labeled water (DLW) is considered the gold standard for measuring energy intake and is used as a reference when looking at other methods. DLW is used over a 7 to 14-day period to allow for variation and helps to estimate the total energy expenditures (TEE). This method is seldom used in research because of its high cost, burden on participants and reliance on high technical skills for analysis (Burrows, Martin, and Collins 2010).

There are a number of methods currently used to measure daily dietary intake. Twenty-four-hour multiple pass recall is a retrospective method that looks at what an individual consumed in the past 24 hours. The more days of recall the more accurate the assessment, and the more likely the results are to show the variability between days (Pearce et al. 2020). Estimated food diaries (EFD) are another method in recording food intake. In this method the participant logs the food and drinks consumed as well as the time of consumption. This method allows participants to write down portion sizes, brand names and preparation methods for optimal analysis. The more days that are logged, the more accurate the diary becomes (Pearce et al. 2020). Weighed food diaries are another type of food diary that is excellent at predicting energy, food, and nutrient intake (Pearce et al. 2020). Food frequency questionnaires (FFQ) are a different method designed

to assess habitual diet by asking about the frequency of consumption over a designated period of time. The reference period usually corresponds to the previous year to capture the difference in seasons (Pearce et al. 2020)

Food questionnaires have been shown to be accurate at analyzing nutrient and food intake for children between the ages of 10-17 years old (Hunsberger et al. 2015). Food questionnaires also provide useful information about individual food intake over a one-year period (Willett et al. 1985). A number of studies have used food frequency questionnaires at large scales to determine nutrient intake to understand the complex interaction between diet-disease relationships (e.g., Greenwood et al. 2000; Riboli et al. 2002). Food frequency surveys have been validated in assessing the dietary intake in all age groups for more than twenty years in countries all over the world (e.g.,Magarey et al. 2011; Moghames et al. 2015; Noor Hafizah et al. 2019). For these reasons, it is determined that the food frequency surveys are a proven, cost effective, and low burden way to collect data on food intake.

2.4 **The Hippo Signaling Pathway**

The Hippo signaling pathway is a central regulator of both tissue homeostasis and organ size development (Maugeri-Saccà and De Maria 2018). The pathway has been an area of interest over the past two decades. Interest began after a study in drosophila, describing an extreme overgrowth of tissue upon loss of the Warts (wts gene) (Justice et al. 1995). In the early 2000s a study showed that mutations in Salvador (sav) and in Hippo (hpo) had similar outcomes leading to the "Salvador-Warts-Hippo (SWH) pathway (Maugeri-Saccà and De Maria 2018). Mutations causing inactivation of these genes lead to hyperproliferation and reduced apoptosis of cells in flies. (Maugeri-Saccà and De Maria 2018). These studies in *drosophilia* were instrumental in

delineating the pathway and function of the mammalian Hippo signaling pathway. The mammalian Hippo pathway was then shown to be a potent regulator of organ size, and its dysregulation leads to tumorigenesis (Dong et al. 2007).

The main function of the Hippo signaling pathway is to relay signals from the plasma membrane to the nucleus where it regulates a myriad of target genes controlling diverse cellular processes such as differentiation, proliferation and survival (Johnson and Halder 2014). The Hippo pathway's main function is to down-regulate YAP and TAZ, two homologous transcriptional co-activators that are downstream mediators of the Hippo signaling pathway (Johnson and Halder 2014). The Hippo signaling pathway has shown to have an effect on growth of different tissues in the digestive system, as well as heart, lung and kidneys. FOXO6 is a regulator of the Hippo Signaling pathway and has been shown to have an effect on facial shape in mice (Sun et al. 2018). It is consistently shown that with inactivation of different parts of the Hippo pathway, an overgrowth and enlargement of tissue occurs (Maugeri-Saccà and De Maria 2018)

A major function of the Hippo pathway is regulation of progenitor cell proliferation during growth and final organ size. Loss of function of Hpo or WTs kinases leads to an overexpression of YAP and TAZ which causes a dramatic overgrowth of adult structures (Johnson and Halder 2014). The overgrowths occur because of two defects found in the mutant cells (Johnson and Halder 2014). First, the mutated cells proliferate faster than the wild-type cells and continue to proliferate when the wild-type cells stop proliferating after tissues have reached the proper size (Johnson and Halder 2014). Secondly, these same mutant cells are resistant to apoptotic signals that are employed to eliminate extra cells. The combination of these two defects leads to an increase in number of cells that cannot be removed leading to an increased organ size. (Johnson

and Halder 2014). In other cells like skin and intestine, an overexpression of YAP causes an enlargement in stem cell compartments due to lack of differentiation but does not lead to an overall increase in organ size (Camargo et al. 2007). This shows that although the general conclusion is that the Hippo pathway in mice and flies drives proliferation of cell growth, it may not drive growth in every tissue.

Dysregulation of the Hippo signaling pathway can lead to tumors in model organisms and also occur in a number of human carcinomas including lung, colorectal, ovarian and liver cancer (Harvey, Zhang, and Thomas 2013). Mutations to the Hippo signaling pathway can lead to uncontrolled cell proliferation as well as insensitivity to apoptosis (Harvey, Zhang, and Thomas 2013). Studies reporting Hippo pathway deregulation rely on the detection of YAP in the nucleus of tumor tissue. In normal tissue, YAP is infrequently found in the nucleus of tissues but nuclear YAP is present in 60% of hepatocellular carcinomas, 15% of ovarian cancers and 65% of non-small cell lung cancers (Harvey, Zhang, and Thomas 2013). YAP and TAZ activity are also linked to drug resistance and cancer relapse. Thus inhibition of the YAP/TAZ will not only target tumor initiation and progression but may also sensitize cancer cells to chemotherapies (Yu, Zhao, and Guan 2015).

Adipose tissue is an energy storage depot that is a key metabolic organ in the regulation of systemic energy homoeostasis (Ardestani, Lupse, and Maedler 2018). The Hippo signaling pathway has been shown to have effects on adiposity. LATS2 is one of the core kinases in the Hippo signaling pathway and is involved in cell growth and survival, and was first linked to adipose development in 2010 (Ardestani, Lupse, and Maedler 2018; Visser and Yang 2010). LATS2 is an important modulator of adipose development because it regulates the balance

between proliferation and differentiation of adipocytes (An et al. 2013). Later studies show that the Hippo gene within the Hippo signaling pathway in *drosophila* is involved in the storage of fat by controlling the number of fat cell (Ardestani, Lupse, and Maedler 2018). Overexpression of the Hippo gene reduces fat cell numbers, while its knockdown promotes fat accumulation and results in weight gain. (Ardestani, Lupse, and Maedler 2018). Therefore, the Hippo signaling pathway has been shown to effect adiposity levels.

2.5 **Single Nucleotide Polymorphisms**

Single nucleotide polymorphisms (SNPs) are the most common genetic variation among individuals (Collins 2020). Each SNP represents a difference in a single nucleotide. SNPs occur about once in every 1,000 nucleotides which correlates to around 4 to 5 million SNPs per person (Collins 2020). These variations can be studied and help in the discovery of links between certain diseases. All members of the same species have an extremely small amount of variation in their DNA (Collins 2020). The variation in the DNA and what makes one individual different from another occurs within the variations of SNPs. The differences at the SNP can be positive, negative, or neutral. The majority of SNPs have no negative effect on health or development (Collins 2020).

2.6 **Geometric Morphometrics**

Morphometrics is the measurement of shape. Geometric morphometrics is the statistical analysis of shape based on cartesian landmark coordinates (Mitteroecker and Gunz 2009). Geometric morphometrics is a system that defines landmarks as not only cartesian coordinates but also as an identifiable landmark or location (nasion, basion, gnathion, etc). The locations are used to compare overall forms of different specimens while taking into account differences in size and shape. Visualization of shape differences and shape changes is a primary strength of geometric

morphometrics which makes it the ideal tool to measure changes in facial structure between individuals (Hallgrimsson et al. 2015). Currently the most commonly used form of superimposition is the Generalized Procrustes Analysis (GPA) (Hallgrimsson et al. 2015). Procrustes superimpositions are done in order to configure centered, scaled and rotated landmarks for comparison. First the shapes are translated to a common origin, next they are scaled to a centroid size and rotated to minimize the squared differences of the homologous landmarks (Hallgrimsson et al. 2015).

Geometric morphometrics has been used to study craniofacial growth and form in healthy individuals, as well growth of patients with cleft lip and or palate (Katsadouris and Halazonetis 2016; Latif et al. 2020; Windhager, Schaefer, and Fink 2011). In one study of normal craniofacial growth in humans aged 12 to 14, 350 Cephalometric radiographs were taken at different time points and 117 points were located which comprehensively covered the craniofacial skeleton. The shape and growth of the craniofacial complex was then studied and compared (Katsadouris and Halazonetis 2016). In another study, geometric morphometrics was utilized to evaluate the maxillary growth of unrepaired cleft patients compared to unaffected individuals (Latif et al. 2020). Geometric morphometrics is now a common tool used in the assessment of facial growth and form. Using two dimensional structures such as radiographs, researchers are able to evaluate and compare growth of large groups of subjects. The effect that childhood obesity has on facial shape has been studied in the past by using geometric morphometrics (Gordon et al. 2021).

3. METHODS AND MATERIALS

3.1 Ethical Approval and Funding

This study examined the relationship between body mass index, genetic variation along the Hippo signaling pathway, and malocclusion as it relates to craniofacial morphology in 2D lateral cephalometric radiographs. Ethical approval was received from the University of Illinois at Chicago Institutional Review Board (protocol #2017-1276) (Appendix A). This study was funded by the American Association of Orthodontists Foundation (Appendix B).

3.2 Subjects

3.2.1 Inclusion and Exclusion Criteria

The criteria for inclusion and exclusion in this study were as follows:

Inclusion Criteria

- Male and female subjects age 7-17 at the time of the study seeking orthodontic treatment at the University of Illinois at Chicago College of Dentistry, Department of Orthodontics
- Comprehensive set of records, including cephalometric radiograph, saliva sample, height, and weight

Exclusion Criteria

- Subjects with craniofacial anomalies
- Subjects with a clef lip and/or palate
- Subjects with syndromes or disorders that potentially affect growth and development

- Medical history of any significant endocrine disorder
- Subjects taking any medications that effect growth
- Subjects under the age of 7 or over the age of 17

3.2.2 **Sample Size**

A total of 117 subjects were recruited to be a part of the study. Three (3) subjects were disqualified from the study because of problems during the DNA analysis, and an additional 6 were lost because of either inaccurate radiographs or because the BMI scores were extreme outliers. Five (5) subjects were missing height and weight data and thus could not be used in the study. In total, 103 subjects were included.

3.3 **Subject Enrollment**

3.3.1 **Eligibility and Screening**

At the initial appointment patients were screened for eligibility and enrollment into the study by one of the University of Illinois at Chicago, College of Dentistry, Department of Orthodontics' residents. When subjects presented at the University of Illinois at Chicago College of Dentistry, Department of Orthodontics for the records appointment, they were asked if they would like to be a part of the study. Patients that were already undergoing treatment at the college that fell within the inclusion criteria were also asked to join the study. No advertising materials were used to recruit patients to this study, and recruitment was verbal by the clinical research team. The patient's determination to participate in the study had no effect on their orthodontic treatment. If patients chose to not be a part of the study, the appointment proceeded as usual. Any data obtained from screen failures that was specifically utilized for research was destroyed. There were no follow up visits required for the subject, and the initial appointment lasted 1-2 hours. After

completion of the initial visit and data collection, each subject was paid $20 for participating in the study.

3.3.2 **Patient Consent**

If the subject agreed to be part of the study, the consent forms were signed by the parents or legal guardians of the subject and assent forms were signed by the subject (Appendix C, D and E). After consent was received, normal orthodontic records were taken. Any records that were used for the study were also stored separately and deidentified. If patients already had components of standard records within the past 6 months, new records were not re-taken. Prior to deciding to be a part of the study, the subject was aware that their decision had no effect on their treatment.

3.3.3 **Expected Risks and Benefits**

There were no expected direct risks or benefits for the patients who participated in the study. Possible benefits of the study for the scientific community include finding a link between BMI and craniofacial form for individuals between the ages of 7 and 17.

3.4 **Data Collection**

The information needed for the study was taken at a standard orthodontic records appointment. Accurate records are important for orthodontic treatment planning so there was no alteration of the records related to their use in the study. At the records appointment, all standard orthodontic records were acquired, including medical history, height, weight, and pre-treatment cephalometric radiograph. For the purposes of our study, we also collected saliva samples and a BFFQ.

3.4.1 **Cephalometric Radiograph**

Cephalometric radiographs were taken on all subjects using an Instrumentarium Orthopantomograph OP300.

3.4.2 **Height and Weight and Body Mass Index Calculation**

All height and weight measurements were made on the same scale to ensure consistency and reliability. The scale used was a HealthO-Meter professional scale with 500lb/220 kg capacity.

BMI was calculated using Centers for Disease Control and Prevention (CDC) guidelines and adjusted factoring in the age and sex of the patient subject (Defining Childhood Obesity | Overweight & Obesity | CDC 2019). Subjects were categorized as underweight if they fell between the 0-5 percentile of children. Subjects who fell between 5^{th} and 85^{th} percentile were categorized as normal BMI. Subjects categorized as 85-95 percentile were categorized as overweight and any subject in the 95^{th} percentile and above were categorized as obese. (Kuczmarski et al. 2002) The CDC has example charts of height/weight depicting the cut-offs for underweight, normal, overweight, and obese children. (Kuczmarski et al. 2002)

3.4.3 **Saliva Samples**

5mL of saliva was collected at the time of the records appointment as part of the research project. This was the only time that saliva was collected for the study. Saliva samples were collected in a sealable test tube, identified with the same six-digit letter and number combination and placed in a locked freezer. DNA was extracted from the saliva and stored in a secure freezer by the genetics team located at the University of Illinois at Chicago DNA Services Facility. The

saliva samples underwent DNA extraction and amplicon sequencing to identify the subjects genotype for the desired SNPs.

3.4.4 **Block Food Frequency Questionnaire**

The Block Food Frequency Questionnaire (BFFQ) was chosen for this study for a number of reasons. To start, the questionnaire was filled out one time, and no follow up was needed. The survey can look at energy and nutrient intake as well as dietary pattern. The questionnaire can be self-administered or administered by an interviewer if help is needed. The survey that was used in this study looked at the past year as a reference period and this allows for variation in seasons to be considered. The list of foods included looks at major sources of nutrients, foods commonly consumed in a population and foods that can contribute to variability between subjects. The specific survey used also allowed for description of cooking methods, types of fat, bread, and milk as well. The frequency of consumption is also looked at within the study and answers can vary from every day, to number of days per week, month or year. Portion sizes are also evaluated in the survey with pictures to assist in describing the size of the food consumed. The relatively low burden on the respondent is one of the reasons this style was used. Typically, it takes 15-25 minutes for the survey to be filled out and there is relatively low cost compared to other dietary assessment models. This study also has some limitations. The survey relies heavily on accuracy of reporting and respondent memory. Respondents may introduce biases towards over documenting healthier foods. Estimating food sizes may also be difficult for the respondents (Pearce et al. 2020)

At the initial visit, the subject filled out the BFFQ. If assistance was needed to fill out the form, a member of the team that was trained in the BFFQ assisted the subject in filling out the form. The BFFQ Surveys were collected, and visually examined to ensure they were filled out

properly. All BFFQ surveys were collected along with consent forms and kept in a protected location. All survey data was sent to Nutrition Quest for analysis. No personal health information was included in the surveys that were sent to Nutrition Quest.

3.4.5 **Subject Information Deidentification and Storage**

All information included in the study was deidentified. The subjects were not required to do any follow up visits. Data that was collected for this study was deidentified and assigned a six-digit letter and number combination.

Radiographs, along with height and weight measurements, were digitally stored in a HIPAA approved location after proper deidentification was completed. Saliva and DNA samples were stored in locked freezers inside locked laboratories. Signed consent forms were stored in a locked cabinet inside a locked office.

3.5 **Digital Landmark Identification**

For each cephalometric radiograph, 45 unique landmarks were identified (Table I, II, III, Figure 1). These points are a mixture of soft and hard tissue landmarks to create a measurable representation of the face.

TABLE I
HARD TISSUE CEPHALOMETRIC LANDMARKS AND DESCRIPTIONS

#	Cephalometric Landmark	Description
1	Porion (Po)	Highest point of the ear canal
2	Orbitale (Or)	Lowest point of the floor of the orbit
3	Sella (S)	Center of the pituitary fossa (sella turcica) of the sphenoid bone
4	Nasion (Na)	Intersection of the internasal suture with the nasofrontal suture in the midsagittal plane
5	Basion (Ba)	Most inferior posterior point of the occipital bone at the anterior margin of the occipital foramen
6	B Point	Most posterior point in the concavity along the anterior border of the symphysis
7	Pogonion (Pog)	Most anterior point on the mid-sagittal symphysis
8	Anatomical Gnathion (Gn)	Midpoint between the most anterior and inferior point on the boney chin
9	Menton (Me)	Most inferior point of the symphysis
10	Gonion (Go)	Most convex point along the inferior border of the ramus
11	R1 Point (Mid Ramus)	Most concave point on the interior of the ramus
12	R2 Point	Most concave point of the exterior border of the ramus along the vertical
13	R3 Point (Sigmoid Notch)	Most inferior border along the top of the ramus (sigmoid notch)
14	Articulare (Ar)	Intersection of the mandible with the temporal bone
15	Condylion (Co)	Most superior point of the condyle
16	A Point	Deepest point of the curve of the maxilla, between anterior nasal spine (ANS) and the dental alveolus
17	Anterior Nasal Spine (ANS)	The tip of the anterior nasal spine
18	Posterior Nasal Spine (PNS)	The tip of the posterior nasal spine

TABLE II
SOFT TISSUE CEPHALOMETRIC LANDMARKS AND DESCRIPTIONS

#	Cephalometric Landmark	Description
19	Soft Tissue Glabella	Most anterior point on the soft tissue over the frontal bone
20	Soft Tissue Nasion	Soft tissue profile's most concave point at the bridge of the nose
21	Tip of Nose	Point of the anterior curve of the nose
22	Subnasale	Point where the nose connects to the center of the upper lip
23	Soft Tissue A Point	Most concave point between subnasale and the anterior point of the upper lip
24	Upper lip	Most anterior point on the curve of the upper lip
25	Stomion Superius	Most inferior point on the curve of the upper lip
26	Stomion Inferius	Most superior point on the curve of the lower lip
27	Lower Lip	Most anterior point on the curve of the lower lip
28	Soft Tissue B Point	Most concave point between the lower lip and the soft tissue chin
29	Soft Tissue Pogonion	Most anterior point on the curve of the soft tissue chin
30	Soft Tissue Gnathion	Midpoint between the most anterior and inferior points of the soft tissue chin in the midsagittal plane
31	Soft Tissue Menton	The most inferior point of the soft tissue chin

TABLE III
DENTAL CEPHALOMETRIC LANDMARKS AND DESCRIPTIONS

#	Cephalometric Landmark	Description
32	U6 Occlusal	Buccal groove of maxillary first molar
33	L6 Occlusal	Buccal groove of mandibular first molar
34	Distal U6	Distal surface of the upper first molar, perpendicular to the occlusal plane
35	Mesial U6	Mesial surface of the upper first molar, perpendicular to the occlusal plane
36	Distal L6	Distal surface of the lower first molar, perpendicular to the occlusal plane
37	Mesial L6	Mesial surface of the lower first molar, perpendicular to the occlusal plane
38	L1 Labial Gingival Border	Labial CEJ of the lower central incisor
39	L1 Tip	Incisal tip of the lower central incisor
40	L1 Root	Root apex of the lower central incisor
41	L1 Lingual Gingival Border	Lingual CEJ of the lower central incisor
42	U1 Labial Gingival Border	Labial CEJ of the upper central incisor
43	U1 Tip	Incisal tip of the upper central incisor
44	U1 Root	Root apex of the upper central incisor
45	U1 Lingual Gingival Border	Lingual CEJ of the upper central incisor

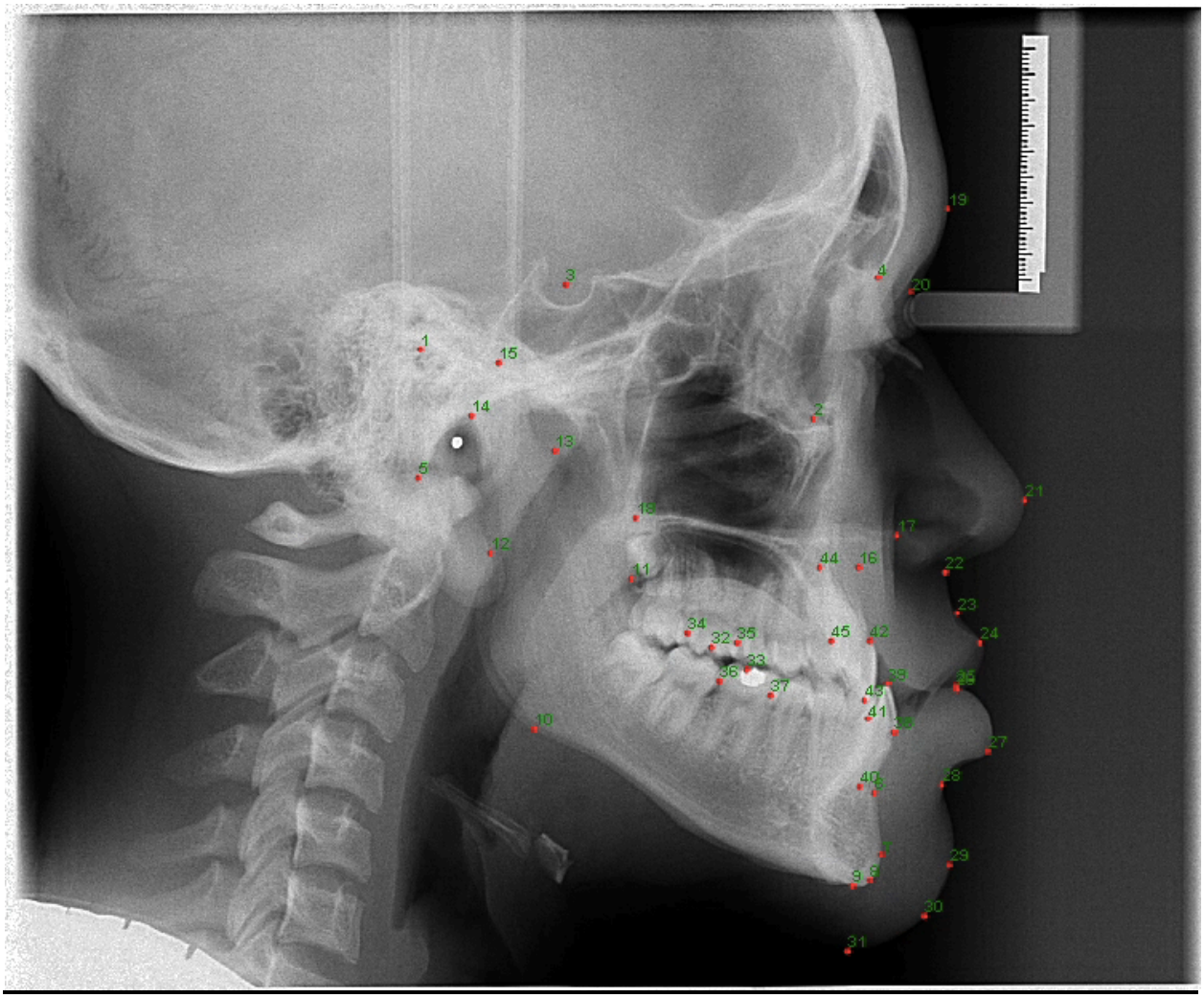

Figure 1: Sample lateral cephalometric radiograph with selected digital landmarks

All cephalometric images were uploaded to a TpsDig2 Version 2.31 software (Copyright 2017 F. James Rohlf, Ecology and Anthropology, Stony Brook Univeristy). This software is used to capture the coordinates of landmarks in a wide variety of 2D image formats (Rohlf 2015). Images can be enhanced so that the landmarks become easier to see. The software allows points to

be captured along outlines and curves. The Tpsdig2 program can also be used to measure distances, angles and areas (Rohlf 2015).

These points can then be compared universally between subjects using the TpsDig2 software. Once completed, Tpsdig2 generated a facial form with the cephalometric points that could be compared across samples. A single operator identified all landmarks on the cephalometric radiographs of all subjects using the Tpsdig2 program (Figure 2).

3.6 **Reliability Testing**

Reliability testing was completed and a threshold of 80% reliability was set in order to move forward with tracing. An initial group of 14 cephs were used to establish reliability. Intra-rater reliability refers to the consistency of the data recorded by one rater over several trials and is determined when multiple trials are administered over a short period of time (Scheel et al. 2018) The reliability was tested for all 45 land marks two weeks apart. The average accuracy after the first round of calibration was 93.4%. Inter-rater reliability refers to consistency of data recorded by two or more raters, measuring the same subjects over a single trial (Scheel et al. 2018). Inter reliability was completed by having two people complete tracing on the same group of cephalograms, and the results were again analyzed. After calibration for inter rater reliability the reliability was greater than 90%. Posterior Nasal Spine (PNS) was the only landmark needing recalibration, and after the second round of calibration the accuracy was at 86%. The R program (R Core Team (2013). R: A language a R Core Team (2013). R, a language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria) was used to analyze and calculate reliability.

3.7 **Phenotypic Analysis**

All landmarking data was uploaded to MorphoJ for further analysis (Klingenberg, C. P. 2011). MorphoJ is an integrated software package for geometric morphometrics. After landmarking was completed for each cephalometric radiograph, the phenotypic data was studied in a regression analysis between the shape of the face and the percentile BMI of the patient. The samples were then broken down further based on sex. Allometric (size related shape information) variation was removed prior to analysis using age as the covariate to control for the effects of sex and age differences in the sample. After this adjustment for age and sex, the samples were then pooled by race for comparison. A linear regression analysis was completed for this sample. The linear regression directly measured how the facial shape varies as a function of BMI.

Next, a principal component analysis (PCA) was completed for the group. A PCA is a way to measure the overall variation of a dataset. We identified 47 principal components (PCs) that account for the total amount of variation in the sample. A T-test was used to identify PCs where there were significant differences in shape between normal and obese patients. Two principal components stood out as being significant, PC8 and PC32. These two principal components were selected for further analysis.

The last phenotypic analysis completed was a canonical variate analysis (CVA). Unlike PCA, a canonical variate analysis identifies only the variation accounted for by a single group (in this case, BMI). While the goal of PCA is to identify patterns shape that drive overall variation within the sample, the goal of CVA is to identify patterns of shape that drive differentiation between pre-defined groups (Zelditch et al. 2012). We looked at three groups; normal, overweight

and obese. In this female sample there were 54 total subjects, 27 normal, 15 overweight and 12 obese.

3.8 Genotype-Phenotype Analysis

Next, genotype-phenotype analysis was completed to examine potential associations between the facial shape and selected SNPs along the Hippo signaling pathway. The specific SNPs chosen on Hippo signaling pathway genes were assessed to see if there was a difference between genetic composition of normal and obese subjects (Table IV). All statistical analyses were completed using SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp).

TABLE IV
SNPS INCLUDED IN THE STUDY WITH ASSOCIATED GENES ALONG THE HIPPO SIGNALING PATHWAY

SNP	GENE	SNP	GENE	SNP	GENE
rs4636447	FOXO6	**rs11758653**	TEAD3	**rs11062462**	TEAD4
rs7522116	FOXO6	**rs72894781**	TEAD3	**rs593390**	LATS2
rs12029493	FOXO6	**rs72894784**	TEAD3	**rs73169516**	LATS2
rs56233836	FOXO6	**rs71002565**	TEAD3	**rs613375**	LATS2
rs1317183	FOXO6	**rs12214749**	RUNX2	**rs58568294**	LATS2
rs55784313	FOXO6	**rs4870529**	LATS1	**rs9509499**	LATS2
rs13085791	MST1	**rs13205080**	LATS1	**rs60842975**	LATS2
rs62262683	MST1	**rs13210297**	LATS1	**rs142801103**	LATS2
rs113893148	MST1	**rs12174349**	LATS1	**rs6490637**	LATS2
rs147997200	MST1	**rs10848754**	TEAD4	**rs112991009**	LATS2
rs7740758	TEAD3	**rs60833991**	TEAD4	**rs62617809**	TAZ
rs10638006	TEAD3	**rs11062461**	TEAD4		
rs61501470	TEAD3	**rs113515288**	TEAD4		

For the first analysis the BMI regression was compared to the SNPs. Each SNP was broken down into three groups: homozygous for the common allele, heterozygous, and homozygous for the rare allele an ANOVA comparing mean BMI across the three SNP variants and evaluated for significant differences along the BMI regression.

Previously it was determined that PC 8 and PC32 showed a significant difference between the normal weight and the obese subjects. In the genotypic analysis these two principal components were compared across allele groups to see if there was a difference in genetic composition between the obese and overweight subjects within each principal component.

Lastly, we looked at the CV scores in relation to allele frequency. Canonical variate analysis was used to highlight shape variation between the three BMI groups being studied; normal, overweight and obese. The last genotypic study looked at the SNPs to see where there was a significant difference between SNPs in each of the three groups. Because there are three groups, we had 2 canonical variates (CV1 and CV2) for the phenotypes of this last analysis.

4. RESULTS

4.1 Phenotypic Results

4.1.1 Regression of BMI and Facial Shape

The first set of phenotypic data that was studied was a regression between the shape of the face and the BMI percentile of the subject (Figure 2). There was a significant correlation between the BMI percentile and facial shape with the full landmark data set (P=0.0295) for the non-pooled sample. By scaling the differences between the normal and obese groups you can get a clearer view of the differences between the groups (Figure 3). This analysis showed a larger difference mostly in the soft tissue. As BMI increases there is an expected increase in adiposity in soft tissue. This can be seen by evaluating the soft tissue in the neck region.

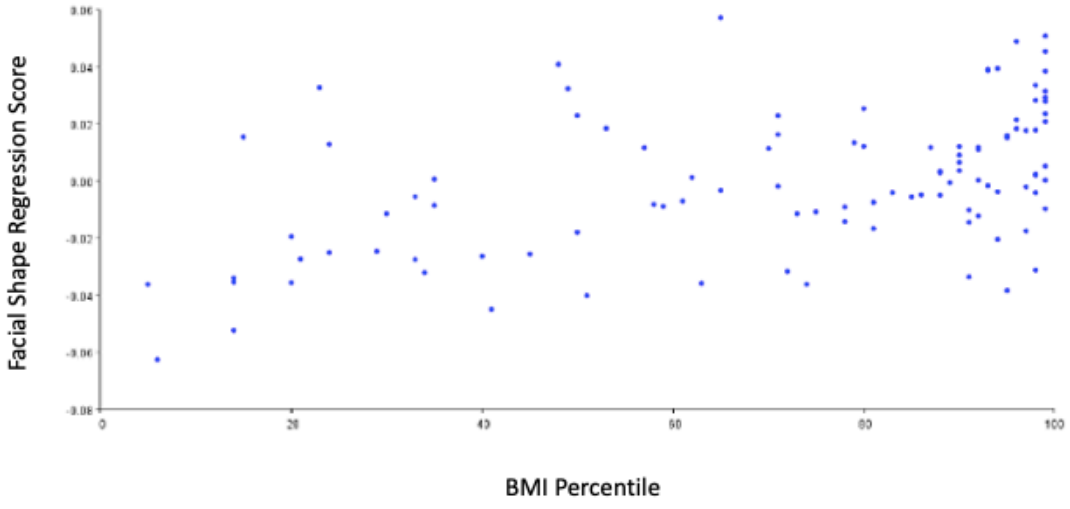

Figure 2: Regression of facial shape as a function of BMI percentile for all subjects with all landmarks

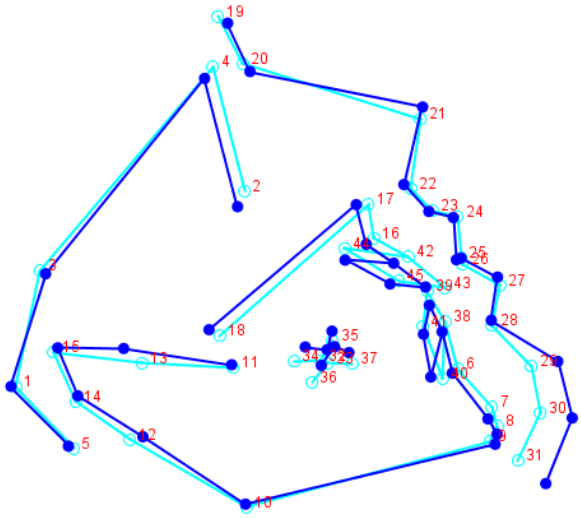

Figure 3: Wireframe diagram comparison of average facial shape of normal and obese subjects. (Dark blue=average facial shape of obese subjects; light blue=average facial shape for whole sample)

Next, the soft tissue points were removed, and the hard tissues shape was analyzed in isolation. We failed to find a statistically significant association between skeletal facial shape and BMI ($p=0.06$). When the same sample was subdivided by race, we still failed to find a statistically significant association ($p=0.22$).

The data was then analyzed by sex. For the males, the results were not significant. For the female sample there was a significant positive correlation between skeletal facial shape and BMI percentage ($p=0.039$; Figure 4). The female group was pooled by race and adjusted for age, and it

was found that BMI accounted for 3.807 percent of the overall shape variation. Given this outcome, only the female subsample underwent full phenotype and genotype-phenotype analysis.

Looking at the shape variation of the obese group there are a number of skeletal changes that stand out (Figure 5). There appears to be a deficiency in the maxillary size. The normal BMI group has markedly larger maxilla. The cranial base angle appears more obtuse in the obese group. When looking at the mandible, the obese group appears to have a steeper vertical angle as well as clockwise rotation of the mandible. Dental changes can be seen between the two samples as well. It appears that the upper and lower incisors are more proclined in the obese group. The obese group tends to have a more class III molar relationship as well. In comparing the two groups, the obese group appears more class III both dentally and skeletally.

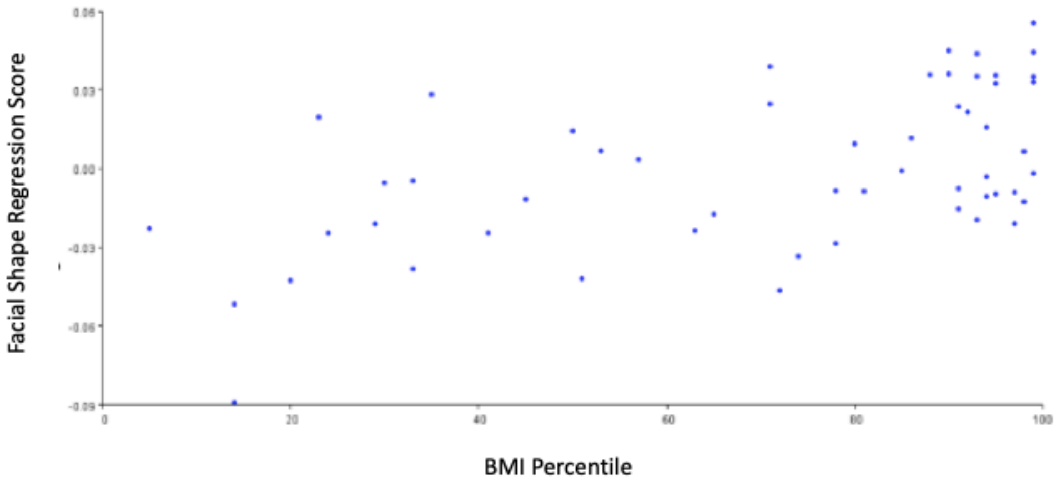

Figure 4: Regression of facial shape as a function of BMI percentage for female subjects pooled by race and adjusted for age

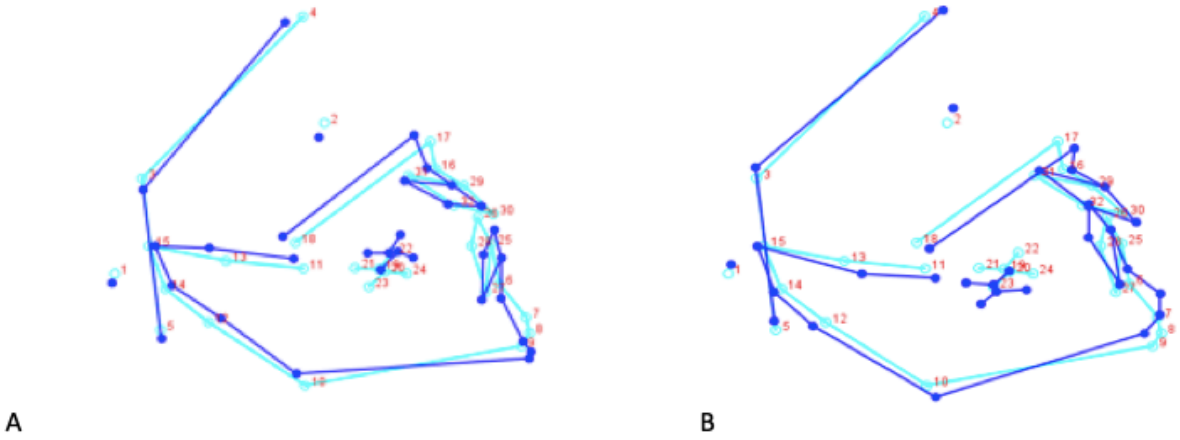

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Figure 5A: Comparison of facial shape of average and Obese Subjects factored by 200 for female subjects pooled by race and adjusted for age. (Dark blue = shape variation of obese individuals, light blue = average shape for comparison.) Figure 5B: Comparison of average facial shape and the facial shape of normal weight Subjects factored by 200 for female subjects pooled by race and adjusted for age. (Dark blue=shape variation of obese facial shape, light blue=average facial shape for comparison.)

4.1.2 **Principal Components Analysis**

Next, a principal component analysis (PCA) was completed. The variation in the data was represented by 47 components.

A t-test was performed on each PC mean to determine if the mean PC score was significantly different between normal weight and high BMI subjects. Only PC8 and PC32 were found to show statistically significant differences. PC8 accounts for 2.81 percent of the variation and PC32 accounts for 0.171 percent of the variation between the normal and obese groups. Principal component scores for PC8 and PC32 were plotted to depict variation in the sample (Figure 6). There is substantial overlap between all groups, though the normal weight subjects tend to have higher PC8 scores and lower PC32 scores.

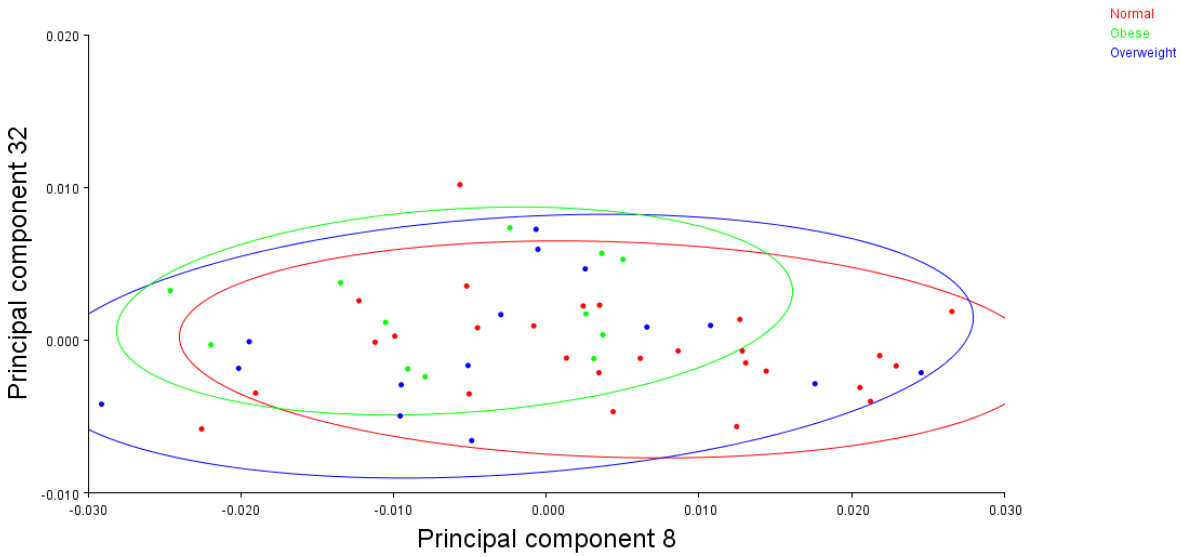

Figure 6: Comparison between principal components 8 and 32 grouped by obesity status. (Red = normal, green = obese, blue = overweight.) Ellipses represent 90% confidence intervals around each group.

When looking at PC8, the obese group again has a more obtuse cranial base, and there appears to be deficient growth of the maxilla. Dentally, the molars of the obese group have a class III relationship and the upper and lower incisors are more proclined than the normal group (Figure 7).

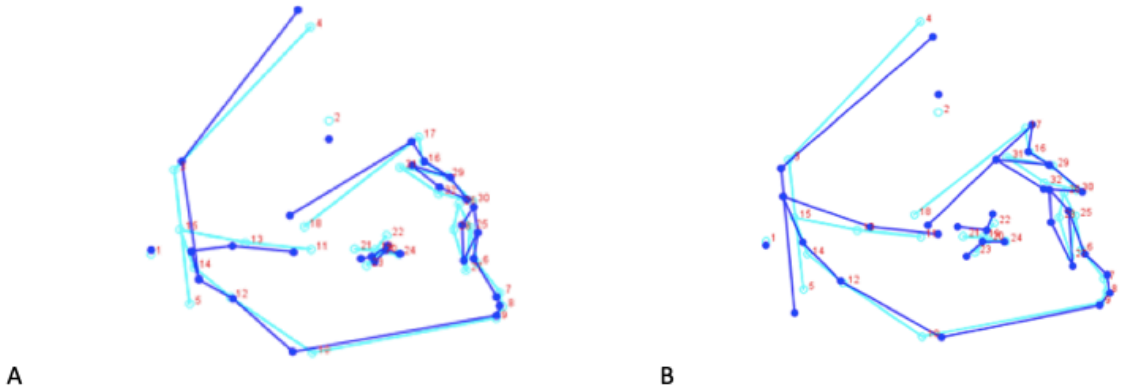

Figure 7A: Comparison of average facial shape with shape variation due to PC8 in obese patients factored by -0.1. (Dark blue = shape variation due to PC8, light blue = average shape for comparison.) Figure 7B: Comparison of average facial shape with shape variation due to PC8 in normal weight patients factored by +0.1. (Dark blue = shape variation due to PC8, light blue = average shape for comparison.)

PC32 accounted for 0.171 percent of the variation in the groups. In looking at the obese group there is a slight clockwise rotation of the mandible. The cranial base is also slightly more obtuse in the obese group. The maxilla also appears to be smaller in the obese group (Figure 8).

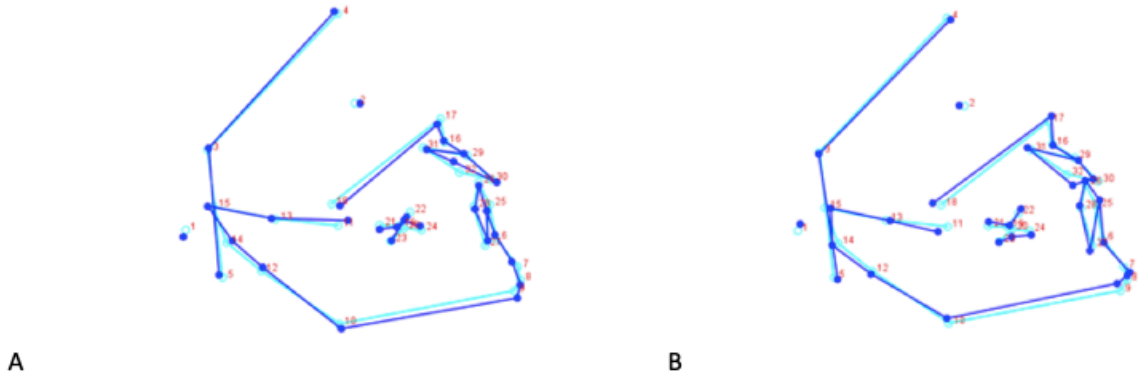

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Figure 8A: Comparison of average facial shape with shape variation due to PC32 in obese subjects factored by +0.05. (Dark blue = shape variation due to PC32, light blue = average shape for comparison.) Figure 8B: Comparison of average facial shape with shape variation due to PC32 in normal weight subjects factored by -0.05. (Dark blue = shape variation due to PC32, light blue = average shape for comparison.)

4.1.3 Canonical Variates Analysis

Due to the fact that we had three groups, our CVA yielded two CVs. When comparing the groups, obese individuals tend to have negative CV scores for both CV1 and CV2 compared to normal individuals (Figure 9). There was no statistically significant difference between the Procrustes distances among the groups. However, using raw Procrustes scores is often not effective for small sample sizes (Klingenberg and Monteiro 2005). When Mahalanobis distances were used, statistically significant differences were seen between the groups ($p<0.001$).

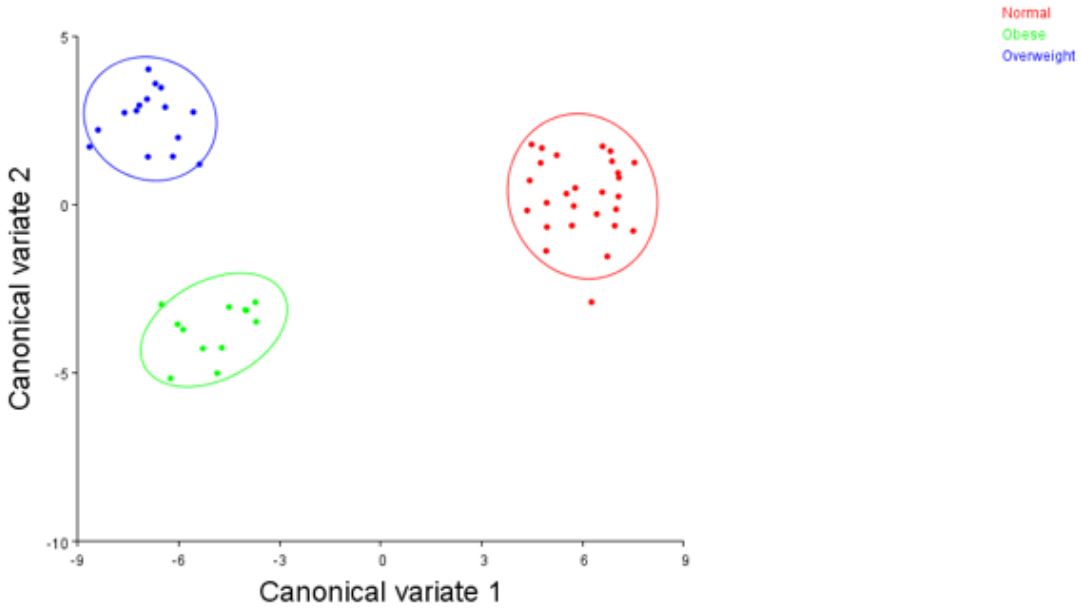

Figure 9: Comparison between CV 1 and 2 grouped by obesity status. (Red = normal, green = obese, blue = overweight.) Ellipses represent 90% confidence intervals.

When looking at CV1, there are similar trends as seen in our PCA analyses when comparing obese and normal individuals. There is a reduction in the size of the maxilla. The cranial base angle is more obtuse and there is more vertical and clockwise rotation of the mandible. The molars have a class III classification and the incisors are more proclined. A decrease in the overjet is also seen in the obese group (Figure 10).

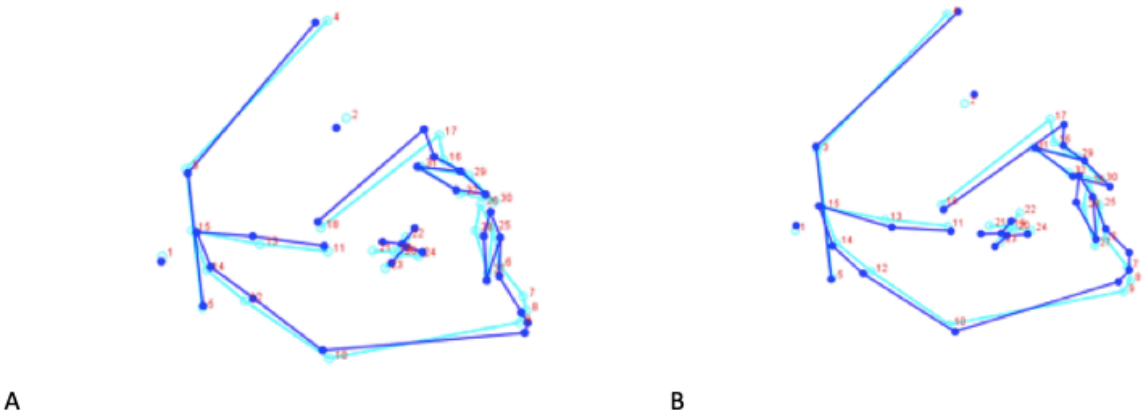

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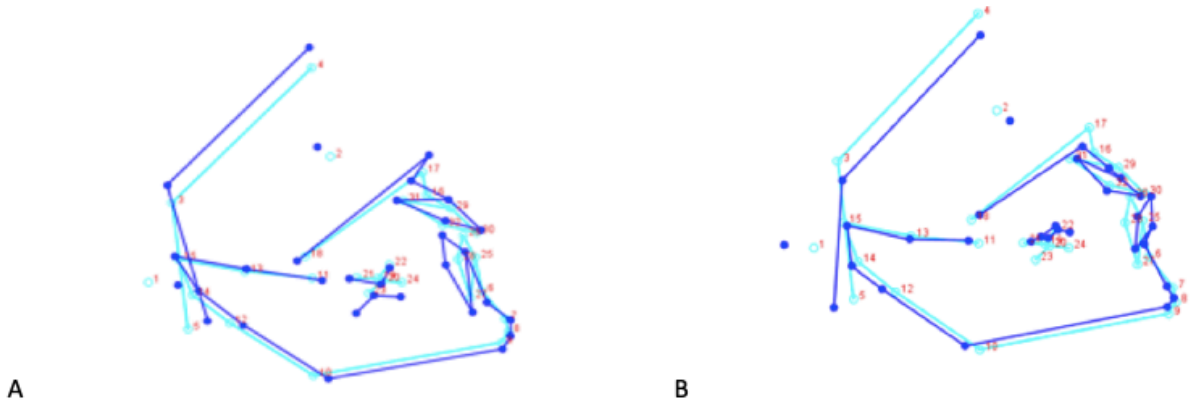
Figure 10A: Comparison of average facial shape with shape variation due to CV1 in obese subjects factored by -30. (Dark blue = shape variation due to CV1, light blue = average shape for comparison.) Figure 10B: Comparison of average facial shape with shape variation due to CV1 in normal weight subjects factored by +30. (Dark blue = shape variation due to CV1, light blue = average shape for comparison.)

Looking at CV2 there is also an increase in the cranial base angle. Maxillae are relatively smaller or more retrusive and there is a proclination of the lower incisors. The overjet is decreased in the obese group the molars are in a class III relationship (Figure 11).



A B

Figure 11A: Comparison of average facial shape with shape variation due to CV2 in normal weight subjects factored by -30. (Dark blue = shape variation due to CV2, light blue = average shape for comparison.) Figure 11B: Comparison of average facial shape with shape variation due to CV2 in obese subjects factored by +30. (Dark blue = shape variation due to CV2, light blue = average shape for comparison.)

4.4 Genotype - Phenotype Results

4.4.1 Regression of BMI and Facial Shape

Of the selected genes along the Hippo Signaling pathway that were analyzed five had statistically significant relationships with facial shape when comparing the percent BMI regression of female only subjects pooled by race. A Welch one-way analysis of variation of rs1317183 (FOX06) showed statistically significant differences by BMI group (p=0.024; Figure 12). This indicates that obese individuals are more likely to be homozygous for the common allele for rs1317183 (FOX06).

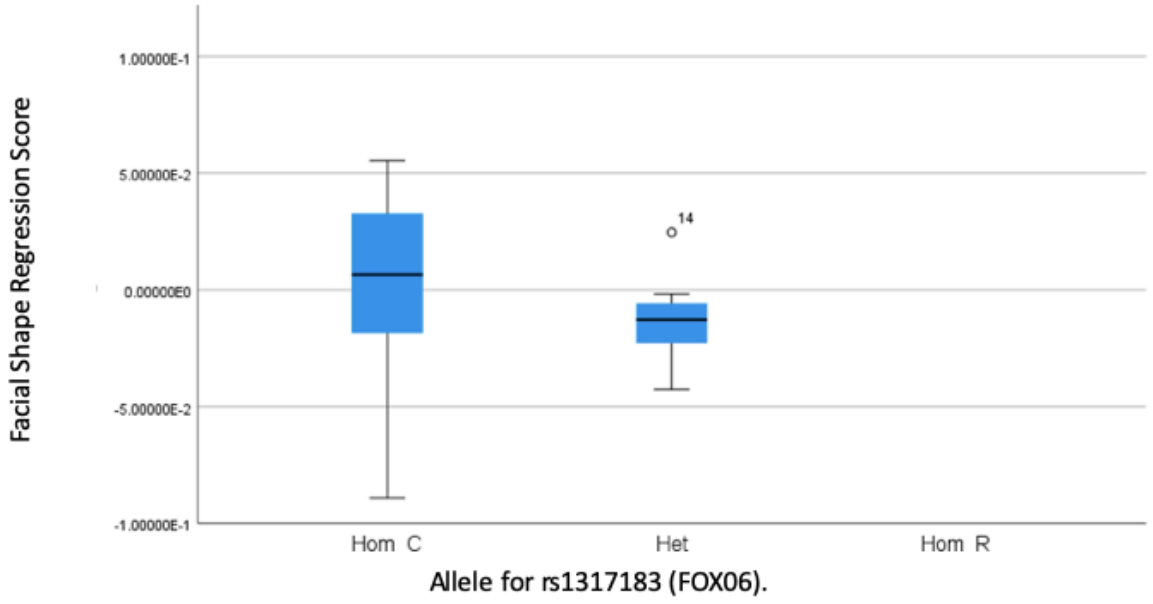


Figure 12: Comparison of individuals who are homozygous common and heterozygous for SNP rs1317183 on FOX06 with regression of facial shape.

A one-way analysis of variance comparing rs11758653 (TEAD3) by BMI group yielded statistically significant differences (p=0.047; Figure 13). This indicates that obese individuals are more likely to be homozygous for the common allele for rs11758653(TEAD3).

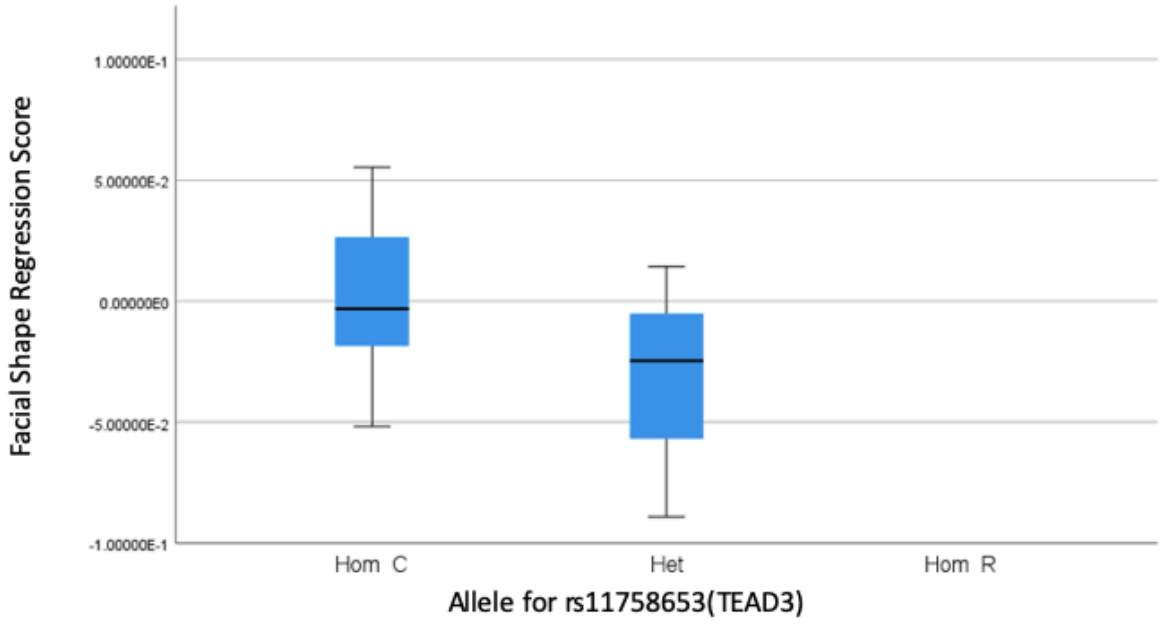


Figure 13: Comparison of individuals who are homozygous common and heterozygous for SNP rs11758653 on TEAD3 with regression of facial shape.

A one-way ANOVA comparing rs72894781 (TEAD3) by BMI group was also statistically significant (p=0.048). This indicates that obese individuals are more likely to be homozygous for the common allele for rs72894781 (TEAD3; Figure 14).

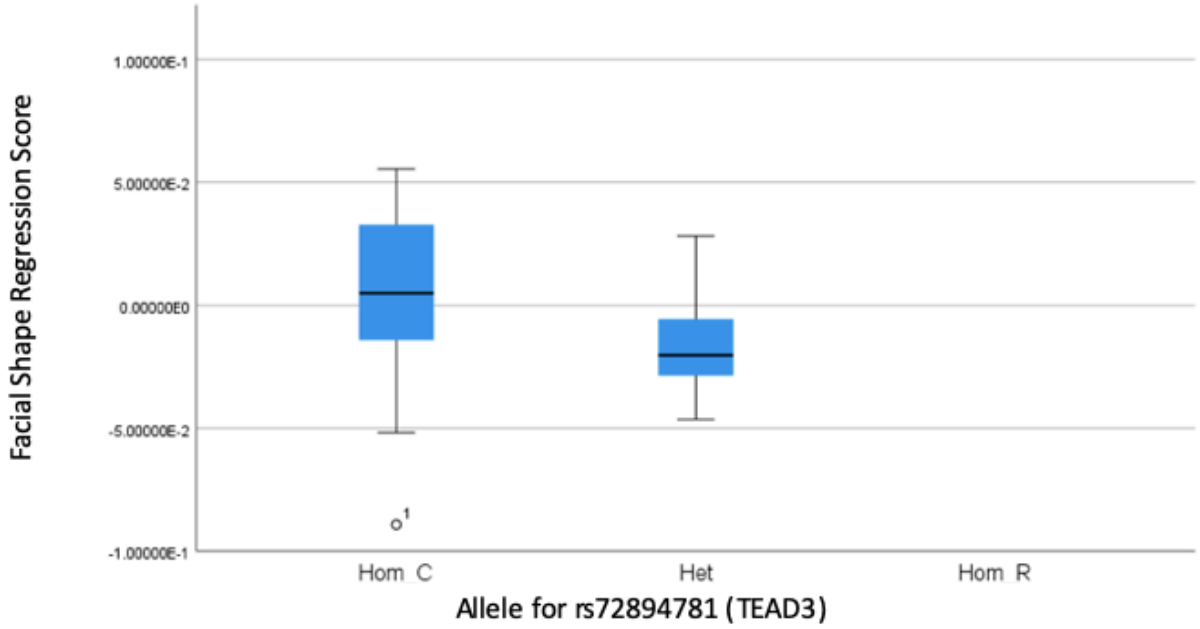


Figure 14: Comparison of individuals who are homozygous common and heterozygous for SNP rs72894781 on TEAD3 with regression of facial shape.

A one-way ANOVA comparing rs72894784 (TEAD3) allele variants by BMI showed statistically significant differences across groups (p=0.048). This indicates that obese individuals are more likely to be homozygous for the common allele for rs72894784 (TEAD3; Figure 15).

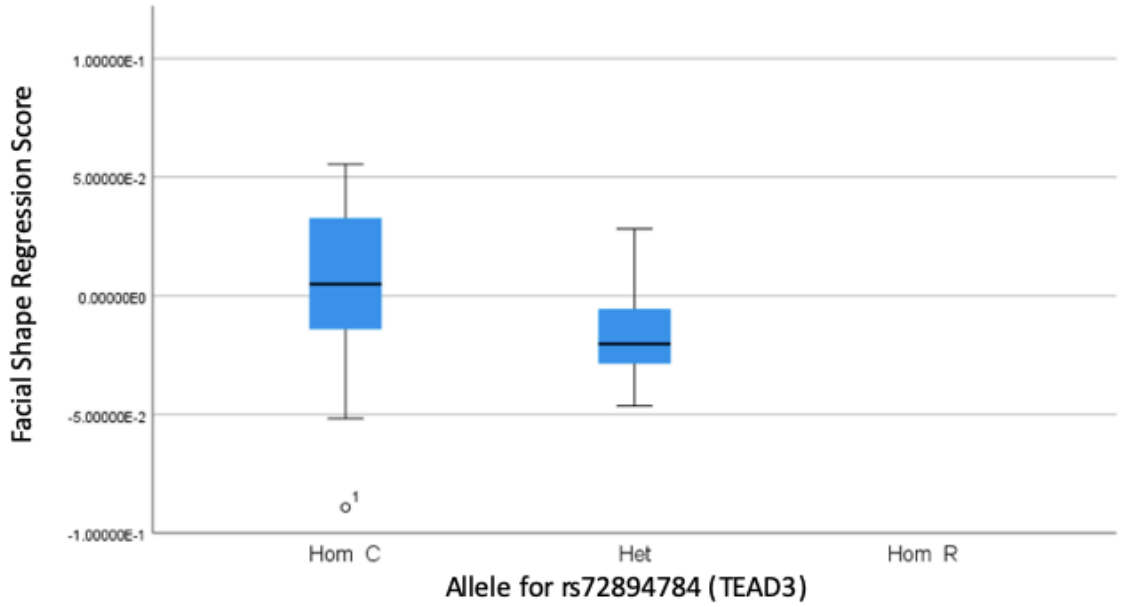


Figure 15: Comparison of individuals who are homozygous common and heterozygous for SNP rs72894784 on TEAD3 with regression of facial shape.

A one-way ANOVA comparing rs112991009 (LATS2) allele variants by BMI group was statistically significant (p=0.012). This indicates that obese individuals are more likely to be homozygous for the common for rs112991009 (LATS2; Figure 16).

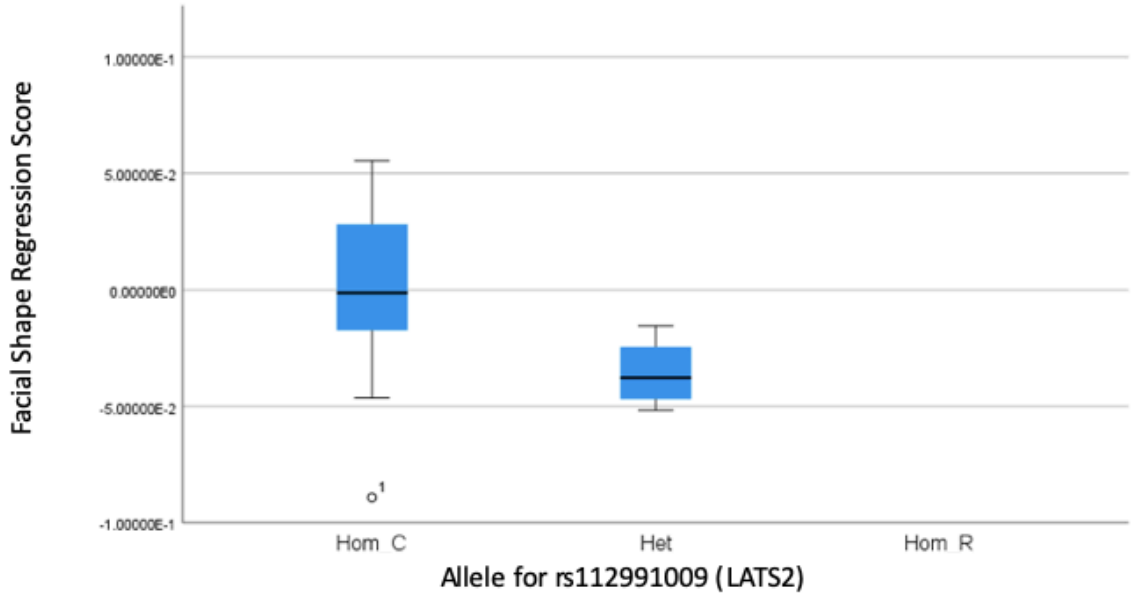


Figure 16: Comparison of individuals who are homozygous common and heterozygous for SNP rs112991009 on LATS2 with regression of facial shape.

4.4.2 **Principal Components Analysis & Genotypes**

Of the selected genes studied along the Hippo signaling pathway that were analyzed, three showed statistically significant relationships with the two PC's that we had previously identified as having significant relationships with facial shape of female only subjects pooled by race. A one-way ANOVA of PC8 scores by the rs12214749 (RUNX2) allele frequencies was statistically significant (p=0.008). For PC8 the positive mean is associated with normal subjects while the negative mean is associated with obese subjects. Our results indicate that being homozygous for the common allele for the rs12214749 (RUNX2) is associated with normal weight subjects while the heterozygous genotype is associated with obese subjects (Figure 17).

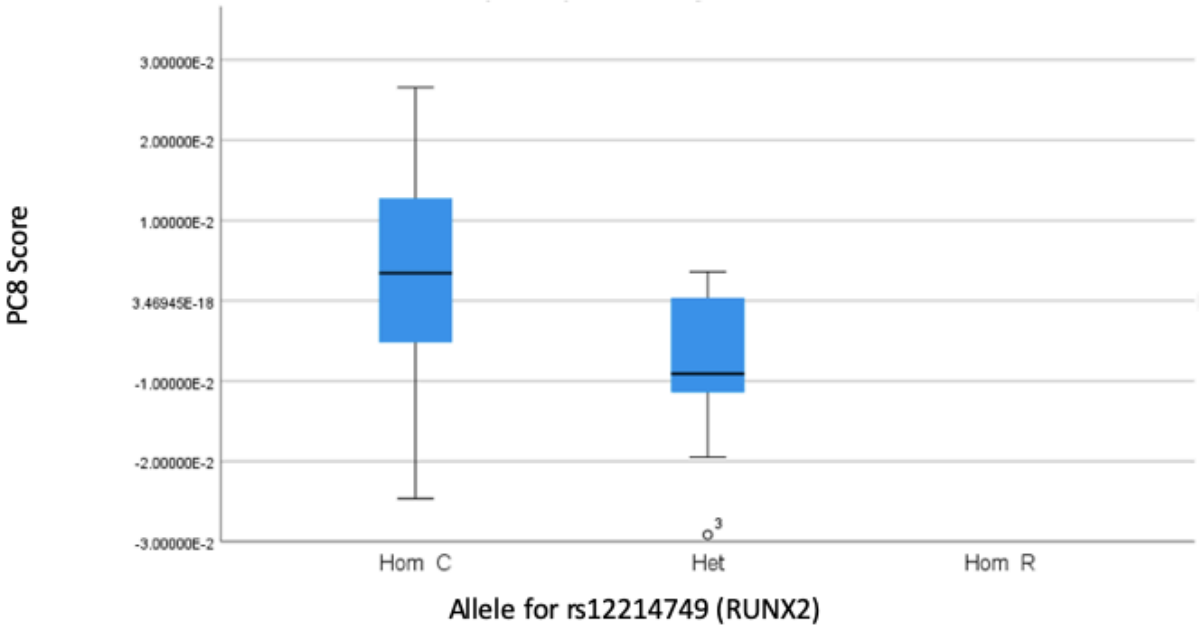


Figure 17: Comparison of individuals who are homozygous common and heterozygous for SNP rs12214749 on RUNX2 with mean of PC8.

A one-way ANOVA of PC8 scores by rs112991009 (LATS2) was statistically significant (p=0.14). For PC8 the positive mean is associated with normal subjects while the negative mean is associated with obese subjects. Thus, our results suggest that being homozygous for the common genotype for rs112991009 (LATS2) is associated with obese subjects while the heterozygous genotype is associated with normal weight subjects (Figure 18). Thus, we infer that subjects who are homozygous for the common for rs112991009 (LATS2) are more likely to have a more vertical and clockwise rotation of the mandible when compared to subjects with a positive mean. Subjects along the negative end of the range of variation were also more likely to exhibit a retrusive maxilla.

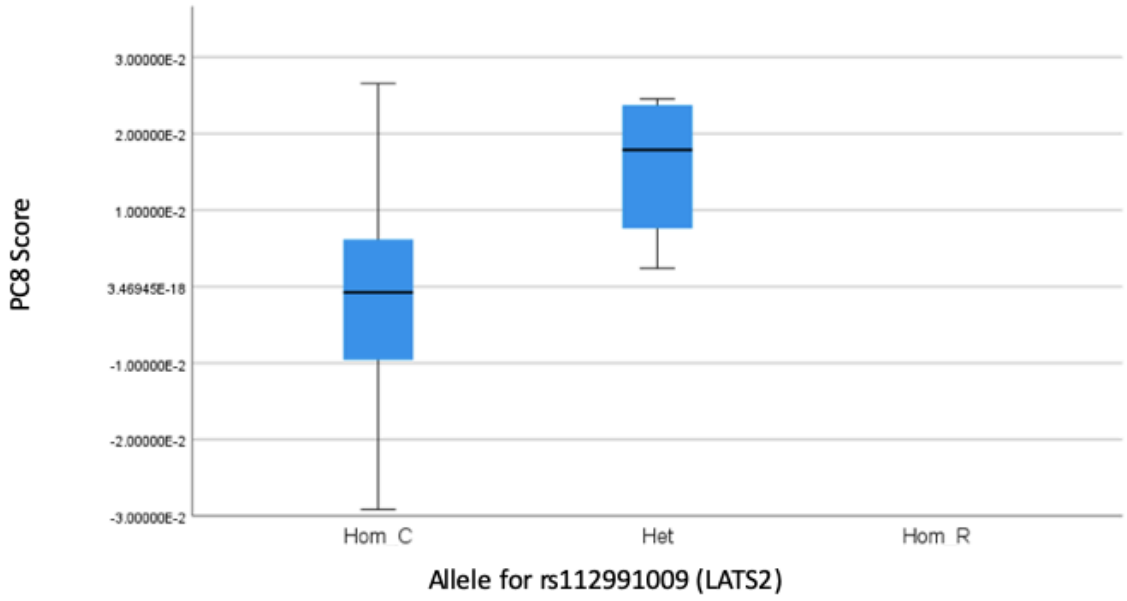


Figure 18: Comparison of individuals who are homozygous common and heterozygous for SNP rs112991009 on LATS2 with mean of PC8.

A one-way Welch's ANOVA of PC32 by rs13085791 (MST1) on was statistically significant (p=0.001). For PC32 the positive mean is associated with obese subjects while the negative mean is associated with normal weight subjects. This indicates that being homozygous for the common allele for rs13085791 (MST1) is associated with obese subjects while being homozygous recessive is associated with normal weight subjects (Figure 19). This suggests that individuals who are homozygous for the common allele for rs13085791 (MST1) may have a greater cranial base angle and more clockwise rotation of the mandible.

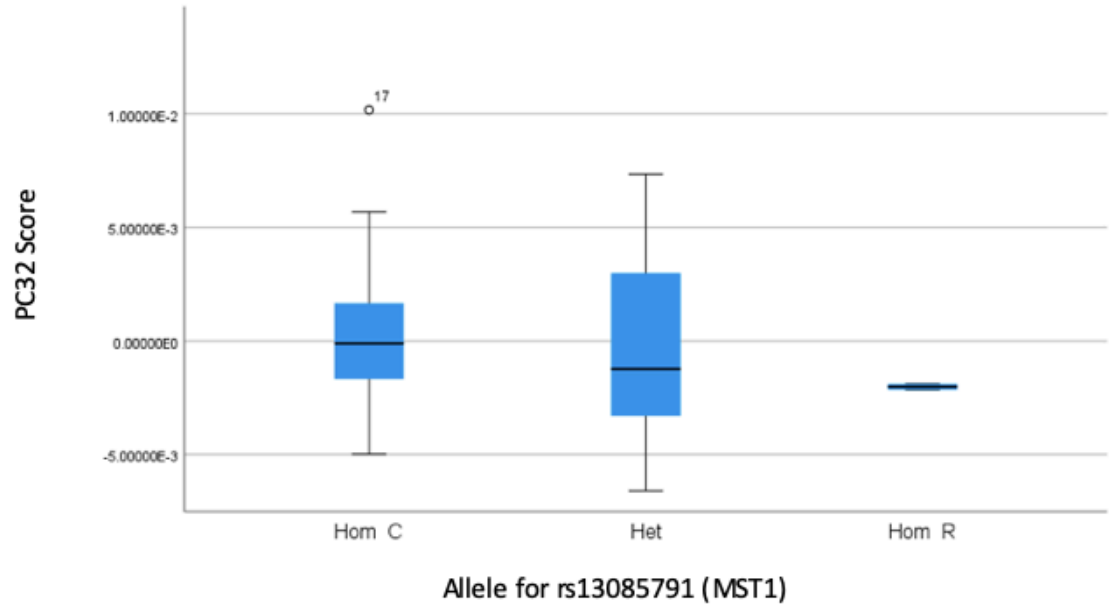


Figure 19: Comparison of individuals who are homozygous common and heterozygous for SNP rs13085791 on MST1 with mean of PC32.

4.4.3 Canonical Variates Analysis & Genotypes

Of the selected genes along the Hippo signaling pathway that were analyzed, three showed a statistically significant relationships to the canonical variates scores. The one-way Welch's test of CV1 by rs62262683 (MST1) was statistically significant (p=0.006). For CV1 the negative mean is associated with obese individuals. This indicates that for rs62262683 (MST1), being homozygous for the common allele is associated with obese individuals (Figure 20). This may indicate that subjects along the negative end of the range of variation for CV1 are likely to display a class III dental and skeletal relationship.

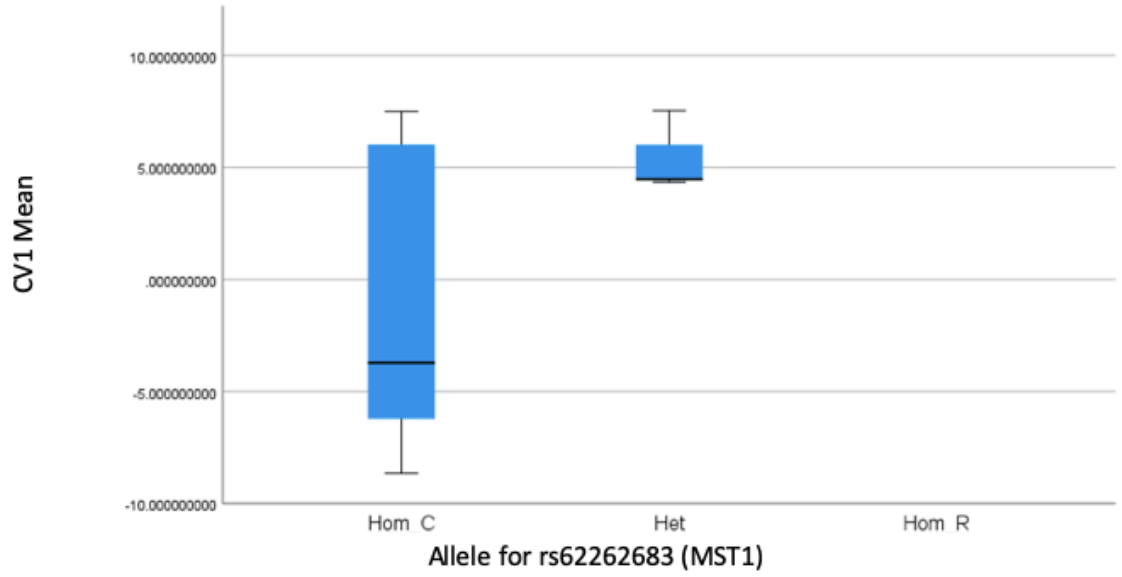


Figure 20: Comparison of individuals who are homozygous common and heterozygous for SNP rs62262683 on MST1 with mean of CV1.

The one-way Welch's test of CV1 by rs11758653 (TEAD3) was statistically significant (p=0.001). For CV1 the negative mean is associated with obese individuals. This indicates that for rs11758653 (TEAD3), being homozygous for the common allele is associated with obese individuals (Figure 21). This suggests that subjects who are homozygous for the common allele for rs11758653 (TEAD3) are likely to have a retrusion of the maxilla, and a more vertical rotation pattern of the mandible compared to those who are heterozygous.

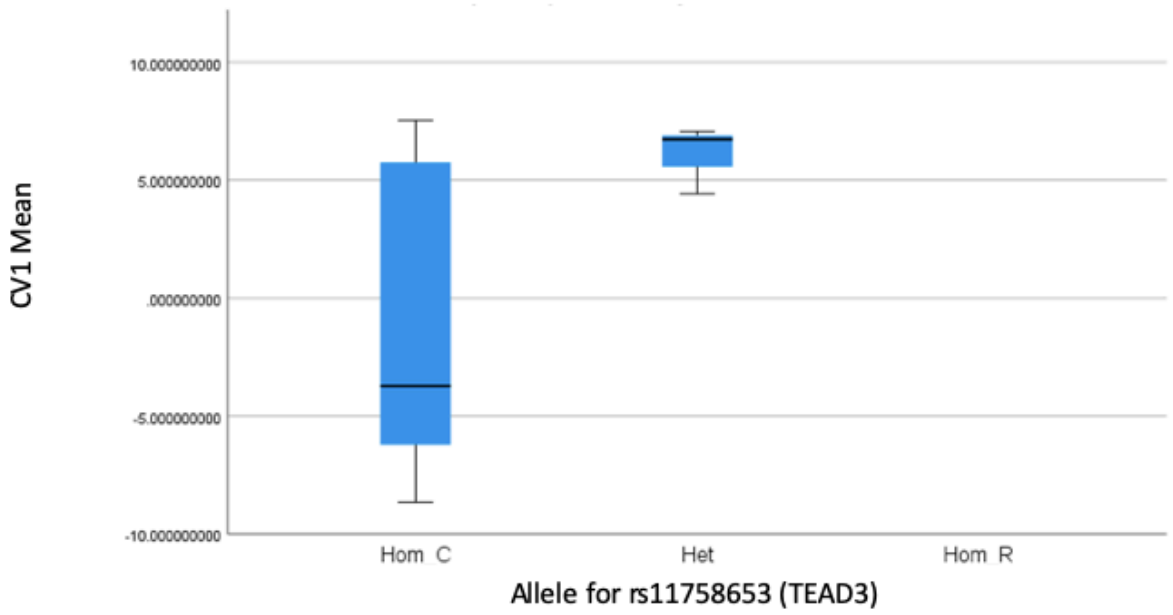


Figure 21: Comparison of individuals who are homozygous common and heterozygous for SNP rs11758653 on TEAD3with mean of CV1.

A one-way Welch's test of CV1 by rs113515288 (TEAD4) was statistically significant (p=0.24). For CV1 the negative mean is associated with obese individuals. This indicates that for rs113515288 (TEAD4), being heterozygous is associated with obese individuals (Figure 22). Subjects that are heterozygous for rs113515288 on TEAD4 are thus more likely to display a counterclockwise rotation of the mandible as well as a retrusive maxilla.

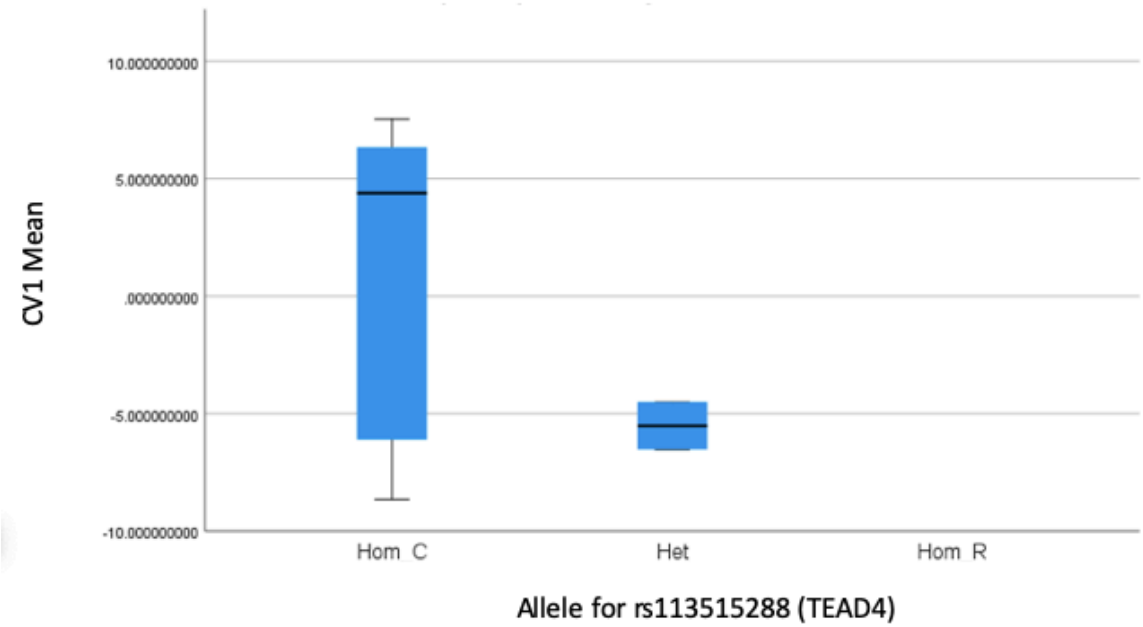


Figure 22: Comparison of individuals who are homozygous common and heterozygous for SNP rs113515288 on TEAD4 with mean of CV1.

5. DISCUSSION

5.1 Phenotype

When comparing normal weight subjects to obese subjects there was a significant facial shape variation among females when pooled by race and adjusted for changes in shape due to age. The obese sample appears to have retrusion of the maxilla along with a taller (supero-inferiorly) mandible with a clockwise rotation. The high BMI group showed significantly higher FMA. There also appeared to be a class III growth pattern with what appears to be a restricted maxilla and protruded mandible. Dentally, the obese group of subjects have more proclined upper and lower incisors as well as a class III tendency in the molar region.

The findings in this study are similar to other studies done in the past and indicate a possible association between facial shape and BMI. Increased mandibular length and prognathic jaws were previously found in obese subjects when compared to normal weight individuals (Ohrn et al. 2002). This matches what is seen in the mandible in our study. There is increased length of the mandible in obese subjects. According to (Gordon et al. 2021), high BMI individuals have taller rami and slightly less prognathic chins. In our study we also see an increase in the vertical growth and potential increase in ramus length. (Sadeghianrizi et al. 2005a) shows that both males and females in the obese group exhibited mandibular and maxillary dimensions. This differs slightly from what we found in this study. In the obese group, we found an increase in the mandibular dimension but usually a decrease in maxillary size.

After breaking down the principal components PC8 and PC32 show a significant difference in facial shape between the obese and normal shape group. When looking at PC8 the obese group shows a class III dental relationship with more proclined upper and lower incisors. (Sadeghianrizi

et al. 2005) finds similar proclination in upper and lower incisors in obese subjects. This may be due to a difference in the maxillary growth and subsequent compensation of the upper and lower incisors to make room for the tongue. When looking at PC32 there is an increase in the mandibular plane angle. This contradicts the findings of (Sadeghianrizi et al. 2005) where there was a decrease in the FMA in males and females of the obese group.

When analyzing the facial phenotype between obese and normal weight individuals for CV1 and CV2 there is a decreased size of the maxilla. This supports our findings from the PC analysis but differs from (Gordon et al. 2021) who found an increase in the size of both the maxilla and mandible. When looking at CV1, obese individuals appear to have a class III dental relationship. Dental relationships can be a factor of skeletal position, and it is possible that the increase in mandibular size along with the decrease of maxillary dimension can lead to a class III dental appearance in obese subjects.

5.2 **Genotype-Phenotype**

There were a number of genes along the Hippo signaling pathway that had significantly different genotypes between the obese and normal weight subjects (FOXO6, TEAD3, TEAD4, MST1, LATS2 and RUNX2). These genes have previously been associated growth and adiposity. For example previous studies demonstrate FOXO6 controls preadipocyte proliferation, apoptosis and early adipogenesis (Abdalla et al. 2021). FOXO6 has also been associated with gluconeogenesis regulation, and FOXO6 inhibition is beneficial in curbing excessive glucose production and improving glycemic control in diabetic patients (Kim et al. 2011).

FOXO6 was shown in this study to be associated with craniofacial form in obese subjects. Previous studies have shown that FOXO6 plays an early regulatory role in facial morphology (Sun et al. 2018). In a knockout study in mice, when FOXO6 was removed, there was an overgrowth in the anteroposterior direction of the maxilla and mandible (Sun et al. 2018). A deeper understanding of FOXO6 gene can give us more insight into how it effects craniofacial form.

TEAD3 has been shown to be associated with final adult height (Perchard et al. 2020). This gene may also have an effect on the craniofacial formation as well. In this study we found that obese individuals were more likely to be homozygous for rs72894784 on TEAD3. It is possible that different alleles on TEAD3 can lead to differential growth of the mandible similar to what was seen in our obese sample. TEAD4 has also been shown to have a direct impact on the regulation of tumoral growth. TEAD4 knockout results in cell cycle arrest in the G1 phase of growth in oral squamous cell carcinoma (Takeuchi et al. 2017). By learning more about the specific role of TEAD4 in craniofacial form, a final facial form can be better predicted, and possibly treated more efficiently in orthodontic cases.

MST1 is present in the mammalian heart and play an important role of regulating the growth and death of cardiomyocytes (Ikeda and Sadoshima 2016). It also may have a role in the muscular changes associated with vertical growth pattern in the obese subject group. In our obese groups we found MST1 to play a role in facial form. As the facial form changes, and muscular adaptations occur and it is possible MST1 plays a role in the regulation of facial muscles.

LATS2 has been argued to play an important role in the pathway that fine-tunes organ growth (Gan et al. 2020). Craniofacial growth may also be affected by the LATS2 gene (Gan et

al. 2020). LATS2 was found to play a significant role in facial form in our study in the obese group. LATS2 has also been discovered to play a significant role in adipocyte proliferation. LATS2 regulates the balance between proliferation and cell differentiation during adipocyte development (An et al. 2013). Obese individuals are more likely to be homozygous for the common for rs112991009 on LATS2. It is possible that individuals with the homozygous allele experience more adipocyte proliferation that other allele forms leading to an increase in BMI, and thus affecting facial form. This study does not provide direct evidence of this, but this may be of interest in future studies.

RUNX2 has been discovered as an instrumental gene in skeletal development (Komori 2017). In our study, individuals who are heterozygous for SNP rs12214749 on RUNX2 is associated with being obese. Because obese individuals appear to have an increased mandibular size, RUNX2 may play a role in craniofacial development as well. The fact that there were significant phenotypic difference between obese and normal weight subjects with the RUNX2 reiterates the role that it plays in skeletal development of the facial region. It is no surprise that the genes found to be significant in this study have been related to growth and development in the past.

5.3 **Clinical Implications**

These skeletal characteristics are consistent with patients who have sleep apnea (Forno et al. 2017). According to Lowe, sleep apnea subjects showed a posteriorly positioned maxilla and mandible, a steep occlusal plane, over-erupted maxillary and mandibular teeth, proclined incisors, a steep mandibular plane, a large gonial angle, and high upper and lower facial heights (Lowe et

al. 1986). Obese individuals are at a much higher risk for getting sleep apnea. An estimated 58% of patients with obstructive sleep apnea have a BMI >30 (Grimm and Becker 2006).

Overweight patients have constricted airways during growth and development (Forno et al. 2017). These changes may cause a more vertical growth pattern. These vertical changes in growth may lead to malocclusions that need orthodontic intervention in the future. It is important to understand the link between obesity, sleep apnea, and facial form to better diagnose, manage and treat these orthodontic patients.

Phenotypic characteristics seen in our obese subjects are also similar to those of mouth breathers. According to a study from 2005, mouth breathers show an increased lower facial height, steeper mandibular plane angle, a shorter maxillary length, and decreased overjet (Agostinho et al. 2015). Another study found that mouth breathing is associated with an open rotation of the mandible and a more vertical mandibular plane (El Aouame, Daoui, and El Quars 2016). Because of the similarities found between mouth breathers and obese patients I think it is important to look further into the connection between the two. For example early screening for obese patients can be done to screen for when mouth breathing begins.

5.4 **Limitations of Study**

Because this is a pilot study there are a number of limitations that exist. To begin with the sample size of the study is relatively small. With a group of 117 subjects it is possible that this sample does not represent the population as a whole. This study was also performed at one location in Chicago. Because it was only completed in one location it may not encompass a full range of ethnic diversity. This study had a majority of normal weight subjects (n=52 for full data set and

n=27 for female only dataset). If there were an equivalent number of obese and underweight subjects there could have been a different conclusion. In this study there was a limited number of subjects with the rare allele for the genes we were studying. With a larger number of subjects, and more subjects with the rare allele, a more comprehensive understanding of the genetic role may be found.

Thorough analysis of the BFFQs could not be completed and that limited our ability to understand the role of diet in our results. In this study we were unable to see if there was a genetic difference between subjects with either a high calorie or low-calorie diet. If there were subjects that had high body weight and no genetic markers it is possible that diet may have played a role in the subject's phenotype. Without the health eating index variable from the BFFQ there was no easy way to factor out diet quality in this analysis.

All subjects in this study were initially presenting for orthodontic records, which poses a risk for inherent bias. It is possible that there is a greater shape variation in these individuals because they are attempting to undergo orthodontic treatment. It is possible that this sample does not represent the population as a whole, and only looks at people who are already seeking care for their facial and dental form. We also don't consider socioeconomic status in this study.

5.5 **Recommendations for Future Studies**

One important recommendation for future studies is to have a much larger sample size. This may improve subject diversity to the study and lead to a better understanding of the genetic role in facial form. For future studies if CBCTs are used instead of panoramic and cephalometric radiographs more precision can be used, and more data can be extracted. CBCT would allow a 3D

analysis, and although the 2D cephs are a good starting point, 3D CBCTs would be best for this. This study could benefit from adding dietary intake into the study. We have a vast amount of raw data on diet, and looking into it could be a full study of its own.

In this study, only a few genes were analyzed. In future studies a much more thorough genetic profile can be used to analyze the genetic role in facial form. A genome wide association study could be a benefit for future studies. Ultimately, the next step after determining the genetic associations with facial shape is to do a knockout study in mice. By knocking out these specific genes, researchers would be able to see if there is a causative relationship between the genes studies and the phenotypic characteristics displayed.

6. CONCLUSIONS

- Higher BMI females show an increase in vertical dimensions of the mandible when compared to normal weight subjects.
- Higher BMI females show retrusive maxillae when compared to normal weight subjects.
- Higher BMI females show an increased FMA and gonial angle when compared to normal weight subjects.
- Higher BMI females show a more class III dental and skeletal relationship when compared to normal weight subjects.
- Obese females show similar skeletal characteristics to individuals with sleep apnea.
- Variations in FOXO6, TEAD3, TEAD4, MST1, LATS2 and RUNX2 show significant phenotypic differences in obese and normal weight female subjects.

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APPENDICES

APPENDIX A

Approval Notice
Initial Review (Response To Modifications)

February 1, 2018

Jennifer Caplin, BS, DMD, MS
Orthodontics
801 S. Paulina St Room 131
M/C 841
Chicago, IL 60612
Phone: (312) 996-0230 / Fax: (312) 996-0893

RE: Protocol # 2017-1276
"Linking Malocclusion and Body Mass Via Genetic Variants Within the Hippo Signaling Pathway and Dietary Factors"

Dear Dr. Caplin:

Your Initial Review (Response To Modifications) was reviewed and approved by the Expedited review process on January 30, 2018. You may now begin your research

Please note the following information about your approved research protocol:

The cover letter response indicated approval from Midwestern University's IRB would be provided, but the document referenced as an approval did not appear to be and IRB approval document (it did not reference the IRB, the FWA, nor the federal regulations governing human subjects research). The Appendices L-2 for the personnel from Midwestern University were not approved, since these documents do not apply if the Midwestern University IRB will review this research. Therefore, Midwestern University was not cited as an approved non-UIC performance site. Once their IRB approval is obtained, and before and research is conducted in conjunction with this site, an amendment will need to be submitted to the UIC IRB to formally add this site.

Protocol Approval Period:	January 30, 2018 - January 30, 2019
Approved Subject Enrollment #:	250
Additional Determinations for Research Involving Minors:	The Board determined that this research satisfies 45CFR46.404, research not involving greater than minimal risk. Therefore, in accordance with 45CFR46.408, the IRB determined that only one parent's/legal guardian's permission/signature is needed. Wards of the State may not be enrolled unless the IRB grants specific approval and assures inclusion of additional protections in the research required under 45CFR46.409. If you wish to enroll Wards of the State contact OPRS and refer to the tip sheet.
Performance Sites:	UIC
Sponsor:	American Association of Orthodontics Foundation
PAF#:	N/A
Grant/Contract No:	N/A
Grant/Contract Title:	N/A
Research Protocol(s):	

Appendix A (Continued)

Approval Notice
Amendment to Research Protocol and/or Consent Document – Expedited Review
UIC Amendment # 1

March 7, 2018

Jennifer Caplin, BS, DMD, MS
Orthodontics
801 S. Paulina St Room 131
M/C 841
Chicago, IL 60612
Phone: (312) 996-0230 / Fax: (312) 996-0893

RE: Protocol # 2017-1276
"Linking Malocclusion and Body Mass Via Genetic Variants Within the Hippo Signaling Pathway and Dietary Factors"

Dear Dr. Caplin:

Members of Institutional Review Board (IRB) #3 have reviewed this amendment to your research and/or consent form under expedited procedures for minor changes to previously approved research allowed by Federal regulations [45 CFR 46.110(b)(2) and/or 21 CFR 56.110(b)(2)]. The amendment to your research was determined to be acceptable and may now be implemented.

Please note the following information about your approved amendment:

Amendment Approval Date: March 7, 2018
Amendment:
Summary: UIC Amendment #1 received on March 5, 2018 involves the addition of Midwestern University as a research site. Appendix K and IRB approval from Midwestern University were provided.
Approved Subject Enrollment #: 250
Performance Sites: Midwestern University, UIC
Sponsor: American Association of Orthodontics Foundation

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
03/05/2018	Amendment	Expedited	03/07/2018	Approved

Please be sure to:

→ Use your research protocol number (2017-1276) on any documents or correspondence with the IRB concerning your research protocol.

APPENDIX B

American Association of Orthodontists

AAOF
Advancing the Specialty™

401 North Lindbergh Blvd.
St. Louis, Missouri 63141-7816

314-292-6546 or 800-424-2841, ext. 546
Fax: 800-708-1364

www.aaofoundation.net

March 8, 2018

Dr. Jennifer Caplin
University of Illinois Chicago
801 S Paulina St., Room 131
Chicago, IL 60612

Dear Dr. Caplin:

Thank you for your 2018 Orthodontic Faculty Development Fellowship Award proposal, entitled ***"Project 1: (Barriers/Access to Care) The Effect of the Implementation of the HLD Index for Medicaid Patients on Access to Orthodontic Care in Illinois / Project 2: Linking Malocclusion and Body Mass Via Genetic Variants within the Hippo Signaling Pathway,"*** requesting $20,000.

Your proposal was reviewed by the Foundation's Planning and Awards Review Committee (PARC) and then considered by the AAO Foundation Board at our meeting in late February.

Congratulations! Your application was among those approved for funding. Your proposal was named the ***2018 Robert E. Gaylord Teaching Fellowship Award***.

- This funding, however, is contingent upon your satisfying the reviewers' concerns for IRB approval for Project #2

This year once again we are providing reviews of all proposals received regardless of the funding status. Attached is your review, along with some important information about the review process which we encourage you to look at carefully and study so that your next proposal will be even stronger.

The entire funding amount of $20,000 will be sent upon receipt of the following:

- completed and signed Letter of Agreement and Promissory Note (copy attached)
- a brief video of the PI and the project sent separately to cyoung@aaortho.org
- a black and white photograph of the P/I, and
- a synopsis (500 words) of the project/research/use of funds, submitted electronically to cyoung@aaortho.org. This synopsis is to include:
  - a short biography
  - a brief description of their project

Appendix B (Continued)

- how orthodontic education will benefit from their award
- why the Foundation is important to the project
- how Foundation funding might help advance your career, and how it has helped advance your career, assuming you have received AAOF funding in the past.

No Progress Report is required for an OFDFA, but a Final Report, in an electronic format, is due no later than July 1, 2019, unless you have received a No Cost Extension. (Final Report form attached.)

Your Final Report will be posted on the AAOF website. Also, it may be summarized and/or distributed to the **AJO/DO** and **Bulletin** as well. See examples of other Final Reports on the AAO Foundation website at: http://www.aaofoundation.net/AwardsProgram/SummaryofAwardResults.aspx.

It is understood that the recipient will make a good faith effort to publish or otherwise disseminate the findings of the project. Publications or presentations made by Recipient relating to the project must contain appropriate reference to support provided by the Foundation.

Should you have any questions, please contact Mr. Robert Hazel, AAOF Executive Vice President, at 800/424-2841, #546.

Kind regards,

David J. Angus, DMD
President

cc: Dr. Budi Kusnoto
Mr. Robert Hazel

Enclosures: Explanation of Review Process (PARC)
Individualized Review
Letter of Agreement/Promissory Note – Fellowship
Final Report Form

APPENDIX C

Linking Malocclusion and Body Mass Via Genetic Variants Within the Hippo Signaling Pathway and Dietary Factors

1. My name is Dr._____.

2. We are asking you to take part in a research study because we are trying to learn more about how body mass and genetics affect the position of your jaws and teeth.

3. If you agree to be in this study, you will be asked to spit into a test tube. You or your parent/guardian will be asked to fill out a survey about what you eat. We will also take an impression of your teeth, take an x-ray of your skull, weigh you on a scale, and measure your height. We will take the impression, the x-ray, your weight, and your height regardless of whether or not you agree to participate in the research, as we need these for your orthodontic treatment. If you have already had your impressions, x-ray, weight, and height taken, we will not re-take them.

4. The biggest risk to you is that other people may discover that you were a part of this study. We will try to prevent that by removing your name, address, birthday, and all other personal information from everything that we use (saliva, survey results, models of your teeth, and x-ray of your skull) as soon as possible.

5. While there is no direct benefit to you for participation in this research, we hope that it will help other children like you in the future who are seeking orthodontic treatment.

6. Please talk this over with your parents before you decide whether or not to participate. We will also ask your parents to give their permission for you to take part in this study. But even if your parents say “yes” you can still decide not to do this.

7. If you don’t want to be in this study, you don’t have to participate. Remember, being in this study is up to you and no one will be upset if you don’t want to participate or even if you change your mind later and want to stop.

8. You can ask any questions that you have about the study. If you have a question later that you didn’t think of now, you can call me at 312-996-0230 or ask me next time.

9. Signing your name at the bottom means that you agree to be in this study. Your doctors will continue to treat you whether or not you participate in this study. You and your parents will be given a copy of this form after you have signed it.

Appendix C (Continued)

_____	_____
Name of Subject	Date

_____	_____	_____
Signature	Age	Grade in School

APPENDIX D

HIPAA Authorization Template V2.9, 03/13/07

University of Illinois at Chicago
Authorization To Use And Disclose (Release) Health Information For a Research Study

Linking Malocclusion and Body Mass Via Genetic Variants Within the Hippo Signaling Pathway and Dietary Factors

State and Federal laws, including the Health Insurance Portability and Accountability Act (HIPAA), require researchers to protect your health information. This form describes how researchers, with your authorization (permission), may use and release (disclose or share) your protected health information in this research study. **Please read this form carefully.**

You have been asked to take part in a research study. The study has already been described to you in a separate consent form. By signing this form you are permitting Dr. Jennifer Caplin, Department of Orthodontics and her research team to create, get, use, store, and share protected health information that identifies you for the purposes of this research study.

Description of protected health information that may be used and released (disclosed or shared)
The health information includes all information created and/or collected during the research as described in the 'Consent for Participation in Research' entitled 'Examining the Relationship between Body Weight and Malocclusion via the Hippo Signaling Pathway and Dietary Factors'. Protected health information may include results of tests, procedures or surveys that are part of the research. Health information in your medical record may be used and released if it is needed for the research; for example, past medical conditions or medications or information related to illness or hospitalizations that occur during your participation in the research

The health information includes: Age, x-ray, digital dental models, height, weight, and genetic data.

Research use of your protected health information:
During the conduct of the research, the researchers may use or share your health information:
- With each other and with other researchers involved with the study;
- With law enforcement or other agencies, when required by law;
- With non-UIC collaborators of the research study: Midwestern University, Chicago College of Osteopathic Medicine, Department of Anthropology;
- With review boards including the University of Illinois at Chicago Institutional Review Board, and other persons who watch over the conduct of research

Protection of your health information

Appendix D (Continued)

The researchers and the American Association of Orthodontics Foundation agree to protect your health information and will only share this information as described in this Authorization and the research consent form.

When your health information is given to people outside of the research study, those agencies that receive your health information may not be required by federal privacy laws (such as the Privacy Rule) to protect it. They may also share your information with others without your permission, if permitted by laws that they have to follow.

Removal of your identifying information (De-Identification)
If all information that identifies you is removed from your health information, the remaining information is no longer subject to the limits of this Authorization or to the HIPAA privacy laws. Therefore, the de-identified information may be used and released by the researchers (as permitted by law) for other purposes, such as other research projects.

Expiration of Authorization
This Authorization does not have an expiration date, but can be canceled sooner if you decide to withdraw your permission.

Withdrawal or removal from the study
You may change your mind and cancel this Authorization at any time. To cancel this Authorization, you must write to:

Jennifer Caplin
University of Illinois at Chicago, College of Dentistry
Department of Orthodontics
801 S. Paulina St., Room 131
Chicago IL, 60612

If you cancel this Authorization, you may no longer be allowed to take part in the research study. Even if you cancel this Authorization, the researchers may still use and disclose health information they have already obtained to maintain the integrity and reliability of the research and to report any adverse (bad) effects that may have happened to you.

Contact information for questions about my rights under HIPAA
If you have questions or concerns regarding your privacy rights under HIPAA, you should contact the University of Illinois at Chicago Privacy Officer at Ph: (312) 996-2271.

If you have not already received a copy of the Notice of Privacy Practices, you should ask for one. You will be given a copy of this Authorization after it has been signed to keep for your records.

Right to Refuse to Sign this Authorization

You do not have to sign this Authorization. If you decide not to sign this Authorization form, it will only mean you cannot take part in this portion of the research that involves the use and release of your health information. Not signing this form will not affect your non-research related treatment, payment or enrollment in any health plans or your eligibility for other medical benefits.

Appendix D (Continued)

Signature of Subject
I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions, and my questions have been answered to my satisfaction. I authorize the use and disclosure of my protected health information for this research.

_____ _____
Signature of Subject Date

_____
Printed Name of Subject

[*OPTIONAL --If all subjects will be adults with the capacity to provide consent/authorization for the research, delete the parent/guardian/legally authorized representative signature lines. If not, replace the previous signatures with the following section*].

_____
Printed name of Subject

_____ _____
Signature of Parent /Guardian or Legally Authorized Representative of Subject Date (must be same as Subject's)

_____
Printed name of Parent / Guardian or Legally Authorized Representative of Subject

Describe relationship to subject including the legal authority this individual has to act on behalf of the subject. (Check one below)
☐ Parent
☐ Medical Power of attorney/representative
☐ Legal guardian
☐ Health care surrogate
☐ Other; specify _____

_____

_____

_____ _____
Signature of Witness Date (must be same as Subject's)

_____
Printed name of Witness

APPENDIX E

University of Illinois at Chicago
Research Information and Parental Permission for Participation in Biomedical Research

Linking Malocclusion and Body Mass Via Genetic Variants Within the Hippo Signaling Pathway and Dietary Factors

Your child is being asked to participate in a research study. Researchers are required to provide a consent form such as this one to tell you about the research, to explain that taking part is voluntary, to describe the risks and benefits of participation, and to help you to make an informed decision. You should feel free to ask the researchers any questions you may have.

Principal Investigator Name and Title: Dr. Jennifer Caplin, Clinical Assistant Professor
Department and Institution: University of Illinois at Chicago, College of Dentistry, Department of Orthodontics
Address and Contact Information:
University of Illinois at Chicago, College of Dentistry
Department of Orthodontics
801 S. Paulina St., Room 131
Chicago IL, 60612
312-996-0320
Emergency Contact Name and Information: Dr. Jennifer Caplin
Sponsor: American Association of Orthodontics Foundation

Conflict of Interest

Your child's health care provider may be an investigator on this research protocol, and as an investigator, is interested in both your child's clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your child's care from a clinician who is not associated with this project. Your child is not obligated to participate in any research project offered by your child's clinician. Your child's participation in this research study is voluntary and your child does not have to participate. The decision to not participate will not affect your child's clinical care now or in the future.

Why am I being asked?

Your child is being asked to be a subject in a research study about the relationship between body mass and malocclusion (crooked teeth and jaw discrepancies) via the Hippo signaling pathway (a collection of genes) and dietary factors. The purpose of this study is to explore the potential links between body mass, the size and shape of the bones of the face, the position of the teeth, diet, and genetics.

Appendix E (Continued)

Your child has been asked to participate in the research because you are seeking orthodontic treatment for your child.

Your child's participation in this research is voluntary. Your decision whether or not to permit your child to participate will not affect your or your child's current or future dealings with the University of Illinois at Chicago. **If you decide to permit your child to participate, you are free to withdraw your child at any time without affecting that relationship.**

Approximately 250 subjects may be involved in this research at UIC.

What is the purpose of this research?

This research is being done to better understand the potential links between body mass, the size and shape of the bones of the face, the position of the teeth, diet, and genetics.

What procedures are involved?

This research will be performed at University of Illinois at Chicago, College of Dentistry Department of Orthodontics, Room 131

Your child will need to come to the study site 1 time.

That visit will take about 1-2 hours

The study procedures are:

- Collection of orthodontic records-digital dental models, x-ray of skull, height, weight, waist circumference, and age by the orthodontic resident.
    - All of these records are collected on all orthodontic patients and therefore will be collected regardless of your child's participation in this study
- Your child will be asked to spit into a test tube to collect saliva.
- Your child, or a representative on behalf of your child, will be asked to fill out a questionnaire (the Block Food Frequency Questionnaire) about your child's diet.

Genetic Testing

The genetic testing will involve analyzing several candidate genes to see how they are unique to your child. We will not test the entire gene, only the segment that differs among people.

Before your child's DNA is analyzed, all identifiers and personal information will be removed, and there will be no way to link the DNA back to your. Your child's DNA will be assigned a random code, which cannot be traced back to your child.

The results of the analysis will be shared with members of the approved research team. All identifiers and personal information will be removed prior to sharing.

Appendix E (Continued)

The results of the analysis will not be shared with you or your child, because we will have no way of identifying your child.

Your child's DNA will be stored for future use. Future research may be conducted to further study the link between genetics and malocclusion (position of the jaws and teeth). The DNA will be stored with no identifiers that can be linked to your child. It will be linked to your child's x-rays, dental models, height, weight, and age. It will be stored indefinitely in an investigator's laboratory.

Unfortunately, once in the bank, we cannot withdraw your child's DNA, as we will not be able to identify which DNA sample belongs to your child.

☐ I agree to allow genetic testing to be performed on my child's saliva sample for the current present research study.
Initials _____.

☐ I agree to allow my child's genetic data to be kept by the University of Illinois at Chicago DNA Services Facility for use by other researchers for future genetic research to learn more about how to prevent, detect, or treat malocclusion.
Initials _____.

☐ I do not agree to allow my child's genetic data to be kept by the University of Illinois at Chicago DNA Services Facility for use by other researchers for future genetic research to learn more about how to prevent, detect, or treat malocclusion.
Initials _____.

☐ I agree to allow my child's genetic data to be kept by University of Illinois at Chicago DNA Services Facility for use by other researchers for future genetic research to learn more about how to prevent, detect, or treat other health problems.
Initials _____.

☐ I do not agree to allow my child's genetic data to be kept by University of Illinois at Chicago DNA Services Facility for use by other researchers for future genetic research to learn more about how to prevent, detect, or treat other health problems.
Initials _____.

What are the potential risks and discomforts?

The less likely risks and discomforts expected in this study are:

The risk of inadvertent or inappropriate use or disclosure of individually identified genetic information, including denial of employment or insurance of a research participant (or a relative or ethnic group or population) and psychosocial harms, such as stress, anxiety, or embarrassment resulting from inadvertent disclosure of information on family relationships, ethnic heritage, or potentially stigmatizing conditions. The researchers will do their best to minimize this risk by removing all personal identifiers from the genetic information prior to analysis. The genetic information will in no way be linked to your child.

Appendix E (Continued)

There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease being tested.

There is a risk that someone could get access to the genetic information we have stored about your child. Genetic testing can create information about a subjects' and their families' personal health risks and can cause or increase anxiety, and/or interfere with your child's ability to get insurance or a job, and can even lead to discrimination. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives. There are laws against this kind of misuse, but they may not give full protection. There may be other unforeseen privacy risks. We believe the chance these things will happen is very small, but we cannot make guarantees. Your child's privacy and the confidentiality of your child's data are very important to us and we will make every effort to protect them. These efforts are described in the section below called "What about privacy and confidentiality?"

Will I be told about new information that may affect my decision to participate?

During the course of the study, you will be informed of any significant new research findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about permitting your child to continuing in the study. If new information is provided to you, your consent to permit your child to continue participating in this study may be re-obtained.

Are there benefits to taking part in the research?

Your child will not directly benefit from participation in the research.

It is hoped that knowledge gained from this research may benefit others with malocclusion (crooked teeth and jaw discrepancies) in the future.

Your child's orthodontic treatment will in no way be affected if you decline to participate in this study.

What other options are there?

You have the option to not participate in this study.

What about privacy and confidentiality?

The people who will know that your child is a research subject are members of the research team, and if appropriate, your child's physicians and nurses. No information about your child, or provided by you or your child, during the research, will be disclosed to others without your written permission, except if necessary to protect your rights or welfare (for example, if you are

Appendix E (Continued)

injured and need emergency care or when the UIC Office for the Protection of Research Subjects monitors the research or consent process) or if required by law.

Study information which identifies your child and the consent form signed by you will be looked at and/or copied for examining the research by:

- The research team
- The University of Illinois at Chicago Institutional Review Board
- State of Illinois Auditors

A possible risk of the research is that your child's participation in the research or information about your child and your child's health might become known to individuals outside the research.

All of your child's personal information will be removed from the data by the research team immediately upon collection of the complete set of records. This information will be destroyed and the records will not link to your child in any way. Your child's records will be assigned a random code that will not link to your child in any way. All records will be stored on a password protected server at the University of Illinois at Chicago College of Dentistry, Department of Orthodontics. Genetics data will be stored at in a secure freezer and secure password protected computer at the University of Illinois at Chicago DNA Services Facility. All personal information will be removed from all records, including genetic information, prior to analysis, and will in no way be linked to you.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your child's identity.

What are the costs for participating in this research?

There are no costs to you or your child for participating in this research.

Will I be reimbursed for any of my expenses or paid for my participation in this research?

You will receive compensation for participation in the study. If your child completes the study, you will receive a total of $20.00. You will receive your payment immediately after your child's visit in person.

Can I withdraw or be removed from the study?

If you decide to permit your child to participate, you are free to withdraw your consent and discontinue participation at any time without affecting your future care at UIC.

You have the right to leave a study at any time without penalty.

The researchers and sponsor also have the right to stop your child's participation in this study without your consent if:

- They believe it is in your child's best interests;

Appendix E (Continued)

In the event you withdraw your child or are asked to leave the study, you will still be compensated as described above.

Who should I contact if I have questions?

Contact the researcher Dr. Jennifer Caplin at 312-996-0230 or email address, jcapli3@uic.edu:

- If you have any questions about this study or your part in it,
- If you feel you have had a research-related injury (or a bad reaction to the study treatment), and/or
- If you have questions, concerns or complaints about the research.

What are my rights as a research subject?

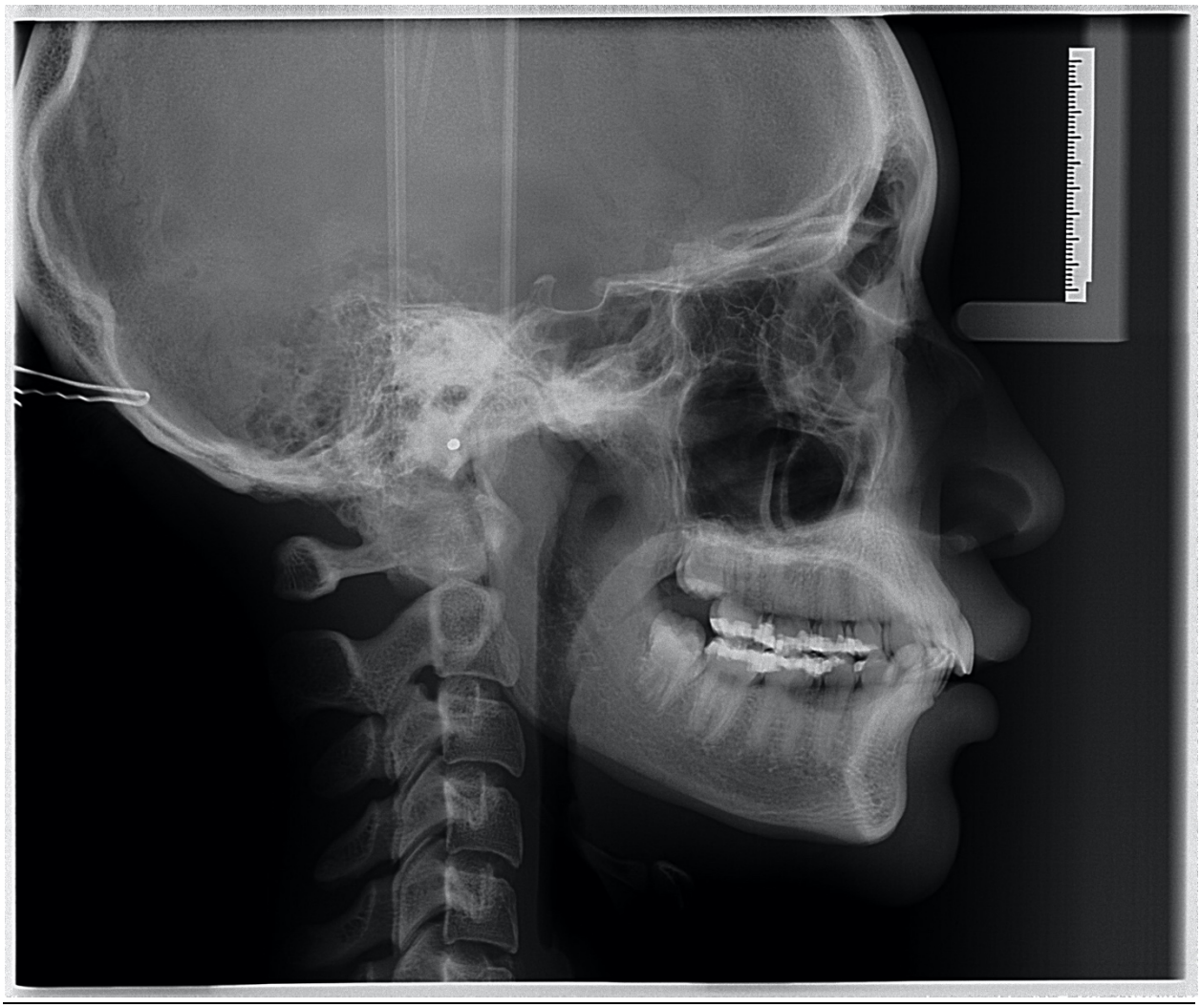
If you have questions about your child's rights as a research subject or concerns, complaints, or to offer input you may call the Office for the Protection of Research Subjects (OPRS) at 312-996-1711 or 1-866-789-6215 (toll-free) or e-mail OPRS at uicirb@uic.edu.

Signature of Subject or Legally Authorized Representative

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to permit my child to participate in this research. I will be given a copy of this signed and dated form.

Signature of Parent	Date
Printed Name of Parent	
Printed Name of Child	Age of Child
Signature of Person Obtaining Parental Permission	Date (must be same as subject's)
Printed Name of Person Obtaining Parental Permission	

APPENDIX F



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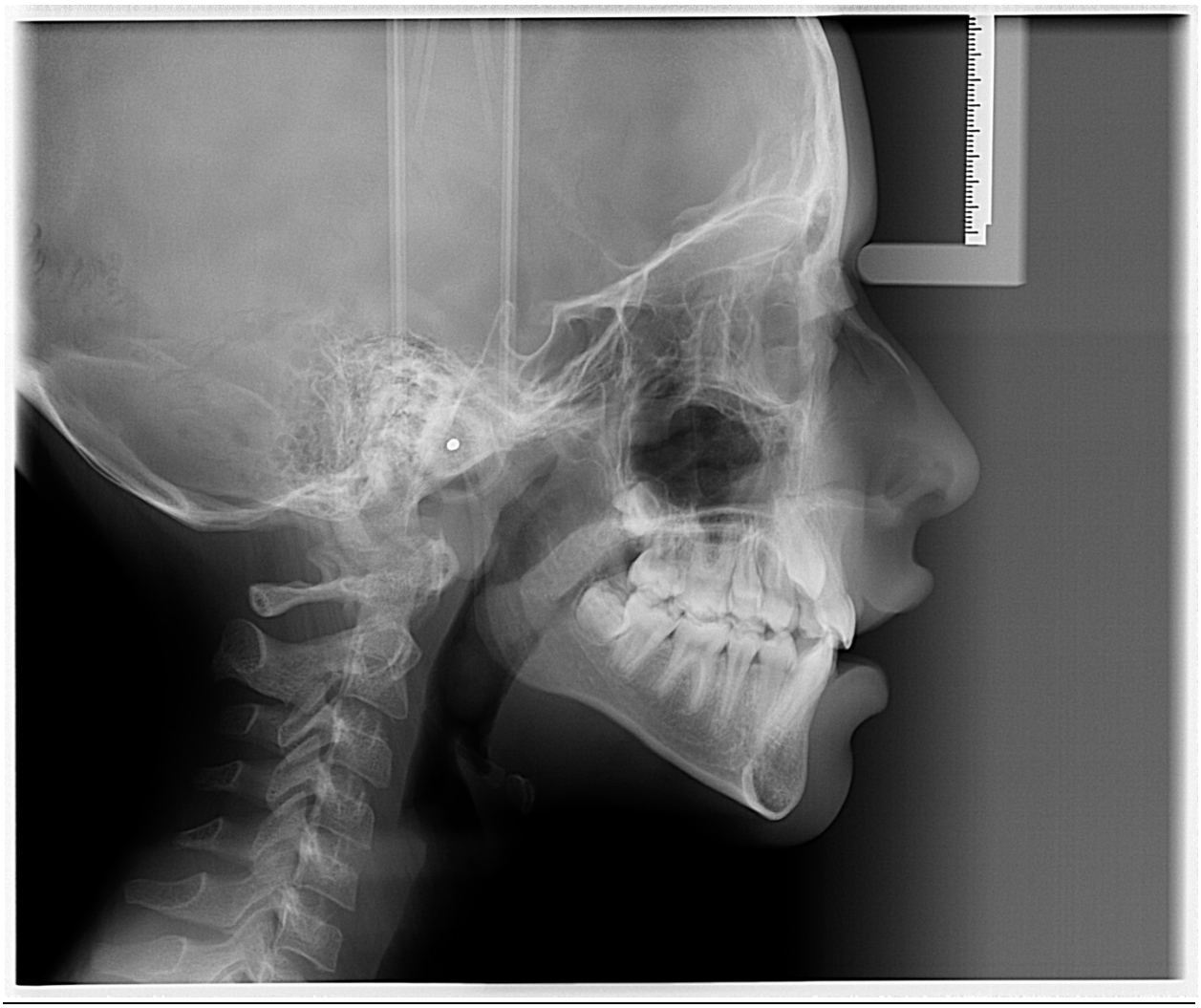

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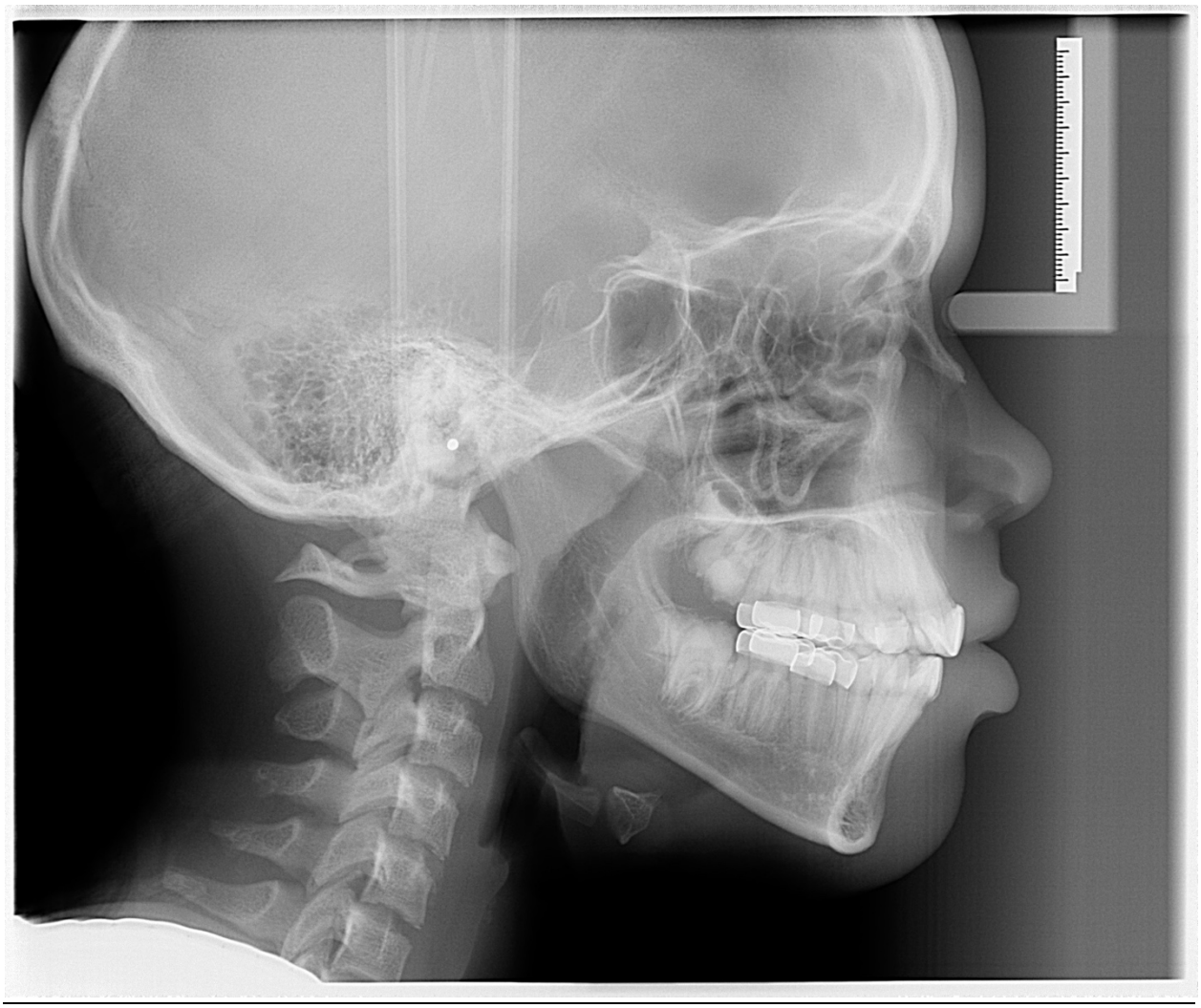

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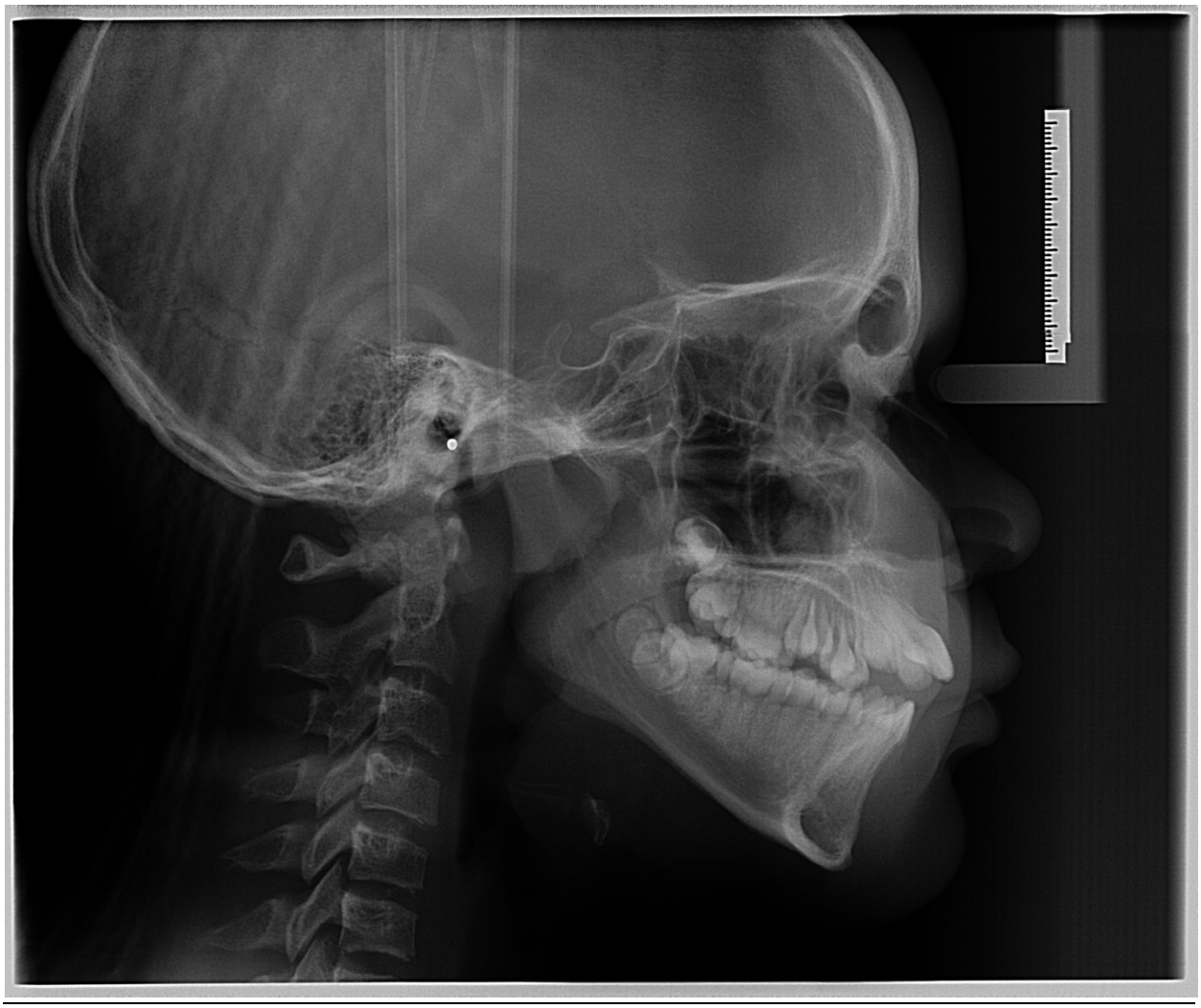

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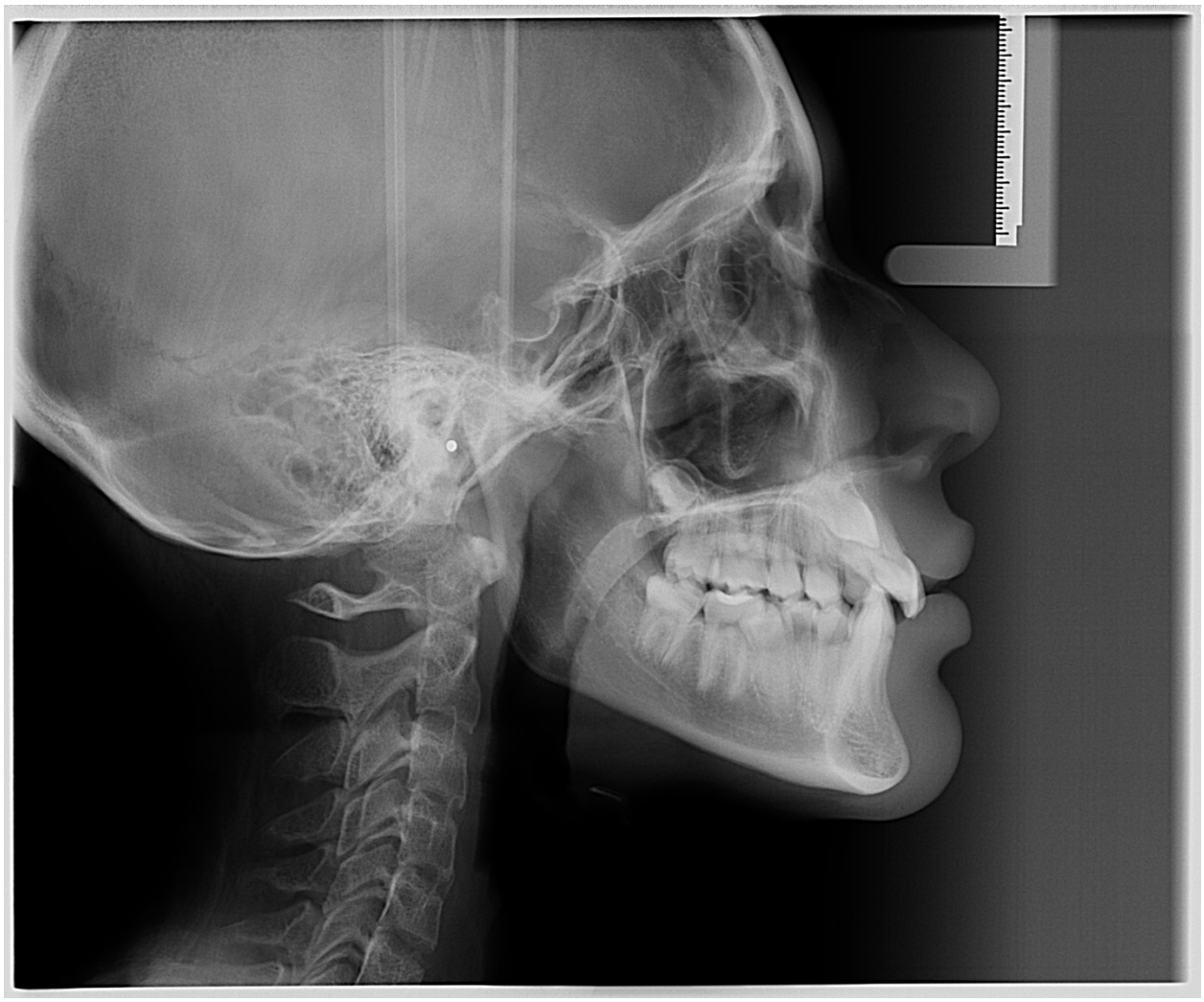

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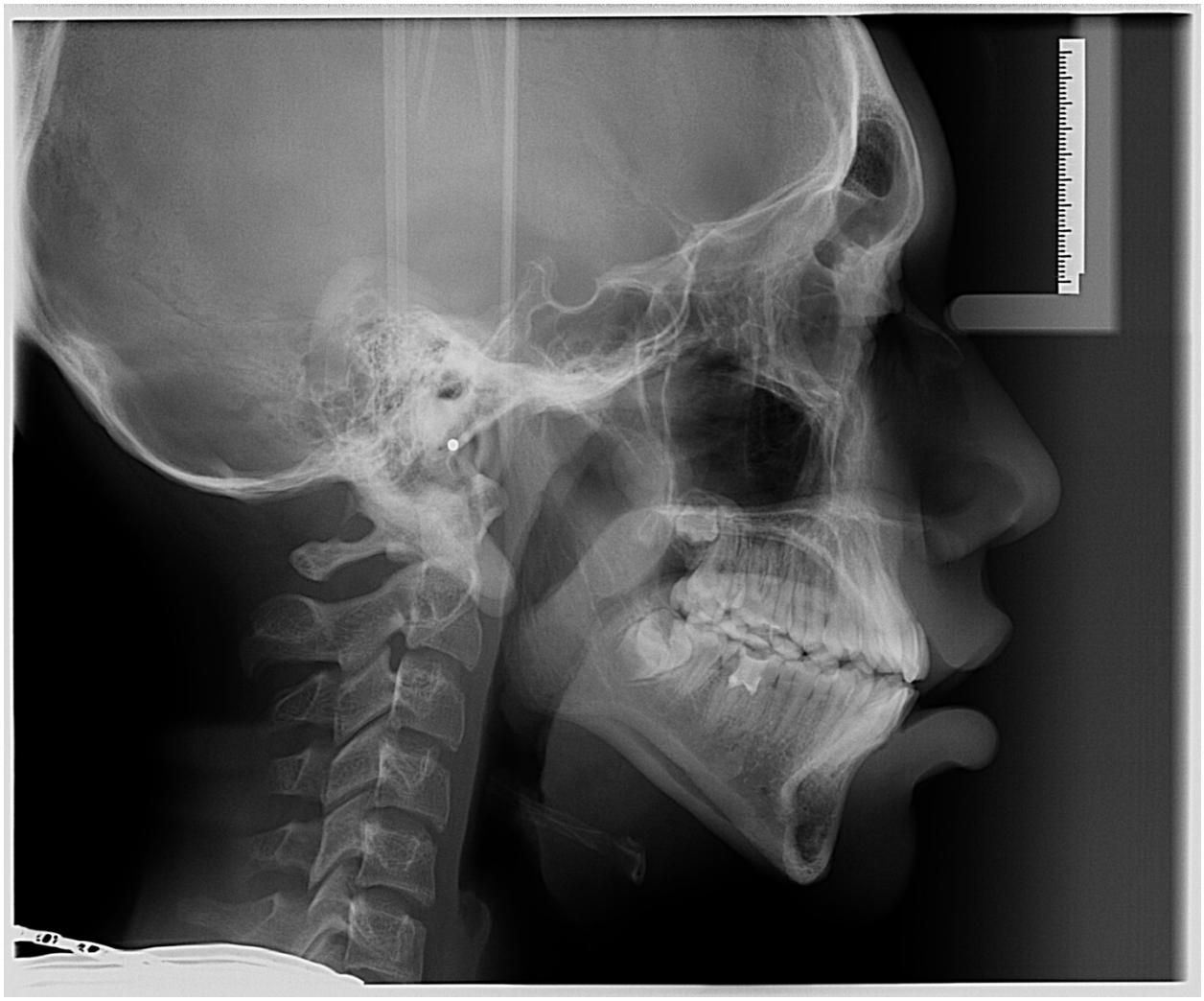

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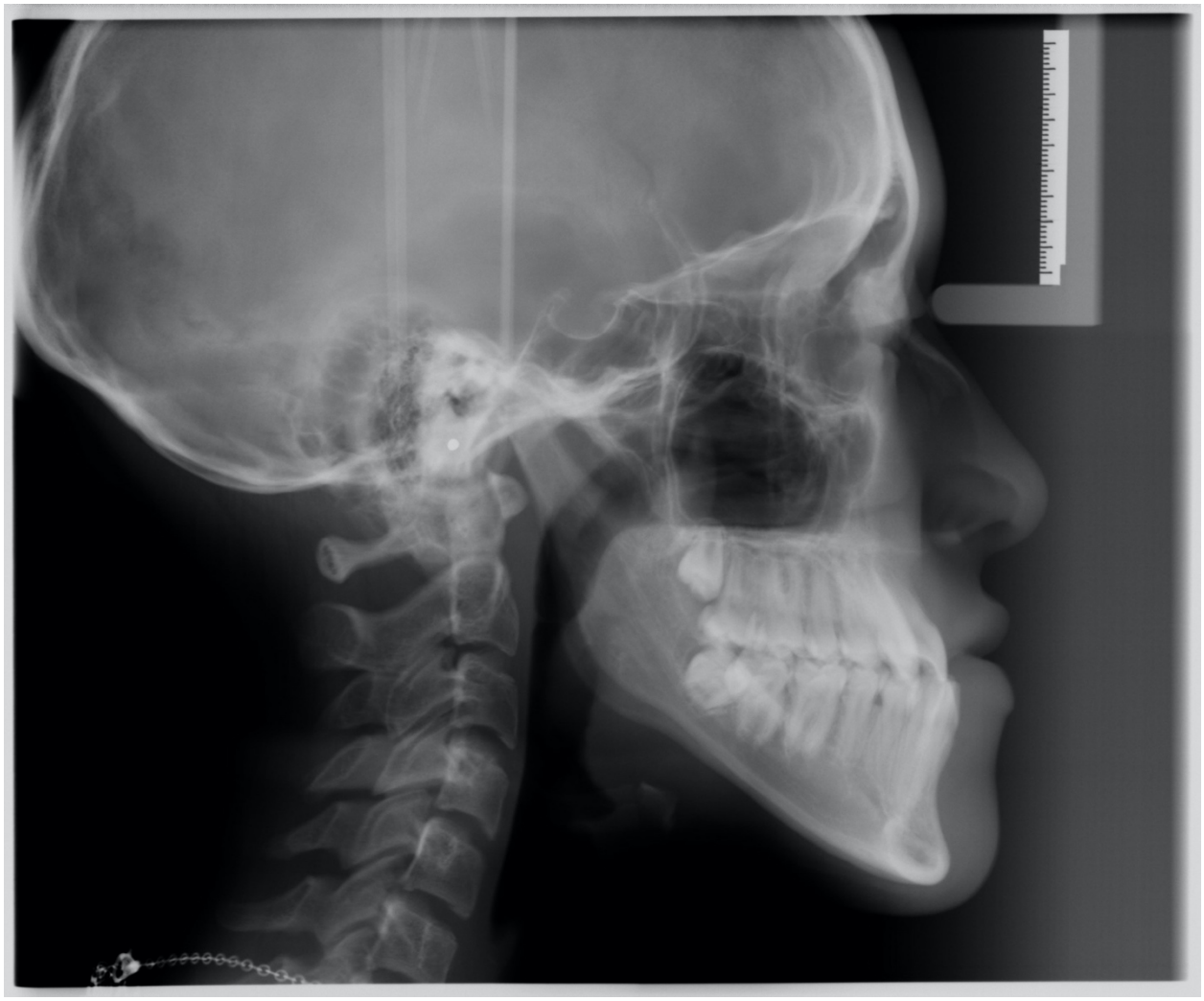

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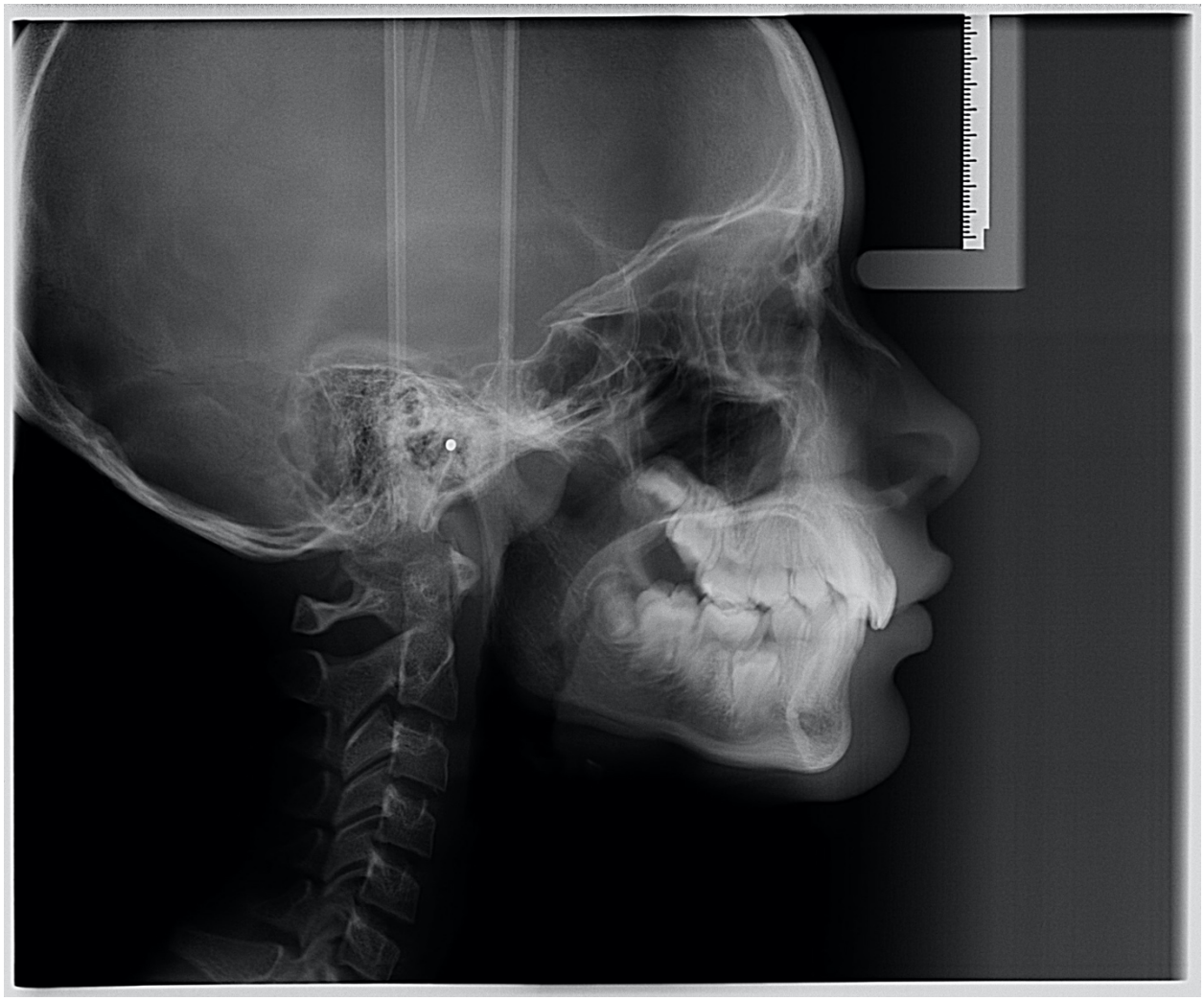

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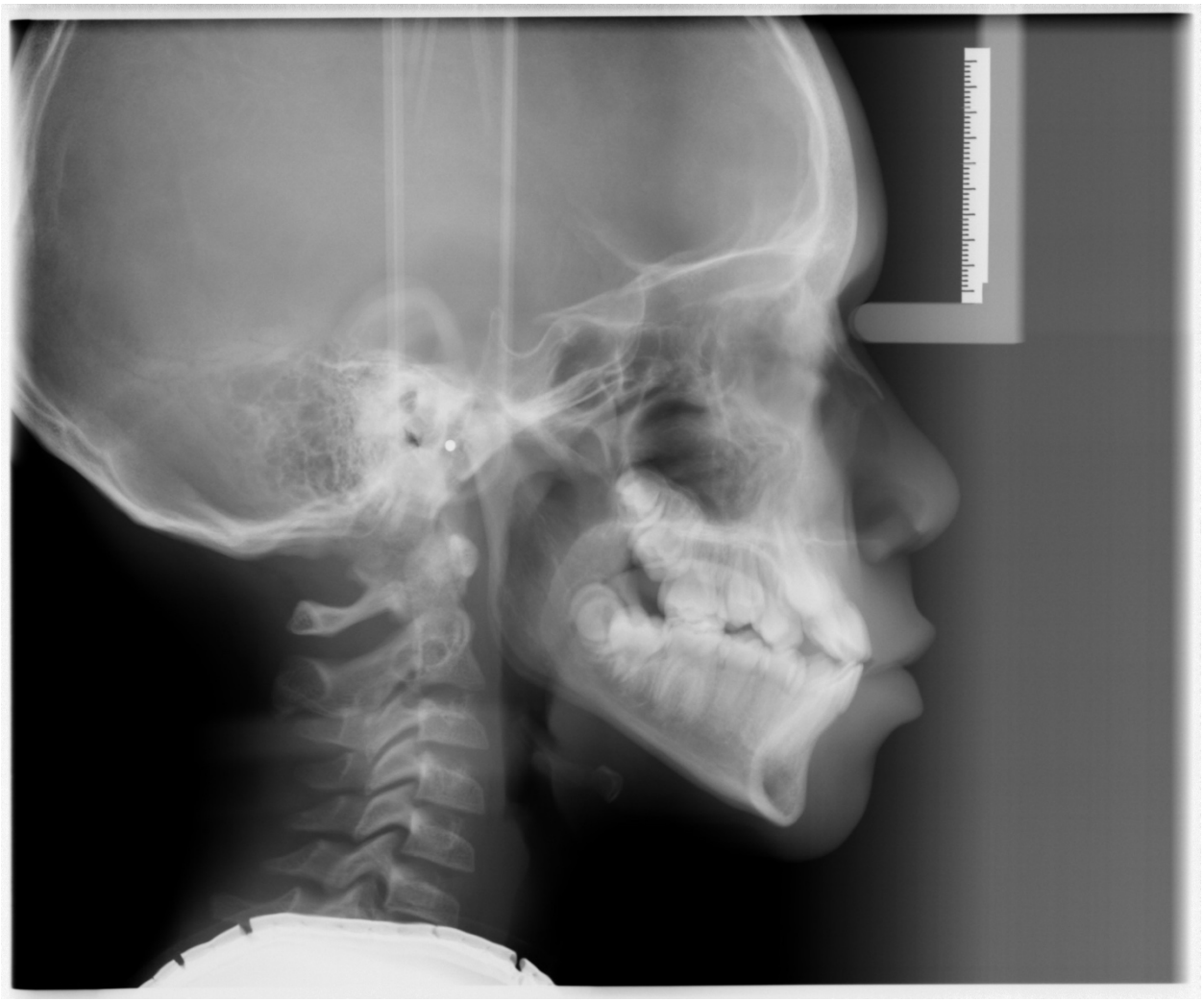

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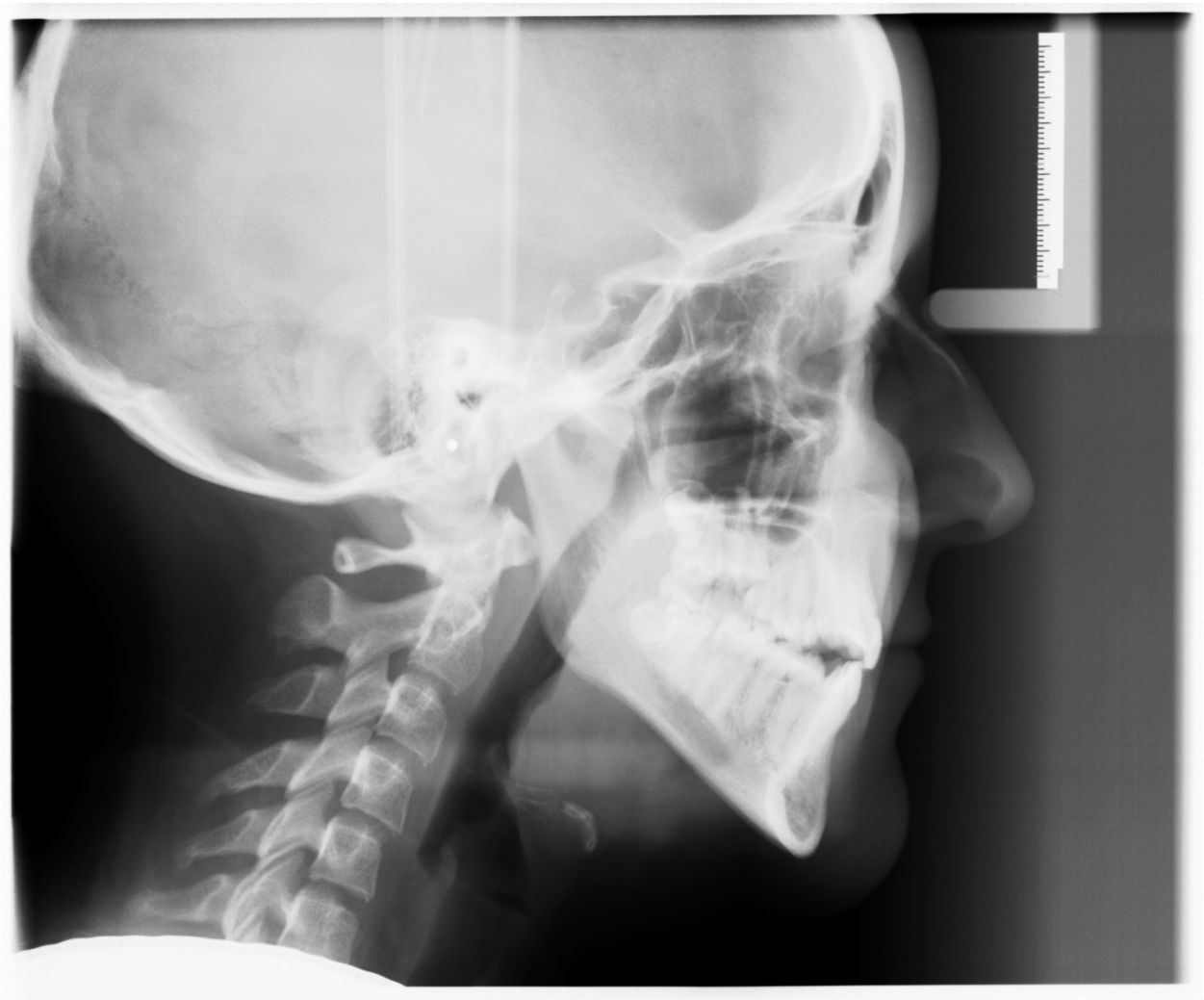

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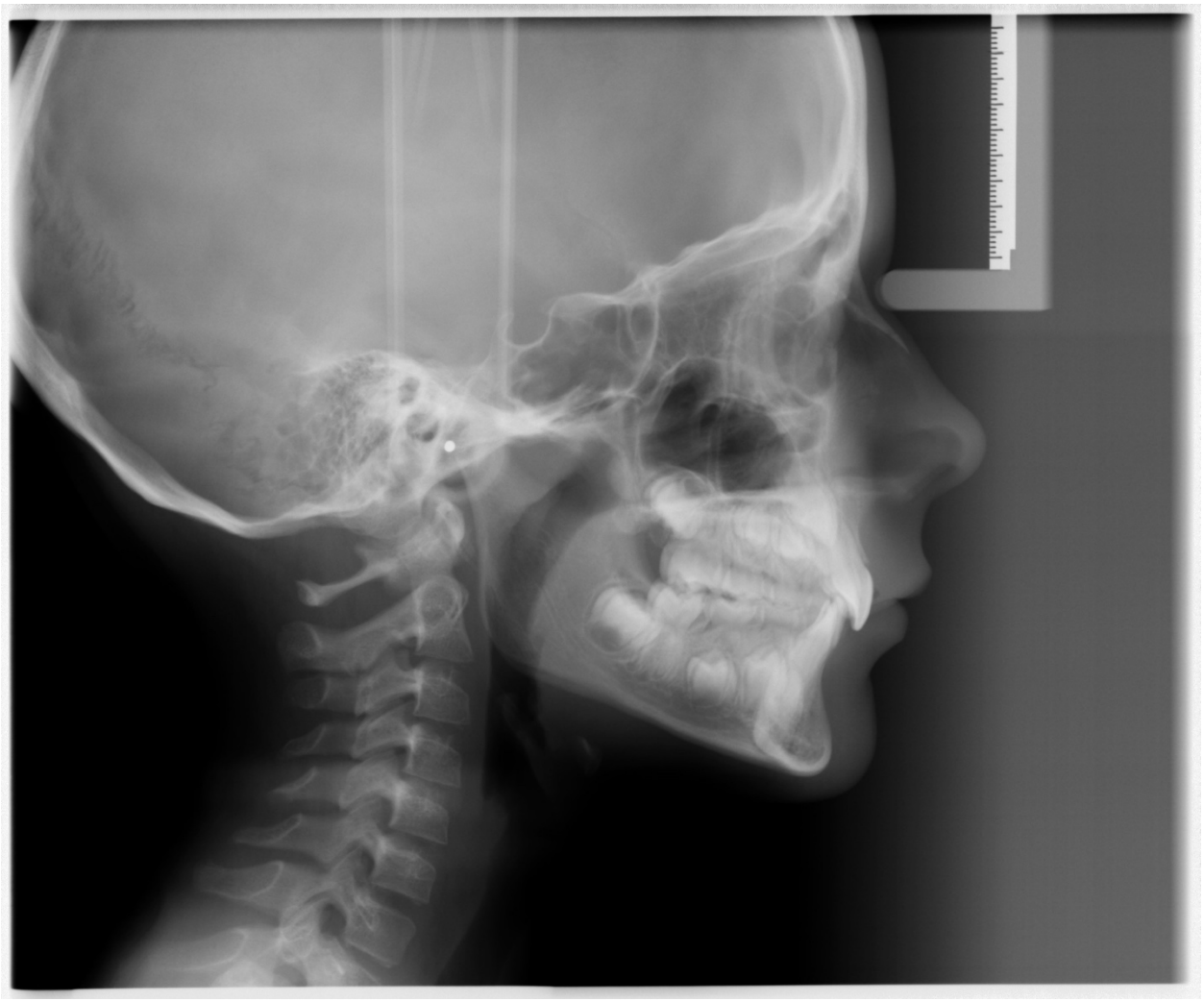

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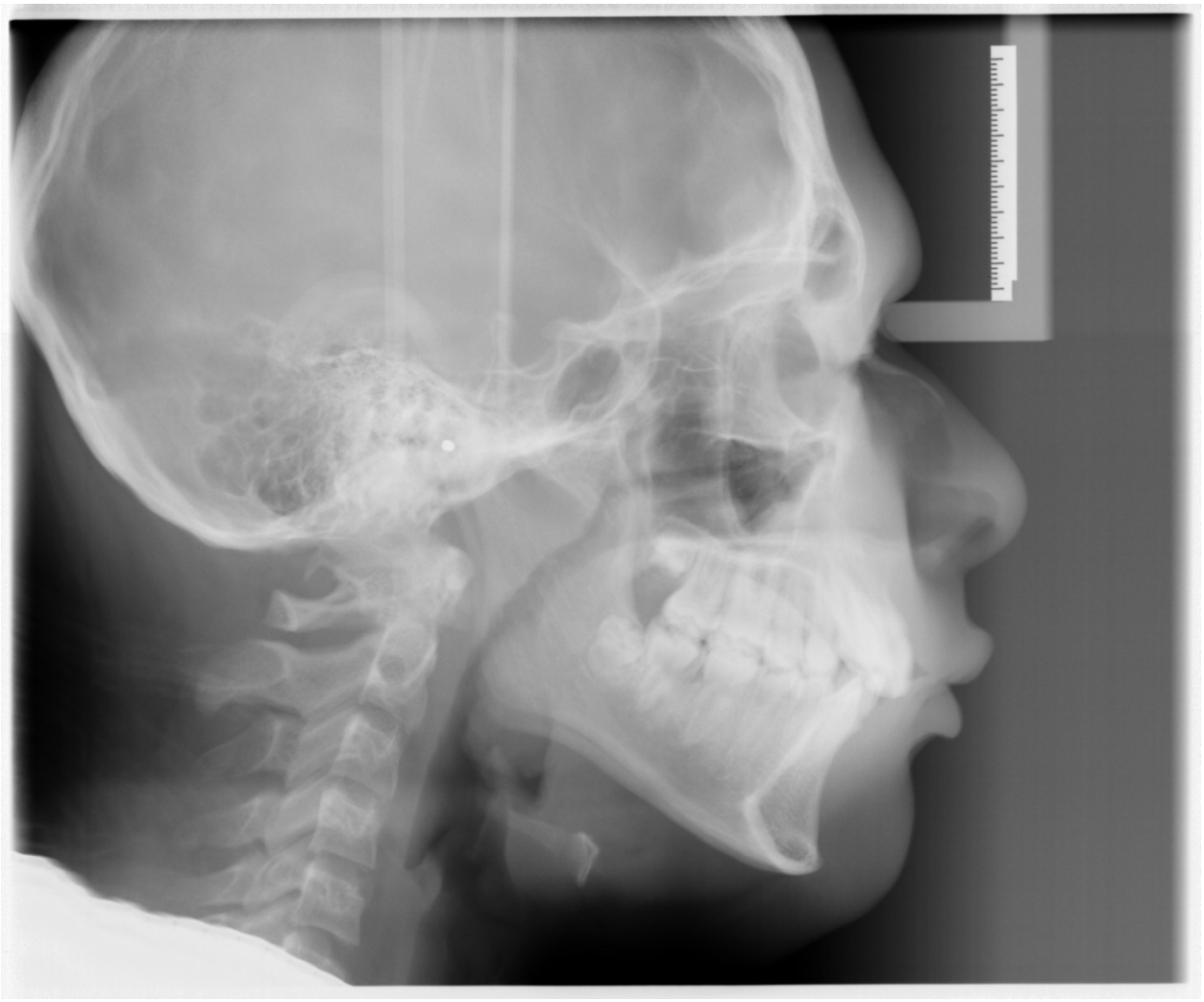

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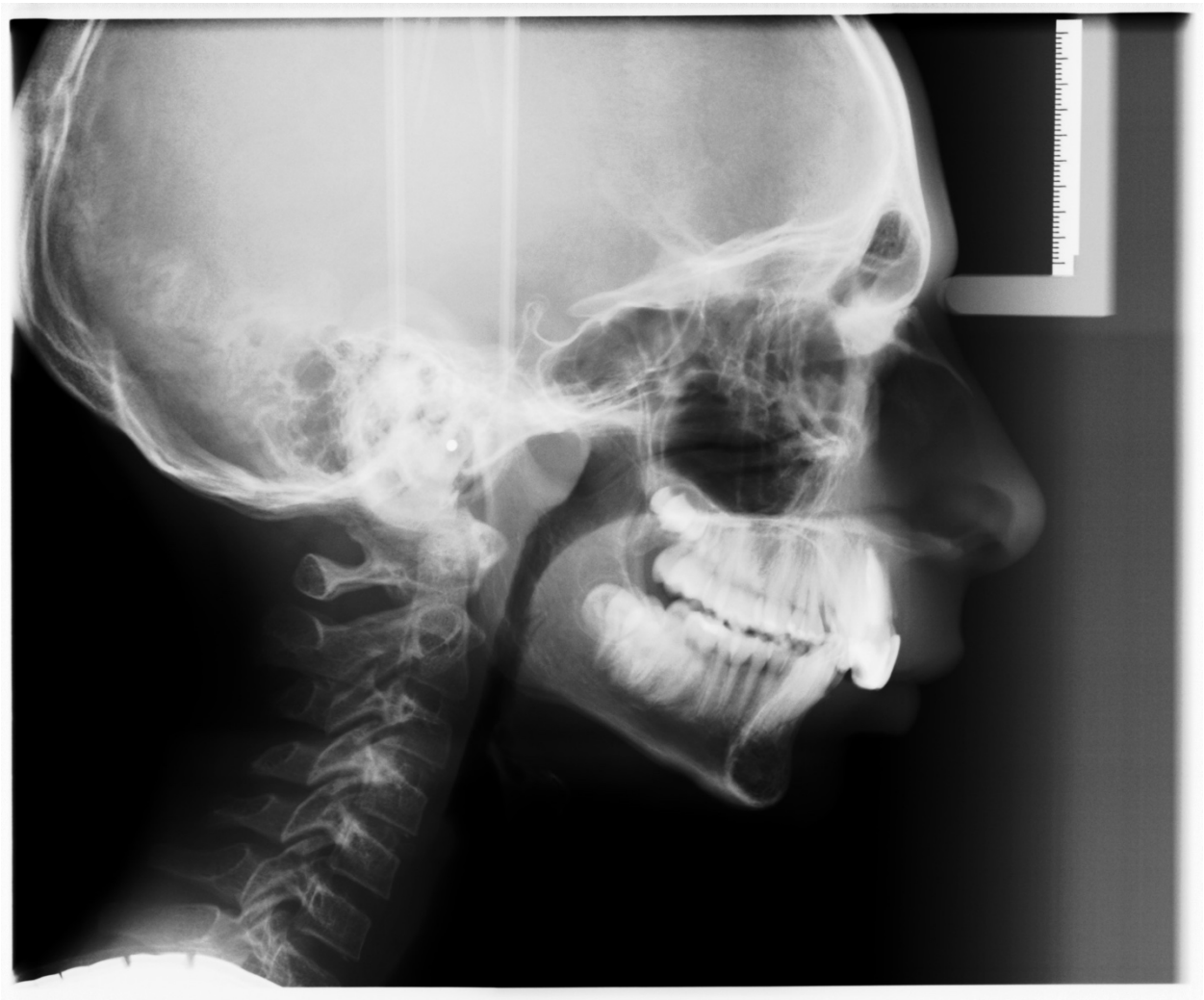

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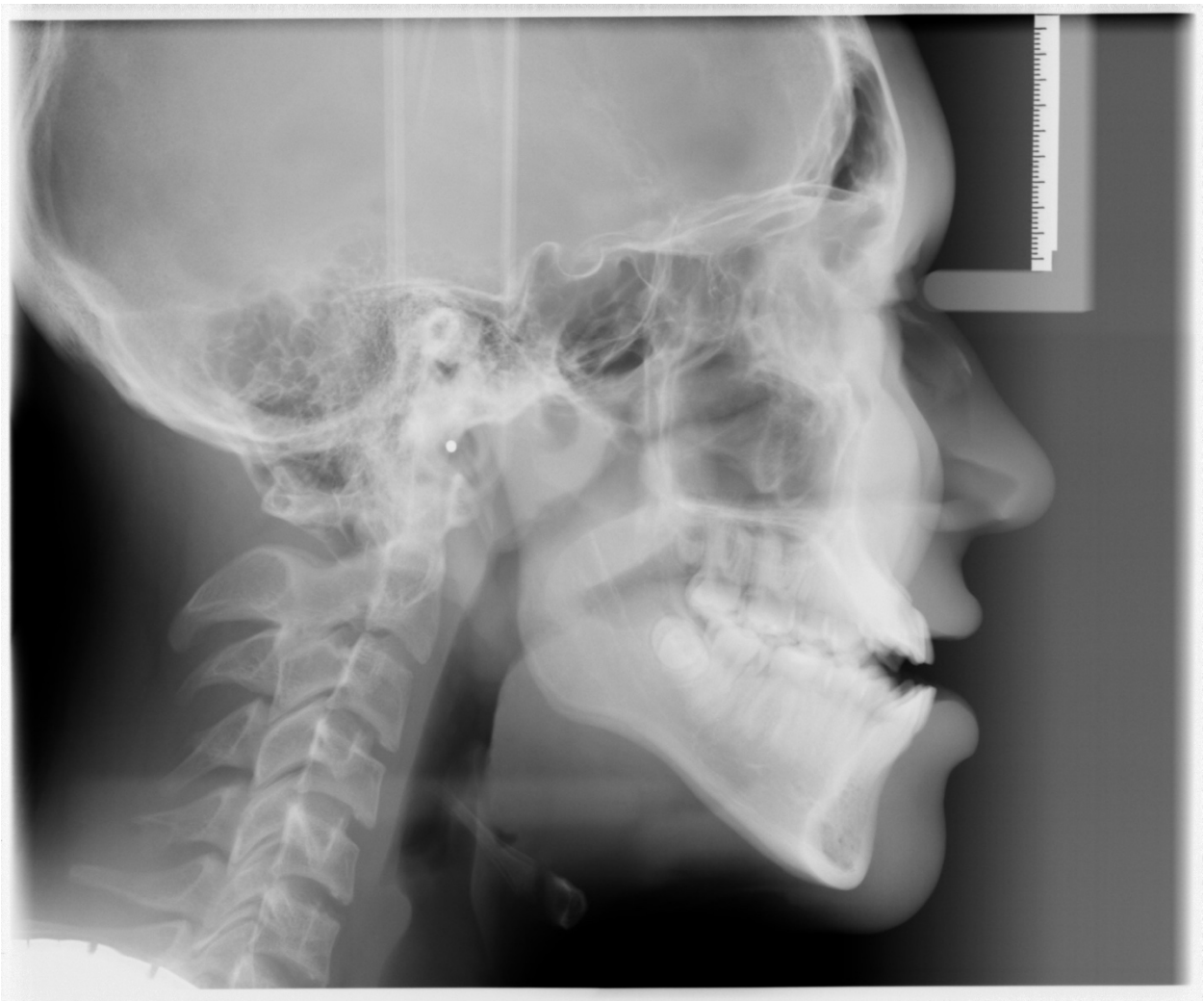

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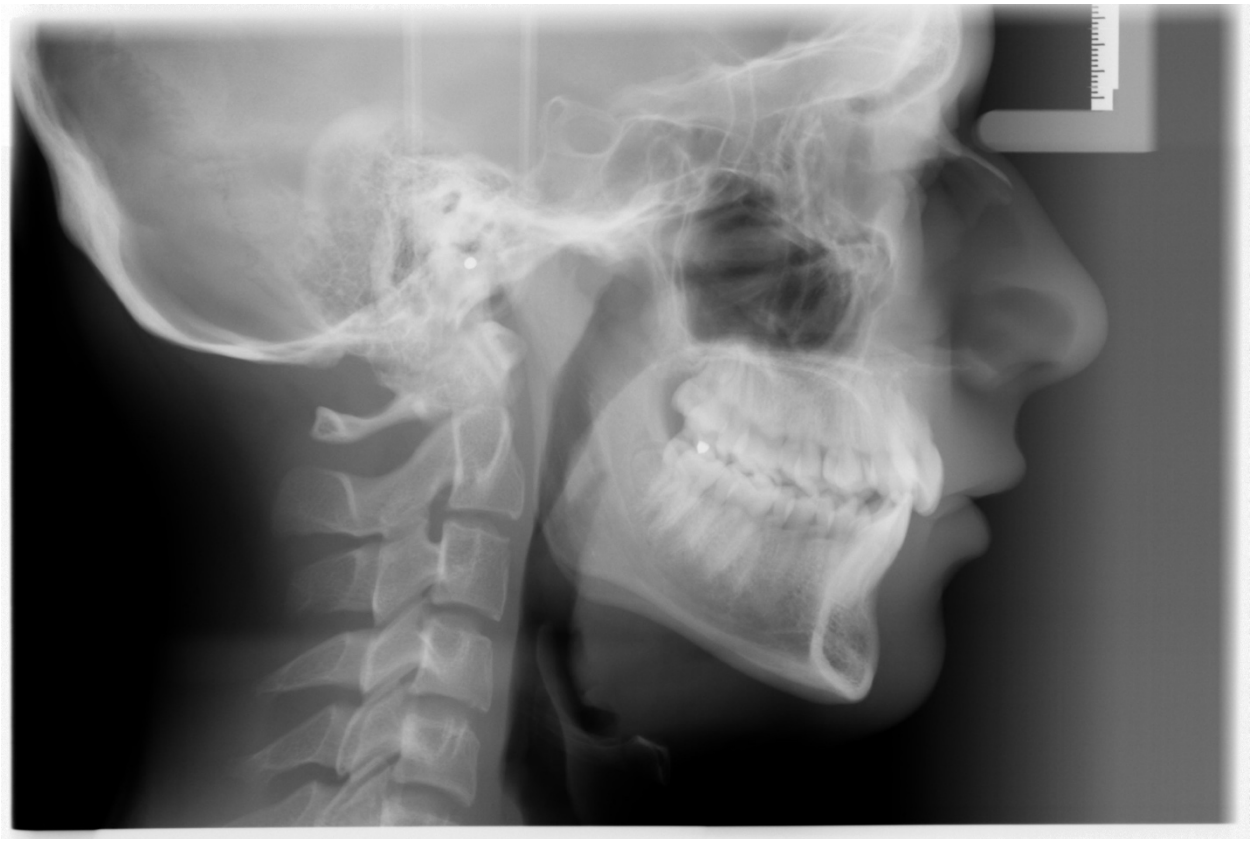

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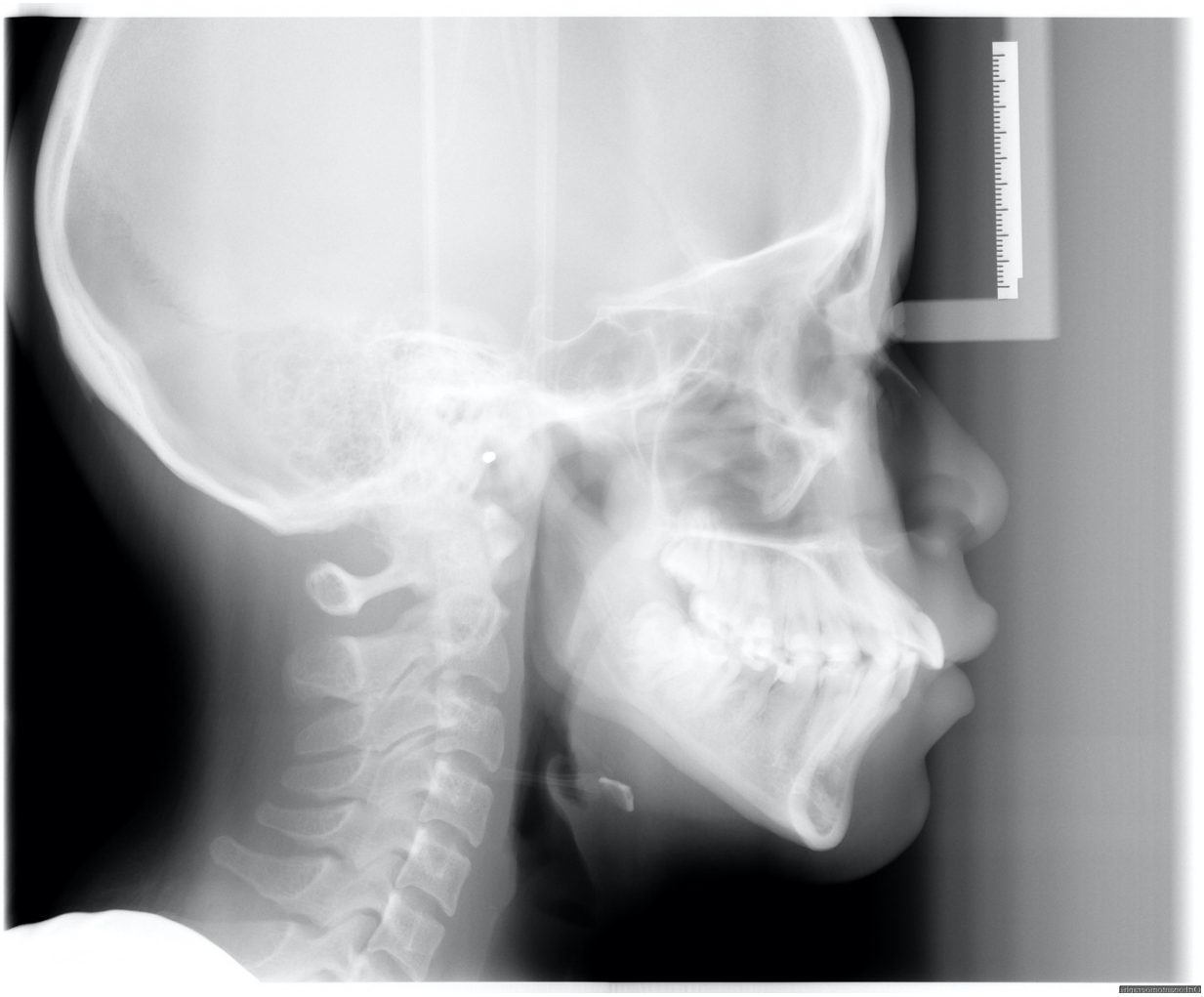

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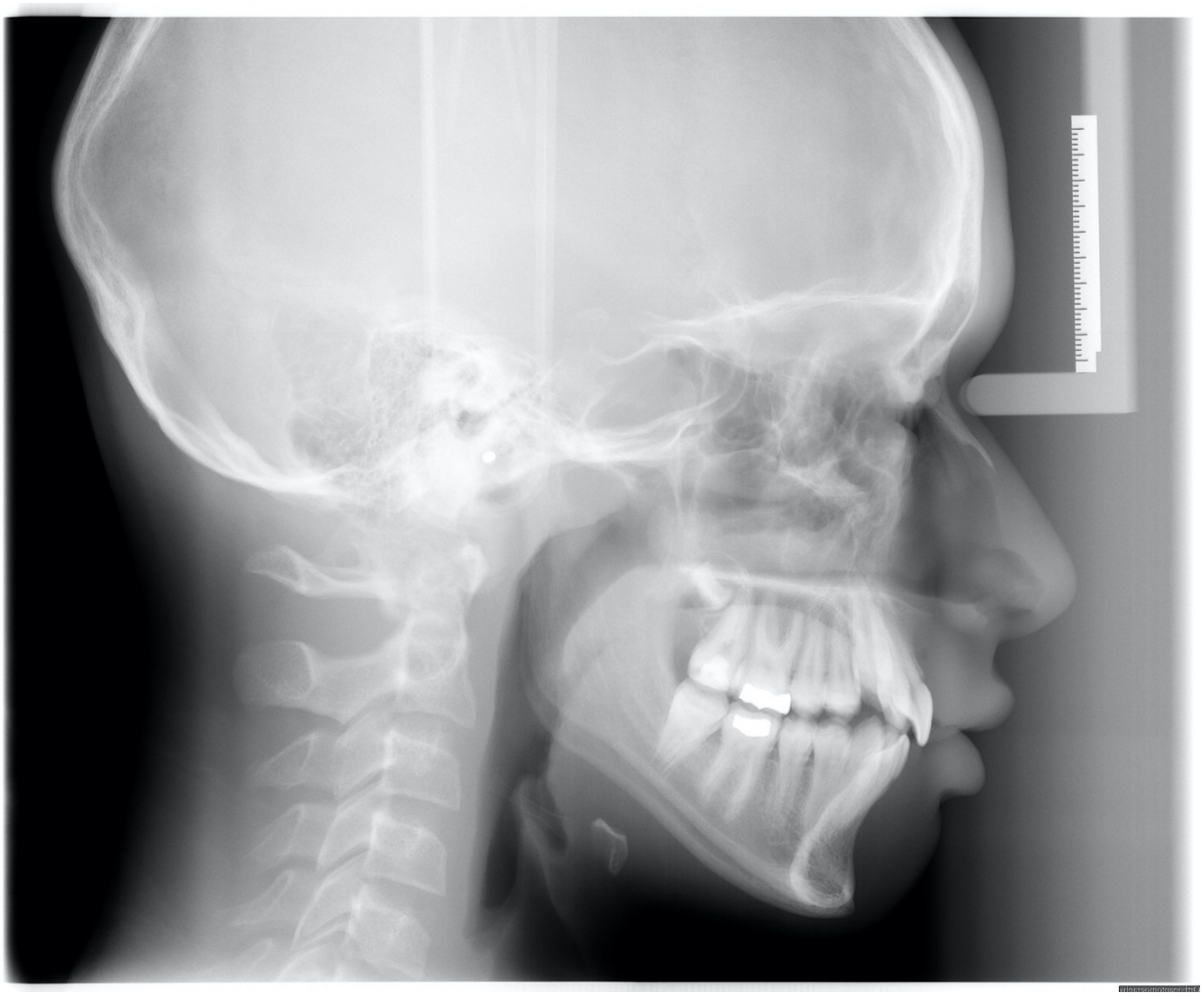

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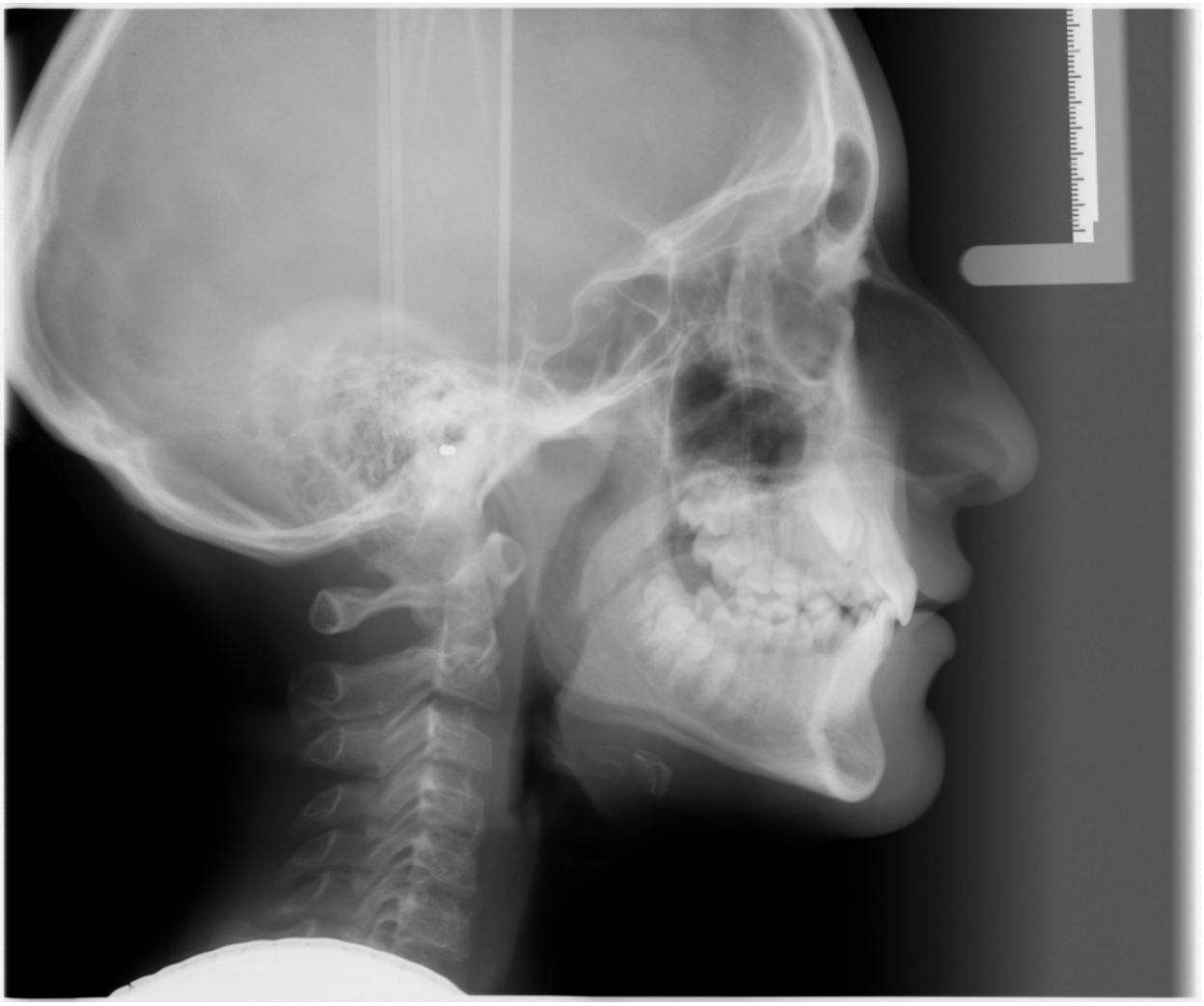

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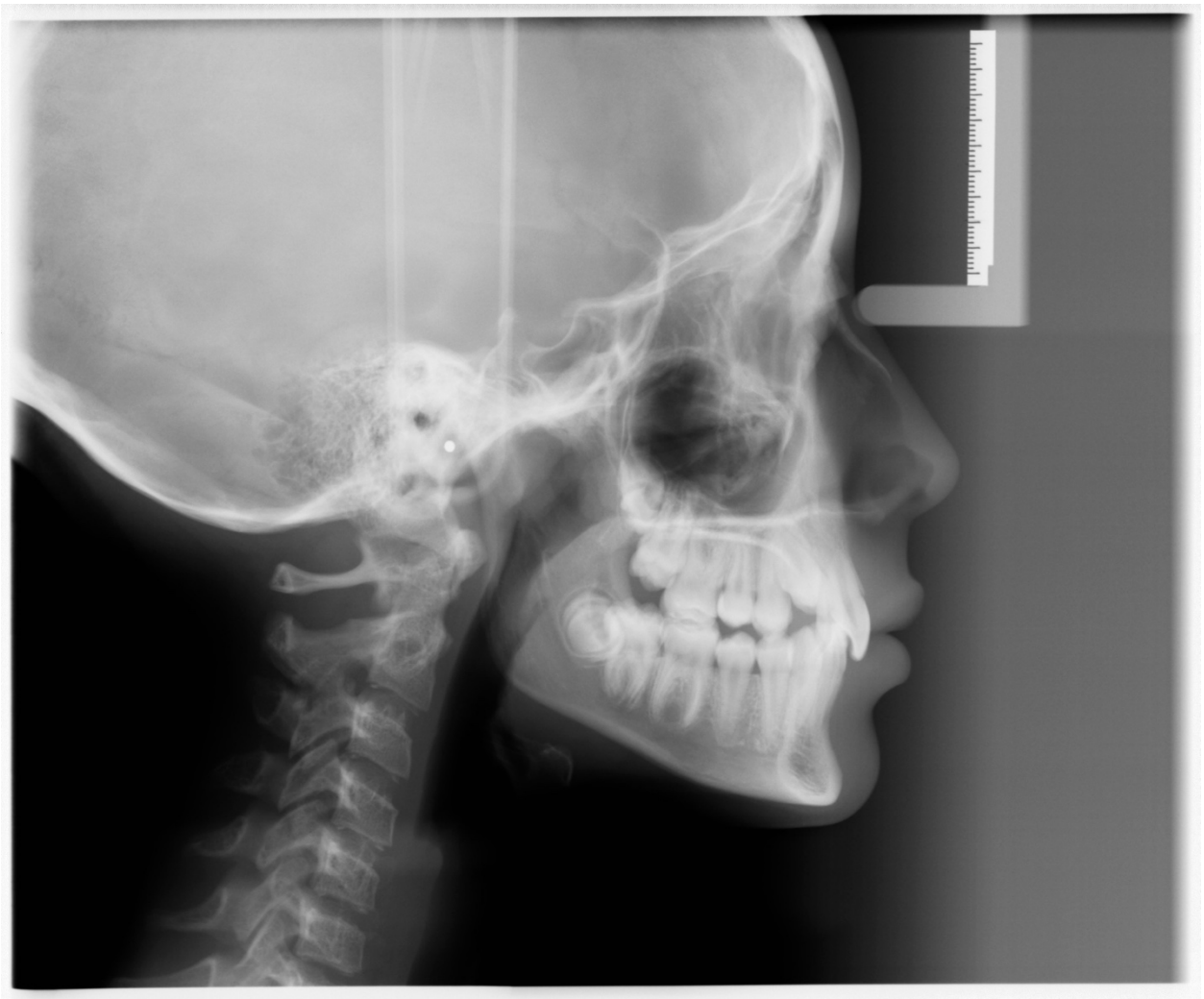

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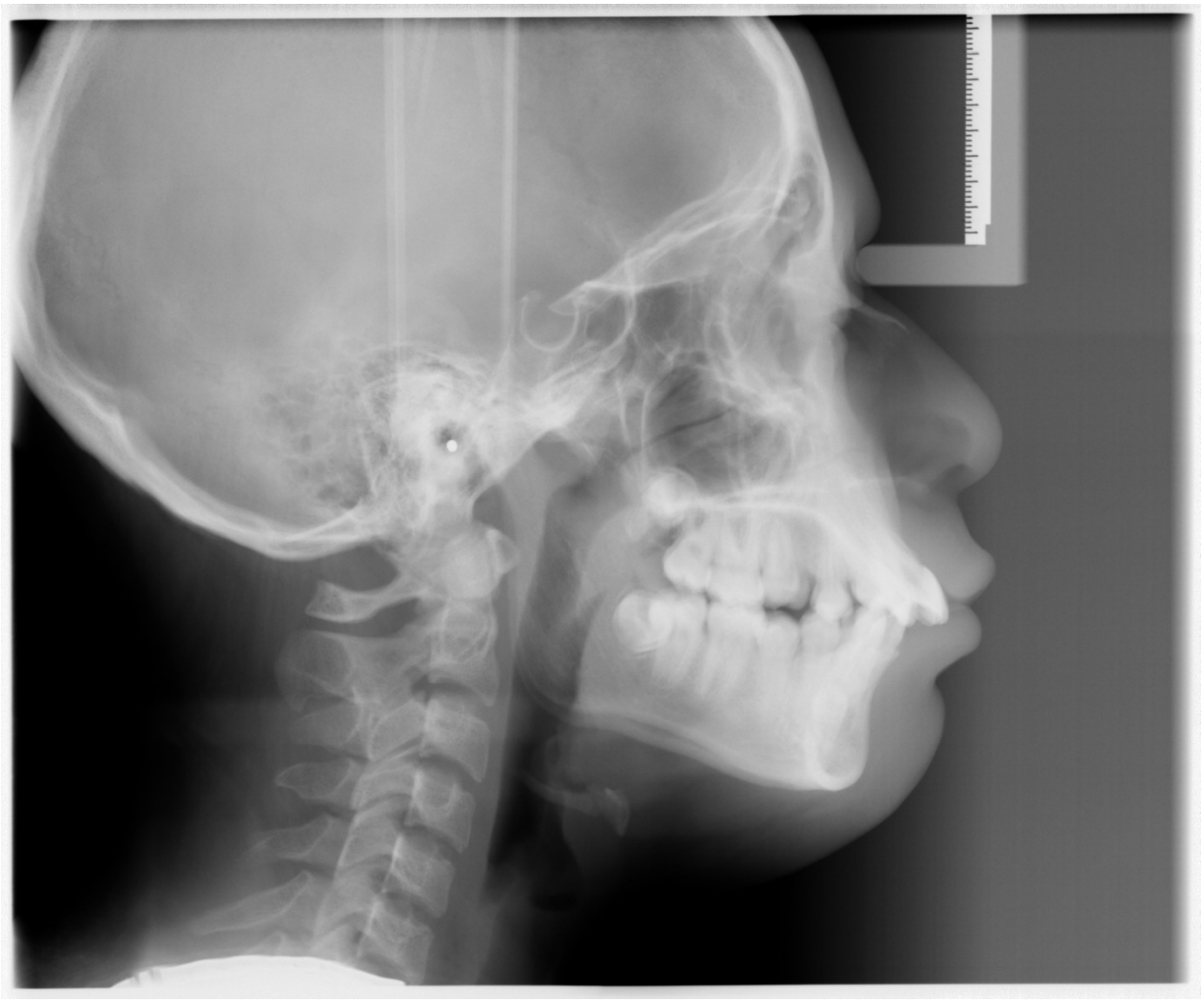

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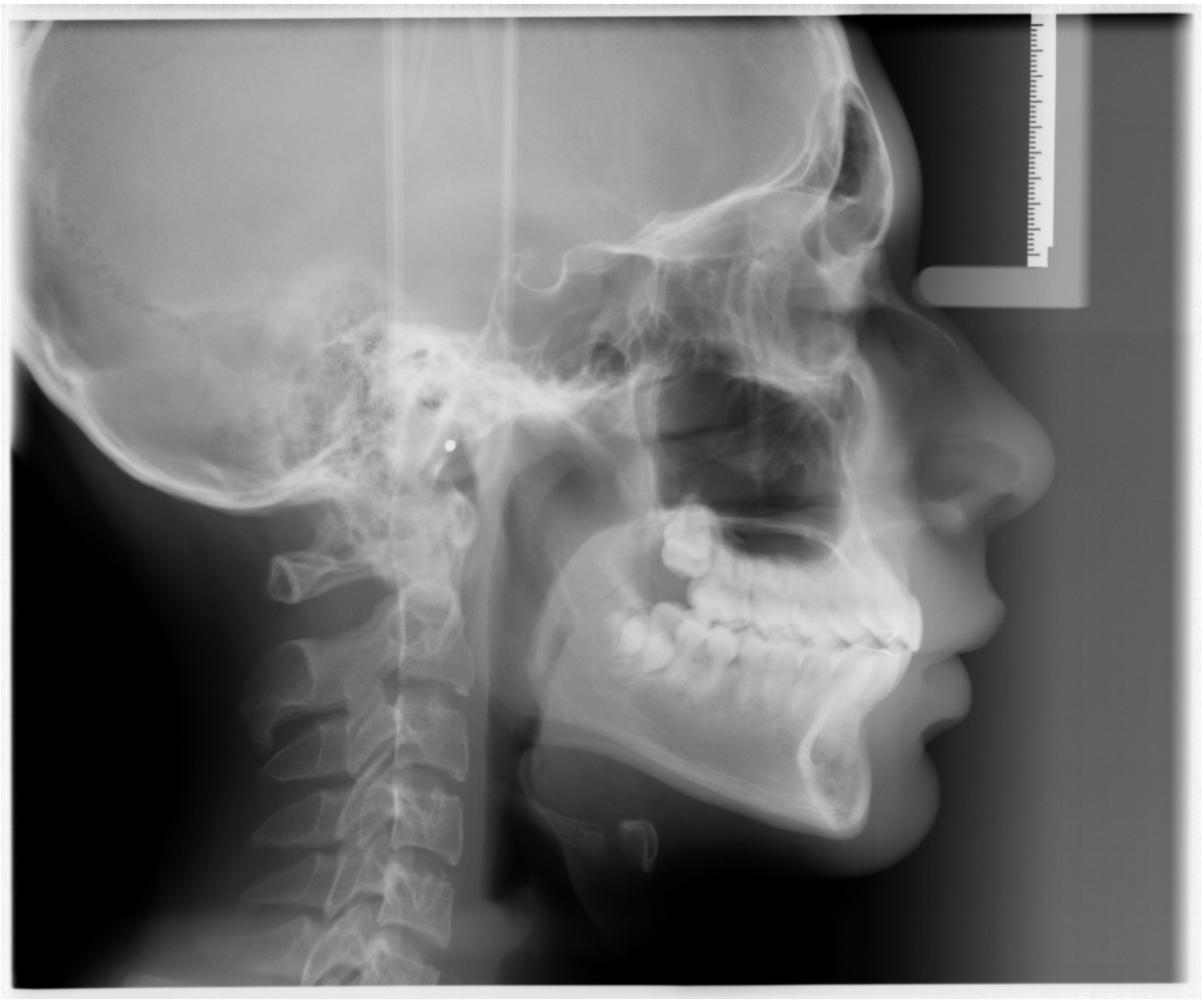

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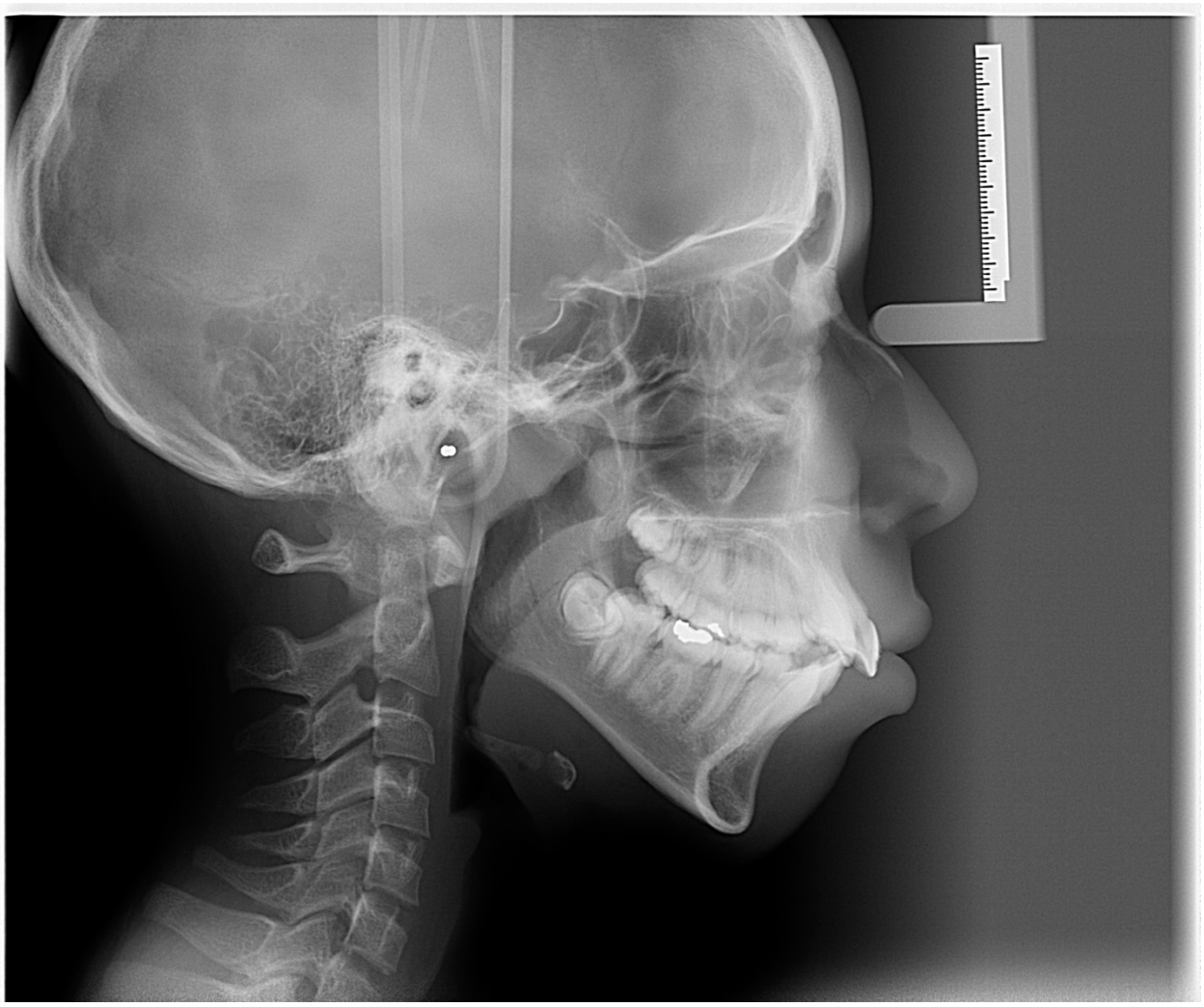

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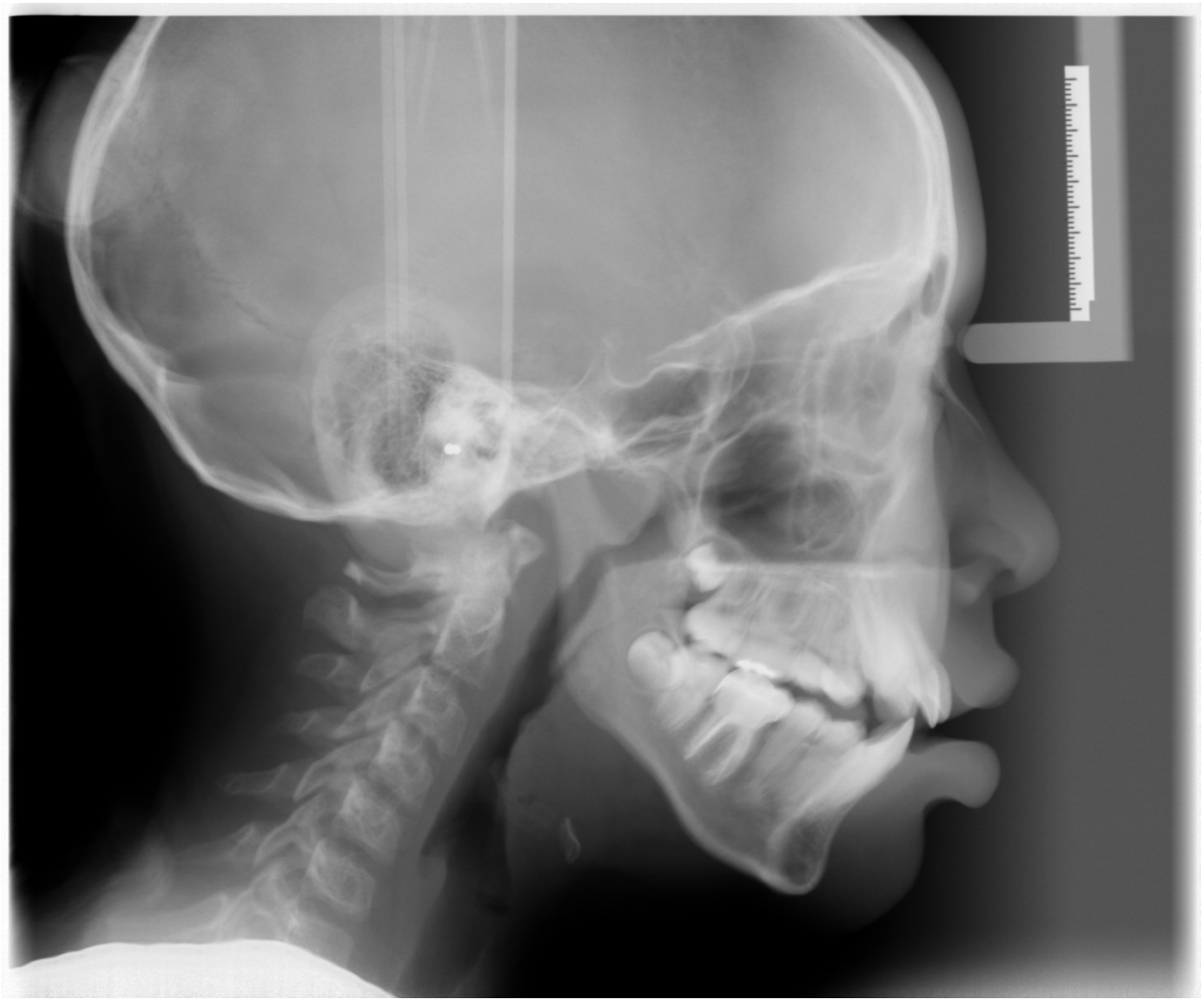

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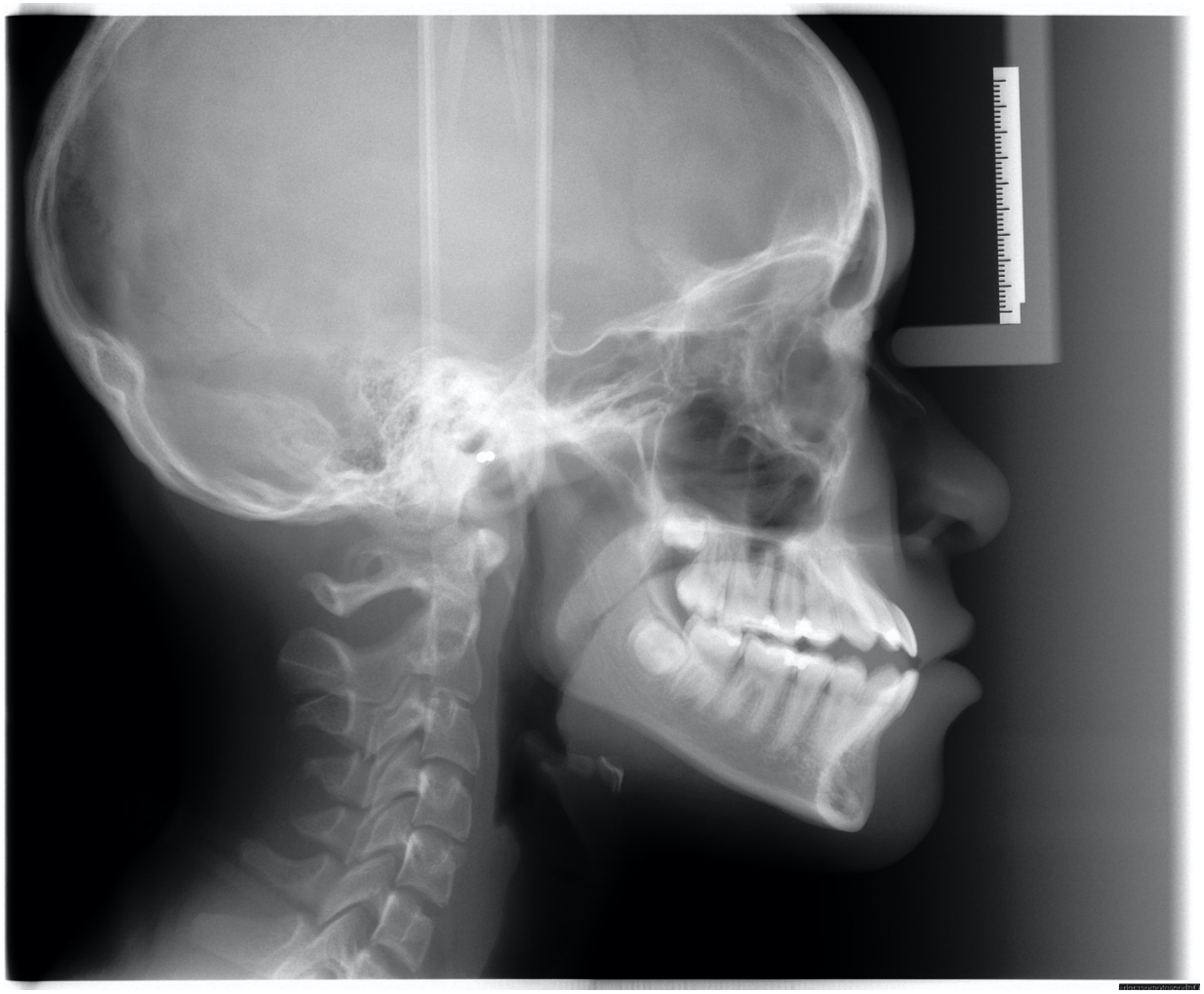

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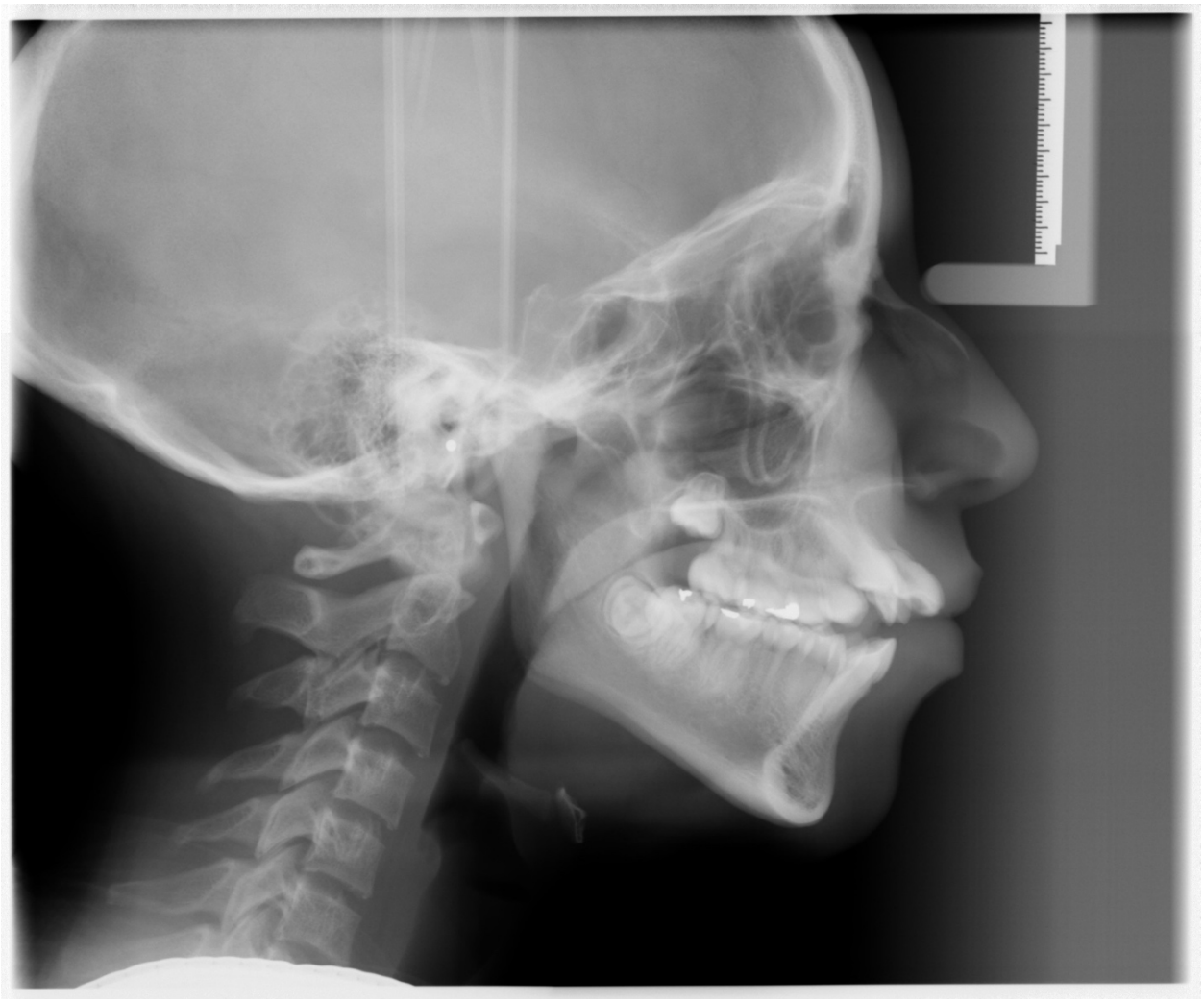

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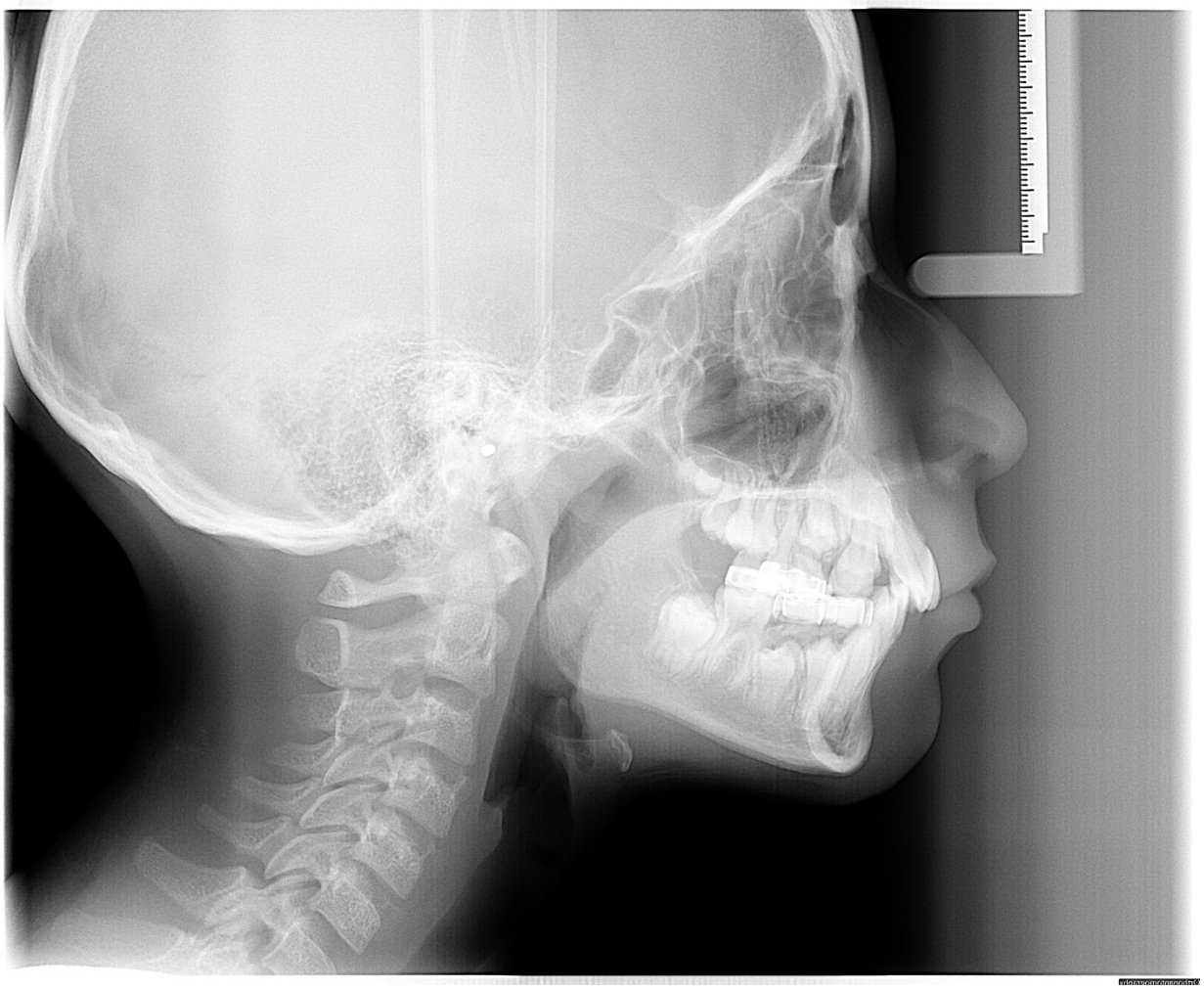

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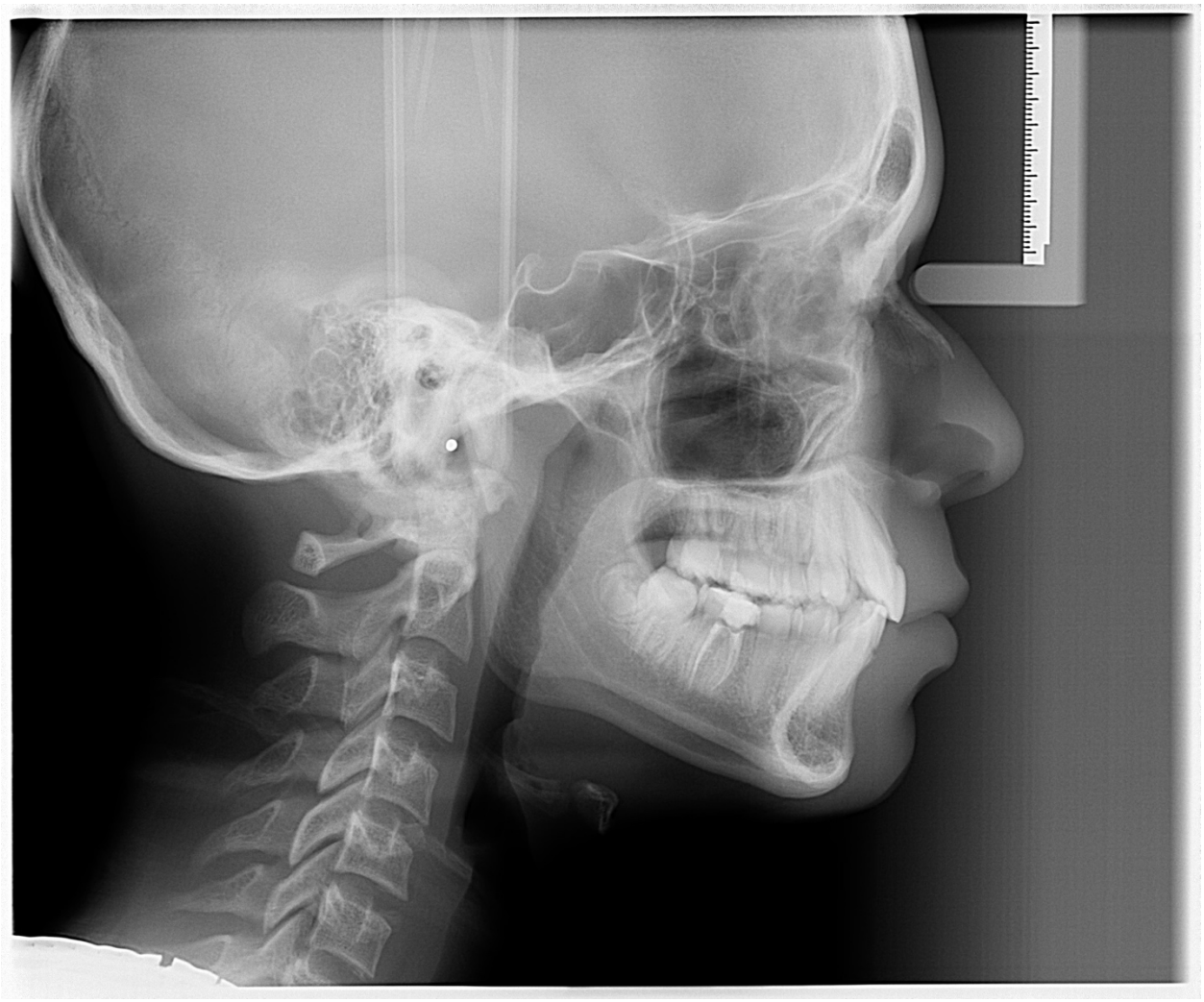

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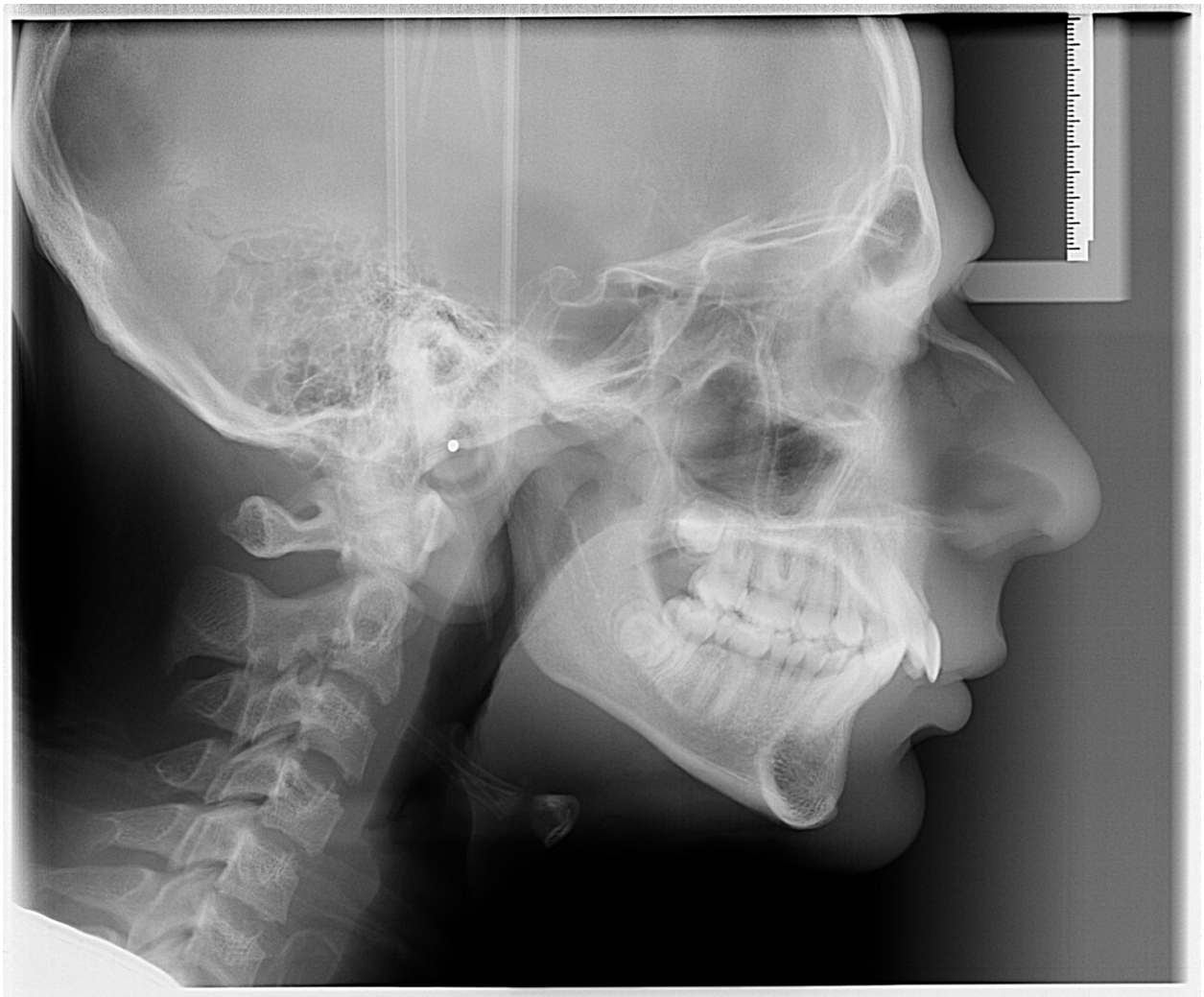

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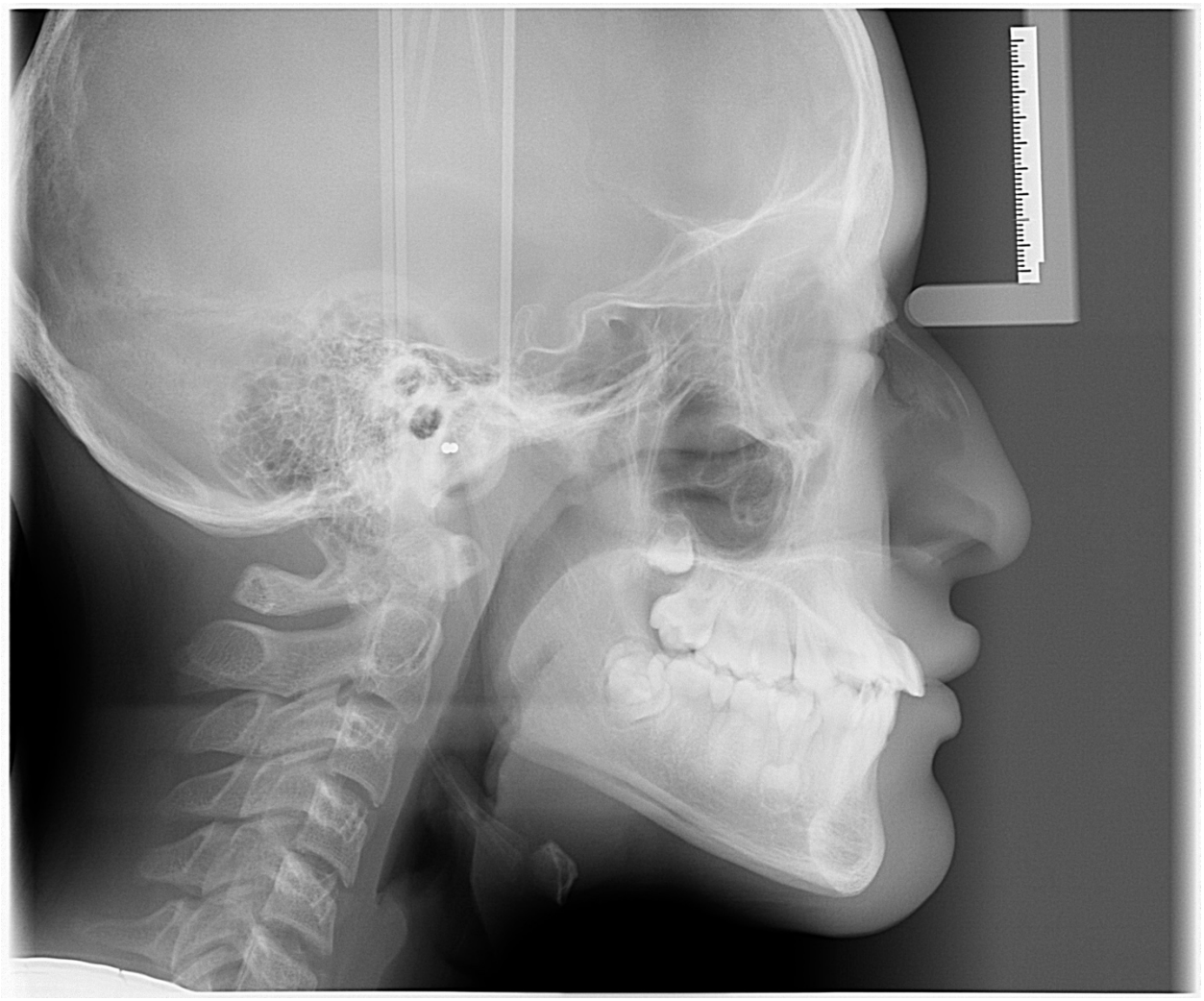

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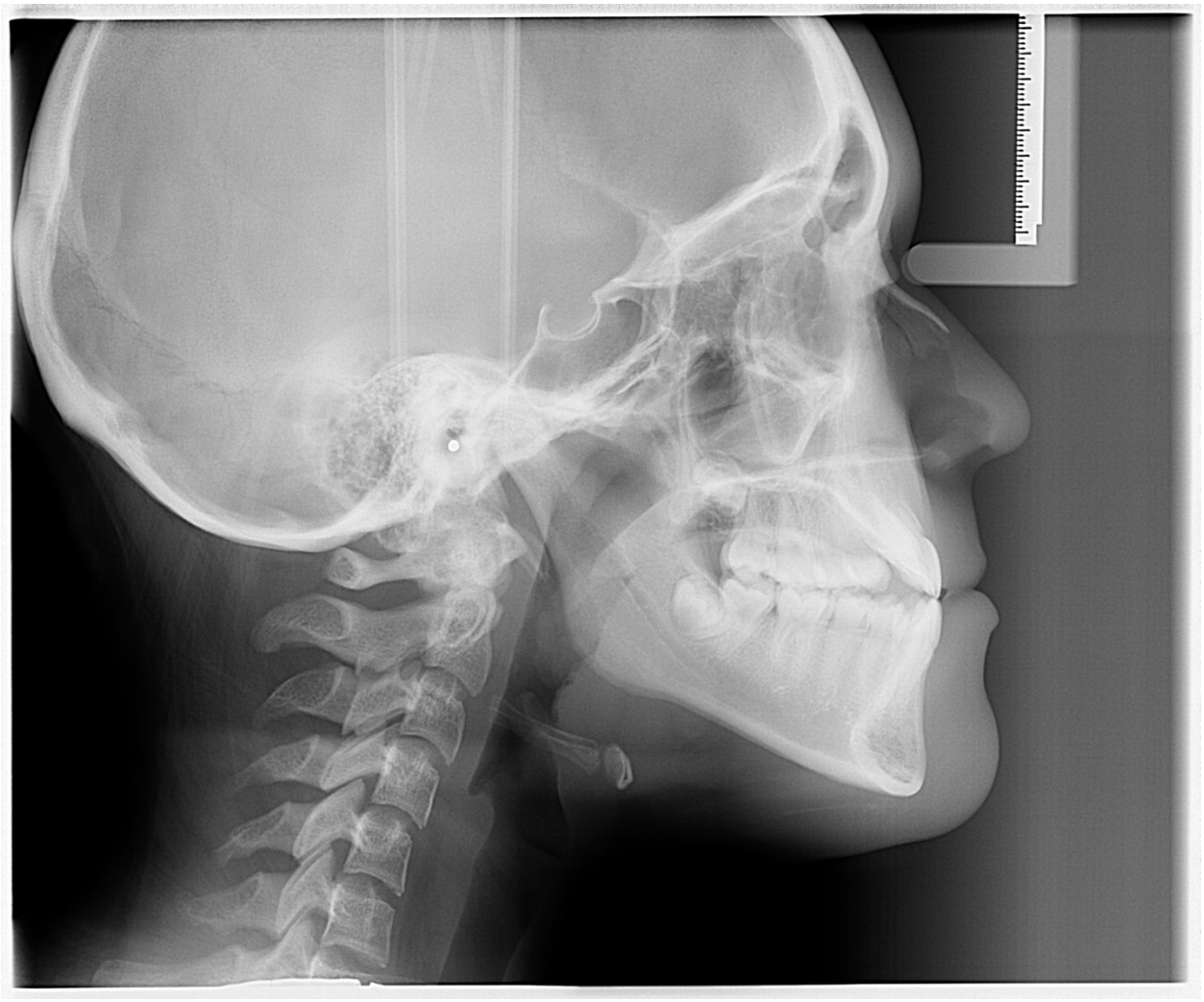

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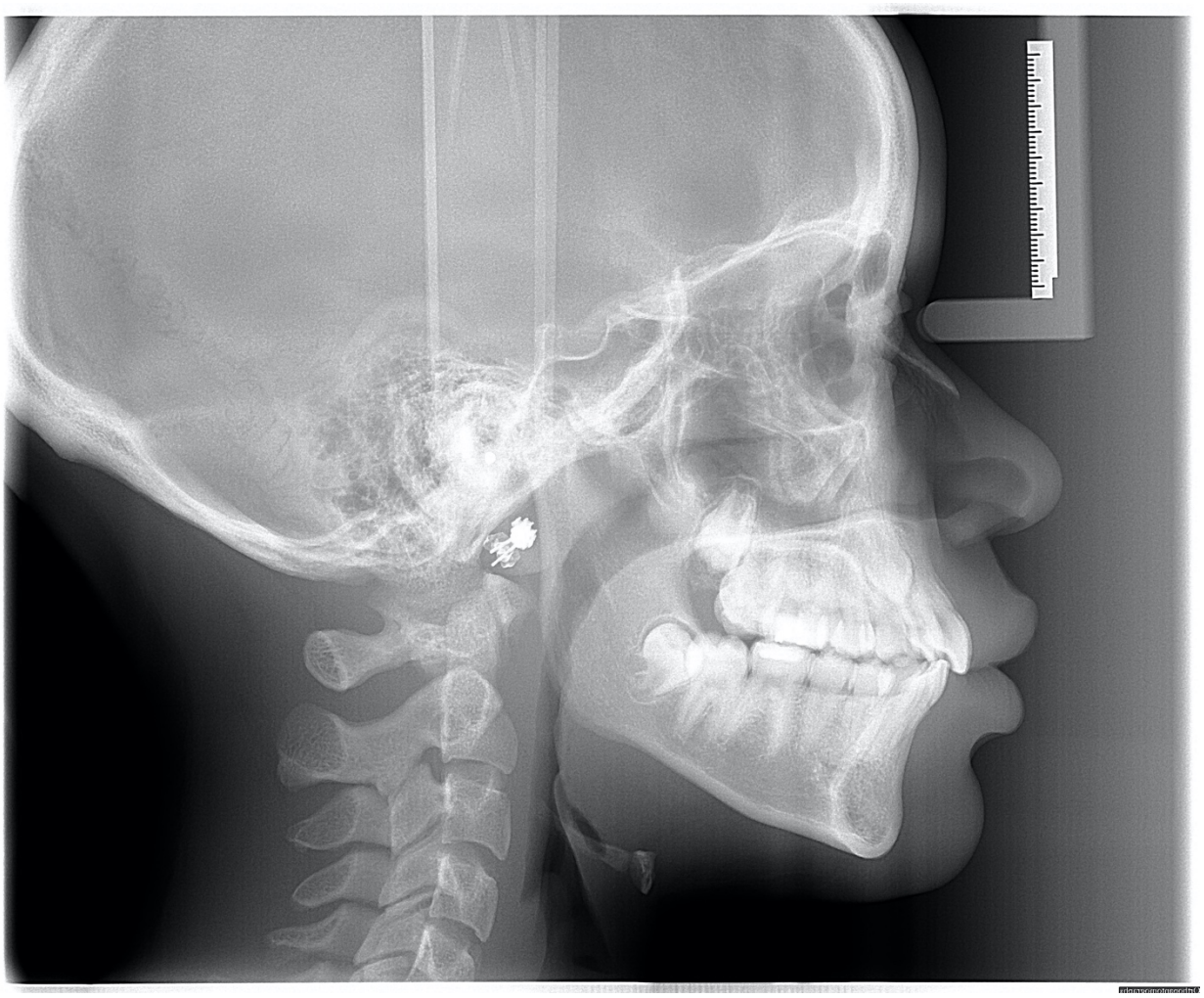

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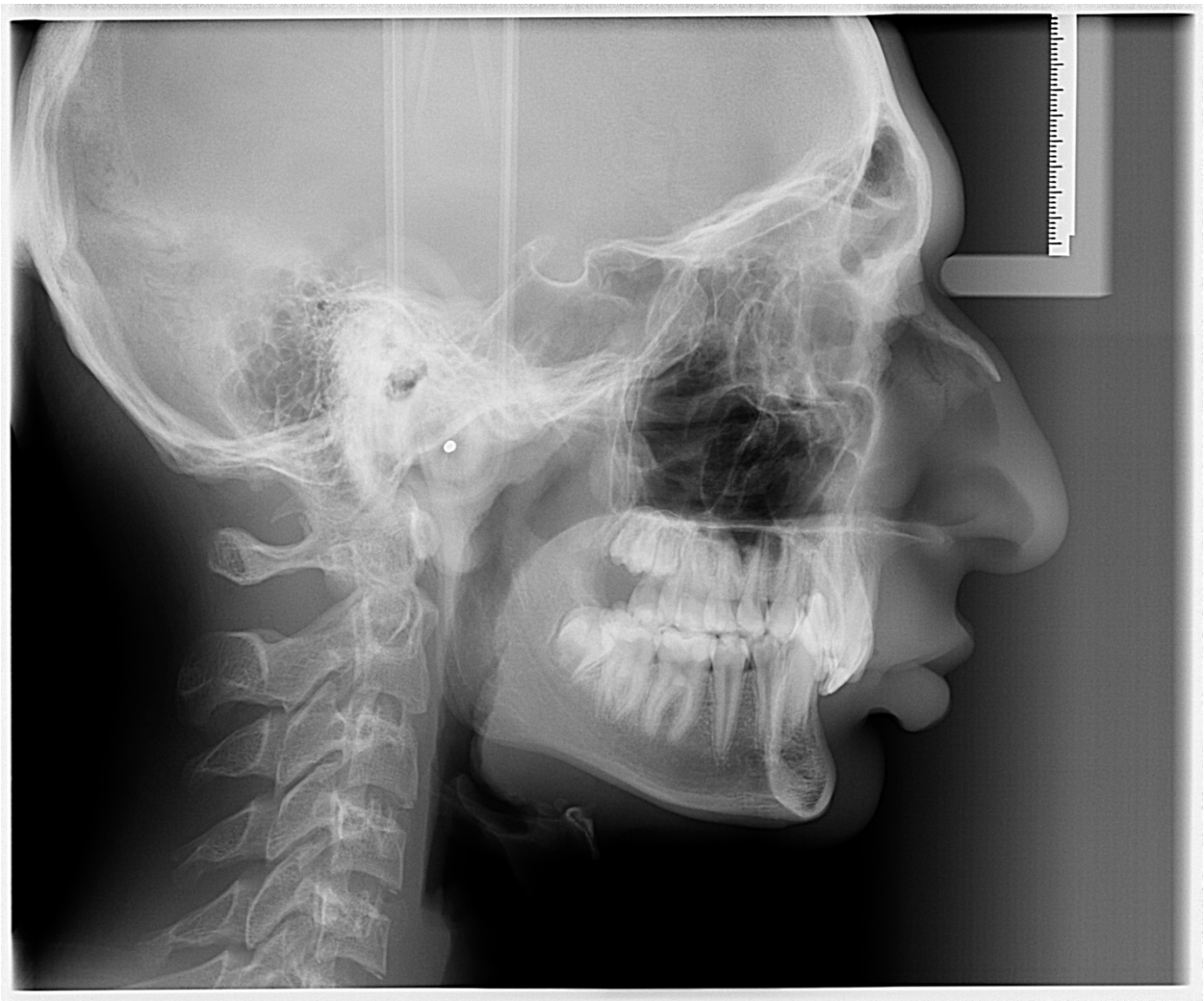

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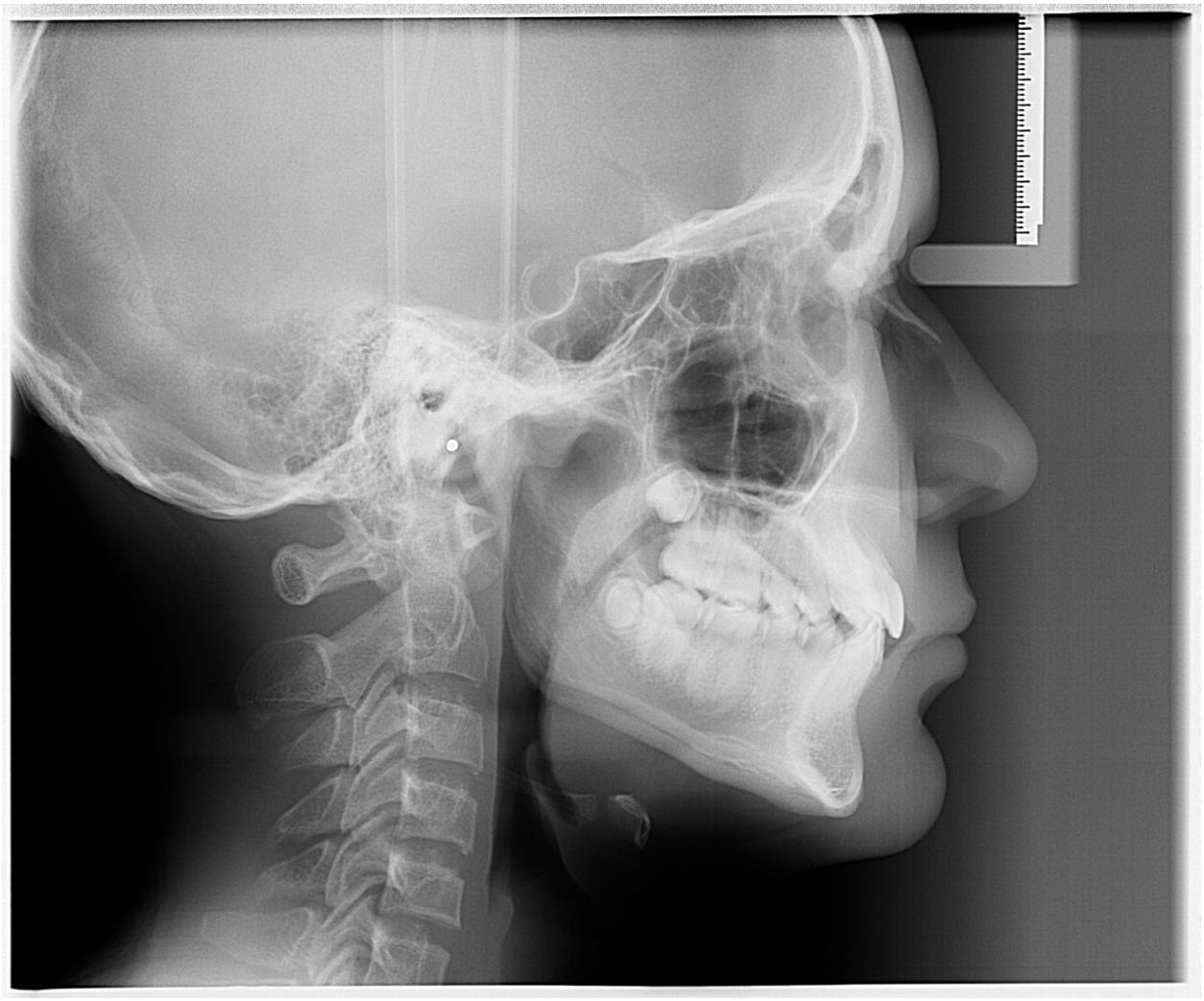

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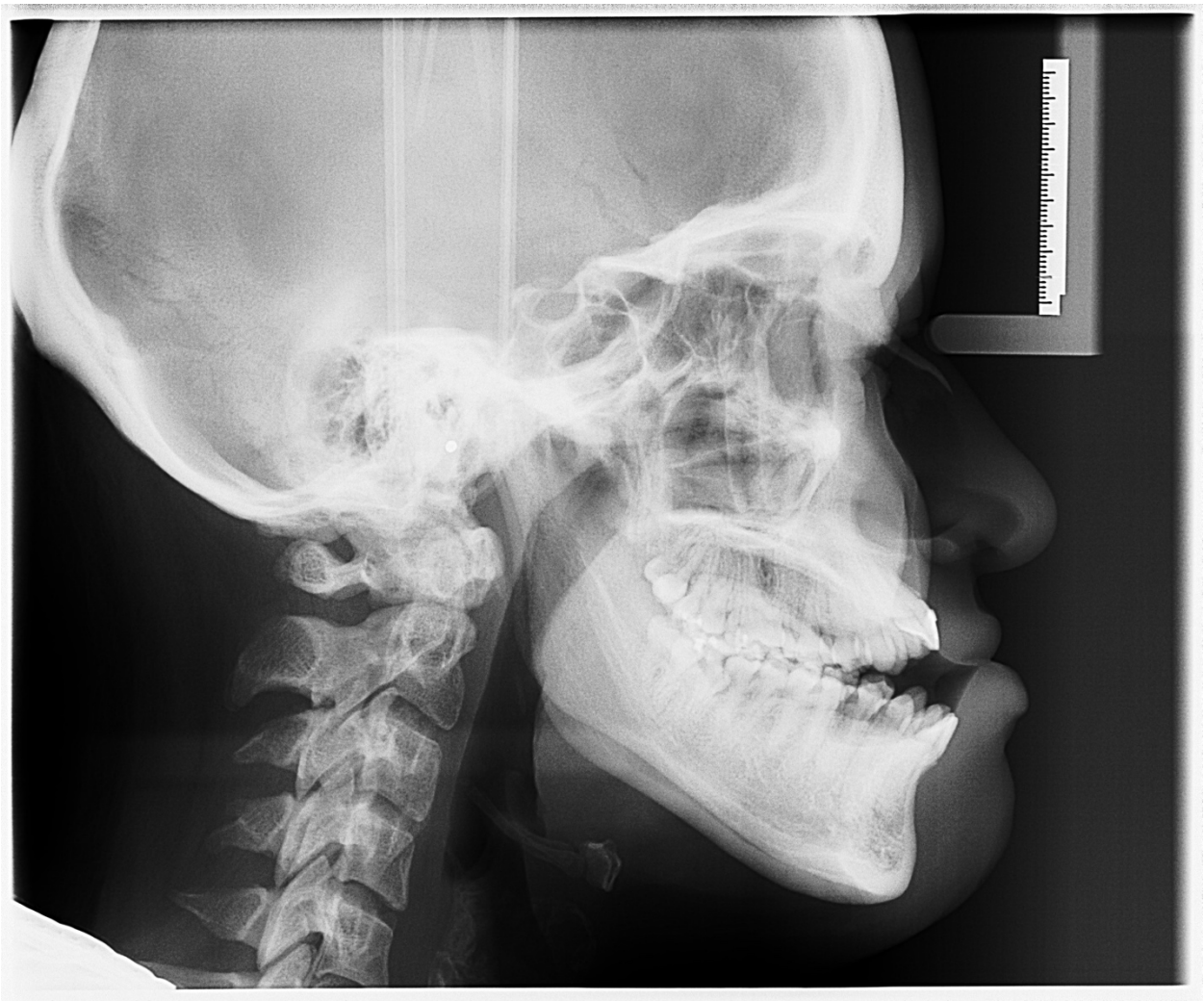

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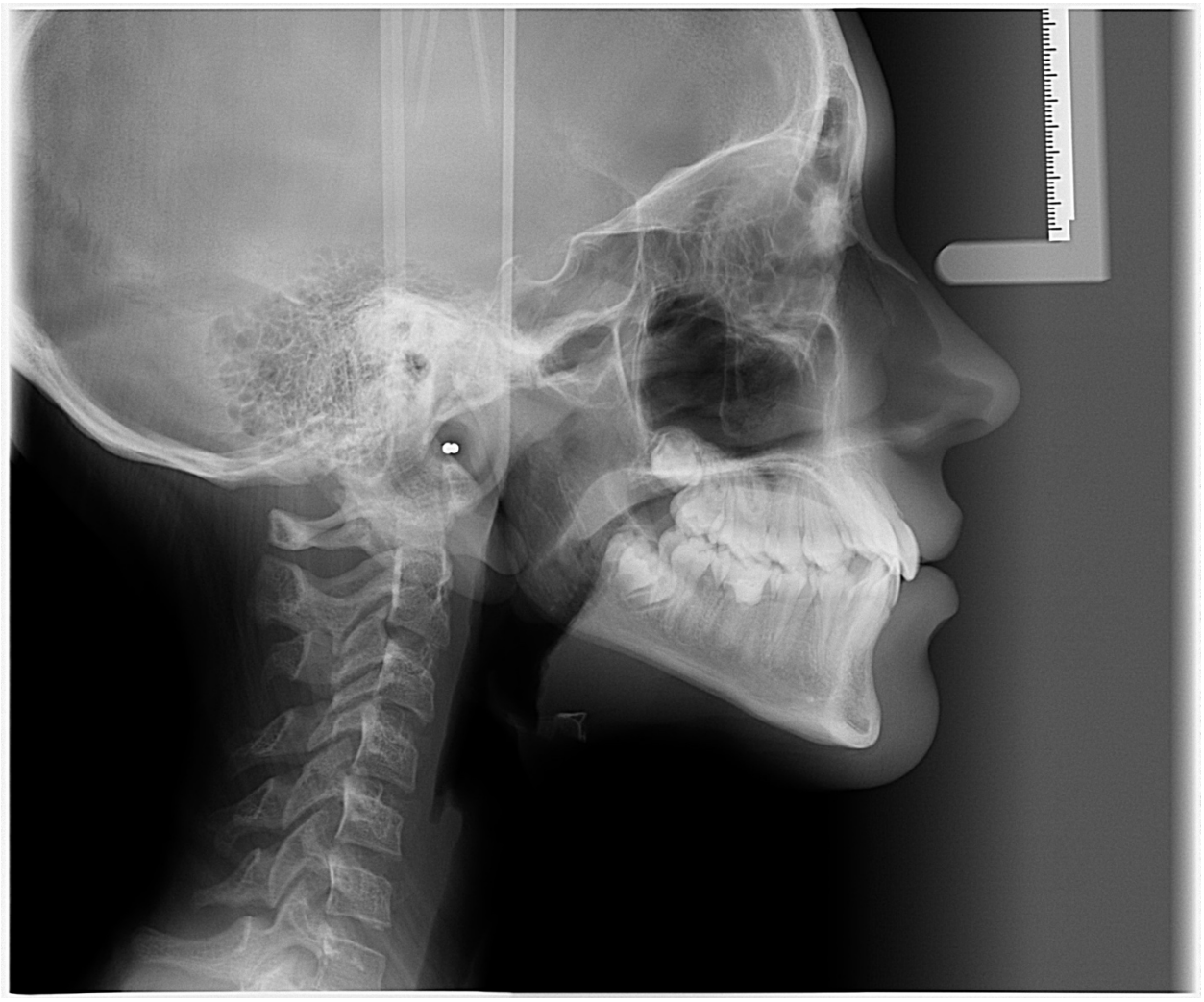

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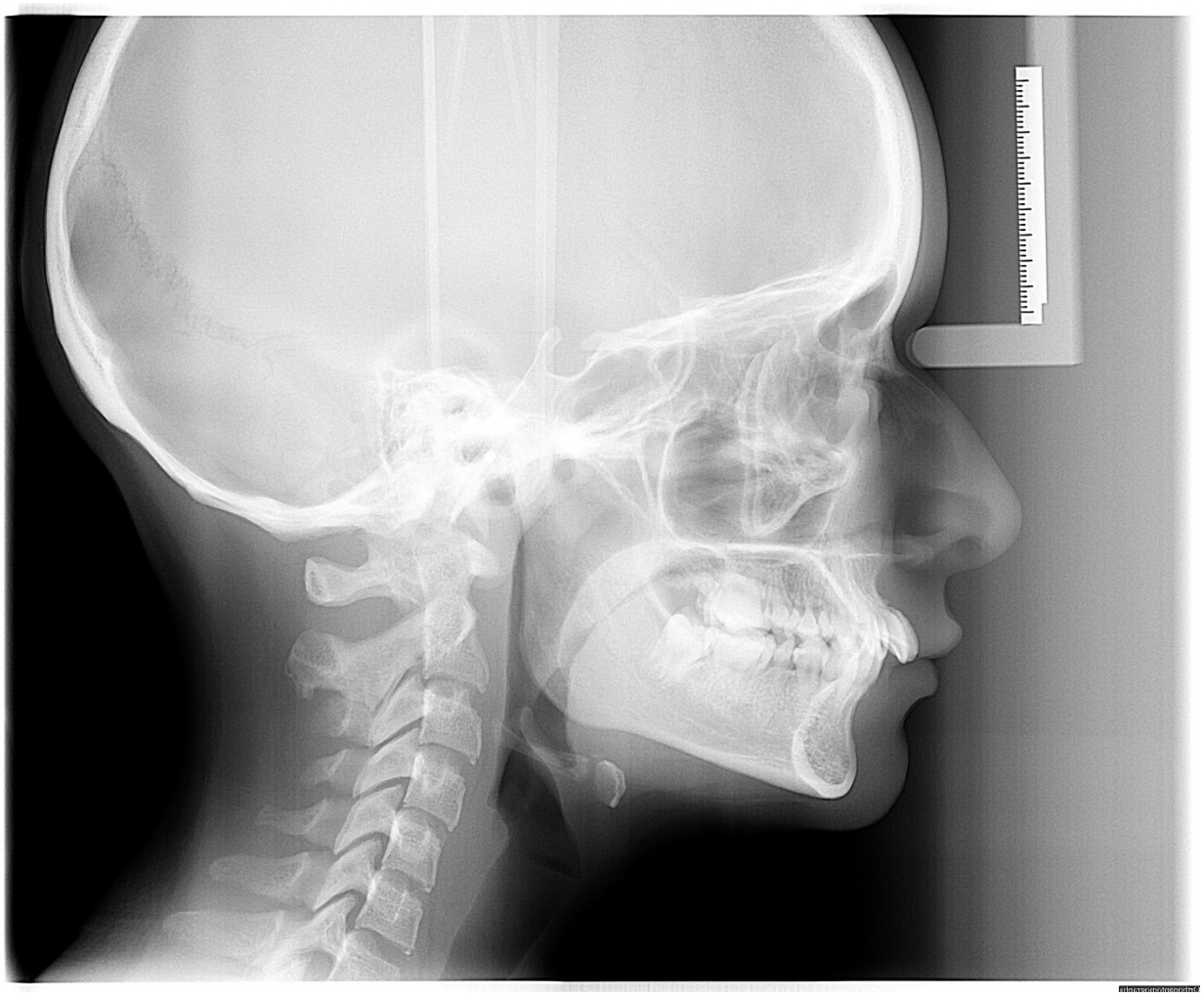

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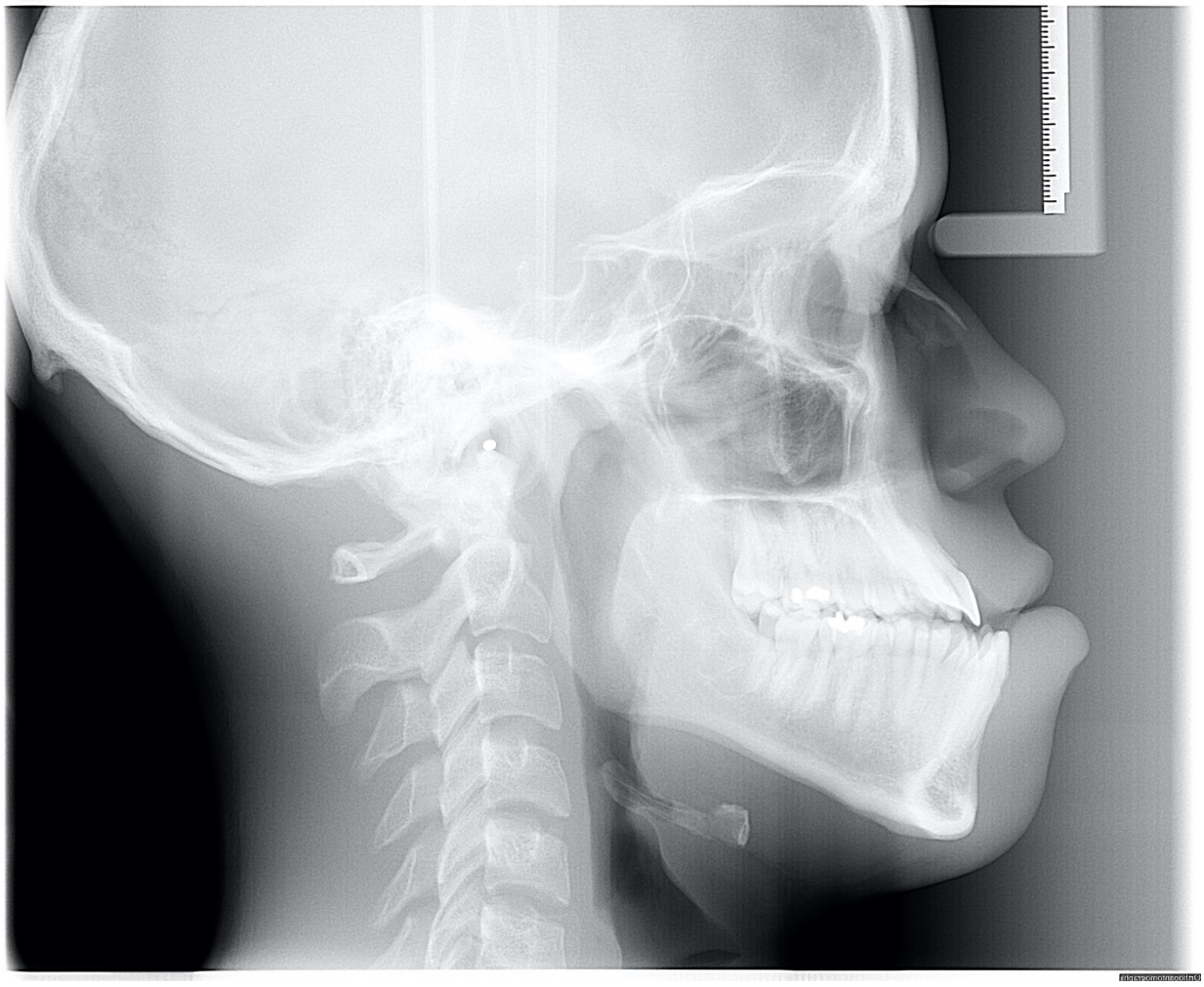

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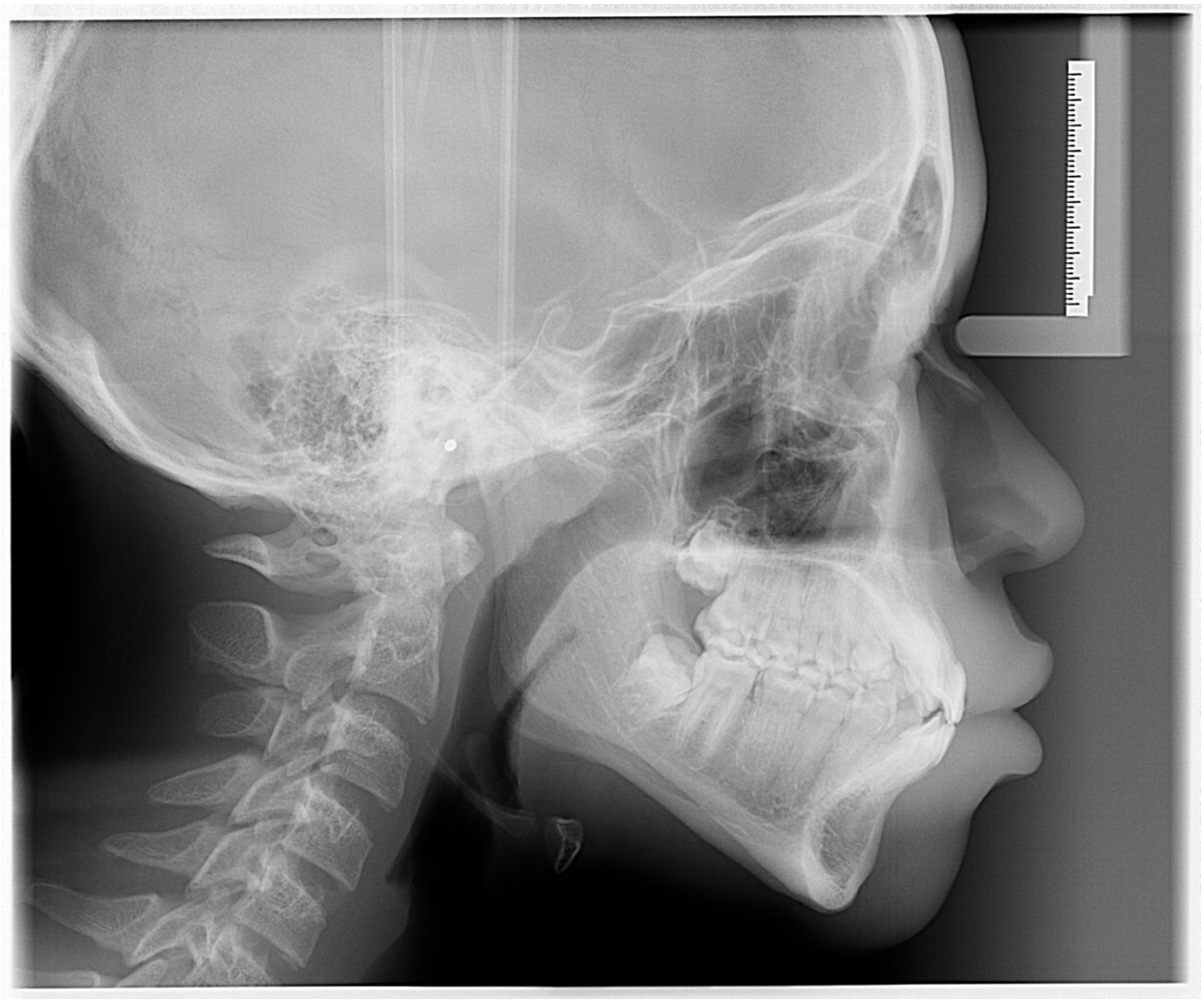

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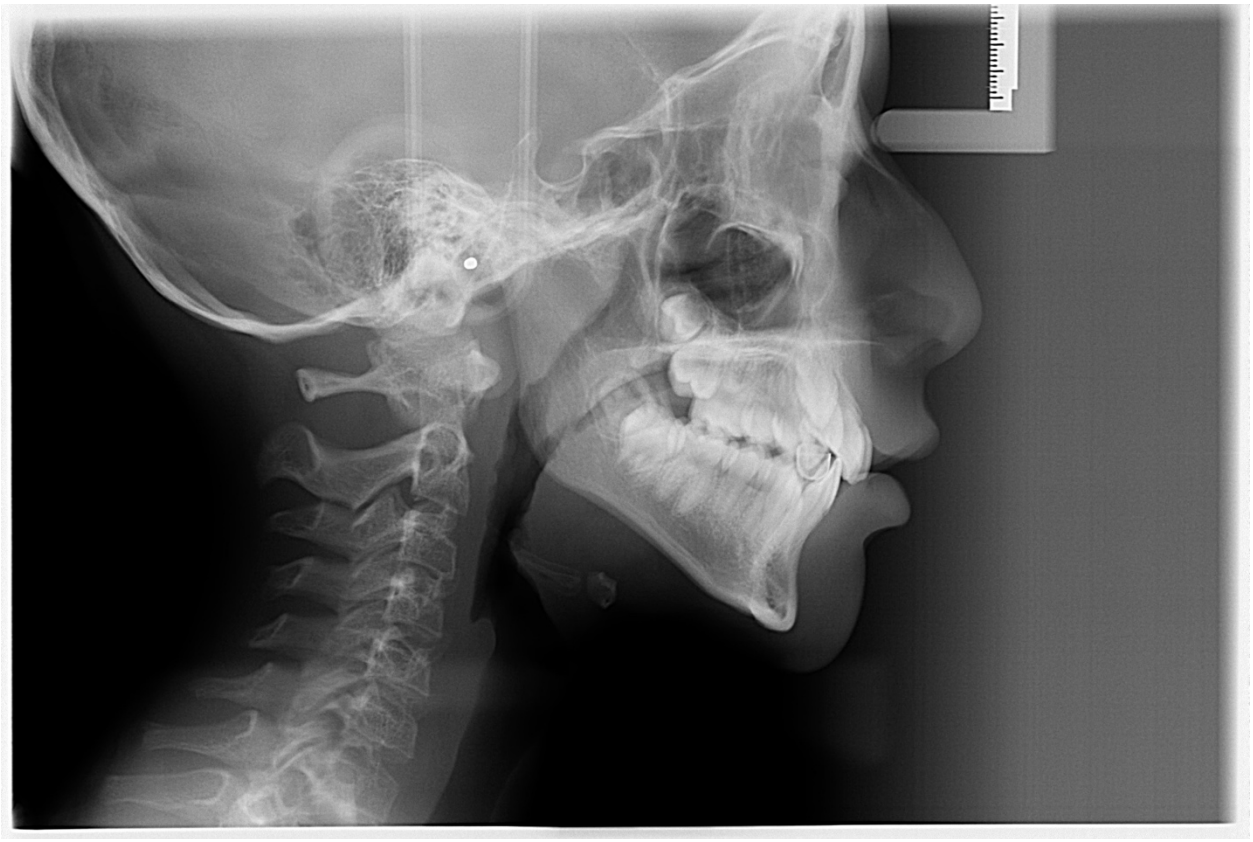

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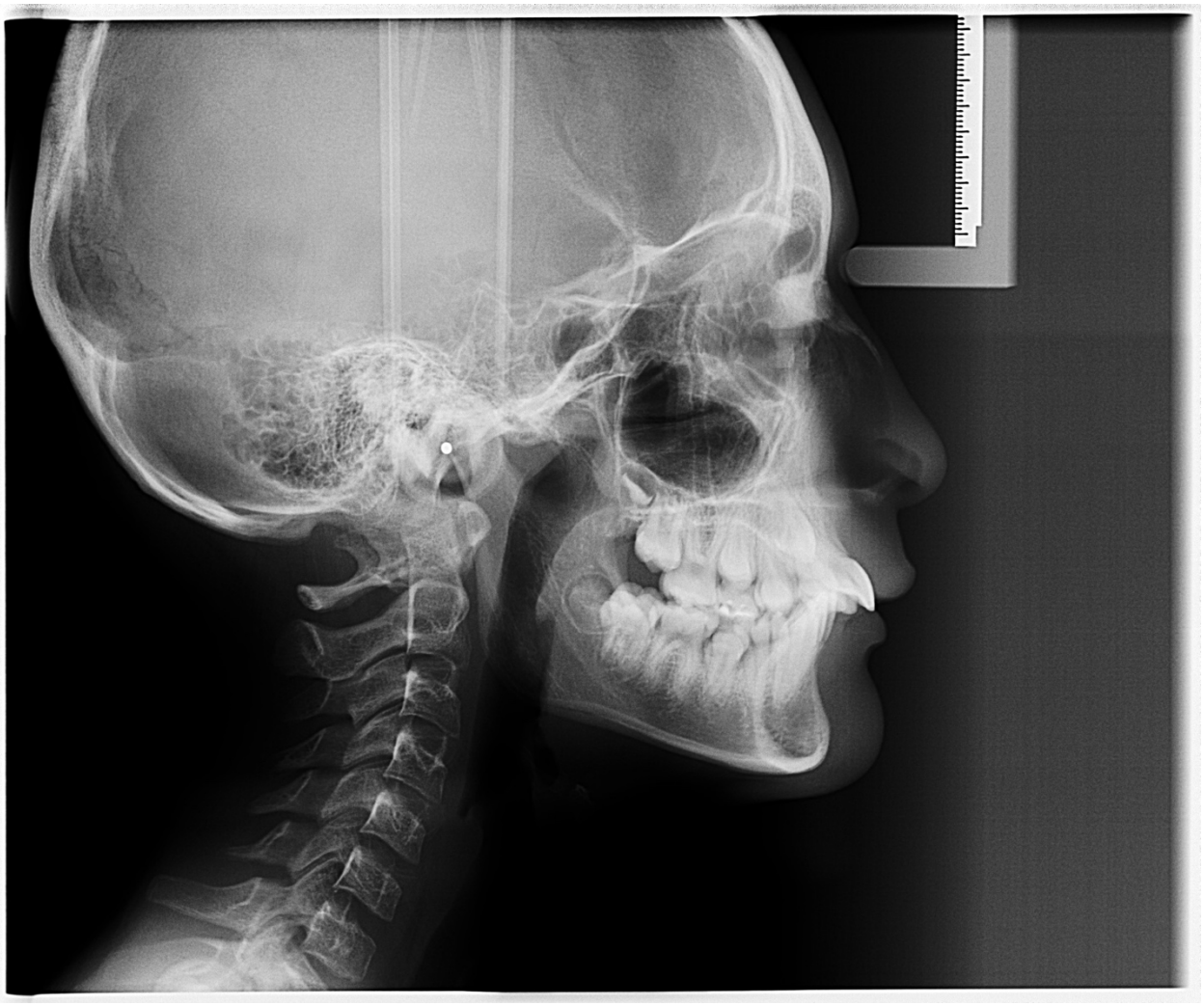

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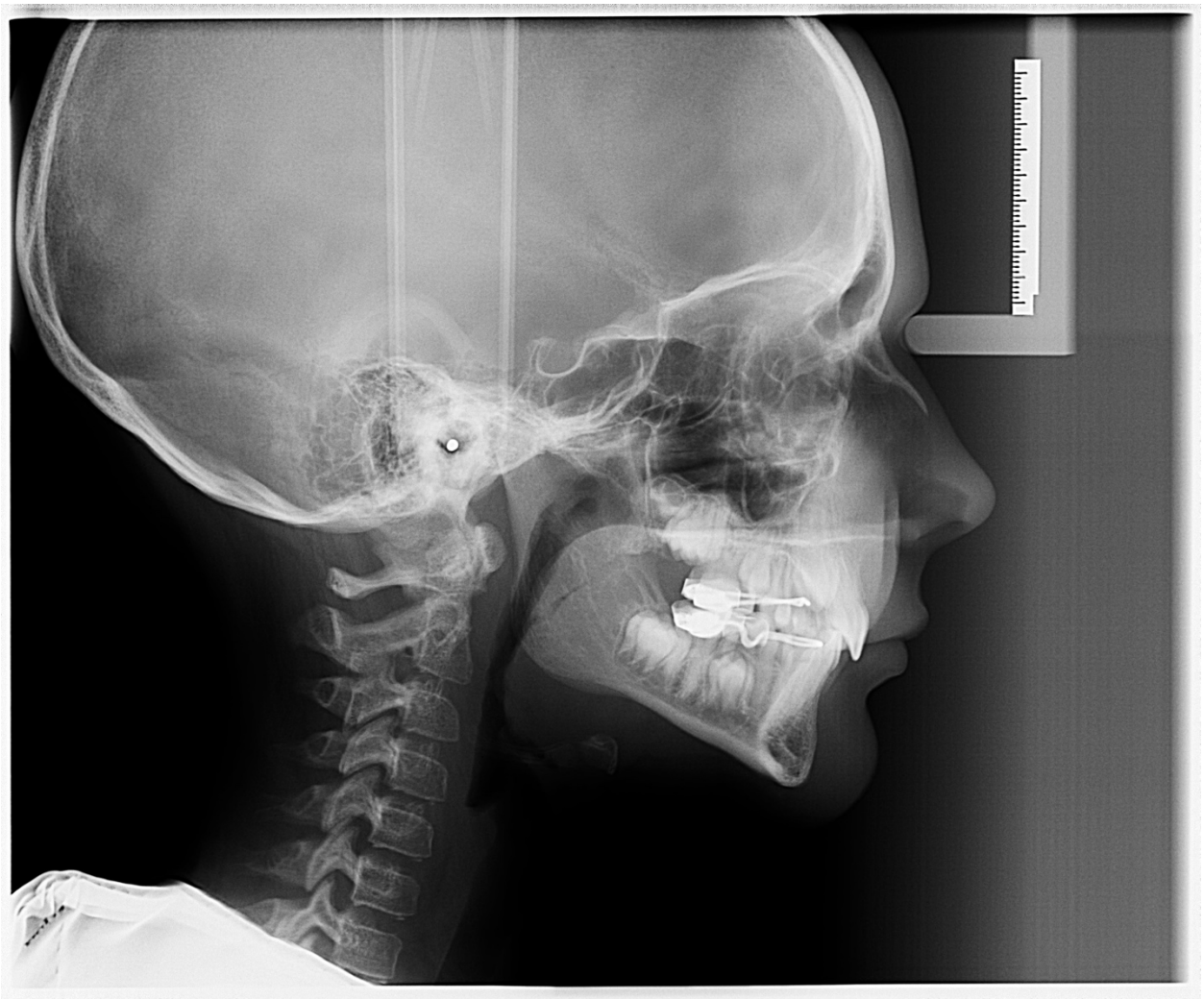

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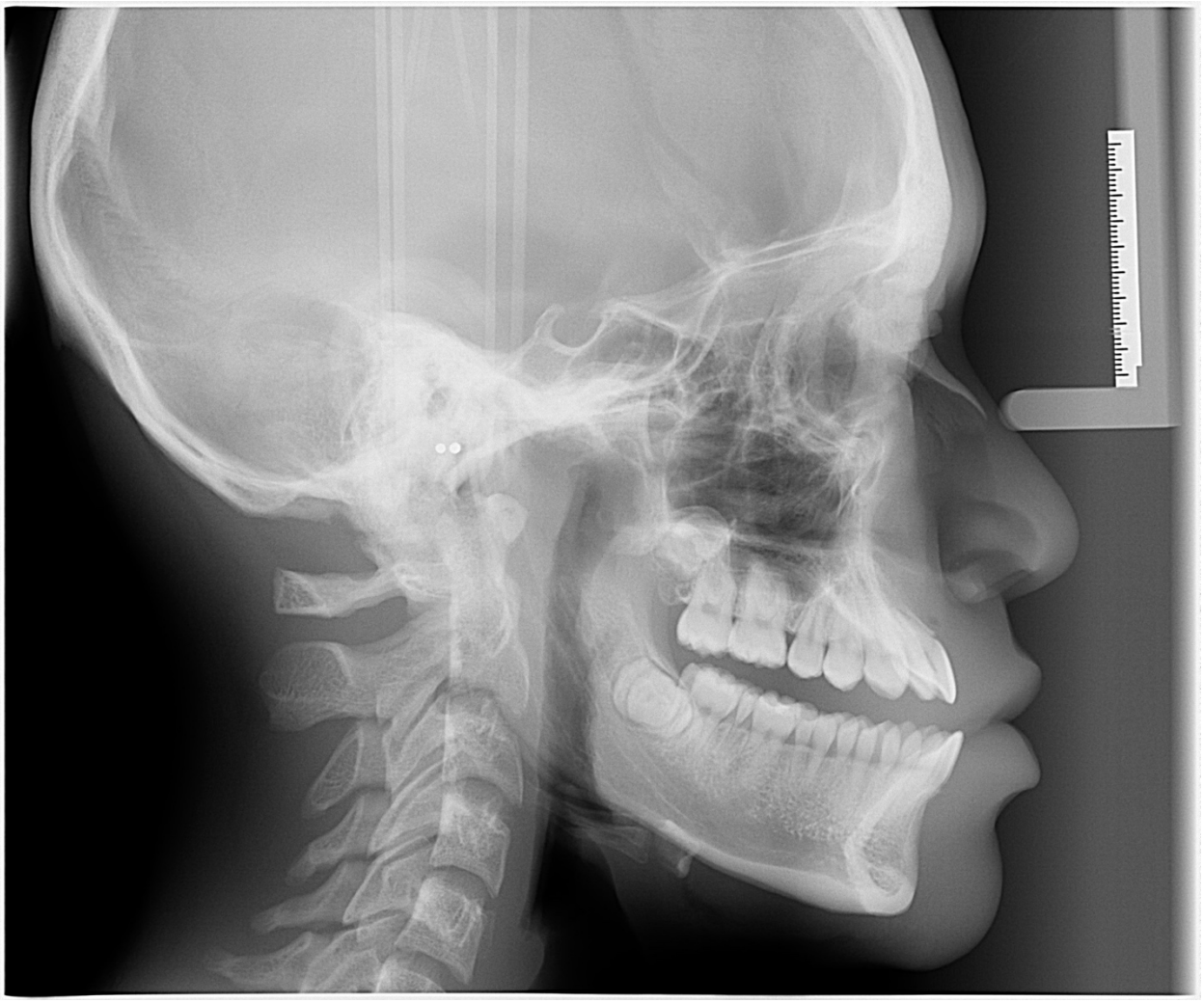

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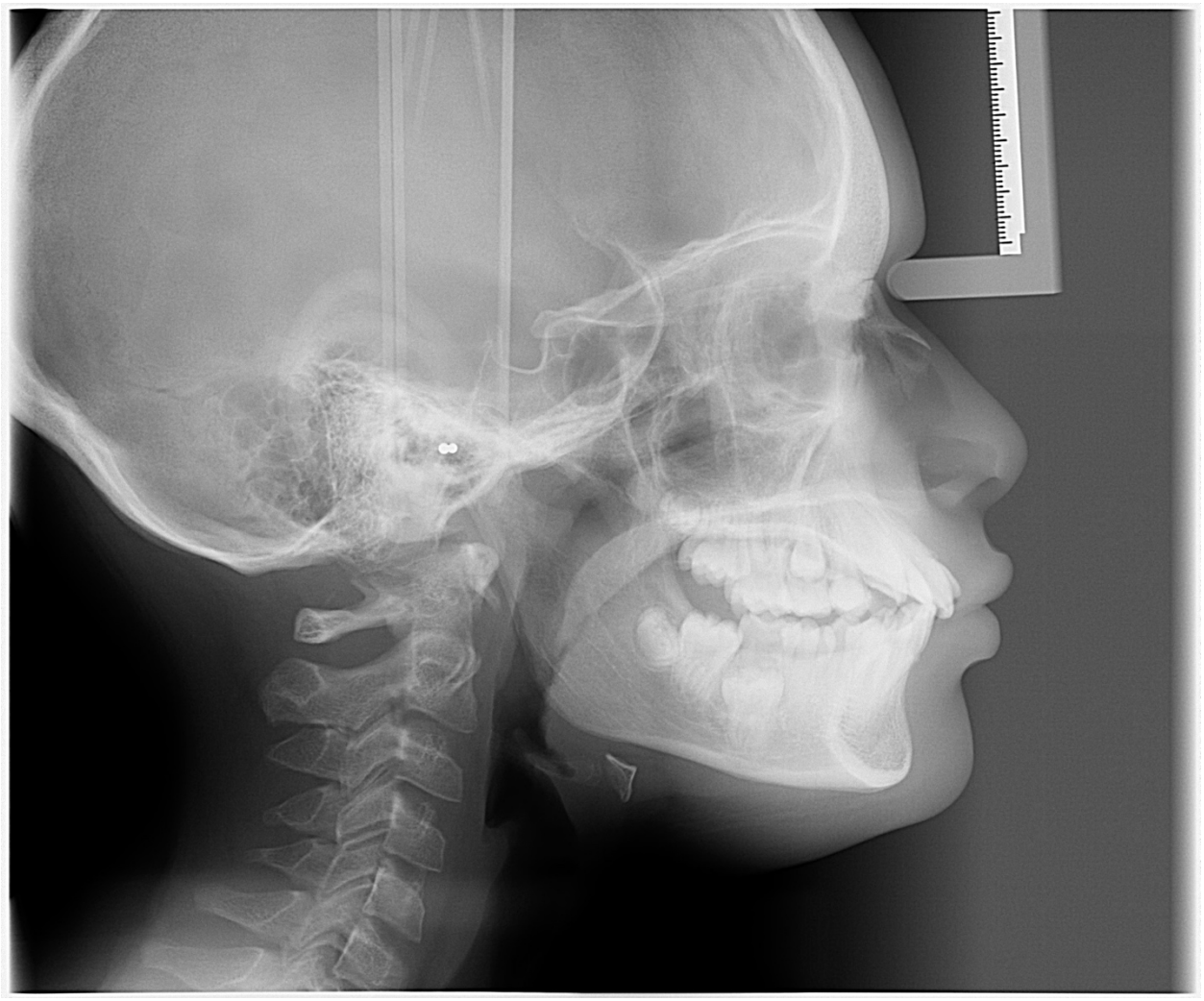

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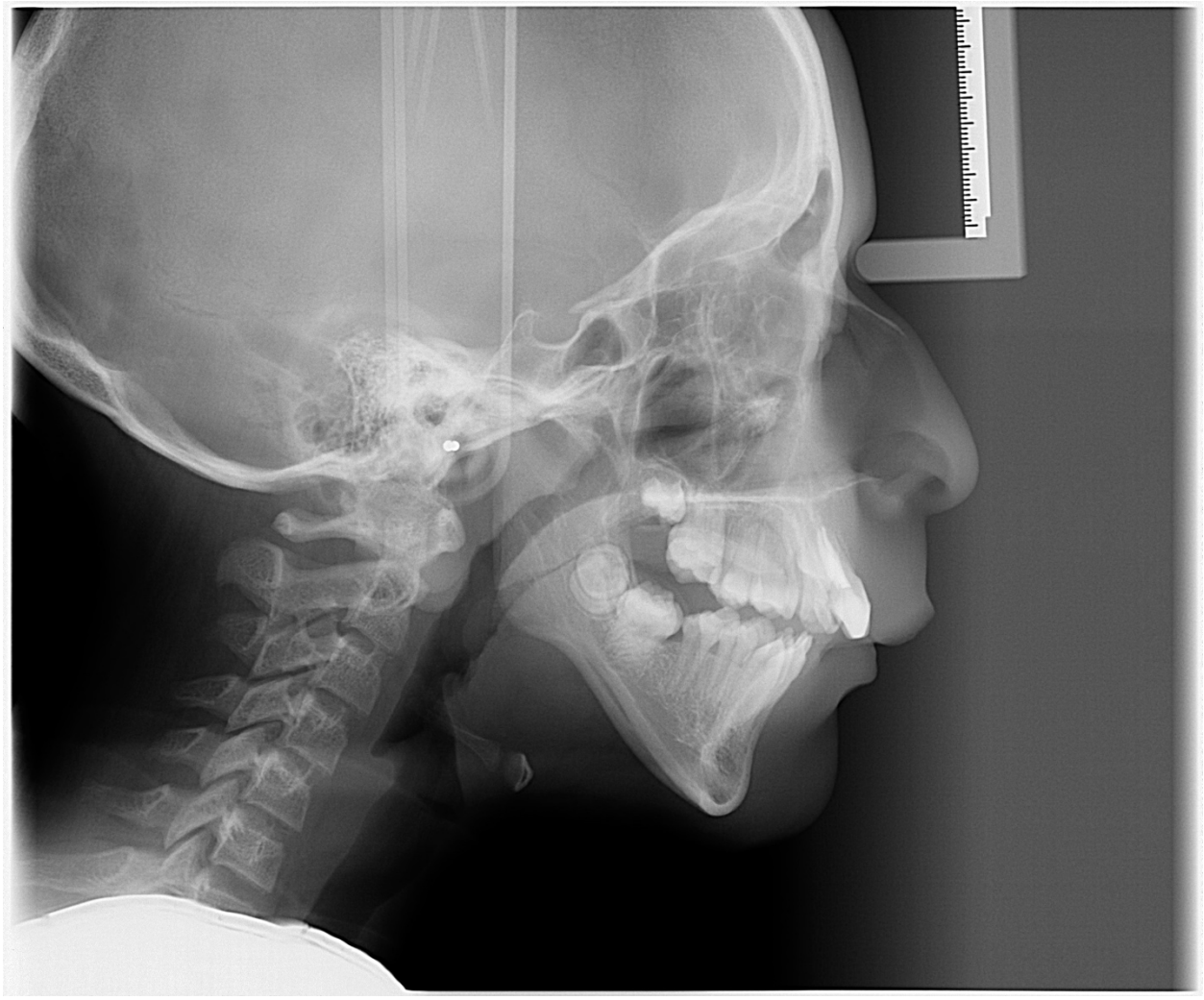

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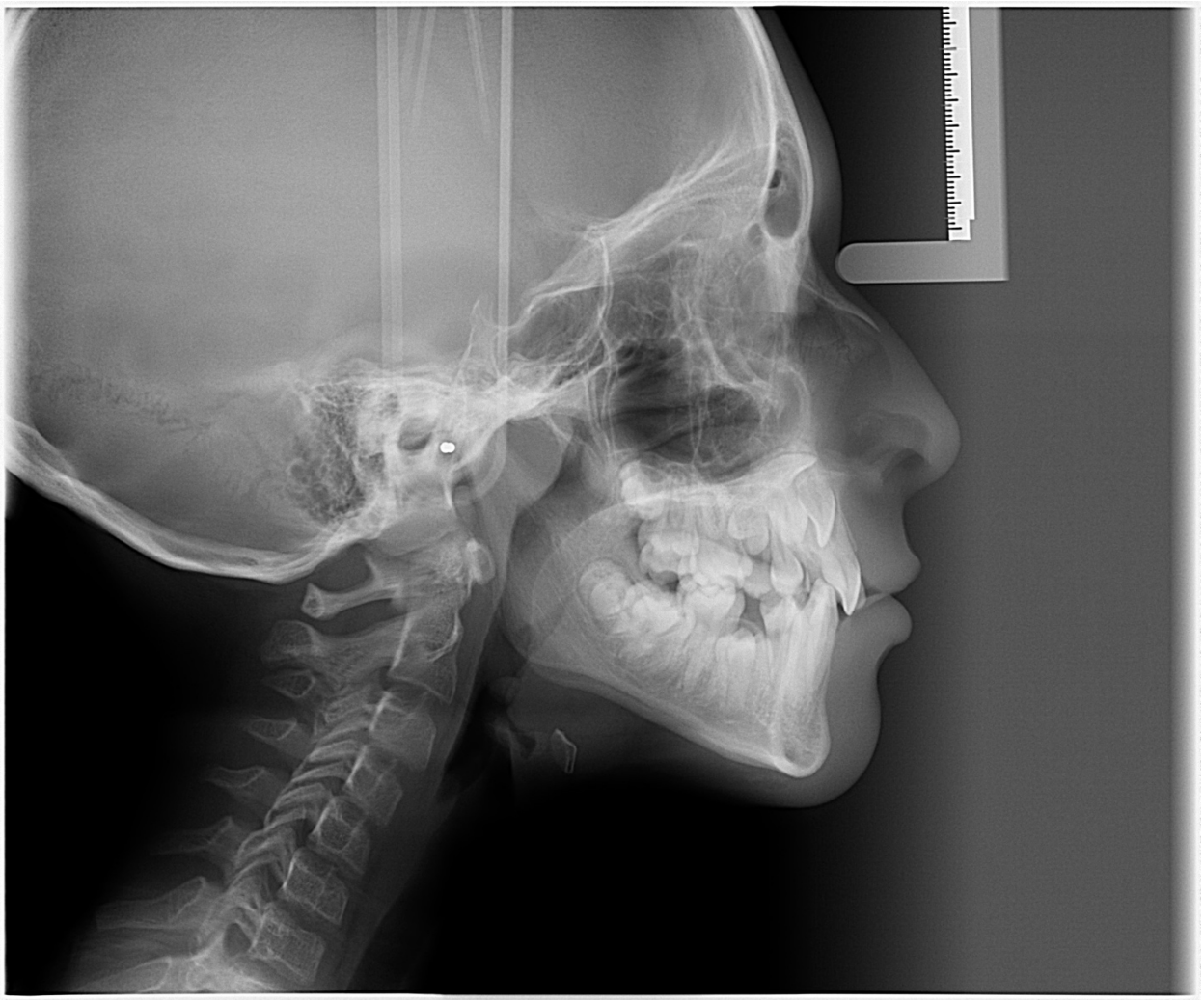

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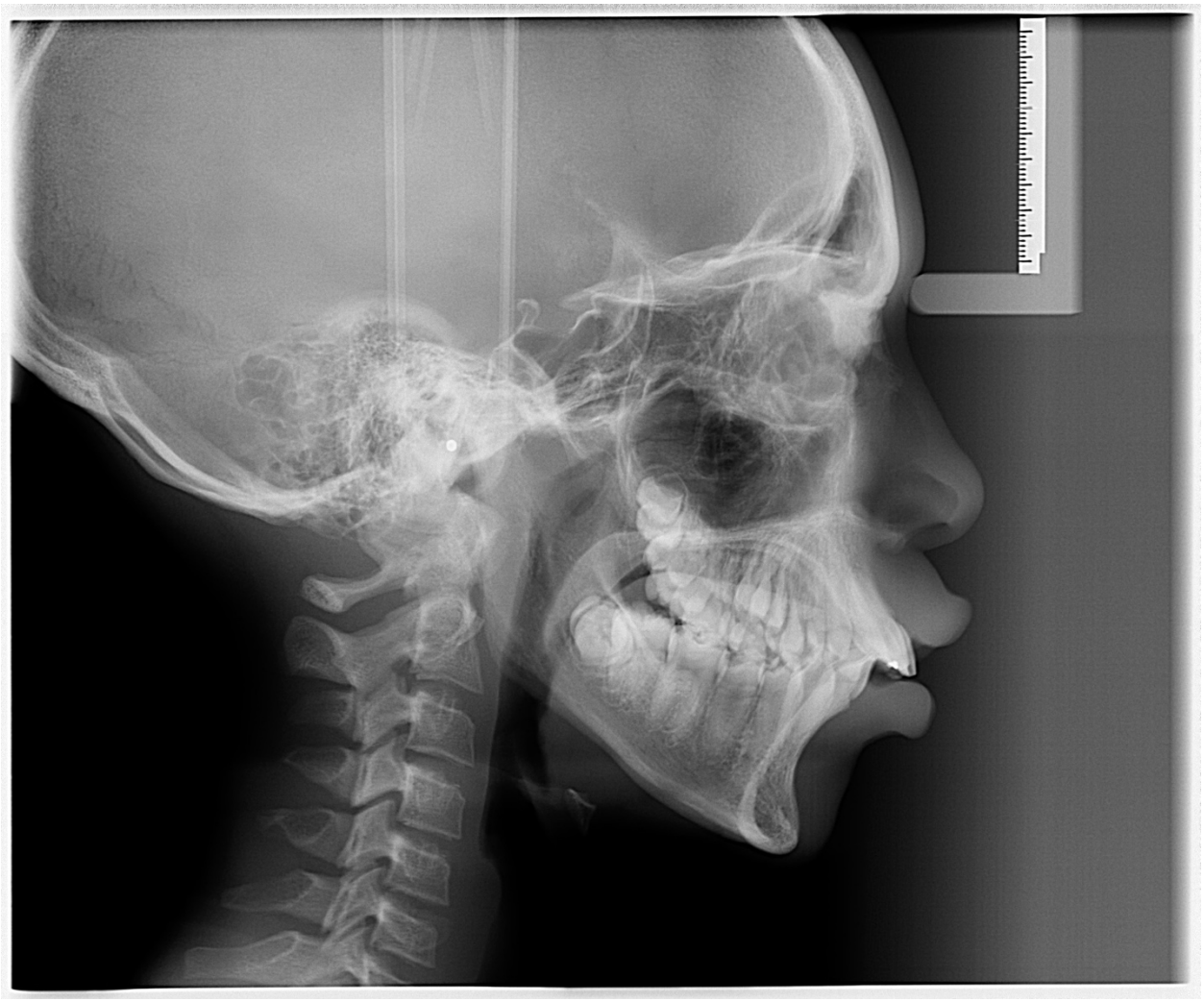

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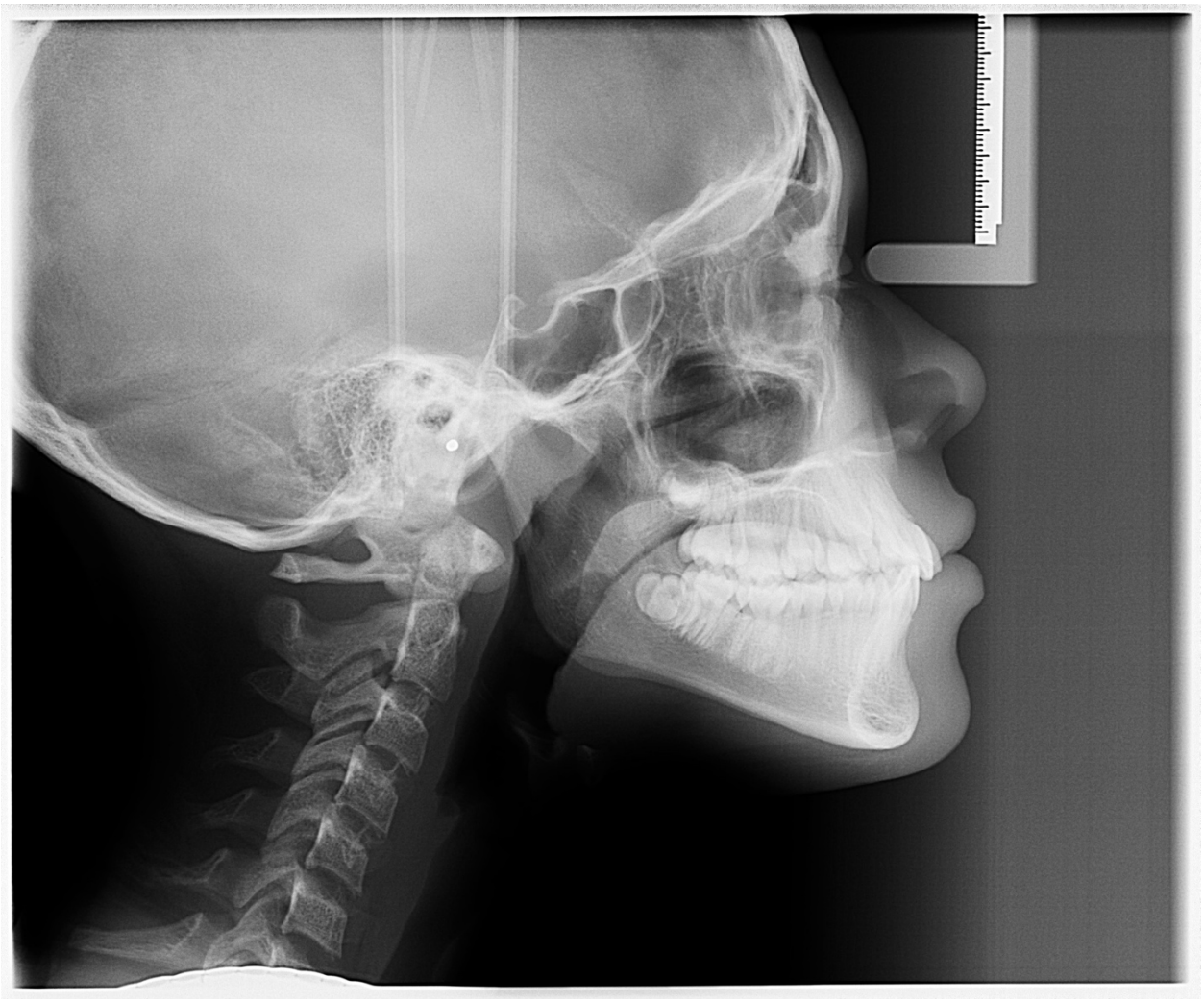

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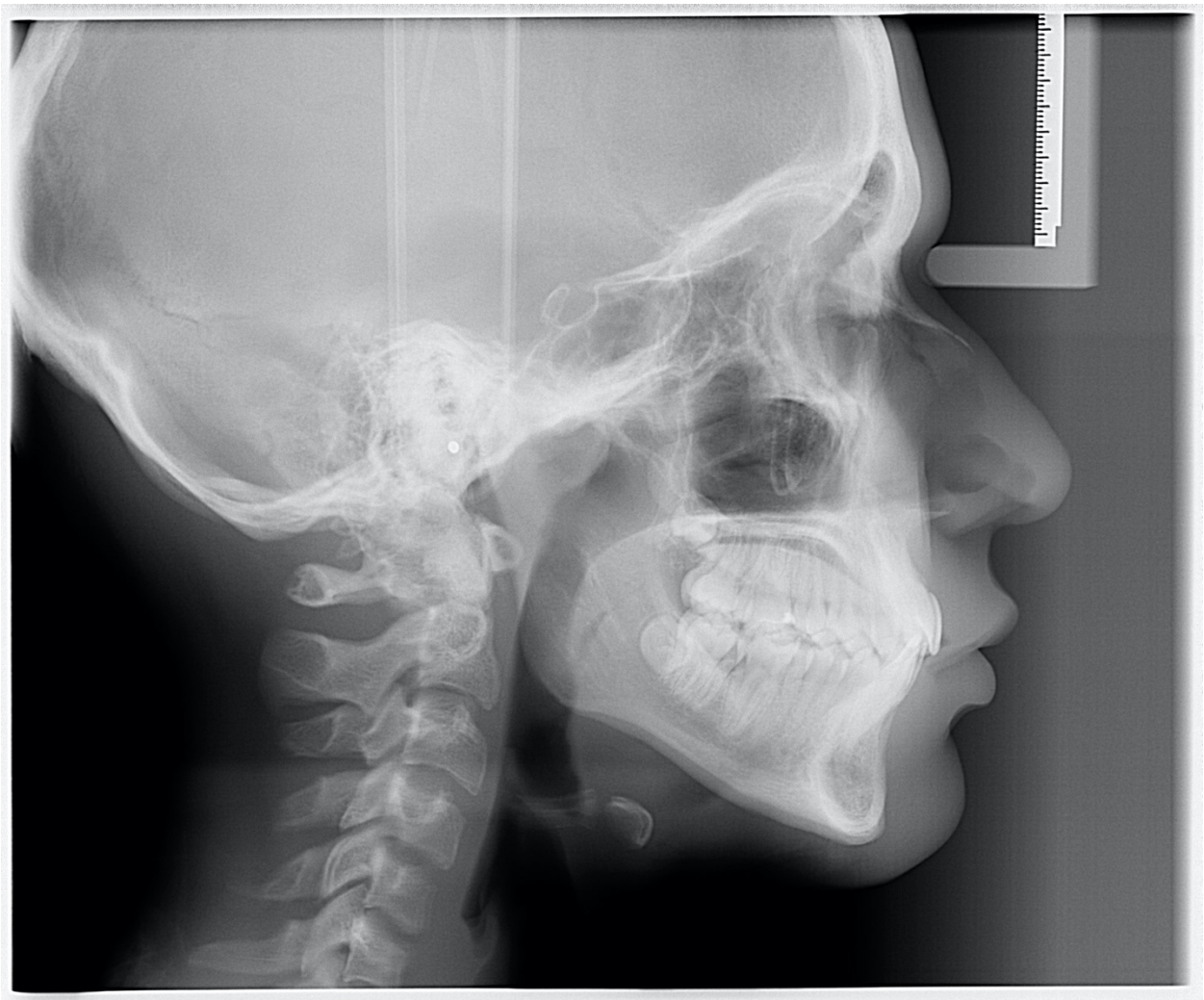

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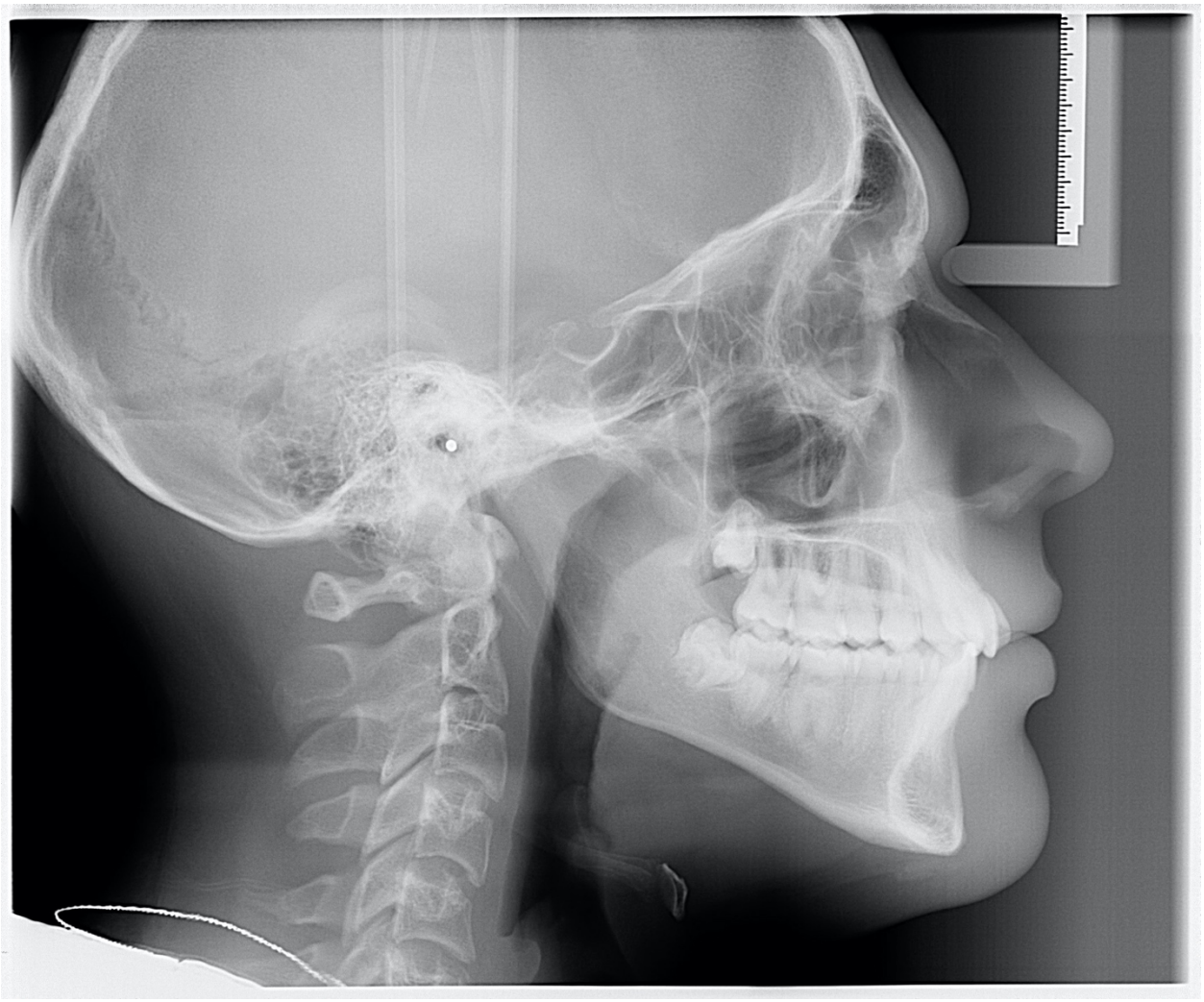

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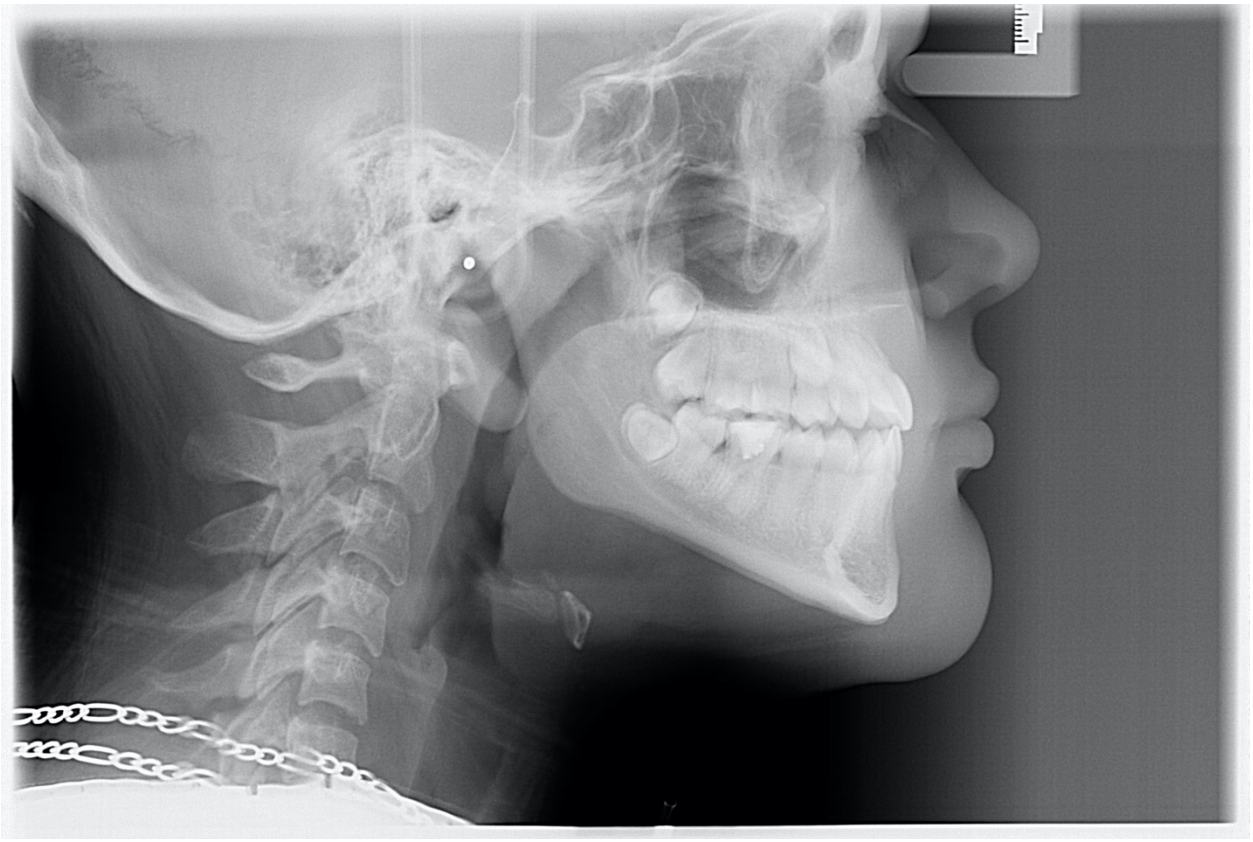

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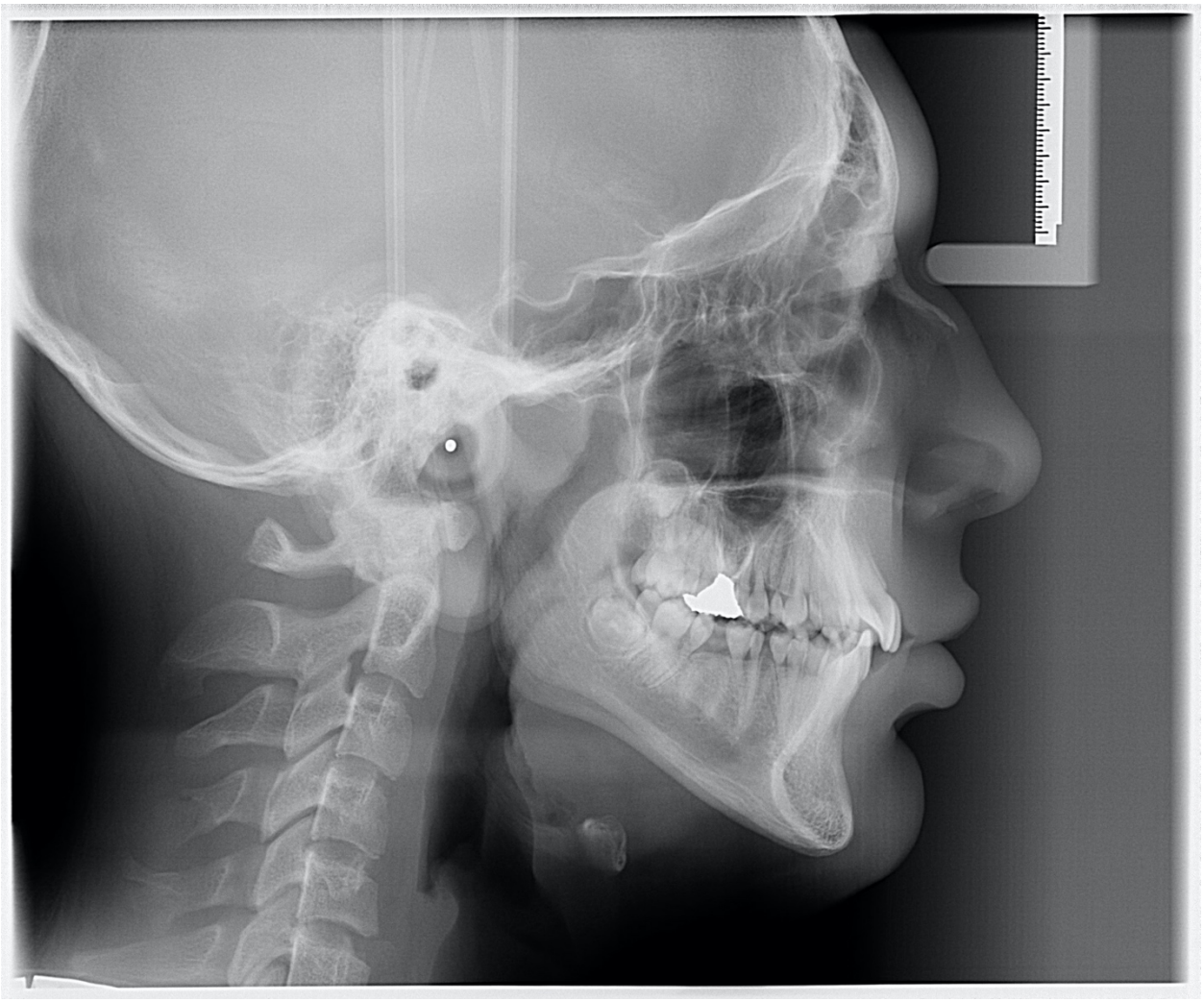

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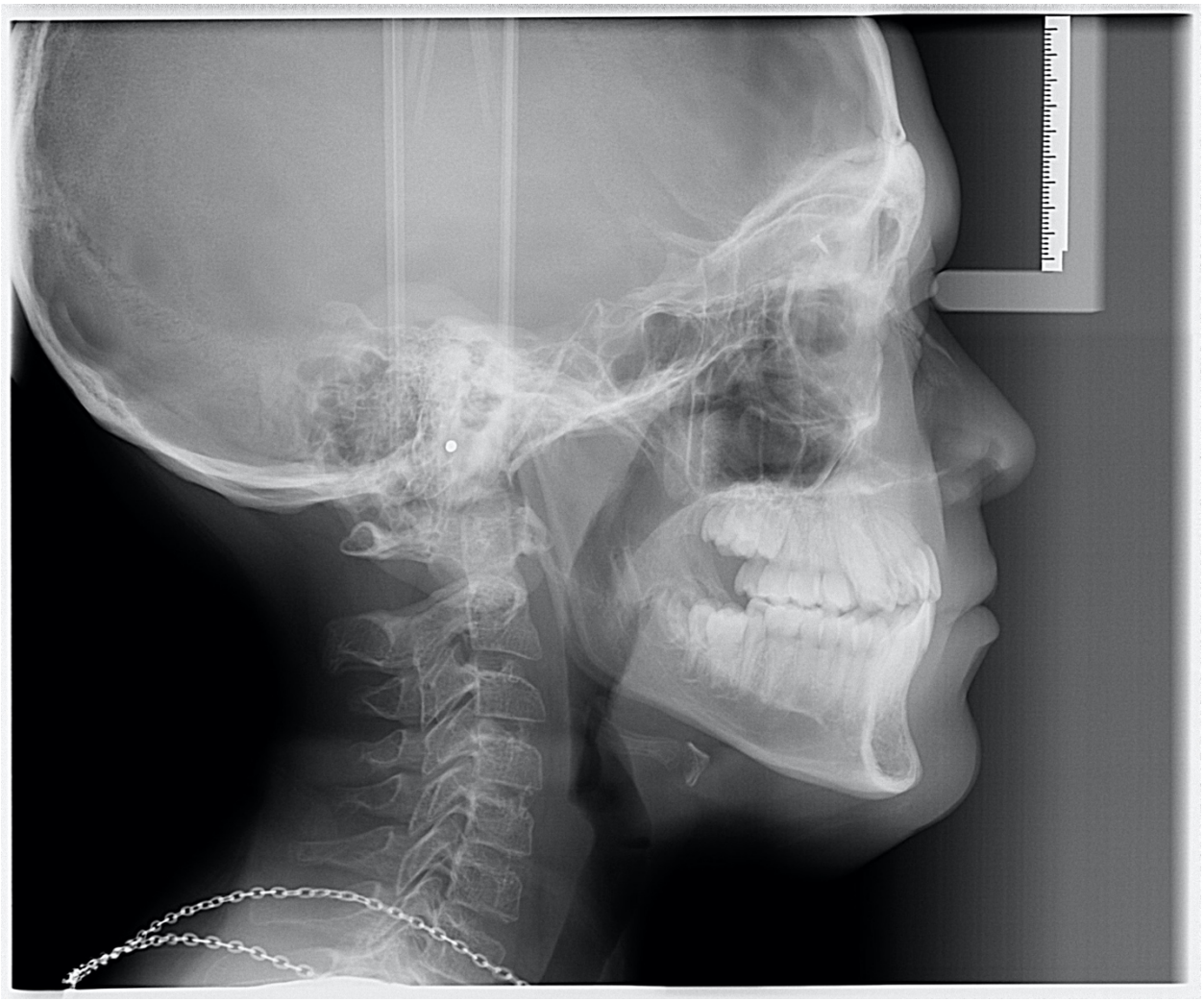

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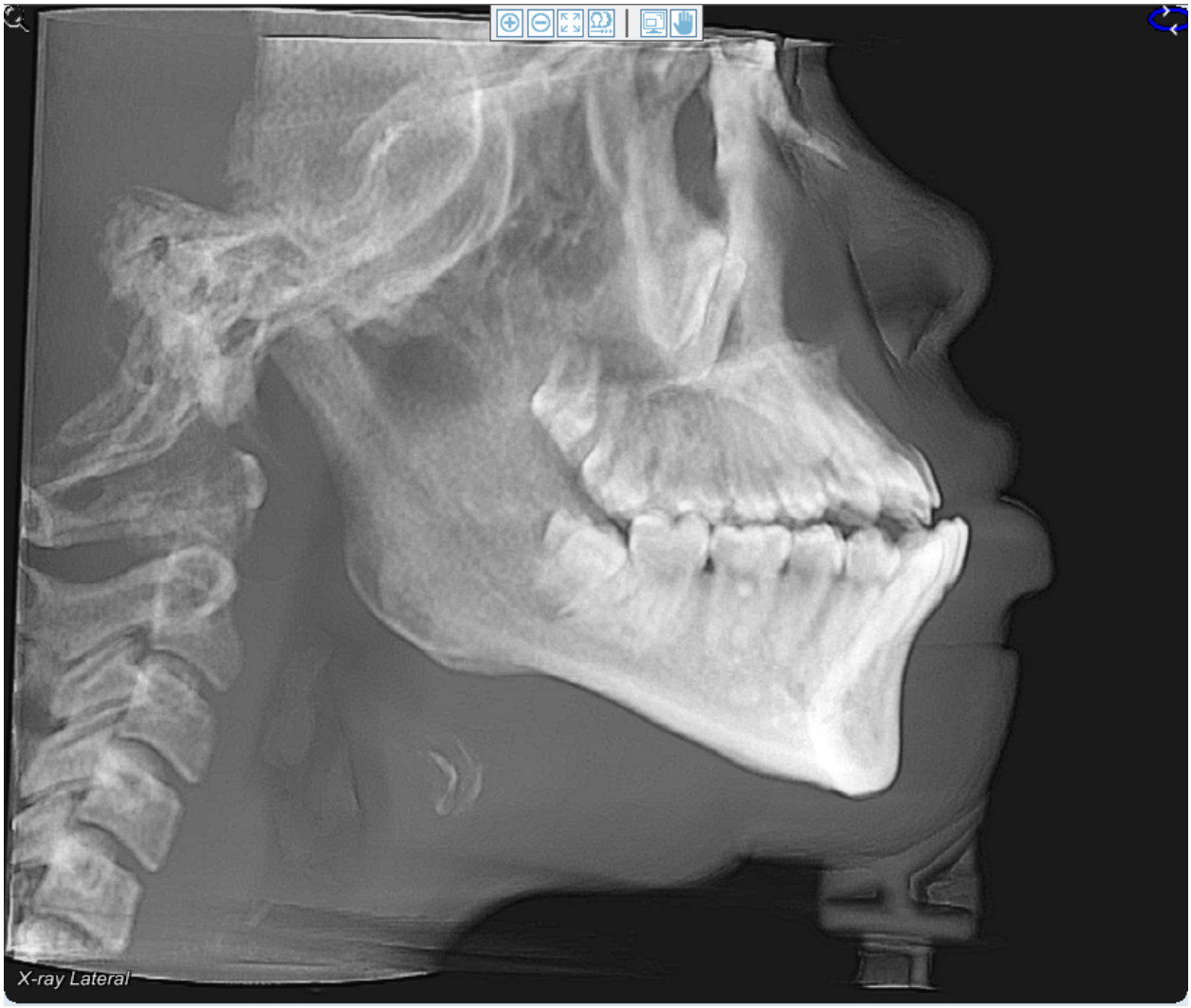

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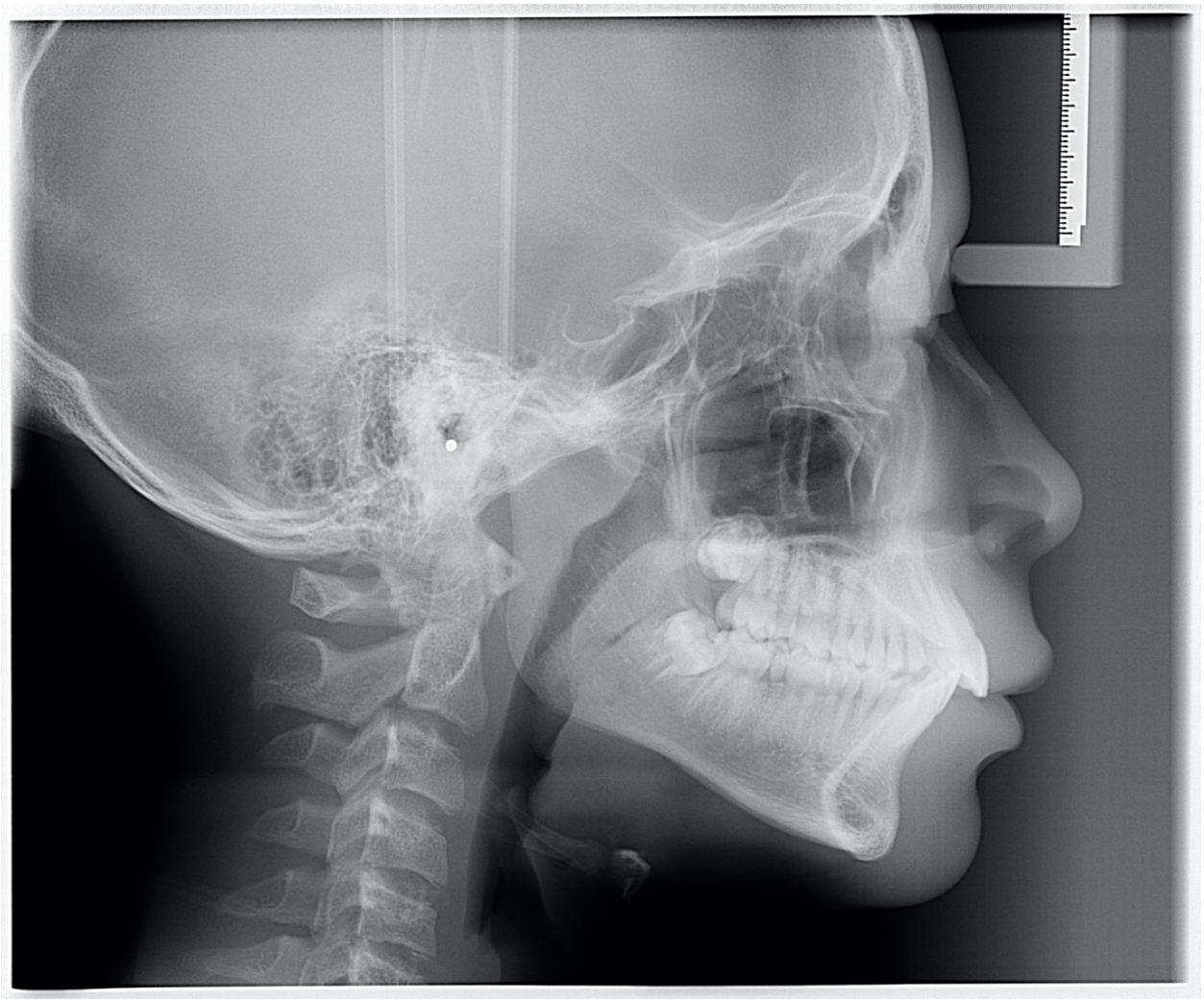

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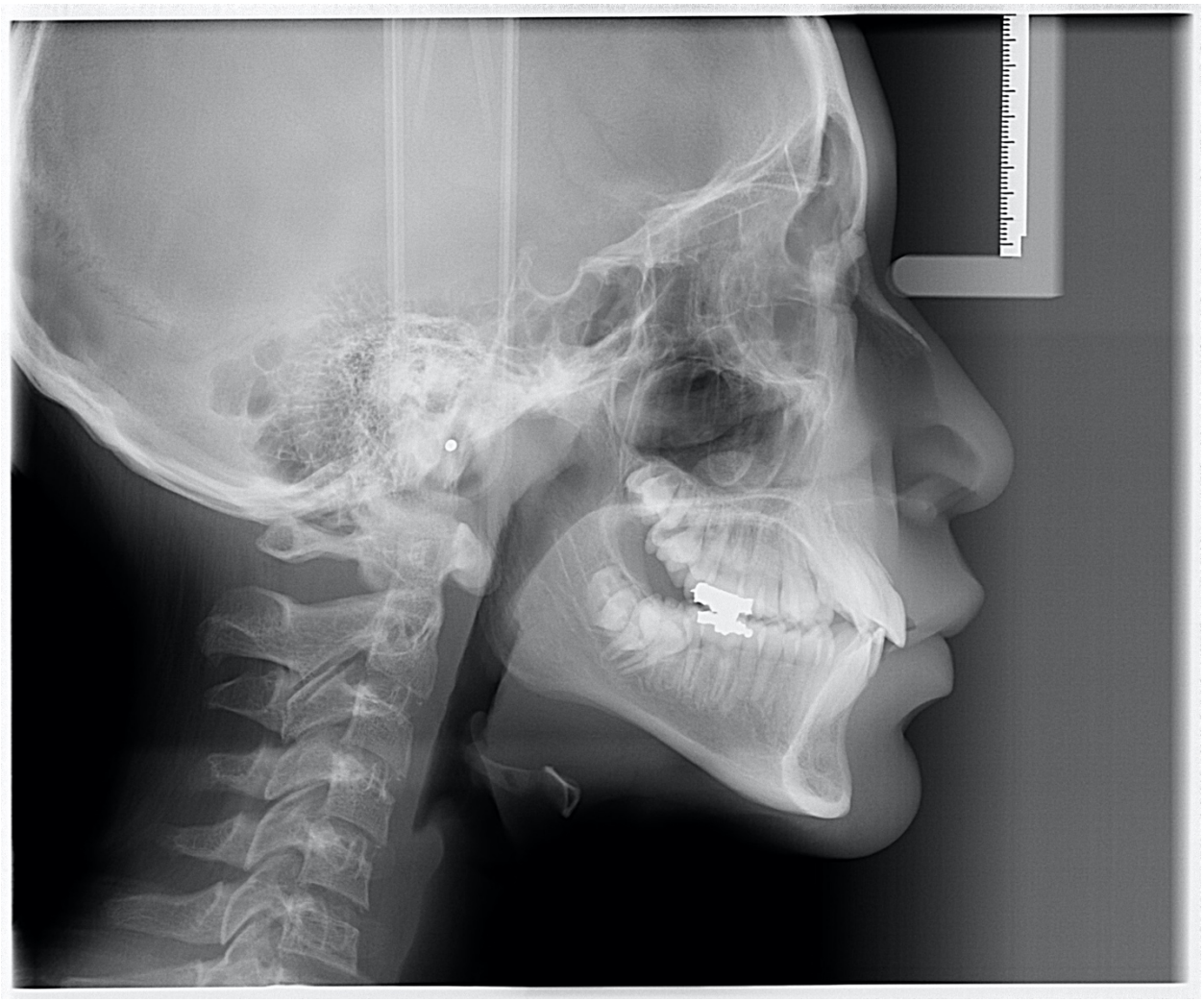

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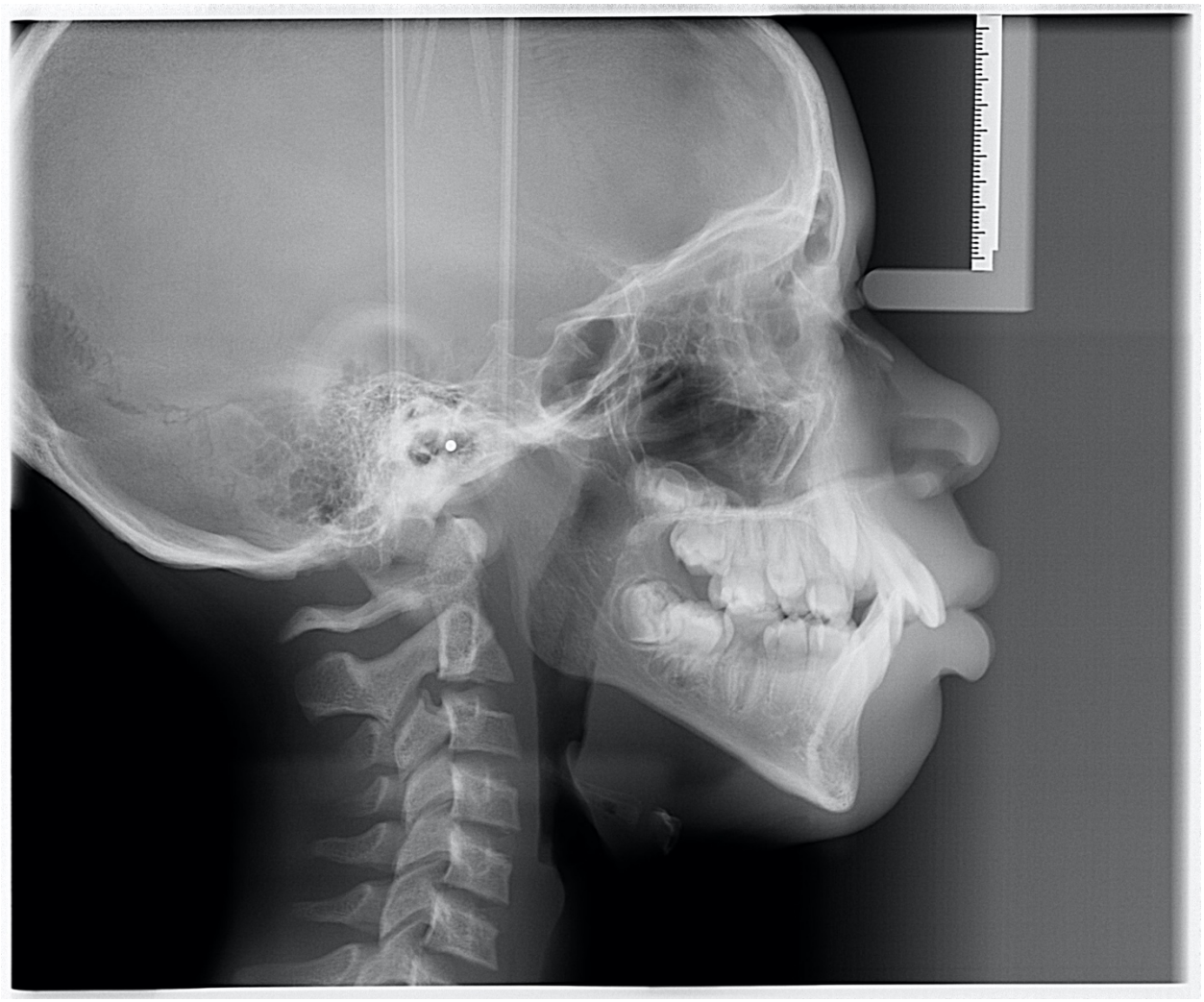

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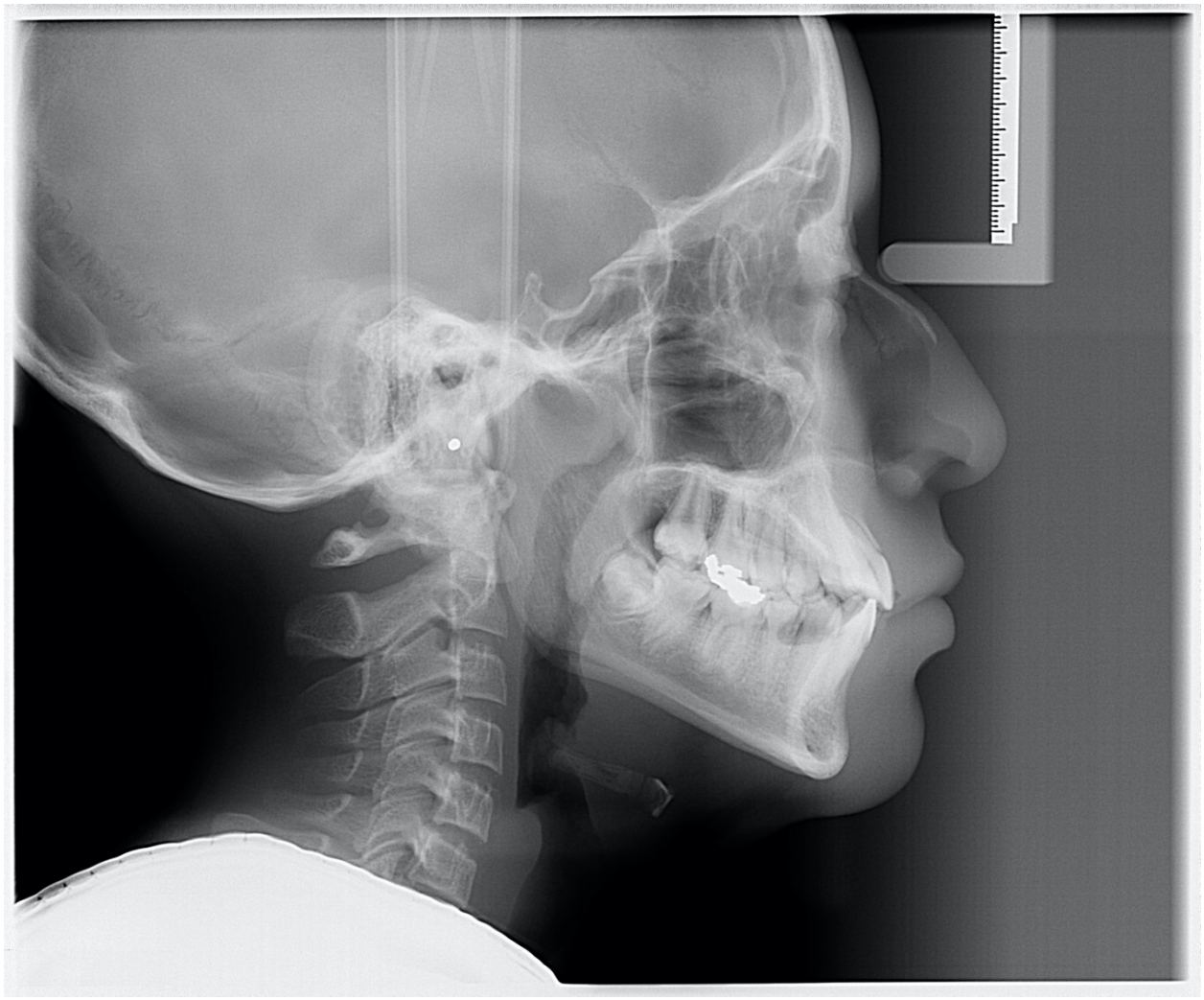

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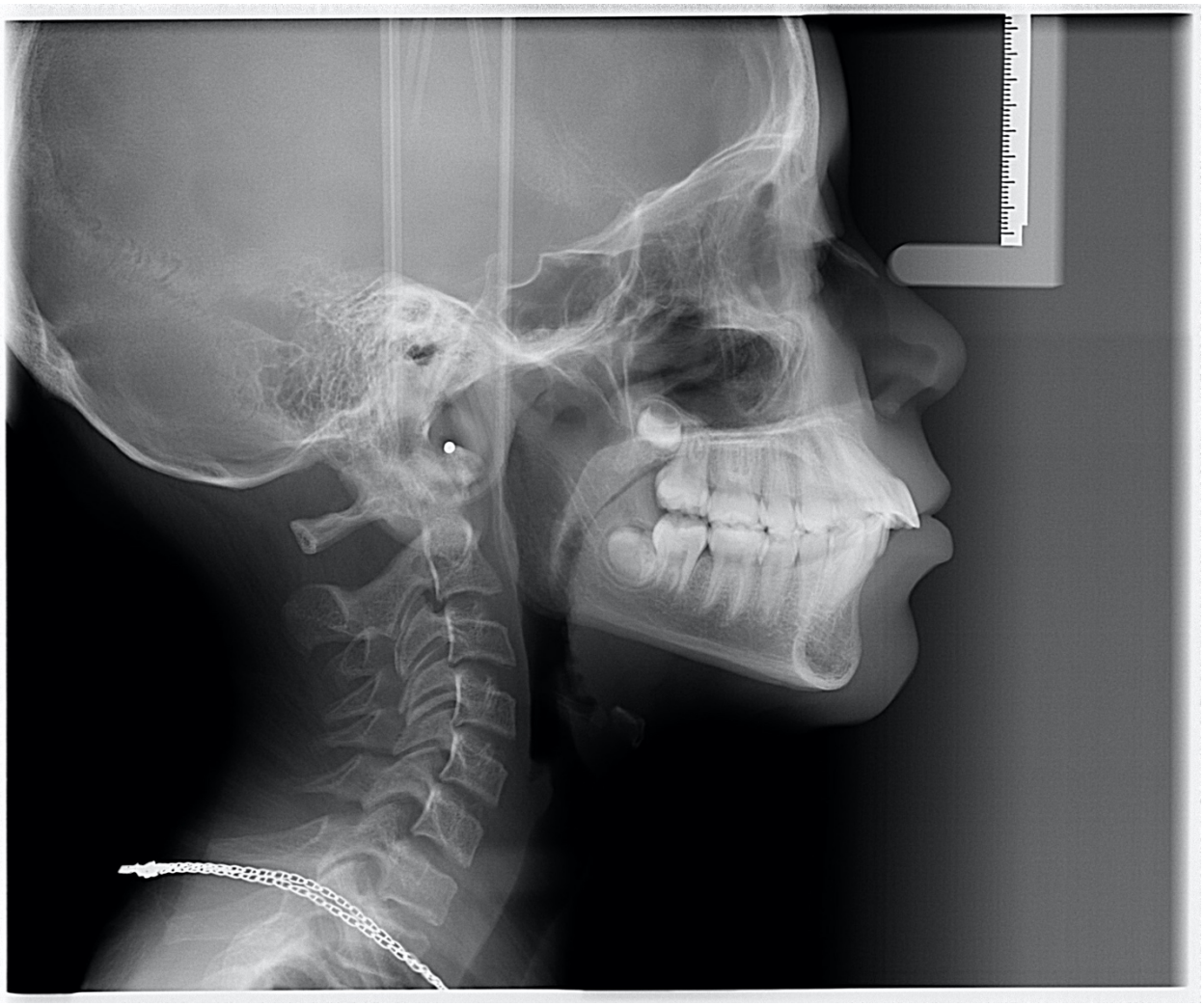

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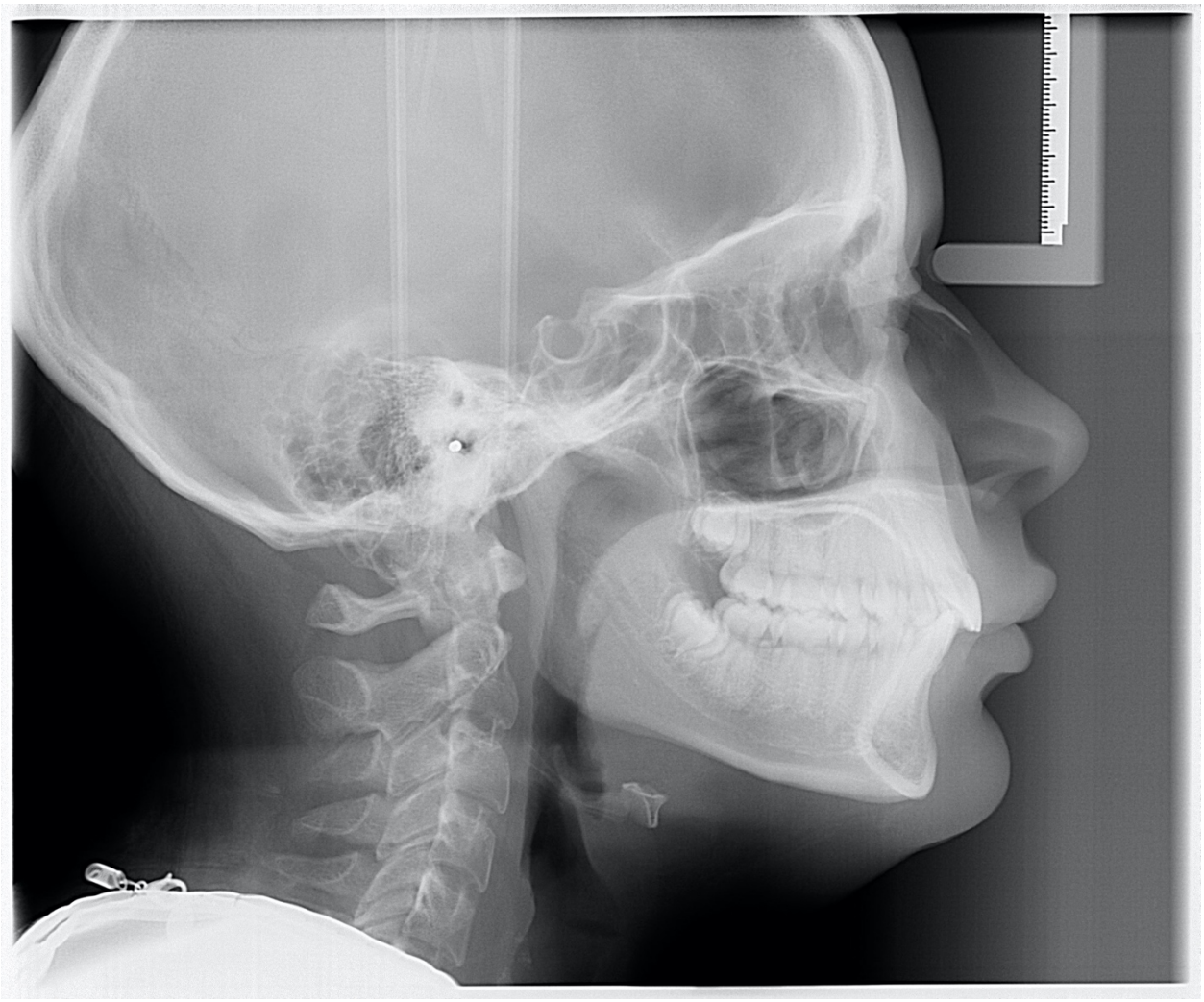

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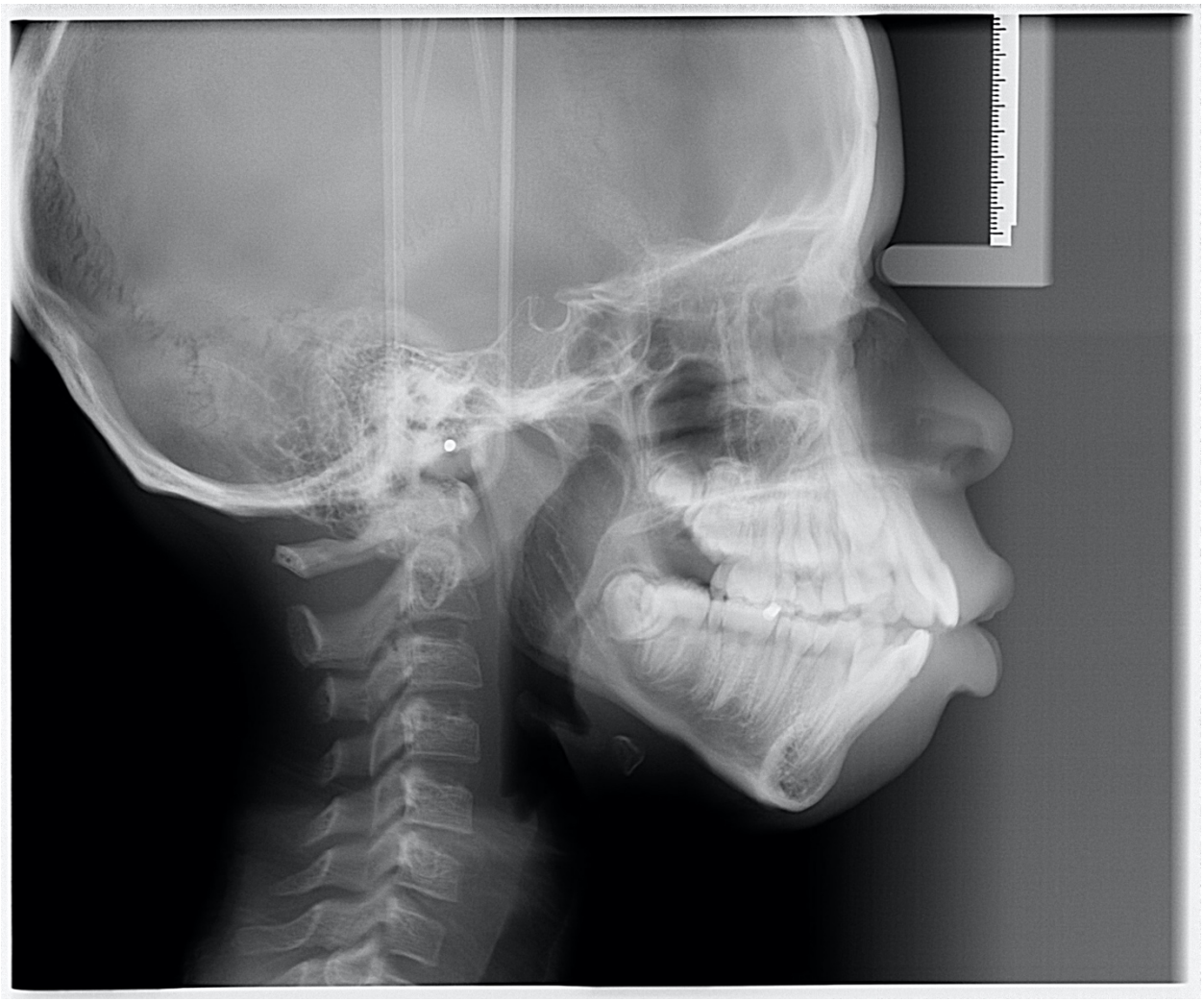

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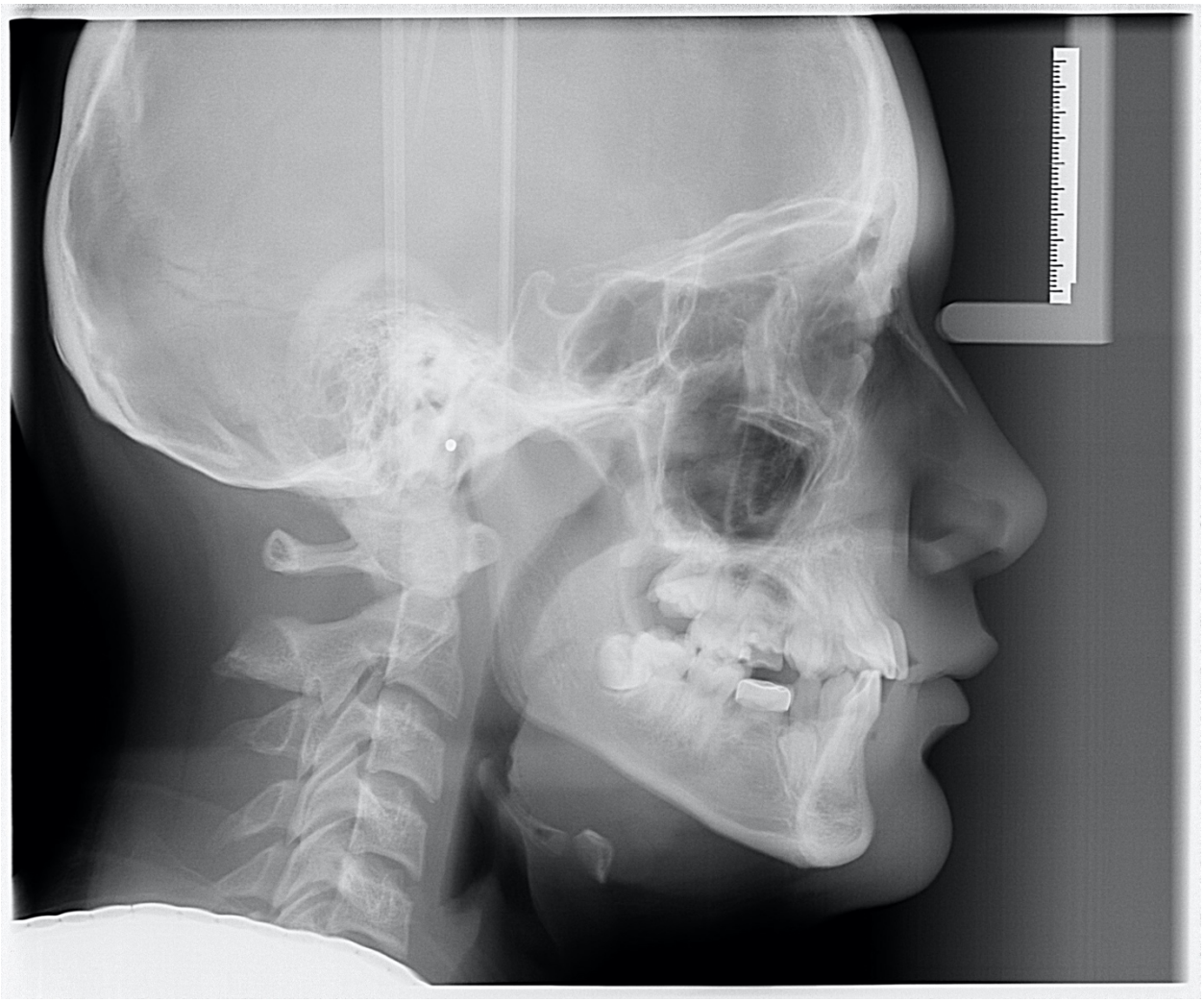

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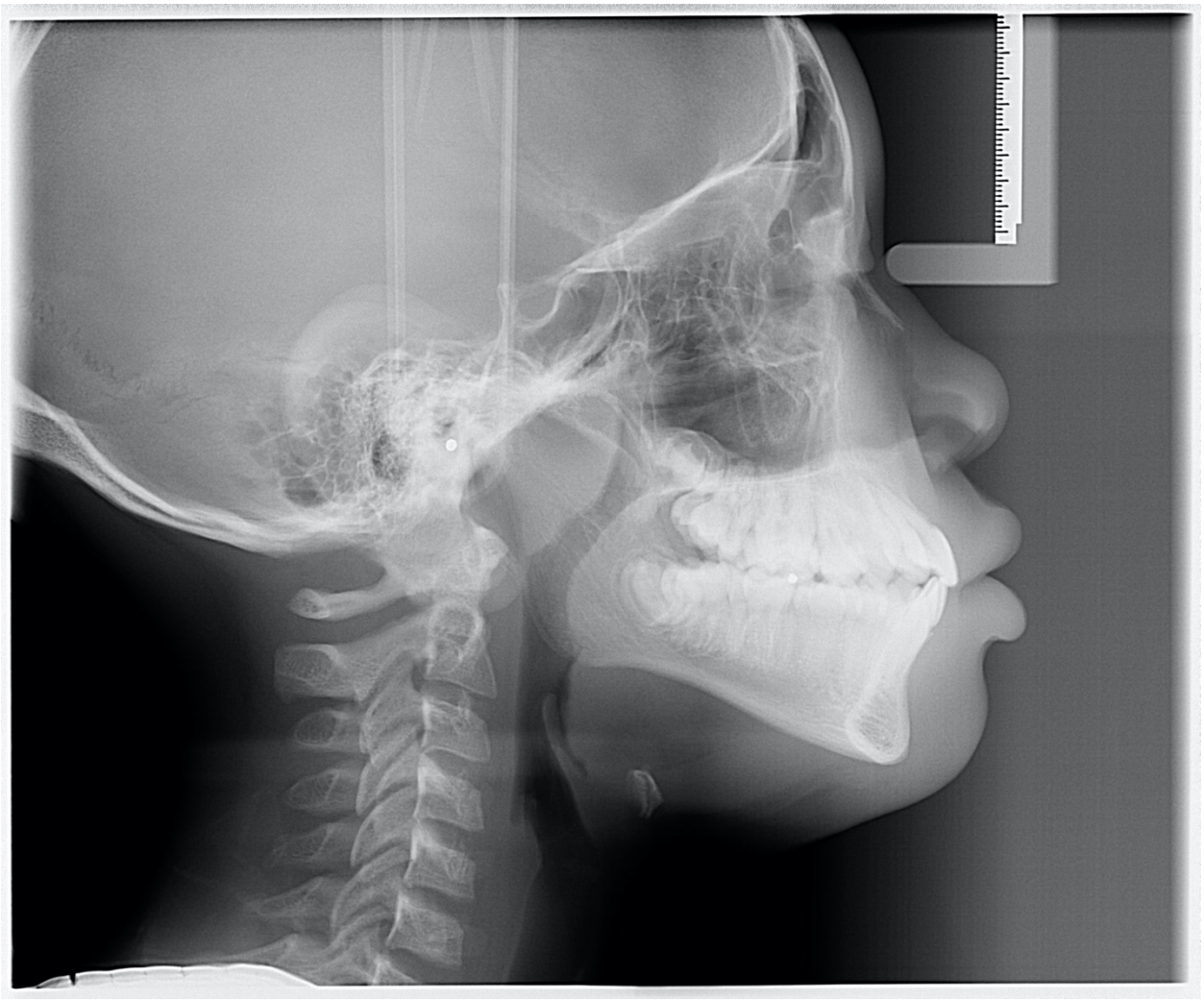

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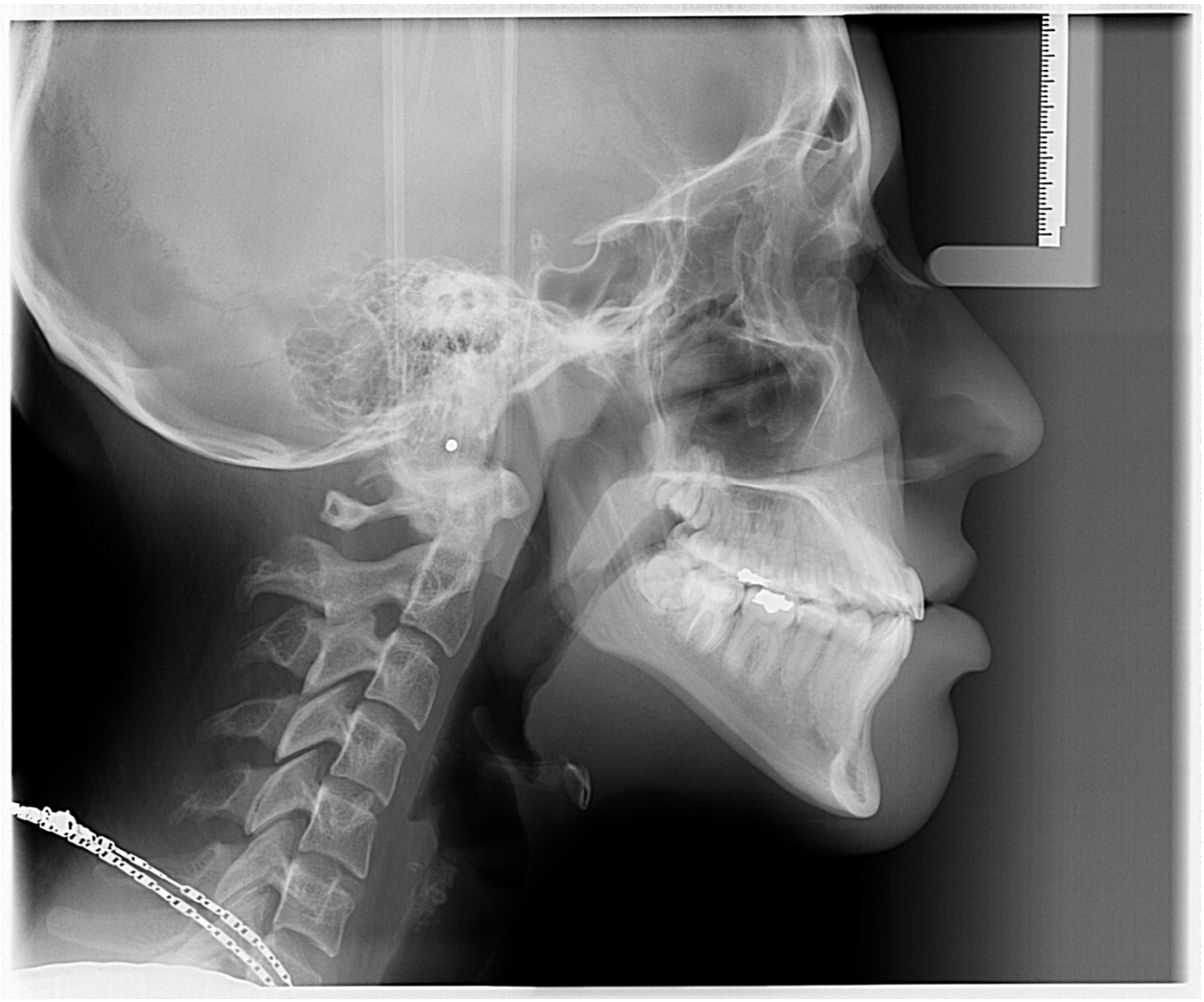

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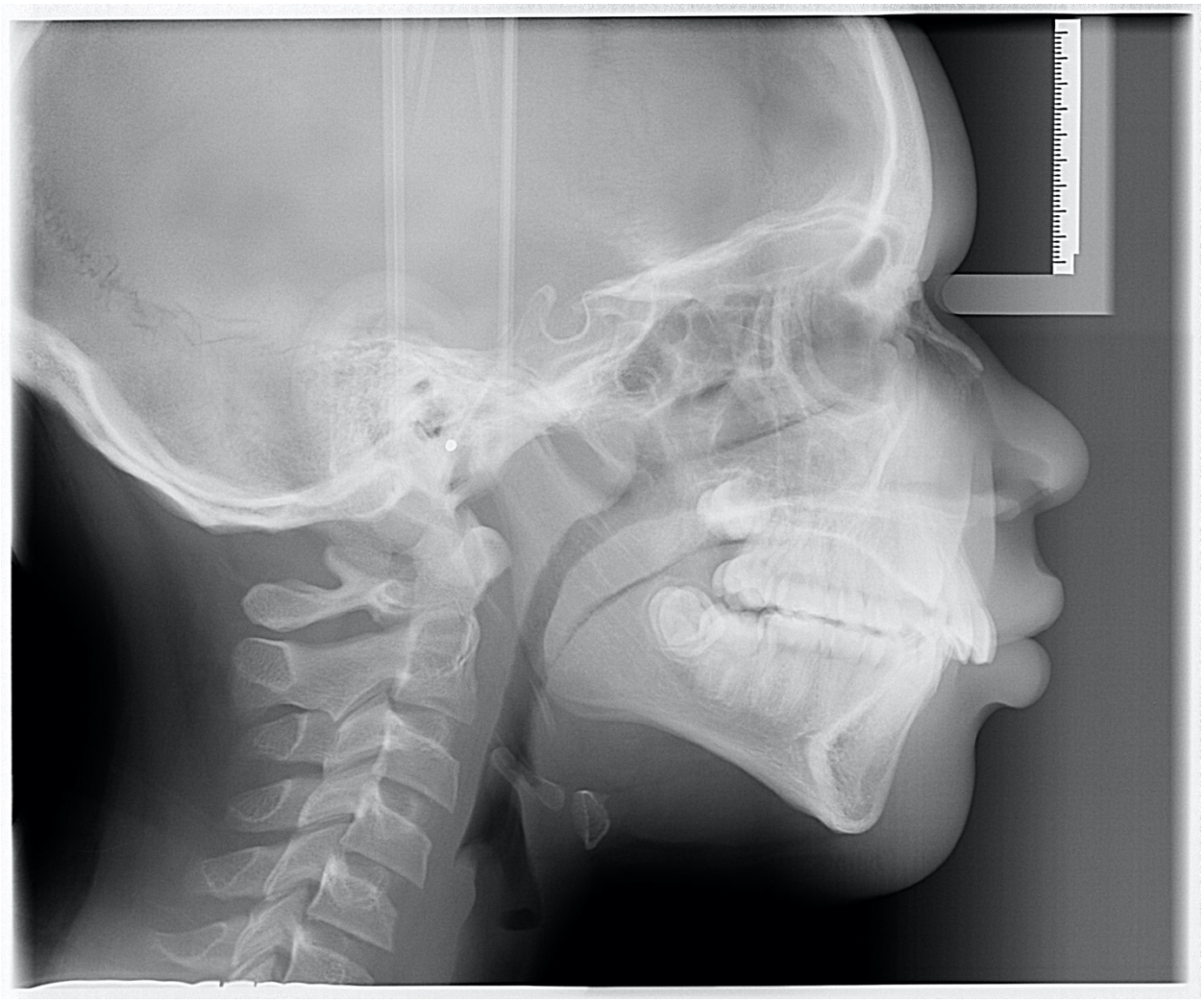

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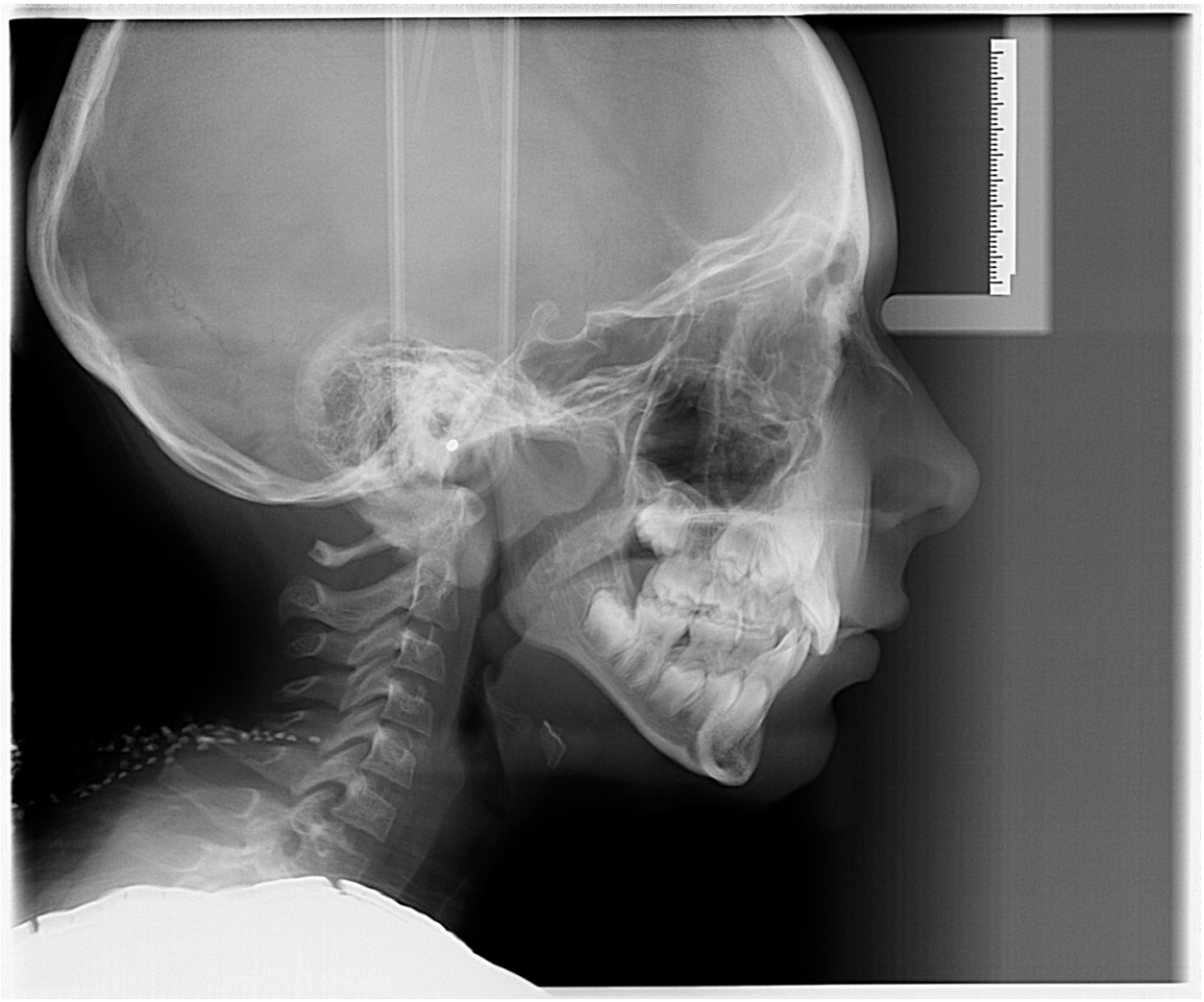

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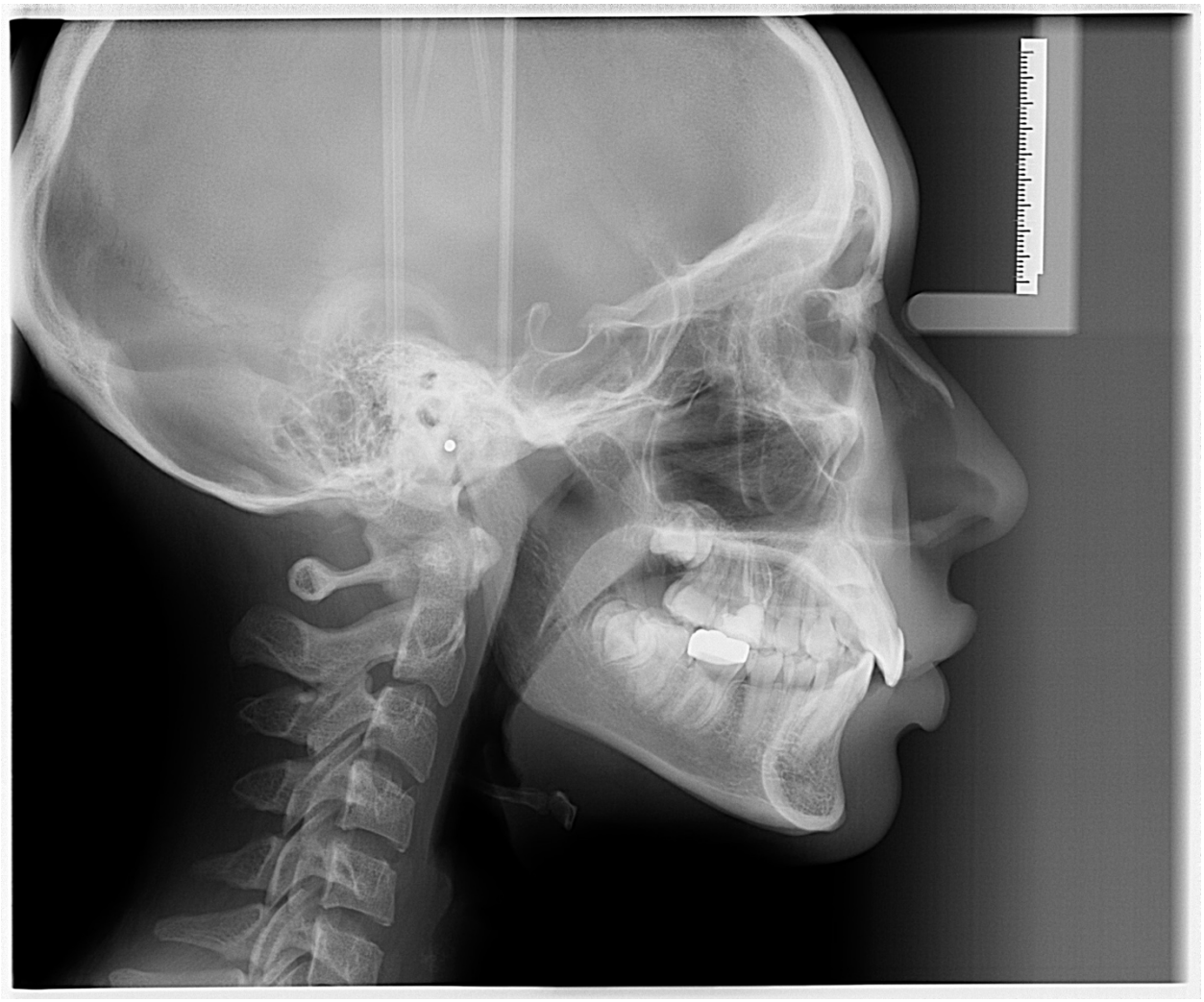

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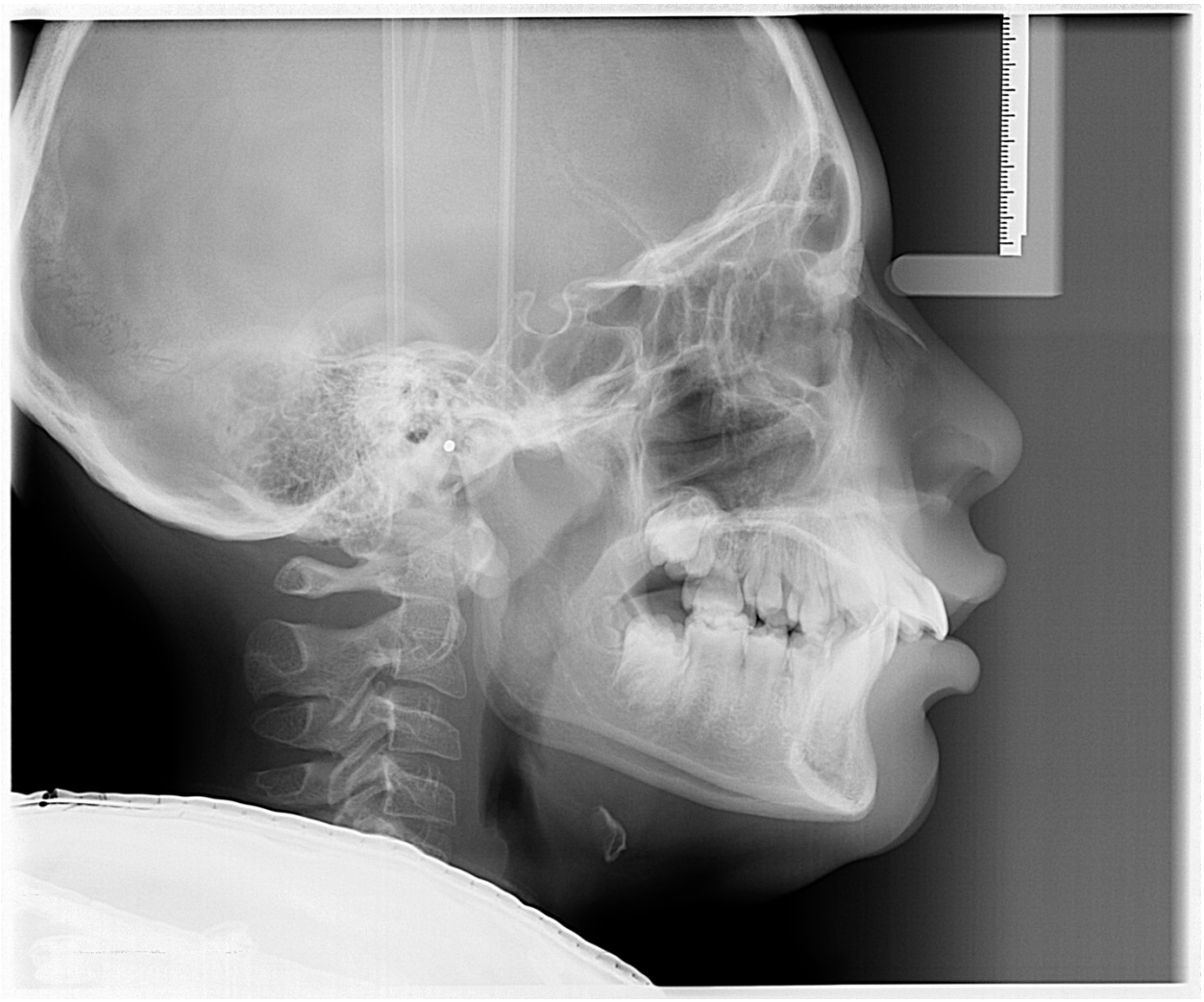

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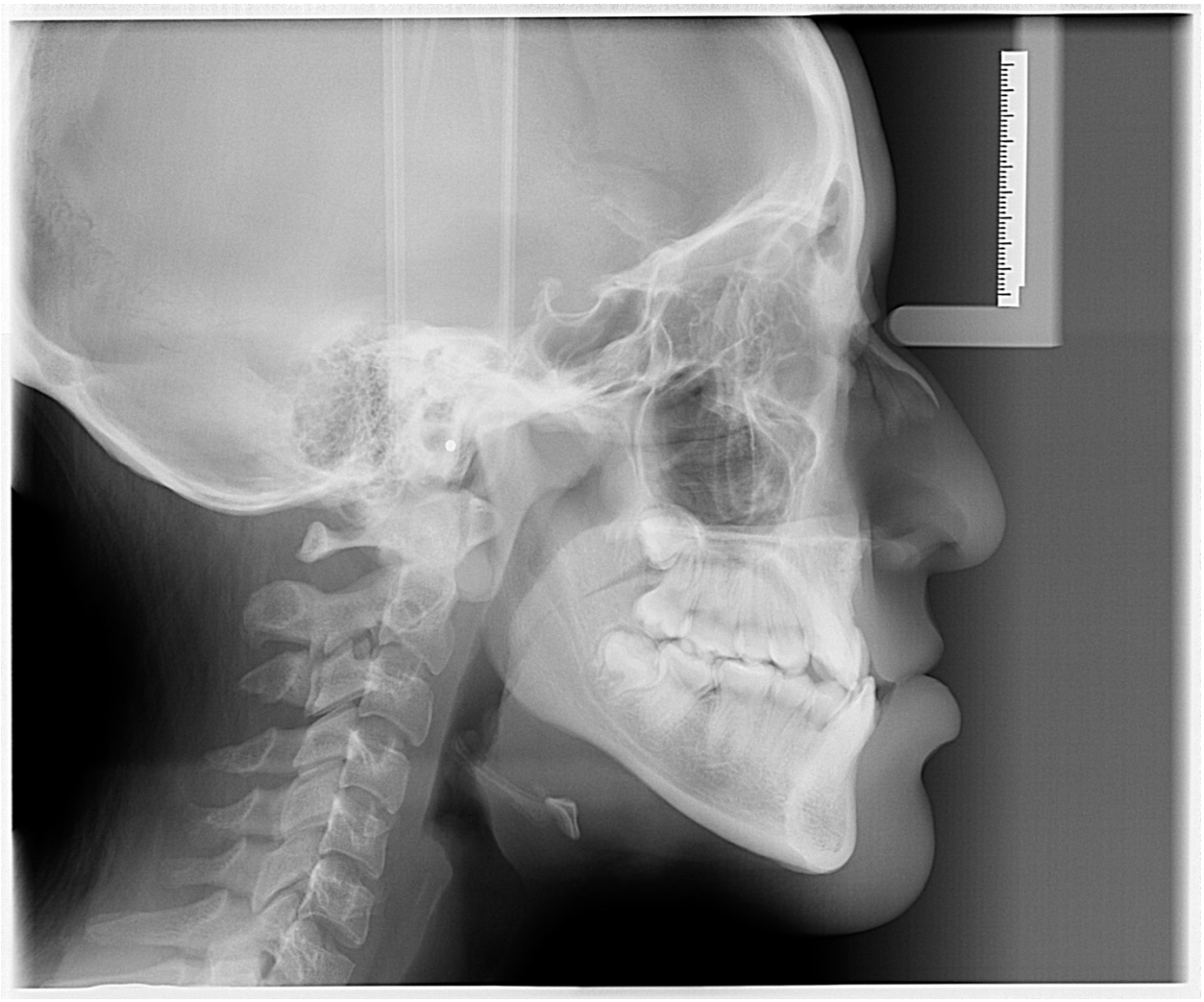

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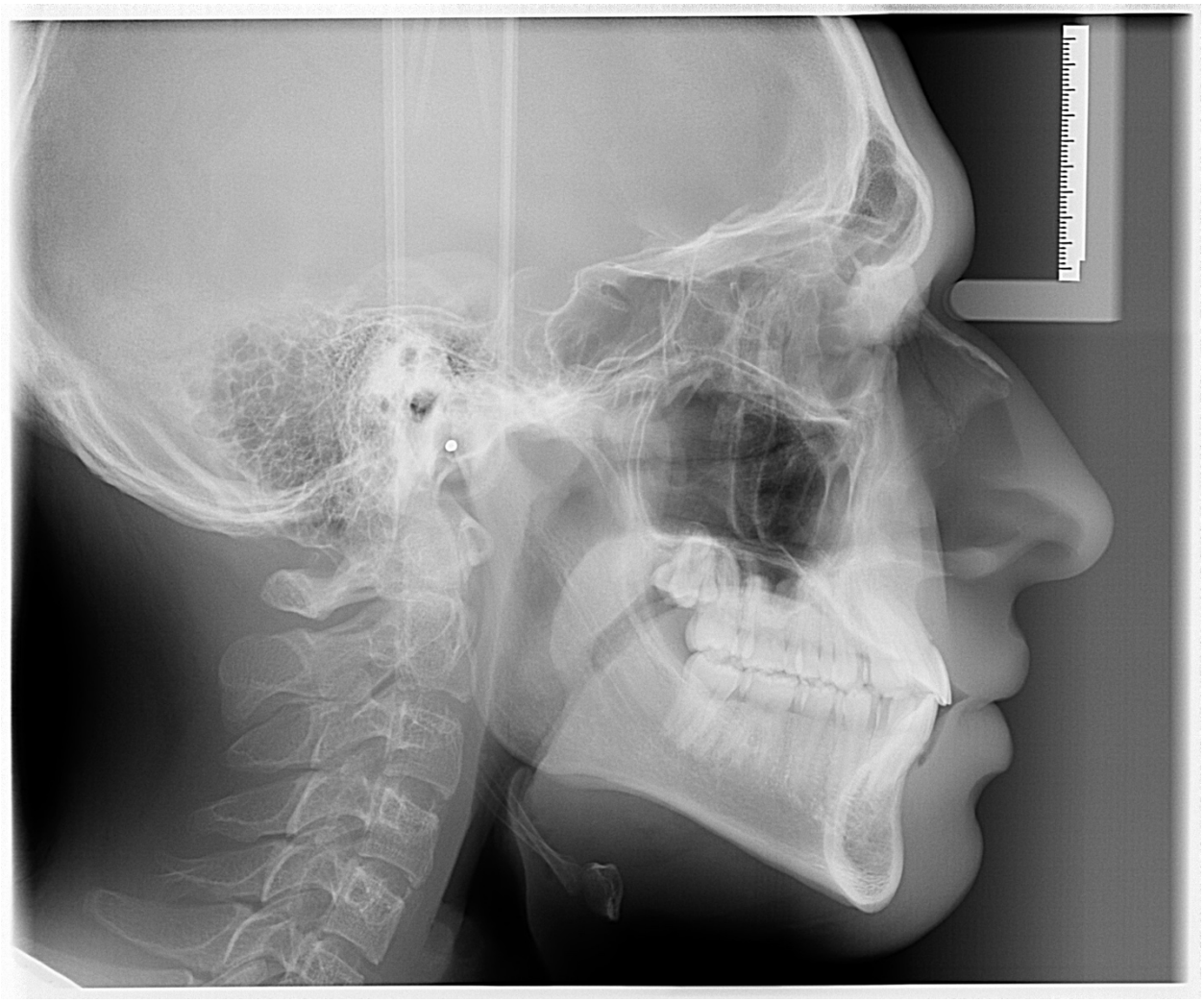

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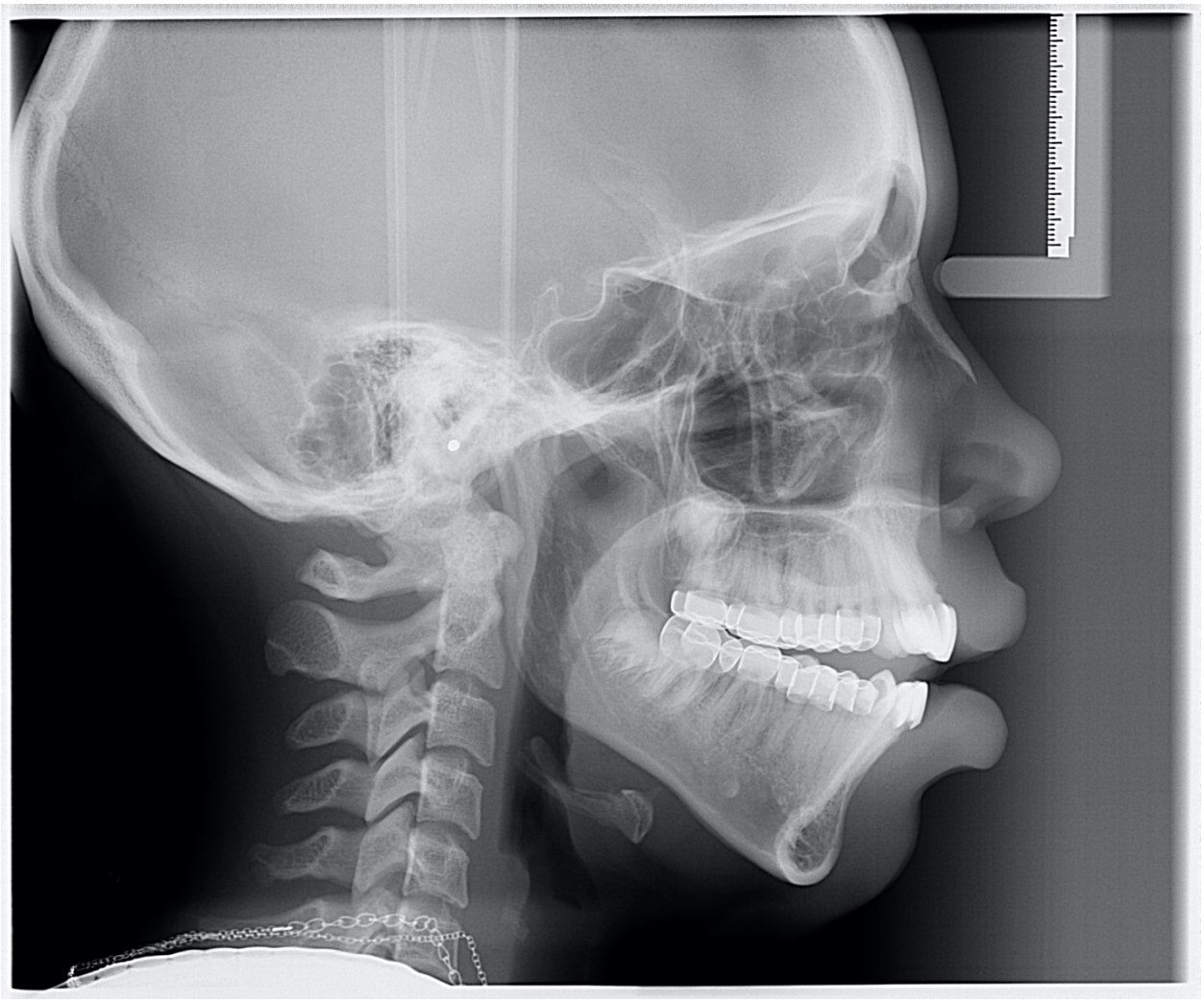

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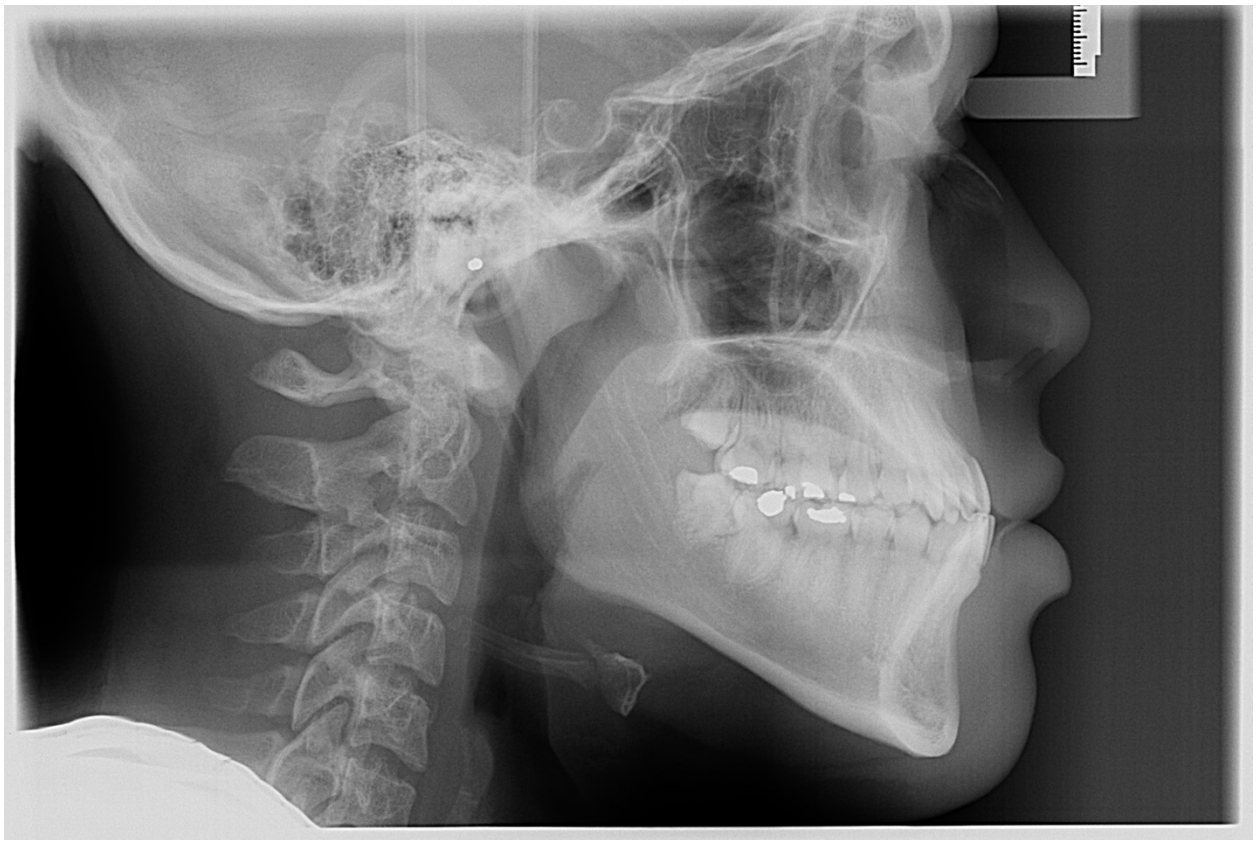

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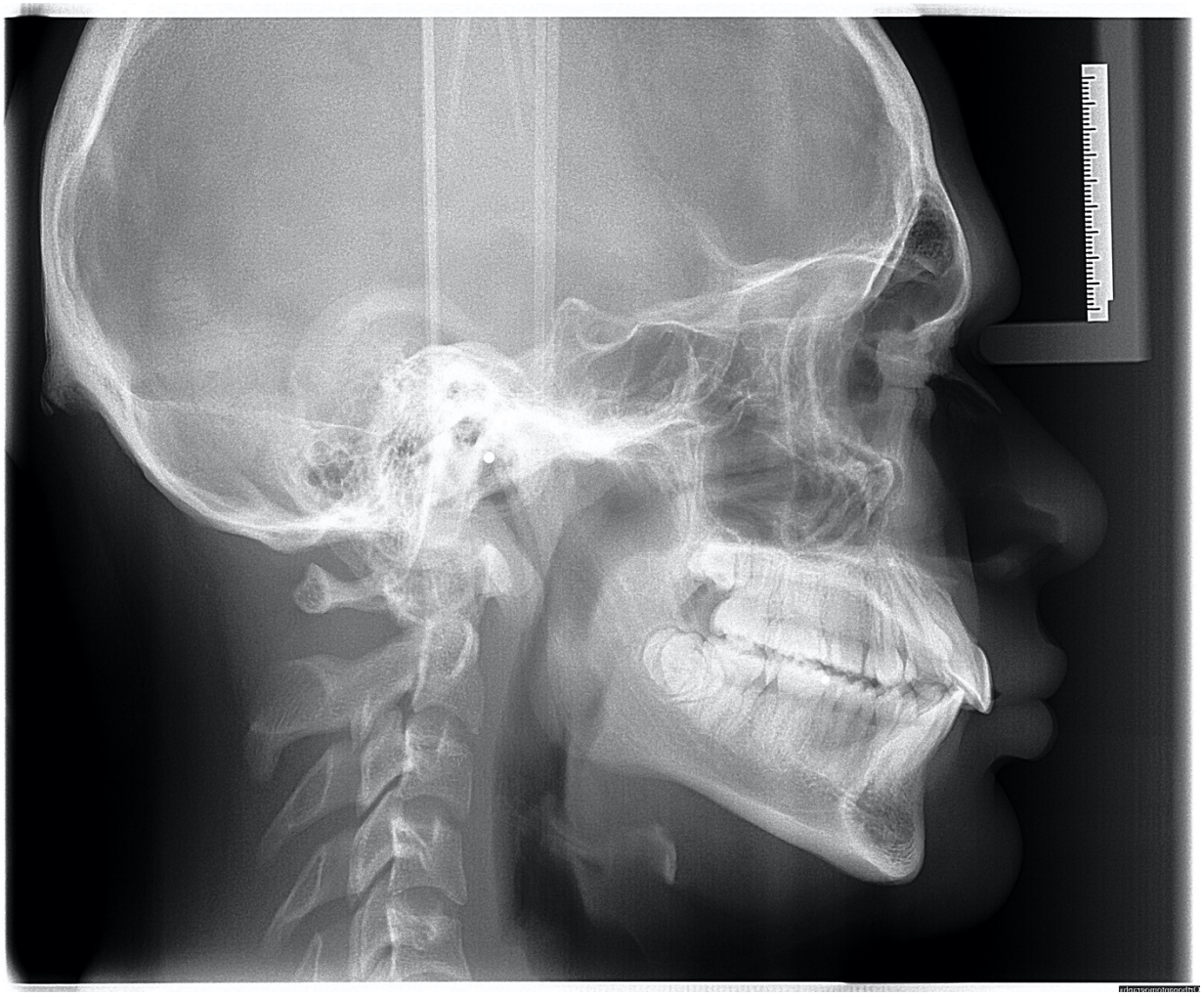

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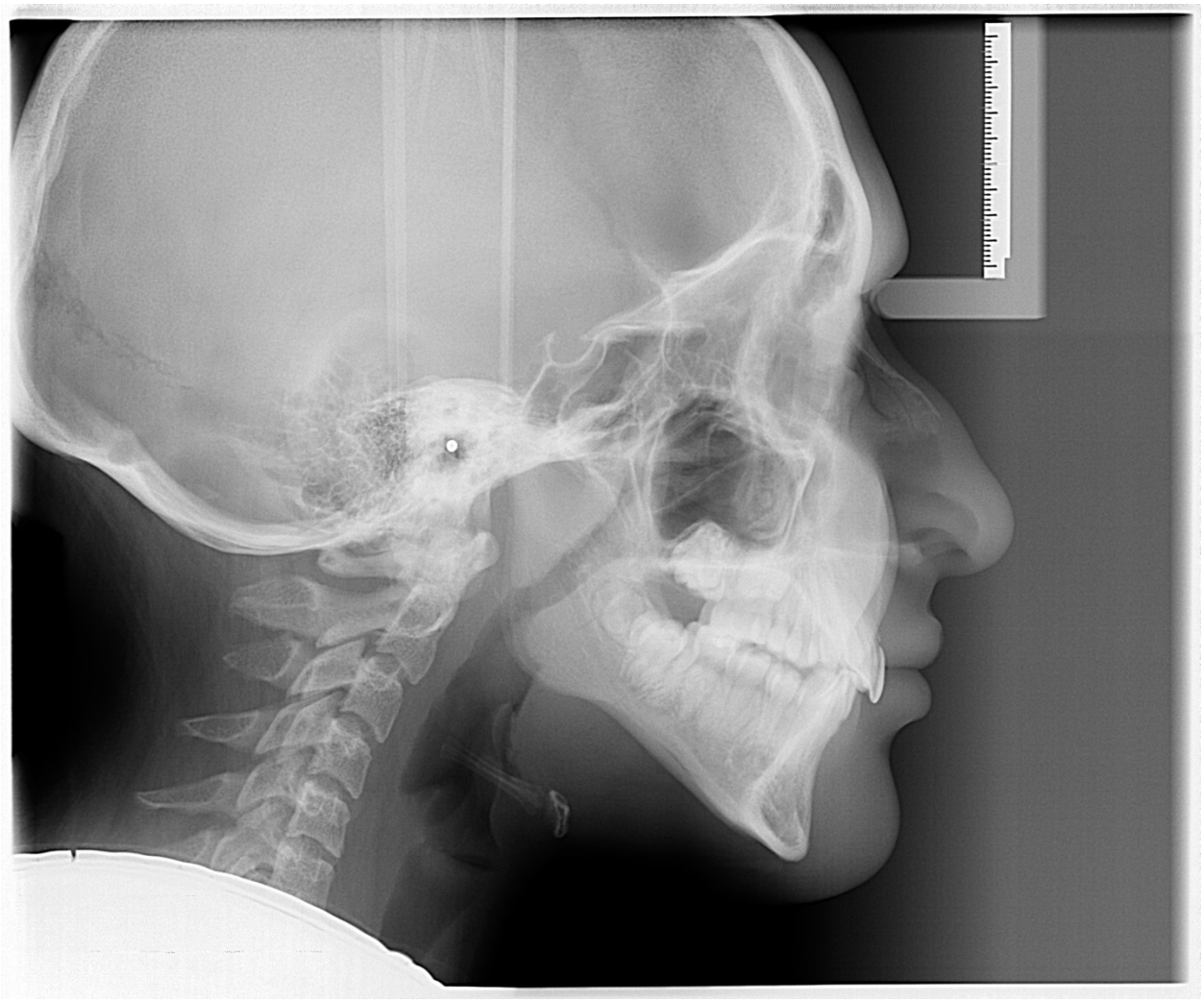

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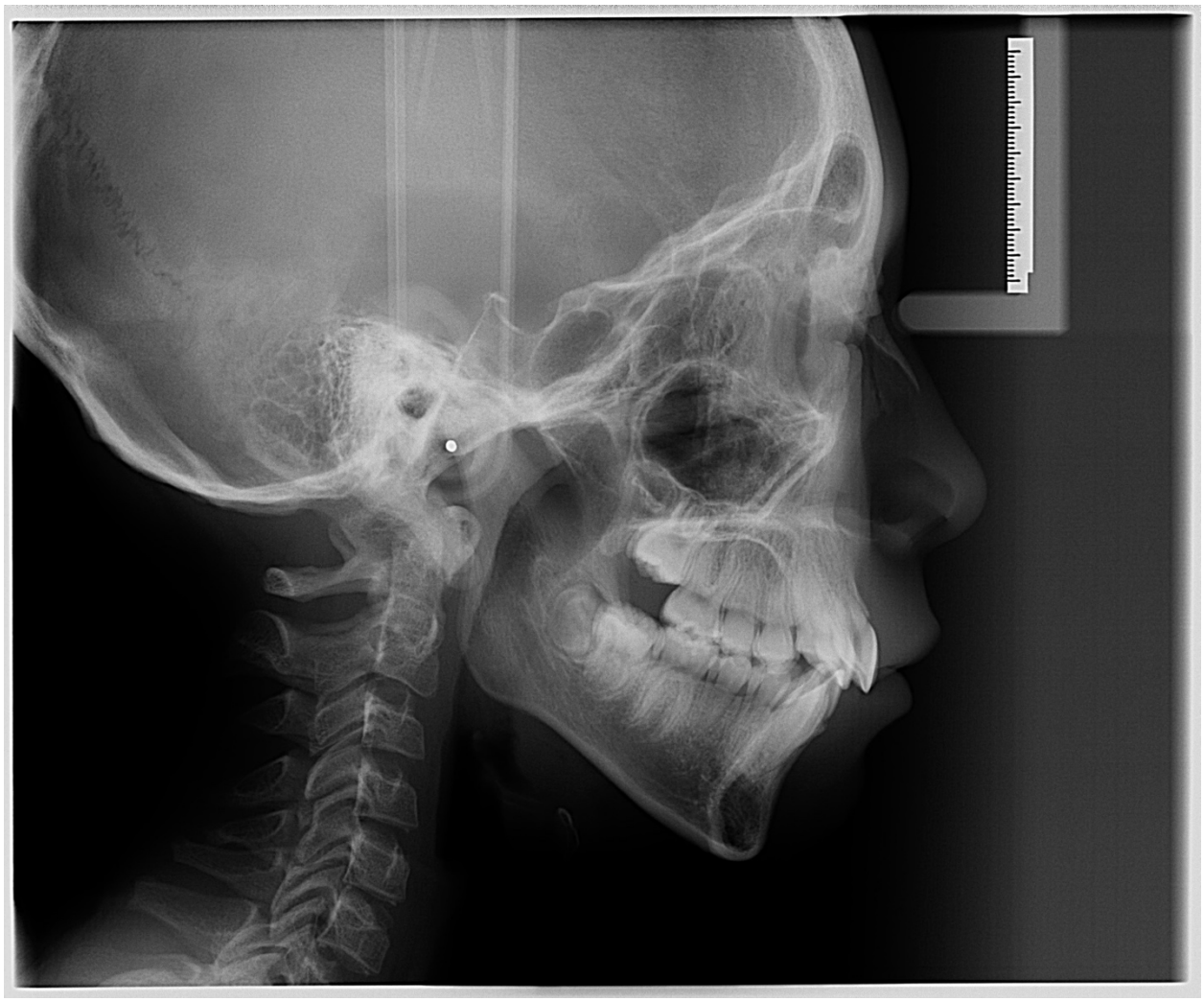

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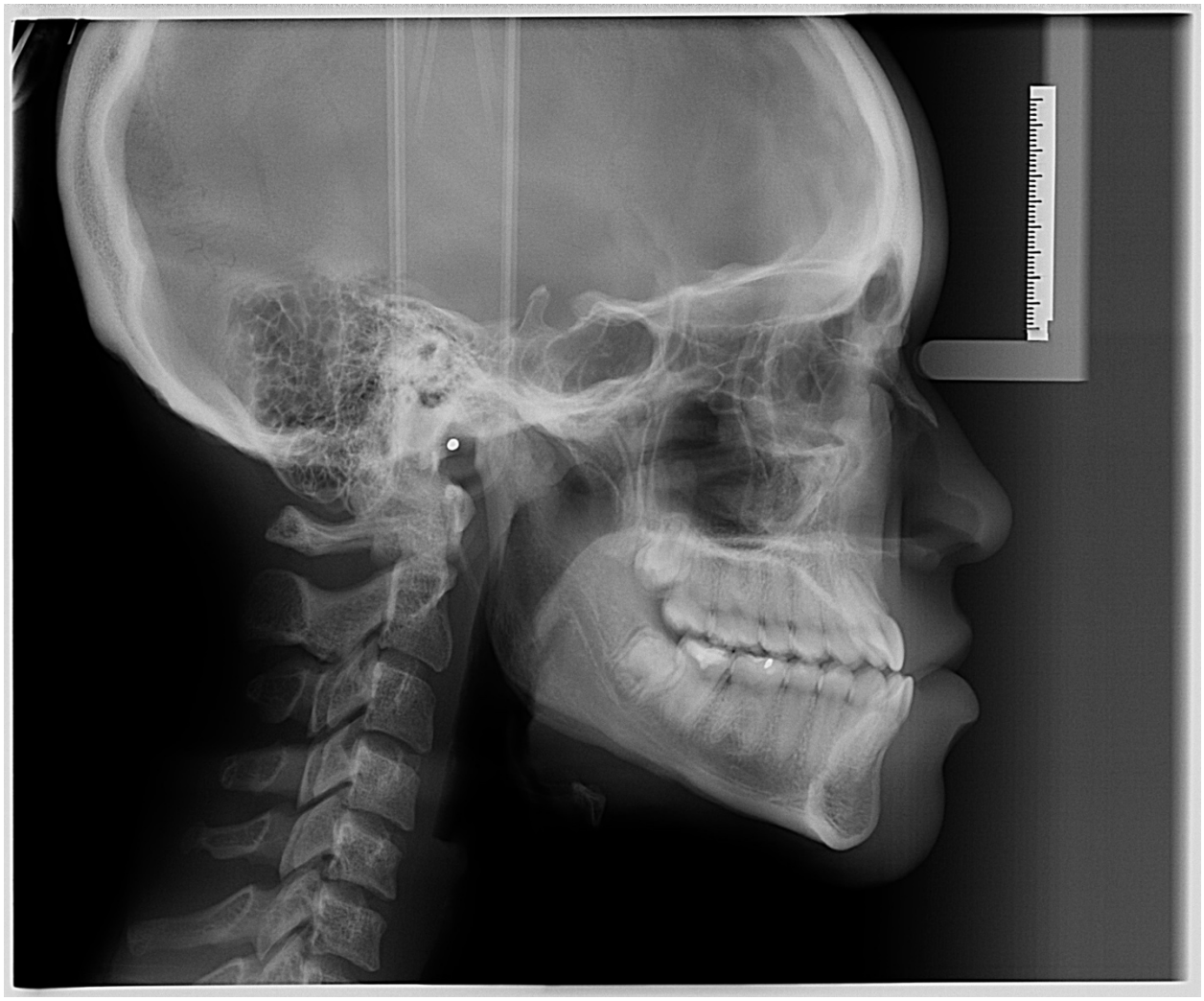

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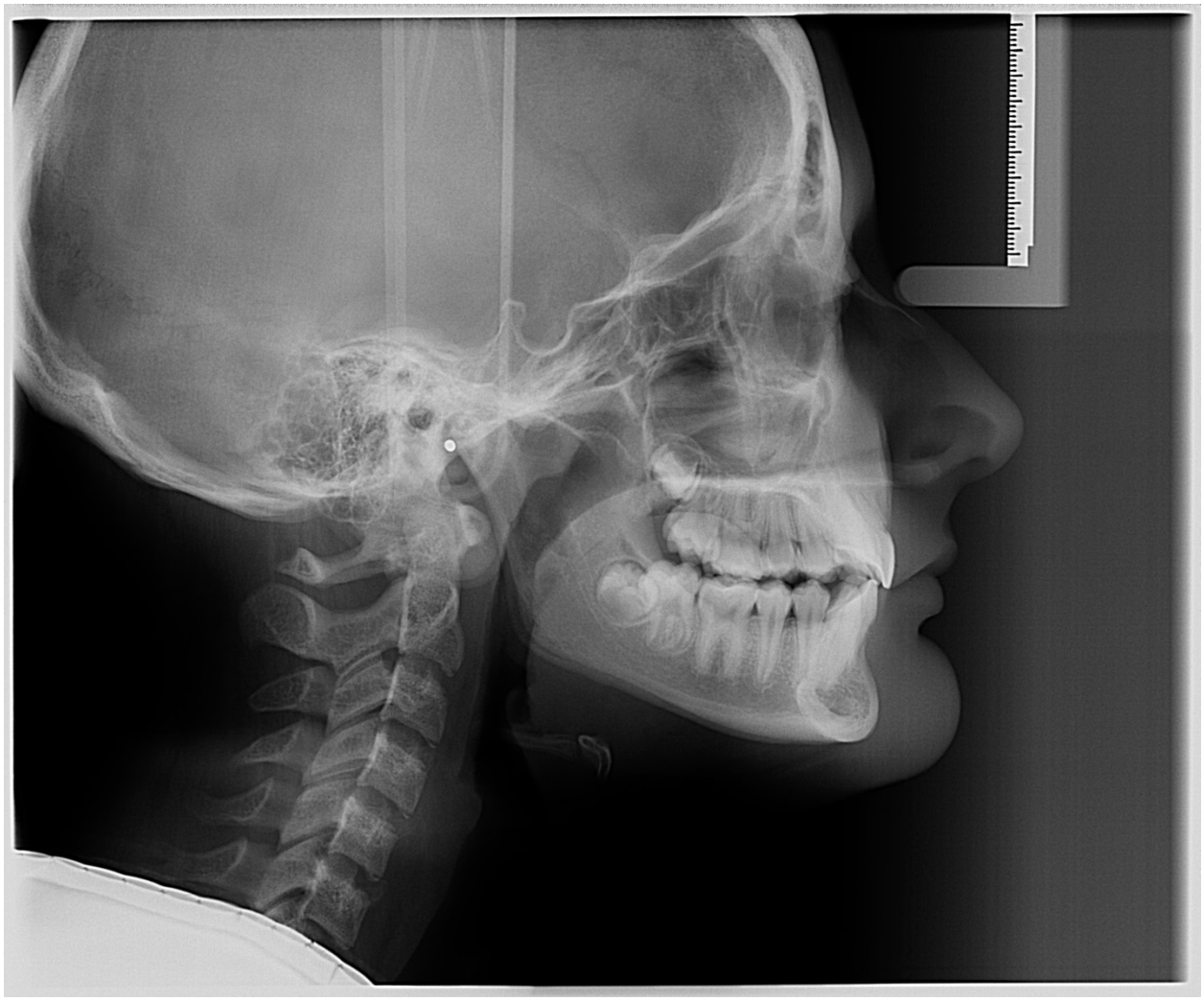

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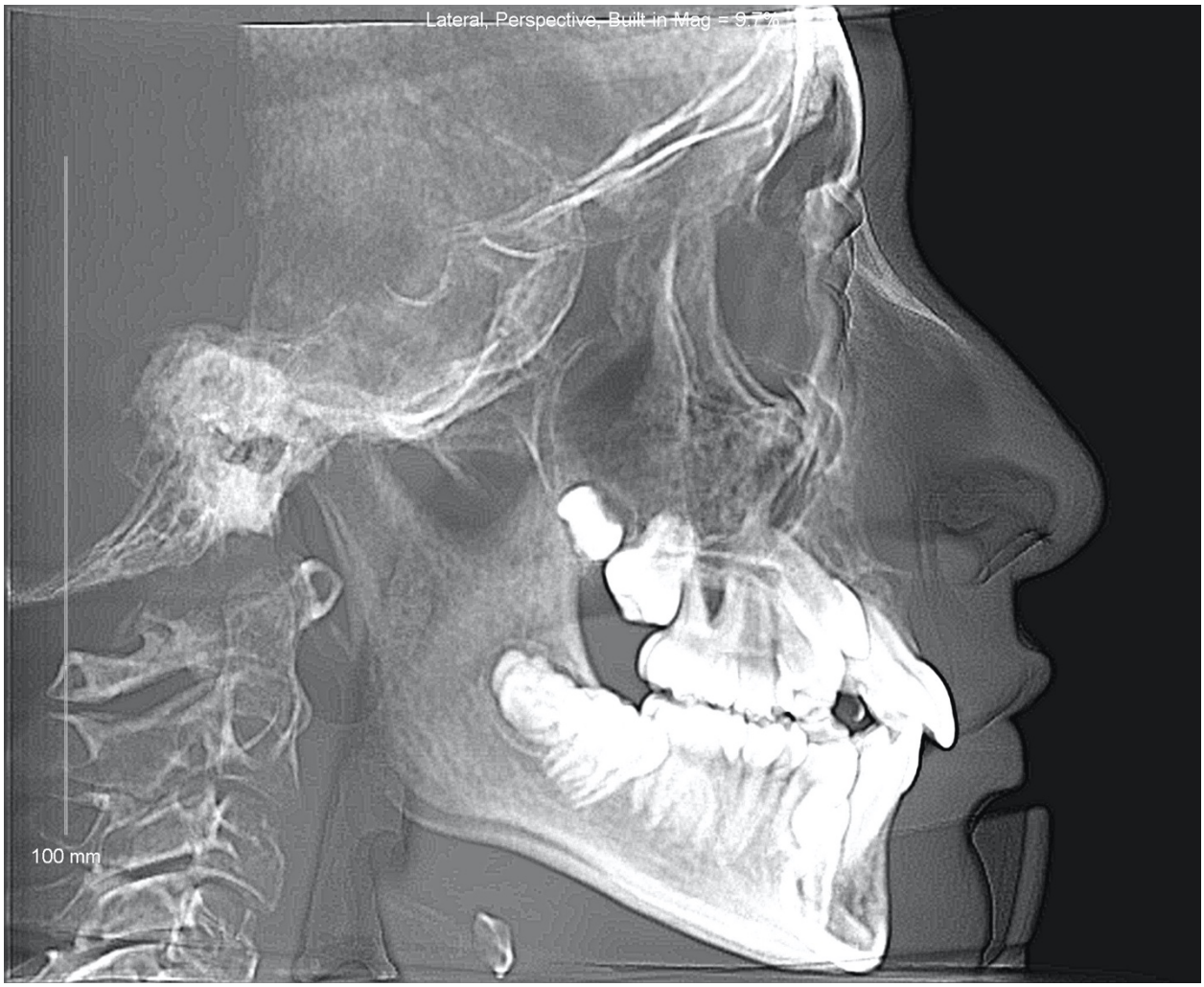

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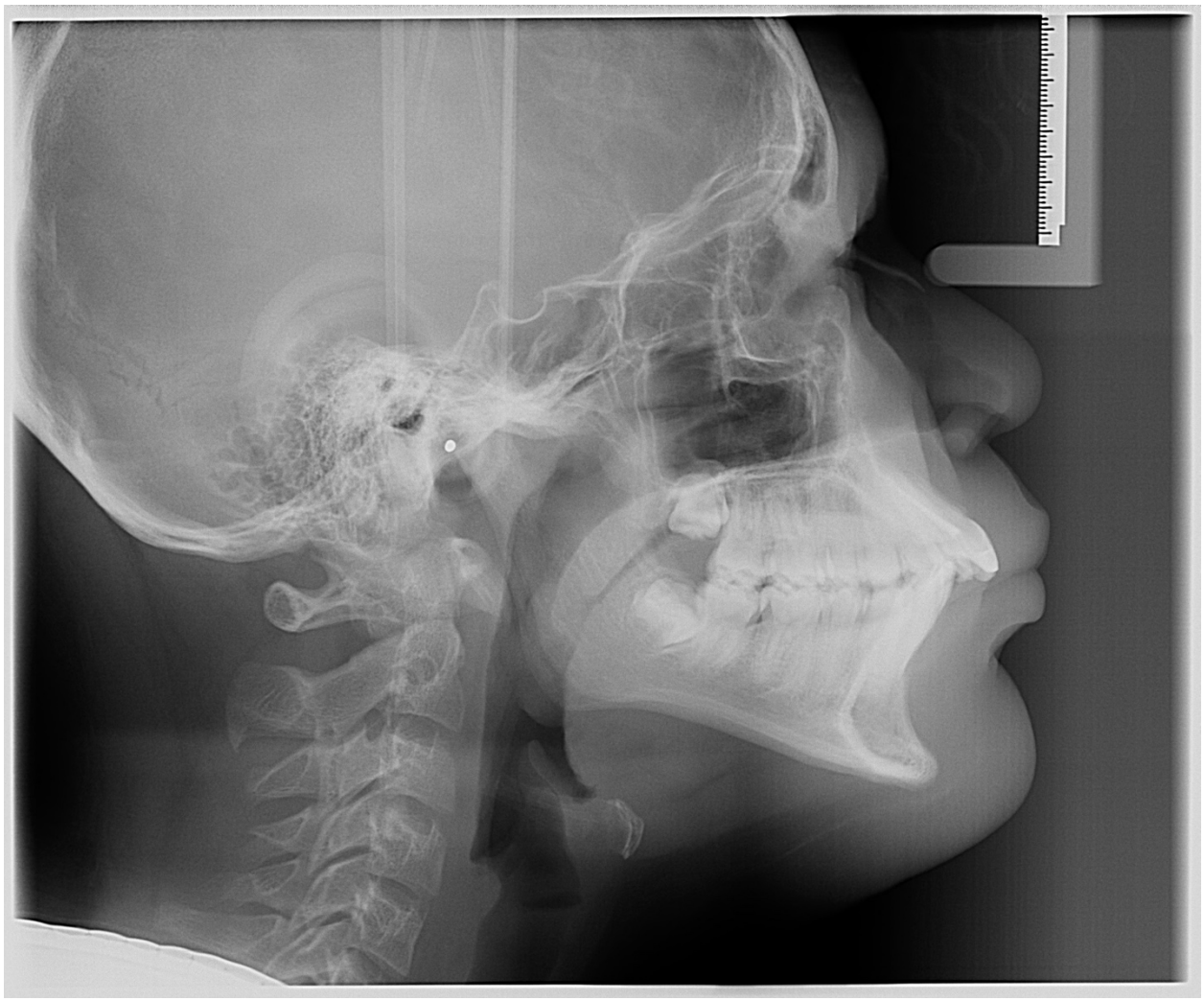

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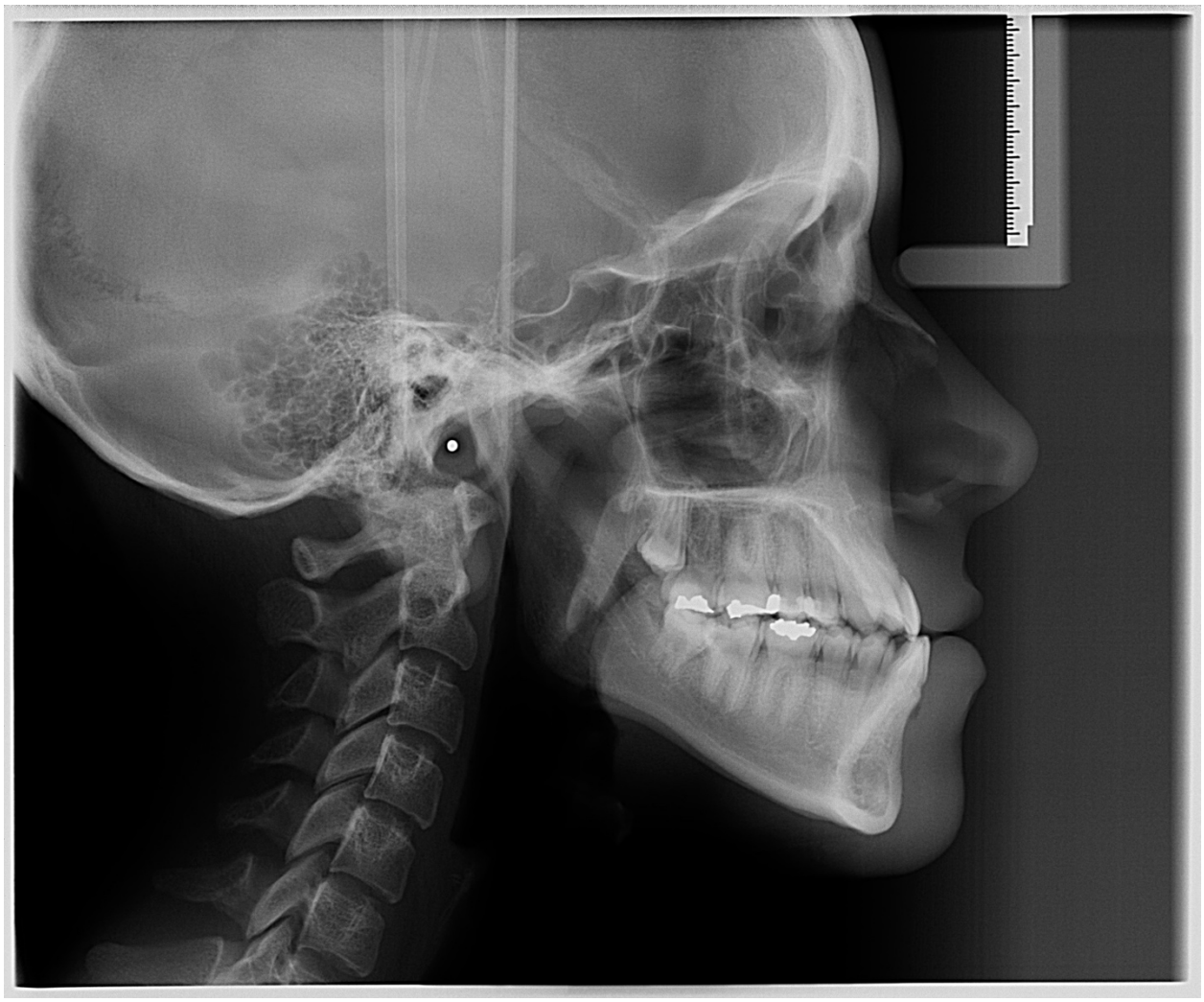

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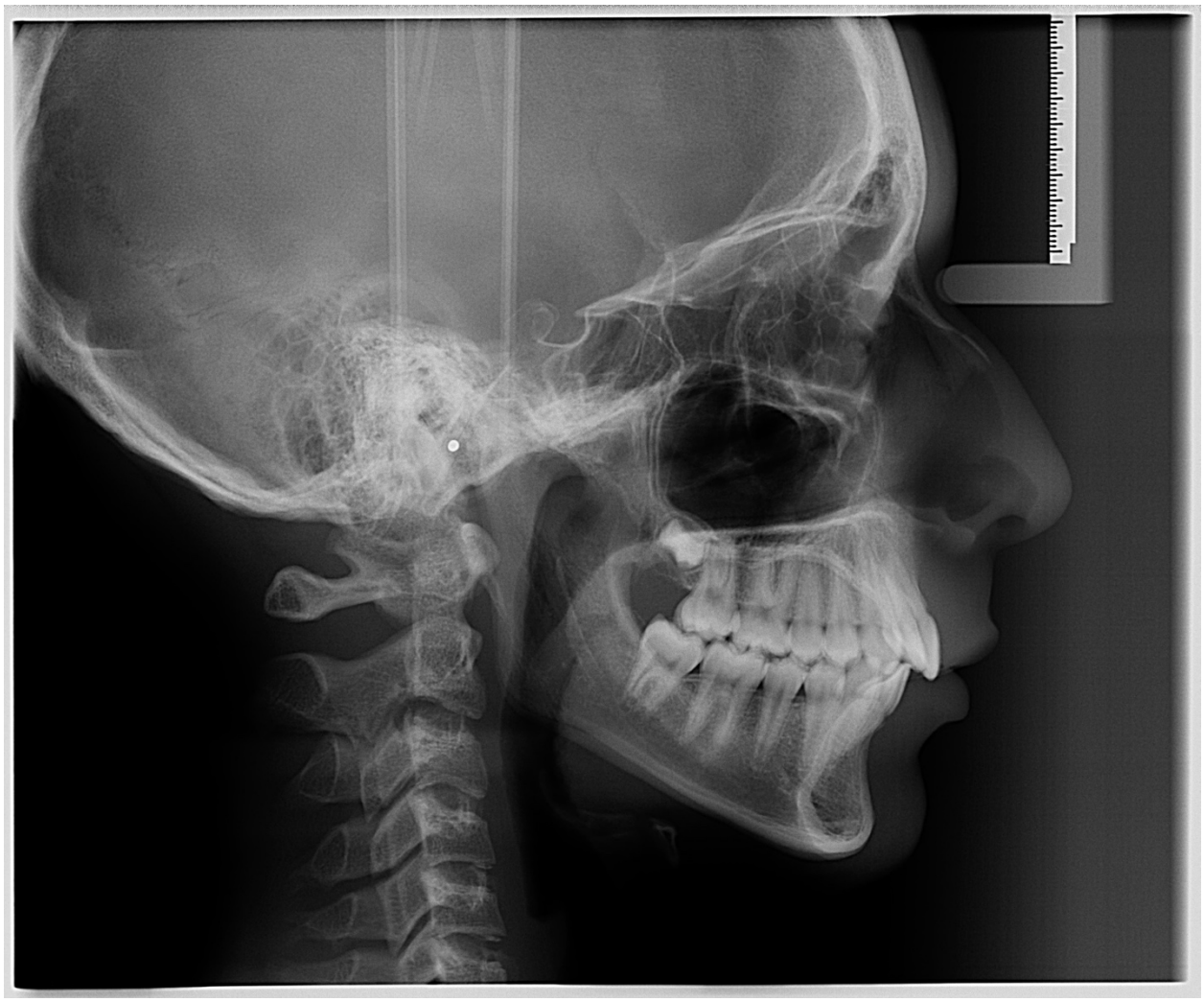
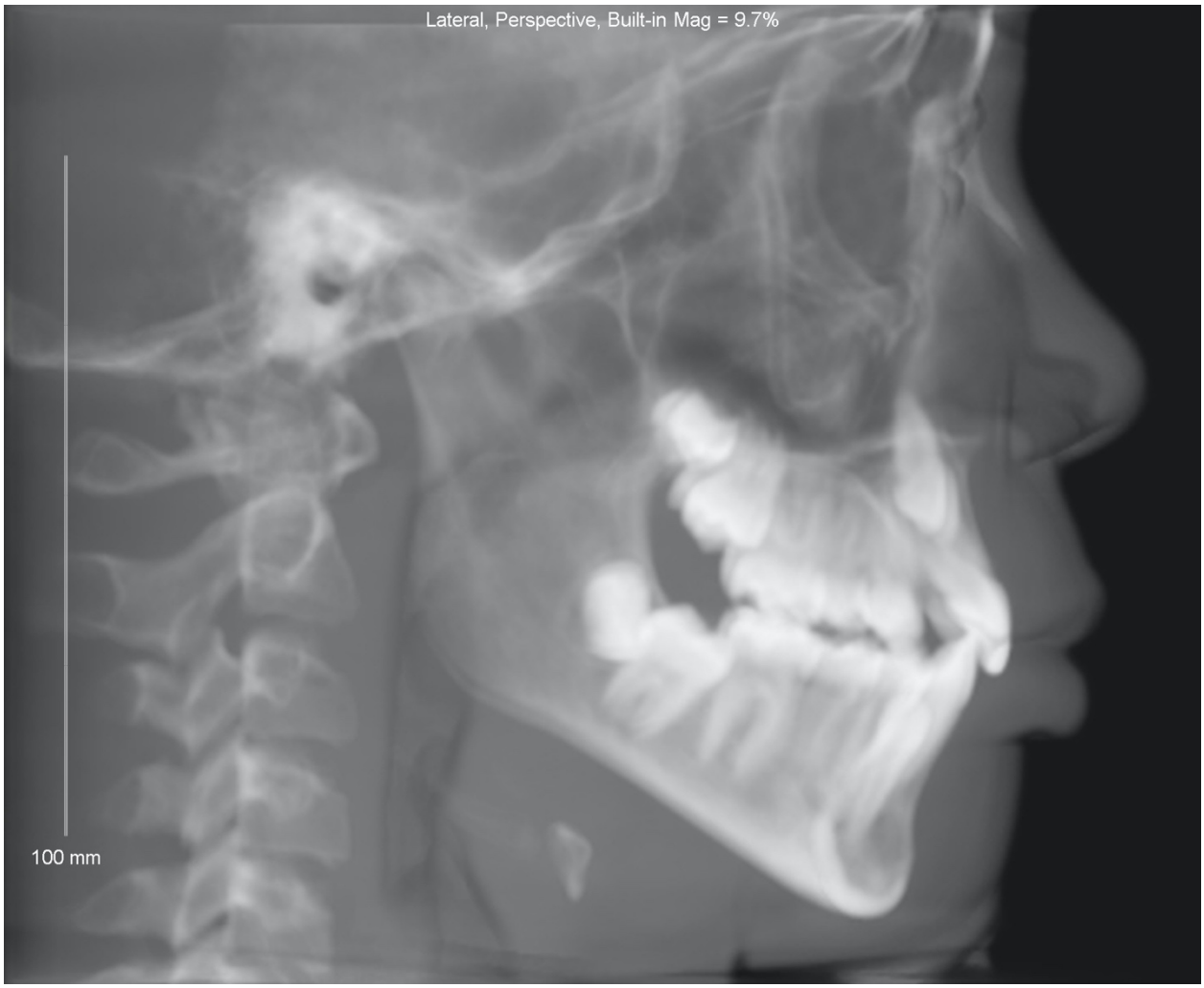
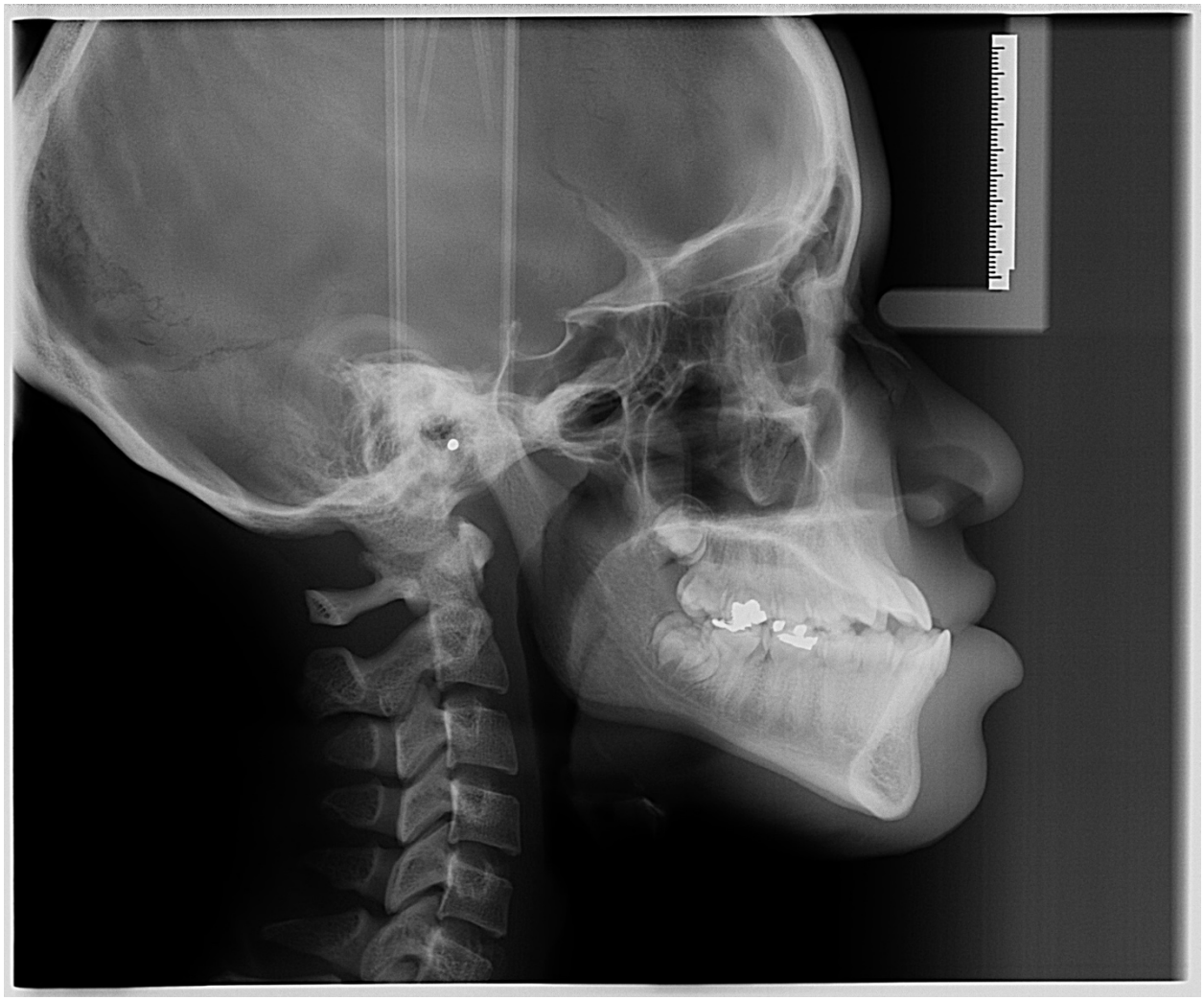


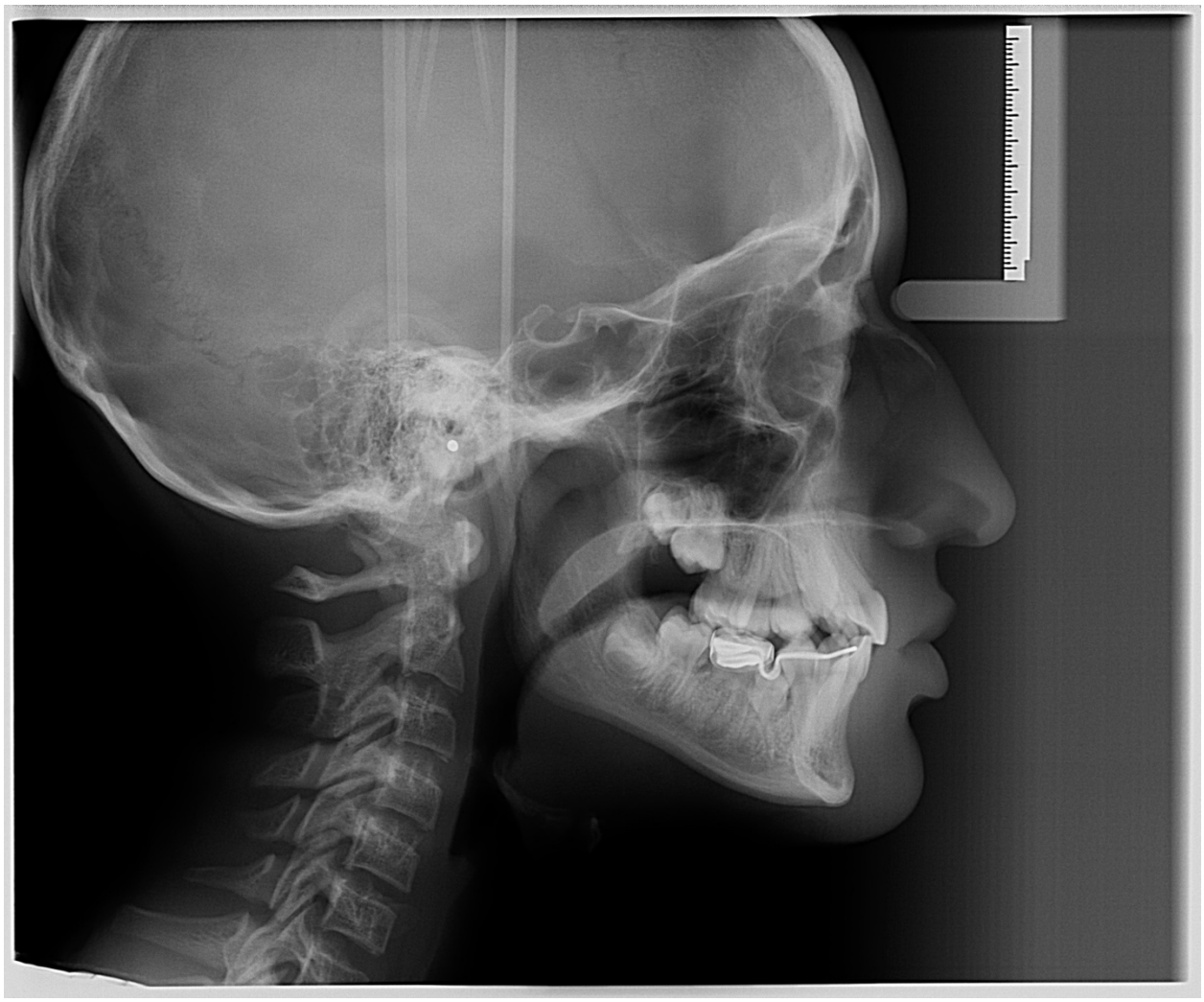
APPENDIX F (Continued



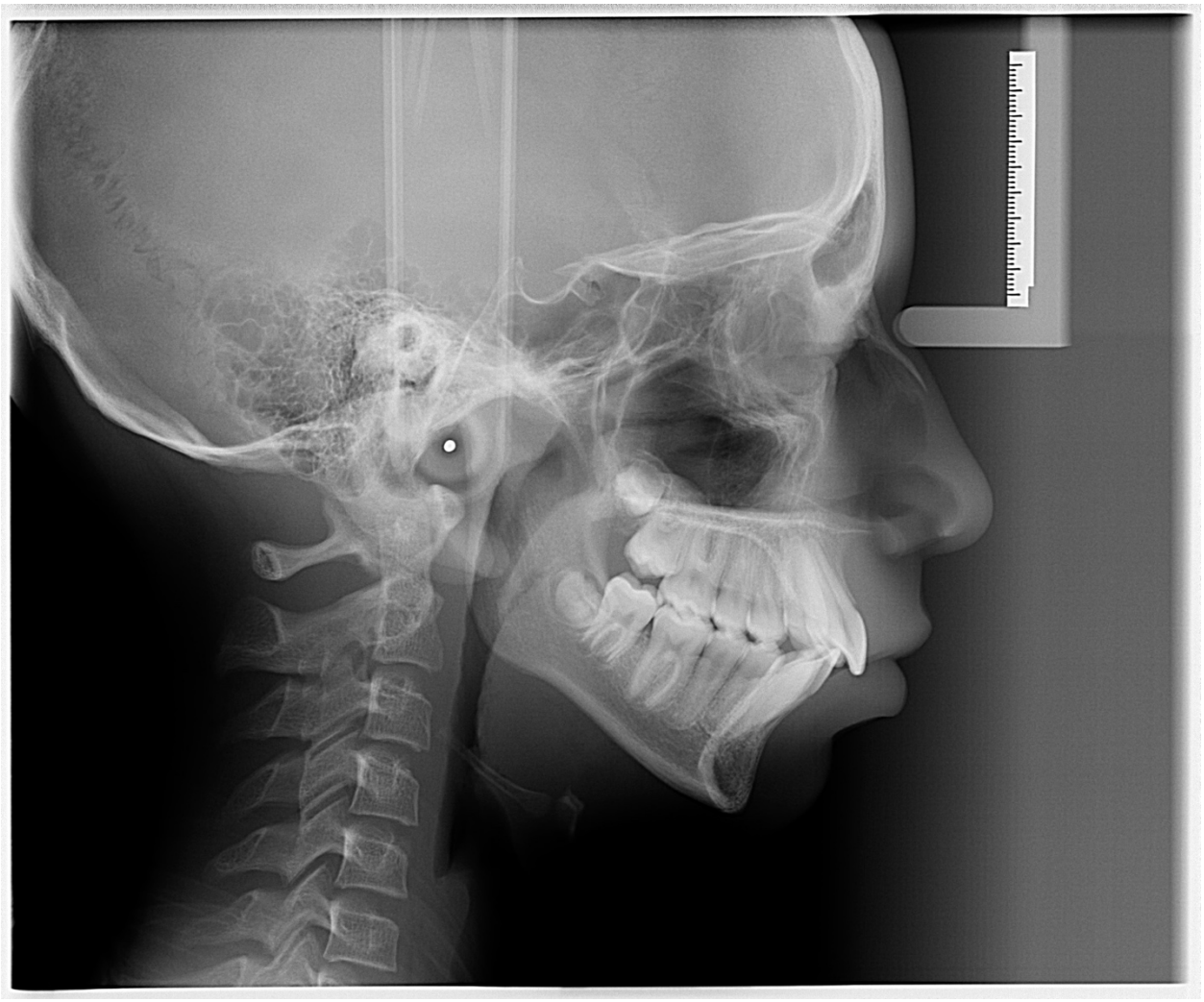
APPENDIX F (Continued)



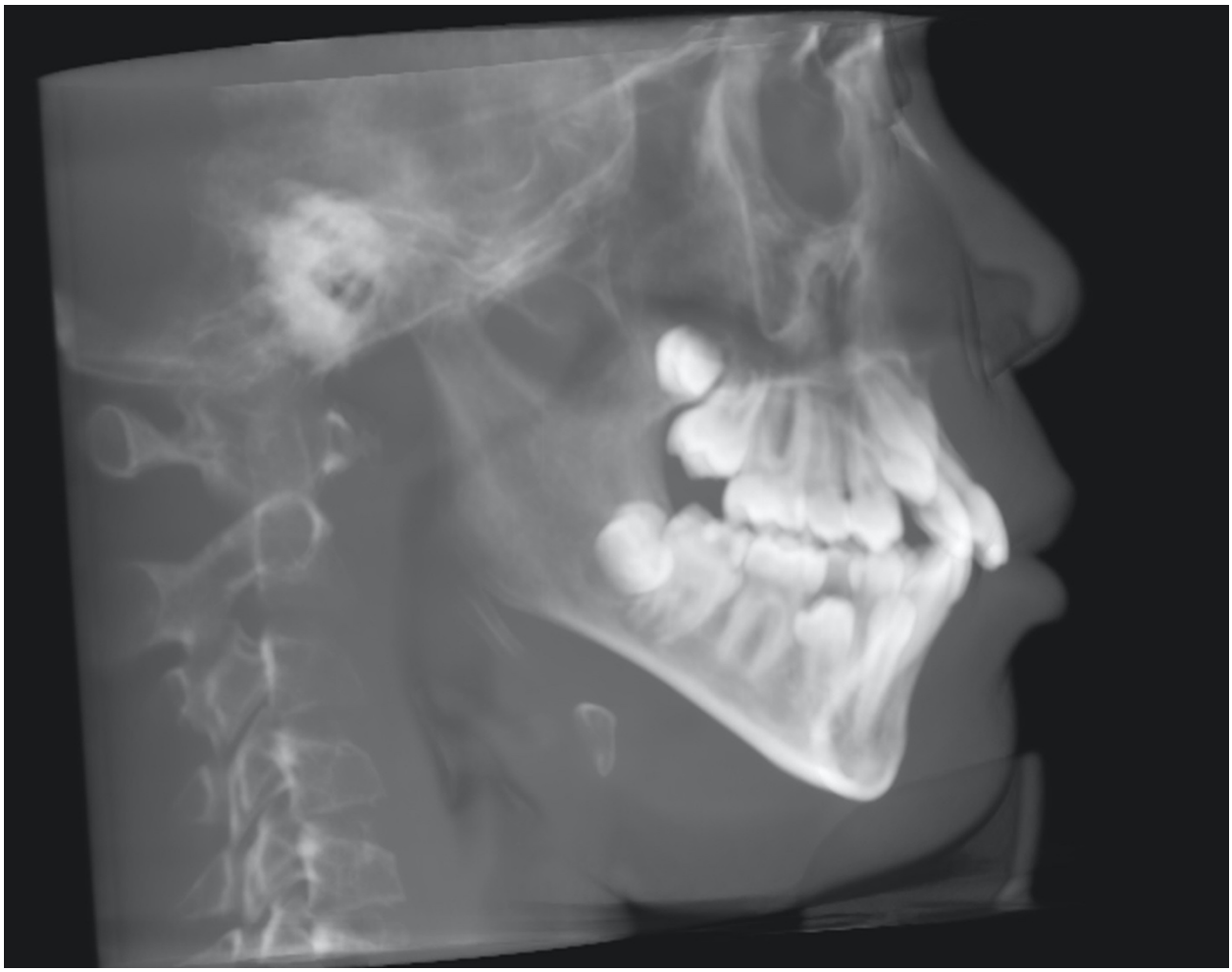
APPENDIX F (Continued)



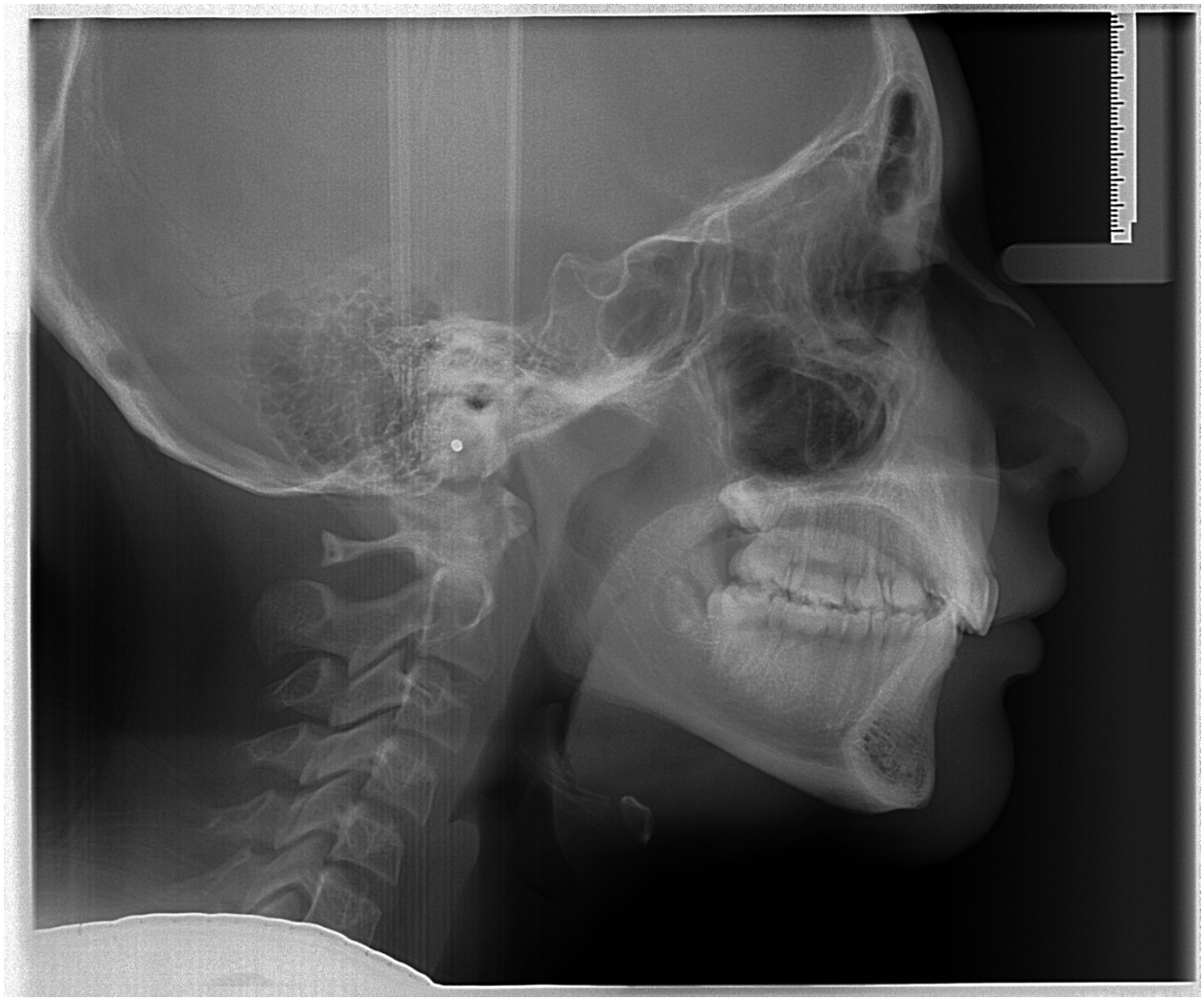
APPENDIX F (Continued)



APPENDIX F (Continued)



APPENDIX F (Continued)

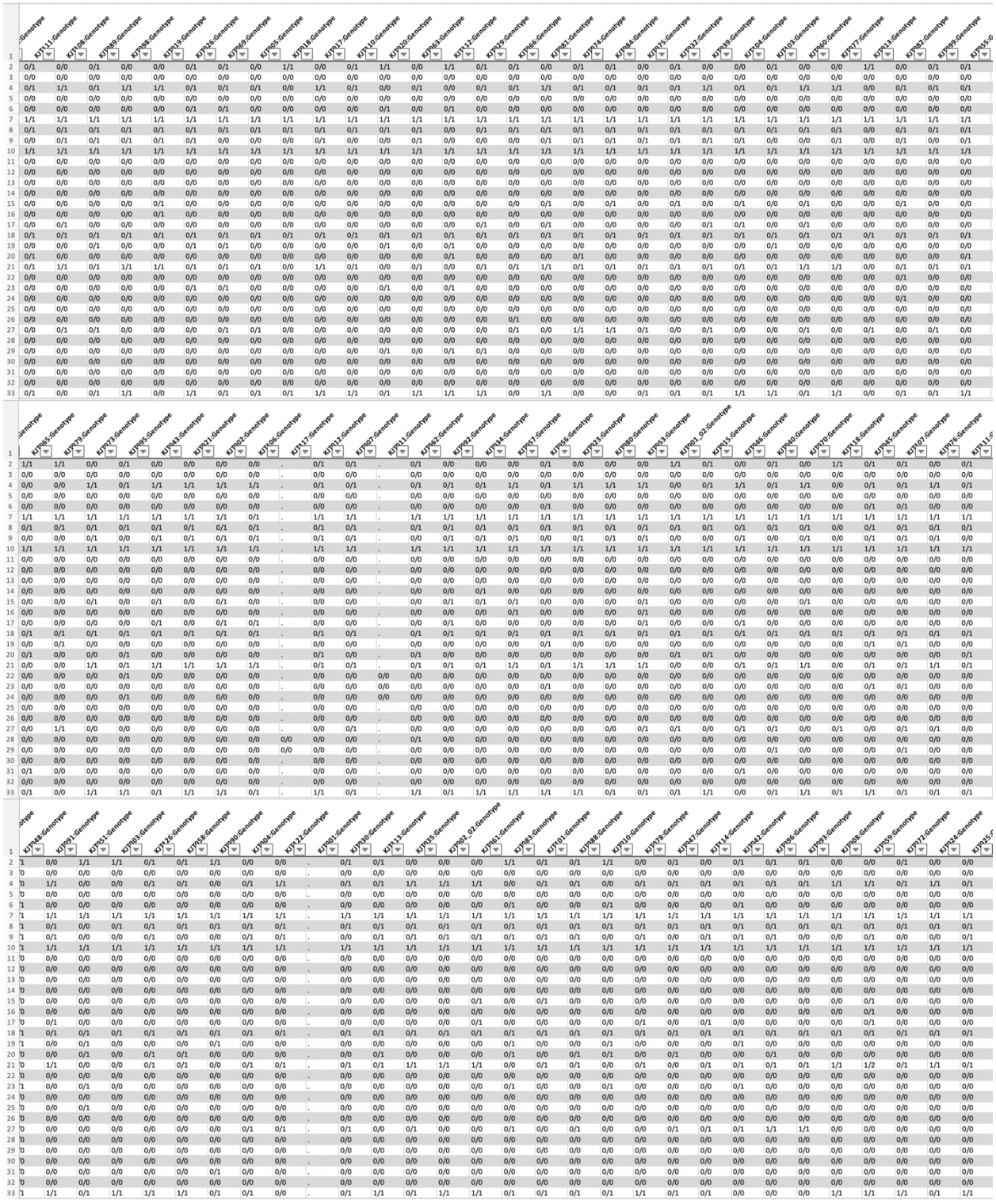


APPENDIX F (Continued)

	Genotype	KJT55:Genotype	KJT54:Genotype	KJT28:Genotype	KJT19:Genotype	KJT68:Genotype	KJT20:Genotype	KJT50:Genotype	KJT16:Genotype	KJT09:Genotype	KJT41:Genotype	KJT09:Genotype	KJT67:Genotype	KJT52:Genotype	KJT31:Genotype	KJT85:Genotype	KJT27:Genotype	KJT22:Genotype
1																		
2	0/1	0/0	0/1	0/1	0/1	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	1/1	0/1	0/0	0/1	
3	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	
4	0/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	1/1	0/1	1/1	0/1	0/0	0/1	1/1	0/1	
5	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
6	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
7	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	
8	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	
9	0/1	0/1	0/0	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/0	0/1	0/1	0/1	
10	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	
11	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
12	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
13	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
14	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
15	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
16	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
17	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
18	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	
19	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
20	0/1	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	
21	0/1	1/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1	0/1	1/1	0/1	0/0	0/1	1/1	0/1	
22	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
23	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
24	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
25	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
26	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
27	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/1	
28	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
29	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
30	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
31	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
32	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	
33	1/1	1/1	1/1	0/0	1/1	0/1	0/1	0/1	1/1	0/0	1/1	1/1	1/1	0/1	0/1	1/1	0/0	

	#CHR	POS	REF	ALT	avsnp147	TYPE	KJT02:Genotype	KJT07:Genotype	KJT16:Genotype	KJT28:Genotype	KJT64:Genotype	KJT49:Genotype	KJT66:Genotype	KJT14:Genotype	KJT86:Genotype	KJT84:Genotype	KJT00:Genotype	KJT21:Genotype	KJT71:Genotype	KJT15:Genotype	KJT48:G
1																					
2	chr1	41369961	A	G	rs4636447	snp	0/1	0/1	1/1	0/1	0/1	0/1	0/0	1/1	0/1	0/0	1/1	0/0	1/1	0/1	1/1
3	chr1	41369981	G	A	rs191294221	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
4	chr1	41370013	C	T	rs7522116	snp	0/1	0/1	0/0	0/1	0/0	0/1	0/1	0/0	0/0	1/1	0/0	1/1	0/0	0/1	0/0
5	chr1	41370069	C	T		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0
6	chr1	41370133	T	C	rs12029493	snp	0/1	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	1/1
7	chr1	41370166	CGGGA	TGGGA	rs4660529	snp	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
8	chr1	41370173	T	G		snp	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/0	0/1	0/1	0/1	0/1
9	chr1	41370176	A	G		snp	0/1	0/1	0/0	0/0	0/1	0/0	0/1	0/0	0/1	0/1	0/0	0/1	0/0	0/0	0/1
10	chr1	41370199	A	G	rs4660191	snp	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
11	chr1	41370202	A	C		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0
12	chr1	41370206	C	A		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
13	chr1	41370209	T	C		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
14	chr1	41370216	T	G		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
15	chr1	41370220	C	G		snp	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0
16	chr1	41370226	A	G		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0
17	chr1	41370234	T	C		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	0/0
18	chr1	41370241	CAAAAAAAAAAAAAAAAG	CAAAAAAAAAAAAAAAG	rs35454700	del	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
19	chr1	41371501	C	T	rs56233836	snp	0/1	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	1/1	0/0	0/0	0/0	1/1
20	chr1	41376652	C	T	rs1317183	snp	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
21	chr1	41376676	TAC	TAT,CAT		snp,complex	0/1	0/1	0/0	0/1	0/0	0/1	0/1	0/0	0/0	1/1	0/0	1/1	0/0	0/1	0/0
22	chr1	41379717	G	A	rs142582620	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
23	chr1	41379869	G	A	rs55784313	snp	0/1	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	1/1	0/0	0/0	0/0	1/1
24	chr1	41379920	C	T	rs150540821	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
25	chr3	49684329	A	G		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
26	chr3	49684333	GC	AA		mnp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
27	chr3	49684365	C	A	rs13085791	snp	0/0	0/0	0/1	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/1	0/1	1/1	0/0	0/0
28	chr3	49685708	A	G	rs144982232	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0
29	chr3	49685714	T	C	rs62262683	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0
30	chr3	49687893	C	T		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
31	chr3	49687907	A	G	rs113893148	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
32	chr3	49687940	A	C		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
33	chr3	49687999	AGG	AG		del	0/1	0/0	0/1	1/1	0/1	0/0	0/1	0/1	1/1	1/1	0/1	0/1	0/0	1/1	1/1

APPENDIX F (Continued)



APPENDIX F (Continued)

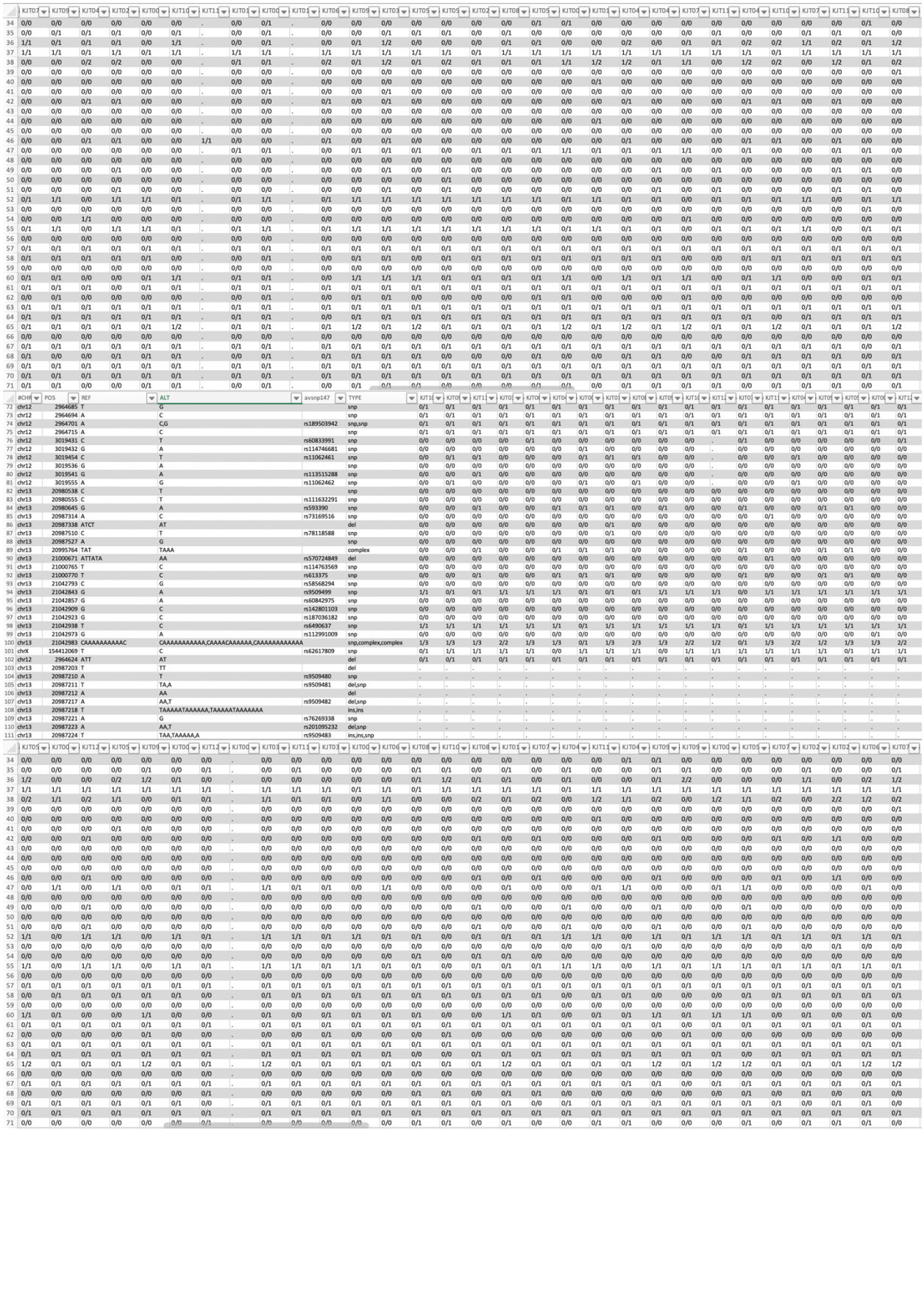
	KJT06	KJT12	KJT05	KJT01	KJT00	KJT04	KJT10	KJT06	KJT05	KJT03	KJT08	KJT02	KJT02
34	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
35	0/1	0/1	0/1	0/0	0/0	0/0	0/0	0/1	0/0	1/1	0/0	0/0	0/1
36	0/1	0/1	0/2	0/1	0/2	0/0	0/0	0/1	0/2	1/1	0/1	0/0	0/1
37	1/1	1/1	0/1	1/1	1/1	0/0	0/1	1/1	0/1	1/1	0/1	1/1	1/1
38	0/1	0/1	0/1	0/0	1/1	0/0	0/1	0/0	0/2	0/0	0/0	1/1	0/1
39	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
40	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
41	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
42	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0
43	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
44	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
45	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
46	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0
47	0/1	0/1	0/1	0/0	0/1	0/0	0/1	0/0	0/0	0/0	0/0	1/1	0/1
48	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
49	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/0
50	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
51	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/0
52	0/1	0/1	0/1	1/1	0/1	0/1	0/1	0/1	1/1	1/1	1/1	0/1	1/1
53	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
54	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
55	0/1	0/1	0/1	1/1	0/1	0/1	0/1	0/1	1/1	1/1	1/1	0/1	1/1
56	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
57	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
58	0/1	0/0	0/0	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0
59	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
60	0/0	0/1	0/0	1/1	0/1	1/1	0/1	0/1	0/0	0/0	0/0	0/1	0/1
61	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
62	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/0
63	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
64	0/1	0/0	0/0	0/1	0/1	0/1	0/1	0/0	0/1	0/0	0/0	0/1	0/1
65	0/1	0/1	0/1	1/2	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/2	0/1
66	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
67	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
68	0/1	0/1	0/1	0/1	0/1	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0
69	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
70	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
71	0/0	0/1	0/1	0/1	0/1	0/0	0/0	0/0	0/1	0/1	0/0	0/1	0/1

APPENDIX F (Continued)

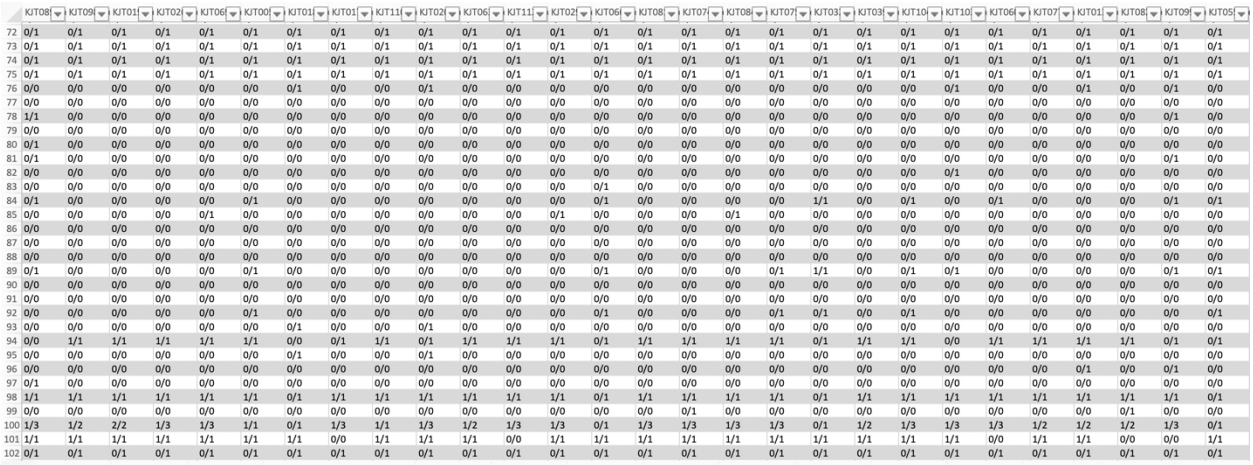
	#CHR	POS	REF	ALT	avsnp147	TYPE	KJT10	KJT09	KJT11	KJT03	KJT06	KJT04	KJT00	KJT01	KJT08	KJT09	KJT10	KJT12	KJT07	KJT11	KJT04
34	chr3	49688745	G	A	rs147997200	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
35	chr6	35489619	G	T	rs7740758	snp	0/1	0/0	1/1	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	1/1	0/1	0/1
36	chr6	35489696	GAG	AAG,CAG,CAT		snp,snp,complex	0/1	0/0	1/1	0/0	0/0	0/3	1/2	2/2	1/2	1/1	0/0	0/0	1/1	0/1	0/1
37	chr6	35493327	CG	CATG	rs10638006	ins	1/1	1/1	1/1	0/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
38	chr6	35493351	A	T,C	rs69255503	snp,snp	0/1	0/2	0/0	0/1	0/2	0/1	0/1	0/2	2/2	0/0	1/1	0/0	2/2	0/2	0/0
39	chr6	35493420	A	G	rs61501470	snp	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	1/1	0/0	0/0
40	chr6	35494021	G	A	rs142812873	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
41	chr6	35494023	G	A	rs11758653	snp	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
42	chr6	35494090	C	A	rs72894781	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
43	chr6	35494091	A	T	rs146976128	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
44	chr6	35494103	C	A	rs138027205	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
45	chr6	35494123	C	T		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0
46	chr6	35494528	T	C	rs72894784	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
47	chr6	35496821	CC	CTC	rs71002565	ins	0/1	0/0	0/0	0/1	0/0	0/1	0/1	0/0	0/0	0/0	1/1	0/0	0/0	0/0	0/0
48	chr6	35496866	C	A		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
49	chr6	45340169	A	G	rs12214749	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/0
50	chr6	45366244	G	T	rs76595706	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
51	chr6	45366370	TAA	TA		del	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/0
52	chr6	149716436	A	G	rs4870529	snp	1/1	1/1	1/1	1/1	1/1	0/1	1/1	0/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1
53	chr6	149716438	C	T	rs13205080	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
54	chr6	149717955	G	A	rs13210297	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
55	chr6	149718012	G	A	rs12174349	snp	1/1	1/1	1/1	1/1	1/1	0/1	1/1	0/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1
56	chr6	149718029	C	T	rs190555603	snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
57	chr12	2964459	CTTTTTTTTTTTTTTG	CTTTTTTTTTTTTG		del	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
58	chr12	2964482	A	G		snp	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
59	chr12	2964493	T	C		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
60	chr12	2964515	T	C	rs10848754	snp	0/1	0/0	0/0	0/1	0/1	0/1	0/1	0/0	0/1	1/1	1/1	0/0	0/1	0/1	0/1
61	chr12	2964553	A	T		snp	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1
62	chr12	2964562	A	T		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/1	0/0	0/0	0/1	0/0
63	chr12	2964594	A	T		snp	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
64	chr12	2964615	A	C		snp	0/0	0/1	0/1	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/0	0/1	0/0
65	chr12	2964624	ATTTTTTTTTTTTTTTTTTTG	ATTTTTTTTTTTTTTTTTTG,ATTTTTTTTTTTTTTTTTG	rs746969503	del,del	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/2	1/2	1/2	0/1	0/1	0/1	0/1
66	chr12	2964653	A	C		snp	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
67	chr12	2964661	A	G		snp	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
68	chr12	2964665	T	G		snp	0/0	0/1	0/0	0/1	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/1	0/1
69	chr12	2964669	T	C		snp	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/1	0/1
70	chr12	2964676	T	G		snp	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
71	chr12	2964681	A	G		snp	0/1	0/1	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/1	0/0	0/0	0/0	0/0	0/1

	KJT09	KJT01	KJT02	KJT06	KJT00	KJT01	KJT11	KJT02	KJT06	KJT11	KJT02	KJT06	KJT08	KJT07	KJT08	KJT07	KJT03	KJT03	KJT10	KJT10	KJT06	KJT07	KJT01	KJT08	KJT09	KJT05	KJT05	KJT02	KJT11
34	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
35	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	1/1	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0
36	0/1	0/0	0/0	0/0	0/0	1/2	0/0	0/1	0/1	0/0	0/0	0/1	0/2	0/0	1/1	0/0	0/0	0/0	0/0	0/2	0/0	0/1	0/0	0/1	0/0	0/0	0/1	0/0	0/2
37	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	0/1
38	0/1	2/2	0/2	0/2	0/1	0/0	0/1	1/1	0/0	1/2	0/1	0/1	1/2	1/1	0/0	0/1	1/1	0/1	1/1	0/2	0/0	0/0	1/2	0/0	0/1	0/0	0/1	1/1	0/2	0/0
39	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
40	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
41	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
42	0/0	1/1	0/1	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
43	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
44	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
45	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
46	0/0	1/1	0/1	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
47	0/1	0/0	0/0	0/0	0/1	0/0	0/1	1/1	0/0	0/1	0/0	0/1	0/1	1/1	0/0	0/1	1/1	0/1	1/1	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/1	1/1	0/0	0/0
48	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
49	0/1	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/1	0/0
50	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0
51	0/1	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/1	0/0
52	1/1	1/1	1/1	1/1	0/0	0/1	1/1	0/1	0/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	1/1	0/1	0/1	0/1	1/1	1/1	0/0	0/1	0/1	1/1	1/1
53	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0
54	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
55	1/1	1/1	1/1	1/1	0/0	0/1	1/1	0/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	1/1	0/1	0/1	0/1	1/1	1/1	0/0	0/1	0/1	1/1	1/1	1/1	1/1
56	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
57	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
58	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0
59	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
60	0/0	0/1	0/1	0/1	1/1	0/0	0/0	0/0	0/1	0/1	0/1	0/0	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/0	0/1	0/1	0/0	0/0
61	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
62	0/0	0/0	0/1	0/0	0/1	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/1	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/1
63	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
64	0/1	0/0	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/1
65	0/1	0/1	0/1	0/1	1/2	0/1	0/1	0/1	0/1	0/1	1/2	0/1	0/1	1/2	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/2	1/2	0/1	0/1	0/1	0/1	0/1	0/1	0/1
66	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
67	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
68	0/0	0/1	0/1	0/1	0/1	0/0	0/1	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/1	0/0	0/1	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1
69	0/1	0/1	0/1	0/1	0/1	0/0	0/0	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/0
70	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
71	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/0	0/0	0/1	0/1	0/1	0/1	0/0	0/1	0/1	0/1	0/0	0/0	0/0	0/1	0/1	0/1	0/1	0/1	0/0	0/0	0/1

APPENDIX F (Continued)



APPENDIX F (Continued)



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72	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
73	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
74	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
75	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
76	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/1	0/0
77	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
78	1/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
79	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
80	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
81	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
82	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0
83	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
84	0/1	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	1/1	0/0	0/1	0/0	0/1	0/0	0/0	0/0	0/0	0/1	0/1
85	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
86	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
87	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
88	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
89	0/1	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/1	1/1	0/0	0/1	0/1	0/0	0/0	0/0	0/0	0/1	0/1
90	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
92	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/1	0/1	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1
93	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
94	0/0	1/1	1/1	1/1	1/1	1/1	0/0	0/1	1/1	0/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	0/0	1/1	1/1	1/1	1/1	0/1	0/1
95	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
96	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
97	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
98	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1
99	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
100	1/3	1/2	2/2	1/3	1/3	1/1	0/1	1/3	1/1	1/3	1/2	1/3	1/3	0/1	1/3	1/3	1/3	1/3	0/1	1/2	1/3	1/3	1/3	1/2	1/2	1/2	1/3	0/1
101	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/0	1/1	1/1	1/1	0/0	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/0	1/1	1/1	0/0	0/0	1/1
102	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1

	KJT05	KJT02	KJT11	KJT06	KJT12	KJT05	KJT01	KJT00	KJT04	KJT10	KJT06	KJT05	KJT03	KJT08	KJT02	KJT02
70	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
71	0/0	0/0	0/1	0/0	0/1	0/1	0/1	0/1	0/0	0/0	0/0	0/1	0/1	0/0	0/1	0/1
72	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
73	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
74	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
75	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
76	0/0	0/0	0/0	0/1	0/0	0/1	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0
77	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
78	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0
79	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
80	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0
81	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
82	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
83	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
84	0/1	0/1	0/0	1/1	1/1	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/1	0/1	0/0	0/0
85	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
86	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
87	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
88	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
89	0/1	0/1	0/0	1/1	1/1	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/1	0/1	0/0	0/0
90	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
92	0/1	0/1	0/0	1/1	1/1	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/1	0/1	0/0	0/0
93	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
94	1/1	0/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	1/1	0/1
95	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
96	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
97	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
98	1/1	0/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1
99	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
100	1/3	0/1	1/3	1/3	0/1	1/2	1/3	1/1	1/3	1/3	1/2	1/3	1/3	0/2	2/2	1/3
101	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/0	1/1	0/1	1/1	1/1	1/1	1/1	1/1
102	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1

APPENDIX F (Continued)

	KJT05	KJT09	KJT00	KJT12	KJT00	KJT03	KJT11	KJT03	KJT00	KJT06	KJT08	KJT10	KJT08	KJT01	KJT07	KJT04	KJT11	KJT04	KJT09	KJT09	KJT00	KJT05	KJT07	KJT02	KJT02	KJT06	KJT07	KJT07
72	0/1	0/1	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
73	0/1	0/1	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
74	0/1	0/1	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
75	0/1	0/1	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
76	0/0	0/1	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	1/1	0/0	0/0	0/0	0/0	0/1	0/0	0/1	0/0
77	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
78	0/0	0/1	0/0	0/0	.	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/1	0/0	0/1	0/0
79	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
80	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0
81	0/0	0/1	0/0	0/0	.	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
82	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
83	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
84	0/0	0/0	0/0	0/1	.	0/0	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/1	0/1	0/1	0/0	0/1	0/0	0/0	1/1	0/1	0/1	0/0	0/0	0/0	0/0	0/1
85	0/0	0/0	0/0	0/0	.	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
86	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
87	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
88	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
89	0/0	0/0	0/0	0/1	.	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/1	0/1	0/1	0/0	0/1	0/0	1/1	0/1	0/1	0/0	0/0	0/0	0/0	0/1
90	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91	0/0	0/0	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
92	0/0	0/0	0/0	0/1	.	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/1	0/0	0/1	0/1	0/1	0/0	0/1	0/0	1/1	0/1	0/1	0/0	0/0	0/0	0/0	0/1
93	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
94	1/1	0/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/0	1/1	1/1	0/1	1/1	0/1	1/1	0/1	1/1	0/1	1/1	0/1	0/1	0/1	1/1	0/1	0/1
95	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
96	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
97	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
98	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	0/1	1/1	0/1	1/1	0/1	1/1	0/1	1/1	0/1	1/1	0/1	1/1	1/1	0/1
99	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1
100	2/2	1/3	1/3	0/0	1/1	1/2	1/2	1/3	1/3	2/2	1/3	0/1	2/2	1/3	0/1	2/2	1/3	0/1	1/1	0/1	1/3	0/1	0/1	1/2	0/2	1/2	0/1	1/3	0/1
101	1/1	1/1	1/1	1/1	.	1/1	1/1	0/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	0/1
102	0/1	0/1	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1

	KJT09	KJT04	KJT02	KJT00	KJT10	KJT11	KJT01	KJT00	KJT01	KJT06	KJT09	KJT03	KJT05	KJT05	KJT02	KJT08	KJT05	KJT00	KJT01	KJT04	KJT04	KJT07	KJT11	KJT04	KJT10	KJT07	KJT11	KJT10
72	0/1	0/1	0/1	0/1	0/1	.	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
73	0/1	0/1	0/1	0/1	0/1	.	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
74	0/1	0/1	0/1	0/1	0/1	.	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
75	0/1	0/1	0/1	0/1	0/1	.	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1
76	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1
77	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
78	0/0	0/0	0/0	0/0	0/0	.	0/0	0/1	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	1/1	0/0
79	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
80	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
81	0/0	0/0	0/0	0/0	0/0	.	0/0	0/1	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	1/1	0/0
82	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
83	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
84	0/0	0/0	0/1	0/1	0/0	.	0/0	0/1	.	0/0	0/0	0/1	0/1	0/0	0/1	0/0	0/0	1/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	1/1	1/1
85	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
86	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
87	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
88	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0
89	0/0	0/0	0/1	0/0	0/0	.	0/0	0/1	.	0/0	0/0	0/1	0/1	0/0	0/1	0/0	0/0	1/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	1/1	1/1
90	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
92	0/0	0/0	0/1	0/0	0/0	.	0/0	0/1	.	0/1	0/0	0/1	0/1	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	1/1	1/1
93	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
94	1/1	1/1	0/1	1/1	1/1	.	1/1	1/1	.	0/1	1/1	1/1	1/1	0/1	0/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	0/1	0/1	0/1	1/1	1/1	0/0
95	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
96	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0
97	0/0	0/0	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
98	1/1	1/1	0/1	1/1	1/1	.	1/1	1/1	.	0/1	1/1	1/1	1/1	1/1	1/1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/1	0/1	1/1	1/1	0/0
99	0/0	0/1	0/0	0/0	0/0	.	0/0	0/0	.	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0
100	1/1	1/3	0/2	1/3	1/3	.	1/3	1/3	.	0/2	2/2	1/3	2/2	1/3	0/1	1/2	1/3	1/3	2/2	1/2	0/1	2/2	1/3	0/1	0/1	1/3	1/3	0/0
101	1/1	1/1	1/1	1/1	1/1	.	1/1	0/0	.	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	0/0	1/1	1/1	1/0
102	0/1	0/1	0/1	0/1	0/1	.	0/1	0/1	.	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1

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ABSTRACTS: "Long-term effects of various cleaning methods on polypropylene/ethylene copolymer January 2019 Retainer material" Wible E, Agarwal M, Altun S, Ramir T, Viana G, Evans C, Lukic H, Megremis S, Atsumasuam P

"Long-term effects of seven cleaning methods on light transmittance, surface roughness, March 2018 And flexural modulus of polyurethane retainer material" Agarwal M, Wible E, Ramir T Altun S, Viana G, Evans C, Lukic H, Megremis S, Atsawasuwan P