ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

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ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

ΕΙΔΙΚΕΥΣΗ ΣΤΗΝ ΟΡΘΟΔΟΝΤΙΚΗ

ΜΟΡΦΟΜΕΤΡΙΚΗ ΑΞΙΟΛΟΓΗΣΗ ΤΩΝ ΑΛΛΑΓΩΝ ΣΚΛΗΡΩΝ ΚΑΙ ΜΑΛΑΚΩΝ ΙΣΤΩΝ ΤΟΥ ΠΡΟΣΩΠΟΥ ΑΣΘΕΝΩΝ ΠΟΥ ΘΕΡΑΠΕΥΤΗΚΑΝ ΜΕ Ή ΧΩΡΙΣ ΕΞΑΓΩΓΕΣ.

A GEOMETRIC MORPHOMETRIC EVALUATION OF HARD AND SOFT TISSUE PROFILE CHANGES IN EXTRACTION VERSUS NON-EXTRACTION PATIENTS.

Αφροδίτη Ε. Κούλη

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Επιβλέπων Καθηγητής για την εκπόνηση της Μεταπτυχιακής Διπλωματικής Εργασίας: Καθηγητής κ. Δημήτριος Χαλαζωνίτης

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Contents

Περίληψη

Σκοπός: Η αξιολόγηση των αλλαγών που παρατηρούνται σε σκληρούς και μαλακούς ιστούς σε περιστατικά εξαγωγών και μη εξαγωγών Τάξης Ι κατά Angle με τη χρήση γεωμετρικής μορφομετρίας.

Υλικό και Μέθοδος: Από ένα αρχικό δείγμα 542 ασθενών με ανωμαλία σύγκλεισης Τάξης Ι, που υπεβλήθη σε διαχωριστική ανάλυση σε μια προηγούμενη μελέτη, συγκεντρώθηκε και αναλύθηκε ένα υποδείγμα 68 οριακών, ως προς τις εξαγωγές, περιστατικών. Τριάντα τέσσερα από τα περιστατικά αυτά θεραπεύτηκαν με εξαγωγές και 34 χωρίς εξαγωγές 4 πρώτων προγομφίων. Η εγκυρότητα της διαχωριστικής ανάλυσης στο να προσδιορίζει επιτυχώς ένα οριακό δείγμα μορφολογικά όμοιων ασθενών εξετάσθηκε με τη χρήση μεθόδων γεωμετρικής μορφομετρίας. Οι αρχικές και οι τελικές κεφαλομετρικές ακτινογραφίες εξετάστηκαν μορφομετρικά προκειμένου να αξιολογηθούν μεταβολές σε σκληρά και μαλακά μόρια ανάμεσα στις εξεταζόμενες ομάδες. Προκειμένου να αξιολογηθεί η στατιστική σημαντικότητα, μετρήθηκε η απόσταση Προκρούστη ανάμεσα στις ομάδες.

Αποτελέσματα: Η διαχωριστική ανάλυση επιβεβαιώθηκε για το δείγμα. Οι μεταβολές των μαλακών μορίων μετά το τέλος της θεραπείας έδειξαν οριακά στατιστικά σημαντικές διαφορές μεταξύ των 2 ομάδων ($P=0.053$, 10000 permutations) κάτι το οποίο δεν παρατηρήθηκε στις σκελετικές δομές ($P=0.078$, 10000 permutations). Τα περιστατικά μη εξαγωγών παρουσίασαν αύξηση στο συνολικό ύψος του προσώπου στα σκληρά μόρια ($P<0.00$, 10000 permutations), με ελαφρώς οπισθιέστερη θέση άνω και προσθιέστερη θέση κάτω χείλους ($P=0.027$, 10000 permutations). Στα περιστατικά εξαγωγών εκτός από αύξηση στο κατακόρυφο παρατηρήθηκε και μια οπισθιέστερη θέση του περιγράμματος της πλάγιας κατατομής του περιγράμματος σκληρών ιστών και μαλακών μορίων ($P<0.00$, 10000 permutations).

Συμπεράσματα: Η επιλογή της εξαγωγής δοντιών παρουσιάζει επίδραση στο περίγραμμα της κατατομής σκληρών και μαλακών μορίων οριακών περιστατικών τάξης Ι. Στους ασθενείς που θεραπεύτηκαν χωρίς εξαγωγές παρατηρήθηκε αύξηση στην κάθετη διάσταση των σκελετικών δομών του προσώπου, ενώ δεν παρατηρηθήκαν ουσιαστικές μεταβολές στα μαλακά μόρια. Οι ασθενείς οι οποίοι θεραπεύτηκαν με εξαγωγές παρουσίασαν παρόμοιες μεταβολές στο κατακόρυφο και οπισθιέστερη θέση του οστικού περιγράμματος άνω και κάτω γνάθου με παρόμοιες μεταβολές στους μαλακούς ιστούς κυρίως στην περιστοματική περιοχή.

Λέξεις κλειδιά: οριακά περιστατικά Τάξης Ι, μεταβολές σκληρών ιστών, μεταβολές μαλακών ιστών, εξαγωγές, μη εξαγωγές, διαχωριστική ανάλυση

Abstract

Objective: To evaluate the hard tissue and facial profile changes in matched extraction and non-extraction Class I patients by the use of geometric morphometrics.

Subjects and Method: From a parent sample of 542 Class I patients, been subjected to discriminant analysis in a previous study, a subsample of 68 borderline cases, in regards to extraction modality, was obtained and analyzed. Of the borderline patients 34 were treated with extraction and 34 without extraction of 4 first premolars. The validity of the discriminant analysis in successfully identifying a borderline group of morphologically similar patients was examined by geometric morphometric methods. Inter- and intragroup skeletal and facial profile changes were evaluated morphometrically using pre- and post-treatment cephalometric radiographs. Permutation tests were conducted to test statistical significance, based on the Procrustes distances between group means.

Results: The discriminant analysis was validated. The post-treatment soft tissue differences were marginally significant ($P=0.053$, 10000 permutations), but not in the hard tissue skeletal component ($P=0.078$, 10000 permutations). The non-extraction group showed increase in overall hard tissue height ($P<0.00$, 10000 permutations), with slightly retruded upper and slightly protruded lower lip ($P=0.027$, 10000 permutations). The extraction group showed a significant retraction of the hard tissue and facial profile outline ($P<0.00$, 10000 permutations).

Conclusions: The choice of treatment modality in regards to extractions has a definite impact on the skeletal and soft tissue profile in Class I borderline patients. In patients treated by non-extraction similar changes were presented in the vertical direction, concerning hard tissue, whereas facial profile altered slightly. Patients treated by extractions exhibited vertical increase of skeletal structures and retroposition of the maxillary and mandibular alveolar osseous contours, followed by similar soft tissue changes mainly in the perioral area.

Key-words: Borderline Class I cases; hard tissue profile; soft tissue changes; extraction vs non-extraction; discriminant analysis

Introduction

Extractions of teeth for orthodontic purposes have been used for decades in addressing a malocclusion. The extraction rate in orthodontics shows strong variations depending on the decade and socioeconomic factors (Weintraub et al., 1989; Proffit. 1994; O'Connor, 1993; Turpin, 1994). The goal of orthodontic treatment to establish function, stability, facial balance and harmony makes the pendulum swing favoring one modality over the other. However, clinicians should be aware that each treatment modality might have a different impact on a patient's features, which are considered important towards the successful completion of an orthodontic treatment.

Despite the plethora of research investigations on the extraction debate, a consensus has not yet been reached whether extractions benefit the patient or not (Drobocky and Smith, 1989; Boley et al., 1998; Kocadereli, 2002; Basciftci et al., 2004; Lim et al., 2008). It has been argued that extraction of 4 first premolars can alter the soft tissue profile by flattening it (Drobocky and Smith, 1989). This concept suggests that incisor retraction causes subsequent retraction of the upper and lower lips which follow the underlying dental and osseous structures. This suggestion though is not always supported by the literature (Young and Smith, 1993; Luppanapornlarp and Jonston, 1993; Bishara et al., 1997). In some cases, 4-premolar extraction results in substantial improvement of soft tissue profile, thus justifying extractions (Kocadereli, 2002; Solem et al., 2013). Contrariwise, non-extraction therapy has been claimed to cause excessive lip strain and lip incompetence (Corbett et al., 2005). Still, Bishara et al. (1997) reported that neither extraction nor non-extraction treatment seem to have a systematically adverse effect on soft tissue profile.

However, the differences observed in soft tissue response between individuals may be attributed to lip morphology, lip thickness, postural tone (Oliver, 1982), type of orthodontic treatment (extraction versus non-extraction, pattern of extraction), gender or age (Wisth, 1972; Wisth, 1974).

The aforementioned studies have used cephalometric analyses in order to evaluate post-treatment differences. However, nowadays geometric morphometric methods are available as an alternative means of soft and hard tissue evaluation. This technique combines tools from geometry, computer graphics for visualization of the outcomes and biometrics for the multivariate analysis of biological shape variation. Landmark data are used so that medical image to be captured, size is separated from shape and subsequent multivariate analysis of shape outline provides us with a thorough understanding of the causes and the effects of the phenomenon under study (Marcus, 1996; Bookstein, 1996; Bookstein, 1997).

In most studies published so far (Bishara et al., 1997; Bishara and Jakobsen, 1997; Saelens and De Smit, 1998; Basciftci and Usumez, 2003; Moseling and Woods, 2004; Xu et al., 2006), the extraction and non-extraction groups are not of the same size, age may not be comparable between groups (Scott and Johnston, 1999; Basciftci and Usumez, 2003, Erdinc et al., 2007) and gender is not equally distributed (Young and Smith, 1993; Scott and Johnston, 1999; Kocadereli, 2002; Lim et al., 2008). Consequently, the derived outcomes are possibly affected either by sexual dimorphism, or by different growth maturation stage existed for all patients. This selection bias has an impact on the research results.

Insufficiently matched extraction and non-extraction subjects may introduce susceptibility bias to a research study, since the resulting differences may probably reflect preexisting differences. Susceptibility bias can be successfully overcome through the use of discriminant analysis (Paquette et al., 1992; Livieratos and Johnston, 1995; Konstantonis et al., 2013; Anthopoulou et al., 2014). This analysis provides a list of variables that have unique discriminating power between the 2 groups. In orthodontic research, apart from specifying groups of clear-cut cases in regards to a treatment modality or technique, discriminant analysis can also distinguish a group of patients that cannot be clearly categorized to one of the groups, thus comprising a borderline group of patients. Borderline subjects have the same probability of being included in different treatment groups and are therefore ideal for treatment comparisons.

It was therefore the purpose of this study to obtain a borderline sample of extraction and non-extraction cases and evaluate their soft and hard tissue post-treatment differences by the use of geometric morphometrics.

Subjects and methods

Identification of a borderline sample – discriminant analysis

The sample used in the present study derived from a previously treated sample of 542 Class I patients, randomly collected from the postgraduate clinic of the Department of Orthodontics (National and Kapodistrian University of Athens) and 5 different orthodontic offices in Athens. Of these patients, 331 were female and 211 male; 397 were treated non-extraction whereas 145 received extraction treatment with removal of the 4 first premolars. All patients were Caucasian and presented with a Class I dental and skeletal malocclusion, a full complement of permanent teeth (excluding the 3rd molars), no dentofacial deformities or orofacial clefts and no history of previous orthodontic or orthognathic surgery treatment. The extraction decision was based solely on orthodontic reasons and not on presence of decay or on periodontal status. All patients were treated with edgewise appliances.

The patients' records included initial and final lateral cephalometric and panoramic radiographs, dental casts and detailed treatment charts. The lateral cephalometric radiographs were taken at natural head position, with teeth occluding in maximum intercuspation and lips relaxed in an unstrained posture. All radiographs depicted a reference ruler on the cephalostat for the exact measurement of the magnification factor.

The parent sample had been subjected to a discriminant analysis (Kostantonis et al., 2013), in order to identify a borderline sample in regards to the extraction modality. The discriminant analysis incorporated 26 cephalometric and 6 dental cast variables along with the 2 variables of age and sex, in order to represent most of the morphological characteristics that might have been considered in forming the treatment decision (Table 1). The computed discriminant score ranged from -3.05 to +3.07 and the optimal cutting score value was 0. Patients with negative scores were more likely to have been treated with extractions and patients with positive scores would have probably received a non-extraction treatment. The farther away the discriminant scores are from 0 the more definite the extraction or non-extraction decision becomes. The patients whose discriminant score was close to the cut-off value might be treated either way and thus constituted the borderline sample of extraction and non-extraction patients.

In this study, we selected patients within the borderline spectrum; each extraction case was matched with a non-extraction case of the same gender and of approximately the same age (six months' deviation), so that these parameters were equally distributed between the two groups. The resulting borderline sample comprised 34 extraction and 34 non-extraction patients. The pre-treatment and post-treatment lateral cephalograms of these patients were scanned at a resolution of 150 dpi (Epson 1600 scanner, Seiko Epson Corporation, Nagano, Japan) and the cephalometric analyses were performed using Viewbox 4.0.1.7. (dHAL Software, Kifissia, Greece). Descriptive statistics are given in Table 2.

Hard and soft-tissue evaluation by geometric morphometrics

All radiographs were traced after being oriented to Frankfurt Horizontal plane. The main craniofacial skeletal structures on the pre- and post-treatment lateral cephalograms were traced with 15 curves and 136 landmarks (126 sliding semilandmarks and 10 fixed landmarks) (Table 3, Figure 1). The fixed landmarks were points either identified by local anatomy, such as anterior nasal spine (ANS), posterior nasal spine (PNS) and basion (Ba), or positioned at the end-points of curves. Upper and lower soft tissue structures were traced by two curves. The upper and lower soft tissue curve were captured by 25 and 23 semilandmarks respectively.

All tracings were superimposed using generalized Procrustes superimposition (Rolf and Slice, 1990), in order to extract Procrustes shape coordinates. The semilandmarks were allowed to slide along tangent vectors to the curves, so that the bending energy against a reference configuration (which was chosen to be the mean shape) could be minimized (Bookstein, 1997; Gunz et al., 2005; Slice, 2007; Gunz and Mitteroecker, 2013). This procedure was repeated four times, until any changes to the mean shape were negligible. Then, Principal Component Analysis (PCA) was applied on the Procrustes shape coordinates in order to identify the samples' variability shape patterns.

Next, in order to validate the discriminant analysis, permutation tests without replacement were used to test the shape difference between the 2 treatment groups at the onset of treatment. The hard and soft tissue differences were assessed based on the Procrustes distances between group means. Procrustes distance is defined as the square root of the sum of the squared differences between corresponding landmarks (Halazonetis, 2004).

Following the validation of morphological homogeneity, permutation tests without replacement were performed to identify the impact of extraction and non-extraction treatment on the patients' hard and soft tissue structures.

Error estimation

In order to calculate intra-observer error, a set of 30 randomly selected cephalograms were redigitized by the same investigator after one month. Intraobserver error was calculated as the mean Procrustes distance between repeated digitizations. These were then compared to the total variation of the sample.

Results

Error estimation

The mean intraobserver error for the hard and soft tissue was 3.28% (range: 0.39% to 10.93%, SD: 2.51%) and 1.91% (range: 0.42% to 6.53%, SD: 1.37%) of total variance respectively.

Shape Variability

Each Principal Component (PC) describes a shape variation pattern. The first ten PCs out of 68 of the hard tissue form were considered to be statistically meaningful (70.9% of the total shape variance, Table 4); while the first five PCs out of 68 of the soft tissue form were considered to be statistically meaningful (85.3% of the total shape variance, Table 4), as assessed by the stopping criteria (broken-stick, Avg-Rnd, Rnd-Lambda) (Peres-Neto et al., 2005) and the scree plots (Figure 2).

Of the PCs describing the shape of the hard tissue, the first four accounting for 21.3, 11.4, 7.1, 6.3 per cent of total variance, respectively, were identified as describing shape patterns easily recognized in everyday clinical practice (Figure 3). PC1 described variability in the vertical direction (long and short face shape pattern), PC2 in the anterior-posterior direction (Class I, II and III relationship), PC3 maxillary and mandibular plane relationship (hypodivergent/hyperdivergent skeletal planes) and PC4 the position of the maxilla and the mandible in regards to the cranial base (bimaxillary protrusion/midface hypoplasia).

Of the PCs describing the soft tissue profile (Figure 4), the first four, accounting for 36.8, 27.4, 9.2, 7.0 per cent of total variance, respectively, were also identified as describing commonly recognized shape patterns. PC1 described the position of the lips relative to nose and chin, PC2 the profile convexity, PC3 the lower face height and PC4 the nasolabial angle and the labiomental sulcus.

Sexual dimorphism

Sexual dimorphism was assessed in the combined pre-treatment groups. Plots showing sample distribution of gender are presented in Figures 5,6. Genders did not differ significantly in hard tissue shape ($P=0.3509$, 10000 permutations) (Figure 7). However, males presented a more convex facial profile with more protruding upper and lower lips compared to females ($P=0.0135$, 10000 permutations) (Figure 8).

Discriminant analysis validation

In order to identify the existence of any intergroup differences at the onset of treatment, the morphometric analysis was performed for hard and soft tissue separately.

Plots showing the sample distribution for pre-treatment hard tissue and facial profile of the two groups of patients are presented graphically in Figures 9, 10.

As far as the hard and soft tissue were concerned, no statistically significant difference was observed between the two groups at the onset of treatment (P=0.1356, 10000 permutations and P=0.1516, 10000 permutations respectively) (Figures 11, 12). Thus, the discriminant analysis was validated.

Impact of extraction versus non-extraction treatment on the patients' hard and soft tissue structures

Intragroup differences:

In the non-extraction group we observed a statistically significant increase in skeletal facial height during the treatment period (P<0.00, 10000 permutations) (Figure 13). In regards to the facial profile, statistically significant difference existed (P=0.0272, 10000 permutations) (Figure 14); the upper lip was slightly retruded while the lower lip slightly protruded.

In the extraction group we observed similar changes in the skeletal structures with an additional backward position of the maxillary and mandibular alveolar contour (P<0.00, 10000 permutations) (Figure 15). The soft tissue changes concerned the perioral area and specifically the upper and lower lips, which were significantly retracted at the end of treatment (P<0.00, 10000 permutations) (Figure 16).

Intergroup differences:

The intergroup post-treatment comparisons showed that the extraction group exhibited a slightly posterior positioning of the osseous contours at the anterior region of the alveolar processes (Figure 17). However, in regards to the hard tissues overall no statistically significant differences were found (P=0.0782, 10000 permutations). In contrast the 2 groups showed a significant difference in soft tissue shape, bordering in the traditional 5% limit (P=0.0539, 10000 permutations). In the extraction group both lips, but especially the lower, were more retruded relative to the nose and chin, compared to the non-extraction group (Figure 18).

The distribution in shapespace of the groups is depicted in Figures 19 and 20.

Considering facial profile shapespace, the Procrustes distance between extraction pre- and post-treatment means was 3.21 times larger than the distance between non-extraction pre- and post-treatment means, demonstrating that the changes to the overall facial profile were approximately three times larger in extraction cases than those observed in non-extraction cases (Figure 21).

Discussion

In this study we selected a sample of extraction and non-extraction patients who presented with similar morphological characteristics at pre-treatment. The sample consisted of equally susceptible to extraction and non-extraction treatment males and females (ratio: 15/19). By the use of discriminant analysis, susceptibility bias, detection bias and inclusion bias were minimized. Furthermore, proficiency bias was successfully overcome since the patients were treated by a large number of orthodontists, hence the changes observed to hard and soft tissue profile cannot be credited to one clinician's therapeutic handlings. Consequently, we managed to gather a mostly bias-free sample and to compare patients matched by age and sex, with similar craniofacial characteristics. The high comparability achieved between the extraction and non-extraction patients leads to the justified assumption that any differences between the two groups at the end of the treatment could be mainly attributed to the treatment modality (extraction or non-extraction) rather to any preexisting differences at the onset of treatment.

The scores of the discriminant analysis, in which the parent sample was subjected to, were based on certain parameters, which were selected as the most significant ones. However, the variables incorporated in the discriminant analysis might not have described the shape of the craniofacial complex comprehensively. As a result, we decided to further validate the effectiveness of the discriminant analysis in identifying a homogenous borderline sample through geometric morphometrics.

The use of geometric morphometrics differentiates the present research from previous studies that have mostly used conventional cephalometric measurements in order to evaluate the impact of the treatment modality on facial profile (Caplan and Shivapuja, 1997; Zierhut et al., 2000; Kocadereli, 2002; Basciftci and Usumez, 2003; Basciftci et al., 2004; Moseling and Woods, 2004; Stephens et al., 2005; Erdinc et al., 2007; Jamilian et al., 2008; Hodges et al., 2009). Conventional cephalometric measurements have limitations in assessing the shape of the craniofacial complex, most of which are overcome by geometric morphometrics (Moyers and Bookstein, 1979). Geometric morphometric analysis is regarded as a valid method of comprehensive shape assessment and evaluation of sample's homogeneity (Bookstein, 1996; Halazonetis, 2004). A fundamental property of geometric morphometrics is that all landmarks are weighted equally, avoiding bias in the reference system. Furthermore, the shape of the craniofacial complex can be captured and described thoroughly, not being subjected to the fragmentary analysis of angles and ratios, considered to be an inherent problem of conventional cephalometrics.

In literature there is lack of geometric morphometric studies regarding extraction versus non-extraction treatment modalities, and their impact on hard tissue and facial profile. Subsequently, no direct comparisons were possible and any changes observed were compared with findings from studies using conventional cephalometric analyses.

Hard tissue changes were as expected. Non-extraction cases increased skeletally in facial height at the end of the treatment ($P<0.00$). The findings in the present study are in agreement to those reported for Class I cases reflecting growth changes and orthodontic intervention (Chua et al., 1993; Sivakumar and Valiathan, 2008). However, Basciftci and Usumez (2003) did not find any difference in vertical height concerning the non-extraction group, finding that could be attributed to the use of a single measurement (GoGn-Sn) for the assessment of vertical changes.

In our study, similar increase regarding vertical facial height was observed in extraction cases at the end of treatment with an additional backward position of the alveolar processes of both jaws ($P<0.00$). Sivakumar and Valiathan (2008) reported that extraction cases showed more statistically significant vertical changes compared to the non-extraction group. Hodges et al. (2009) reported statistically significant increase in anterior face height in the adolescent group. These were contradictory to the findings of Chua et al. (1993) and Basciftci and Usumez (2003) who found no difference in the vertical height in the extraction group, in Class I cases. Furthermore, few studies report statistically significant changes in A and B points in the extraction cases after incisor retraction and subsequent bone remodeling (LaMastra, 1981; Sharma, 2010).

As for the extraction and non-extraction post-treatment comparison, no statistically significant difference was found in the skeletal component ($P=0.078$). This finding is in accordance with the existing literature (Basciftci and Usumez, (2003); Sivakumar and Valiathan, 2008).

The mean facial profile shape of the non-extraction group presented upper lip retrusion of approximately 0.5 mm and lower lip protrusion of approximately 0.2 mm after treatment compared to pre-treatment ($P=0.027$). Relative upper lip retrusion might be explained by the growth of the nose while lower lip protrusion might be attributed to the position of the anterior teeth and especially the upper incisor (Moseling and Woods, 2004). Our findings differentiate the present study from the existing literature where minor, yet not statistically significant changes were reported (Kocadereli, 2002; Basciftci and Usumez, 2003).

More pronounced changes regarding facial profile were observed in the extraction cases after treatment. In our study, we observed retrusion of the upper lip (approximately 1.5 mm) and even greater retrusion of the lower lip (approximately 2 mm). The association of treatment with extractions and lip retrusion is confirmed in the literature (Caplan and Shivapuja, 1997; Kocadereli, 2002; Jamilian et al., 2008; Hodges et al., 2009). The overall changes should be attributed to both treatment modality and growth. The posterior placement of lips relative to the growing nose and chin is expected (Nanda et al., 1990; Bishara et al, 1998). Hodges et al. (2009) showed that in Class I adolescents, growth dampened the extractions effect on facial profile compared to adults.

The position that the lip acquires after treatment in extraction and non-extraction cases remains a controversial issue. Lip retrusion in extraction treatment relative to non-extraction Class I patients has been reported in studies using either conventional cephalometric analyses or digital subtraction radiography (Kocadereli, 2002; Akyalçin et al., 2007). Such retrusion of the lips is questioned by several investigators (Basciftci and Usumez, 2003; Stephens et al., 2005; Erdinc et al., 2007), who showed that extraction and non-extraction cases had similar soft tissue facial profiles after treatment. This conflict is explained by the findings of the present study. Since the difference found was marginal to the traditional level of 5%, treatment modality appears to have an impact on facial profile, but this impact may be overshadowed by potential pre-treatment group differences, if not compensated, as done by the discriminant analysis in this study.

Since the Procrustes distance between pre- and post-treatment soft tissue means of the extraction cases was 3.21 times larger than the corresponding distance of the non-extraction cases, treatment with extractions causes three times more changes in overall facial profile. However, since treatment time was larger for the extraction cases, part of the shape change may be attributed to continuing soft-tissue growth post-treatment (Bishara et al., 1998).

The results of the present study may influence the perception about the decision of tooth extraction. Clinicians should be aware of the shape patterns described in this study, so that facial profile may not be deteriorated at the end of treatment. Although the statistical significance of the outcomes does not provide us with sound evidence towards choosing one modality over the other, nonetheless, the clinical significance of the results may be important. Cases in which upper and lower lips are more retruded relatively to nose and chin, teeth should be extracted with caution. On the contrary, in cases with protruded upper and lower lips the extraction of teeth would be recommended.

Limitations

The results deriving from studies using cephalometric radiographs for assessing facial profile should be interpreted with caution. Soft tissue are dynamic, three dimensional structures with complex anatomy, that cannot be thoroughly described by a profile projection. The relationship between dentoalveolar movement and perioral soft tissue changes is multifactorial and takes places in all three planes of space (Solem et al., 2013).

The borderline sample derived from a discriminant analysis in which the extraction cases accounted for 27% of the total sample (145 out of 542 cases). By matching extraction and non-extraction cases, a sample of 34 patients per group was collected. It would be interesting to conduct the study using a substantially larger borderline sample in order to evaluate whether substantial difference between the two groups exists.

Moreover, the duration of treatment was significantly larger in extraction cases (mean: 2.59y, SD: 1.03y, range: 1.45 to 5.04) compared to non-extraction cases (mean: 1.68y, SD: 0.65y, range: 0.82 to 3.72) ($P<0.00$). So, residual growth is a factor that should be taken into consideration for the evaluation of the study outcomes.

In the literature, dental factors have been found to be better correlated with lip profile changes than skeletal factors (Wisth, 1974; Young and Smith, 1993; Caplan and Shivapuja, 1997; Kocadereli, 2002; Moseling and Woods, 2004; Jamilian et al., 2008; Lim et al., 2008). In our research teeth were not digitized and no dental measurements were performed. If we consider incisor positioning and soft tissue response, it could be assumed that in extraction cases retraction of incisors led to bone remodeling and lip retrusion, whereas in non-extraction cases incisor proclination led to remodeling in the alveolar region of the mandible and protrusion of the lower lip. Further investigation is needed in order for this issue to be clarified.

Conclusions

- Geometric morphometrics validated the discriminant analysis as a successful method in identifying a borderline spectrum of extraction and non-extraction patients.
- Geometric morphometrics suggested that extraction and non-extraction treatment had a definite impact on the patients' hard and soft tissue structures.
- Concerning the hard tissue profile, the changes between the groups were focused to the alveolar maxillary and mandibular contour as well as to the skeletal vertical component.
- Concerning the soft tissue profile, changes between the groups were located at the perioral area, mainly described as changes in the position of the upper and lower lips. In contrast to non-extraction cases, the extraction group showed more retracted lips at the end of treatment.
- Changes to the overall soft tissue profile were approximately three times larger in extraction cases than those observed in non-extraction cases, as shown by the Procrustes distance in shapespace.
- Facial profile is a parameter that could guide the clinicians to choose the one treatment modality over the other (extraction versus non-extraction).

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Tables

Table 1: Cephalometric and dental cast variables considered in the discriminant analysis

Cephalometric variables		*Characteristics*
1.	SNA	Maxillary position
2.	SNB	Mandibular position
3.	ANB	Maxillo-mandibular relationship
4.	NSGn	Mandibular size/position
5.	S-Go	Mandibular position
6.	S-Ar	Mandibular position
7.	N-Me	Total face height
8.	N-ANS	Upper face height
9.	ANS-Me	Lower face height
10.	FMA	Facial height/orientation of the mandible
11.	SN-PP	Palatal position/cant
12.	SN-OP	Occlusal plane cant/position
13.	PNS-A	Maxillary size
14.	Pg-NB	Bony chin size
15.	WITS	Maxillo-mandibular relationship
16.	U1-SN	Upper incisor inclination relative to SN
17.	U1-NA (°)	Upper incisor inclination relative to NA
18.	U1-NA (mm)	Upper incisor position relative to NA
19.	L1-NB (°)	Lower incisor inclination in relation to NB
20.	L1-NB (mm)	Lower incisor position relative to NB
21.	FMIA	Lower incisor inclination in relation to FH
22.	IMPA	Lower incisor inclination in relation to MP
23.	L1-A Pg	Lower incisor position
24.	U1-L1	Upper-lower incisor relationship
25.	Z angle	Profile convexity
26.	LL-Eplane	Lower lip position
Dental cast variables		
1.	Overbite	
2.	Overjet	
3.	Upper crowding	
4.	Lower crowding	
5.	Upper midline deviation	
6.	Lower midline deviation	

<u>Table 2</u>: Age descriptive statistics (in years)

	Non-Extraction Group		Extraction Group	
Gender	MALE (n=15)	FEMALE (n=19)	MALE (n=15)	FEMALE (n=19)
Mean (SD)	14.32 (2.05)	13.65 (3.95)	14.36 (1.85)	13.68 (4.24)
Median	14.41	12.61	14.06	12.66
Range	10.65 to 18.57	10.45 to 25.60	10.44 to 17.17	10.56 to 25.47

<u>Table 3</u>: Description of the curves (Cocos and Halazonetis, 2016)

	Curve	Anatomical structures described	Number of Points
1	Porion	External auditory meatus	4
2	External frontal – Nasal	External cortical plate of frontal bone and nasal bone	12
3	Sella – Basion	From tuberculum sellae to posterior clinoid process, dorsum sellae, along clivus, to Basion	12
4	Endocranial frontal	From frontal sinus, along roof of orbit and planum sphenoidale, to anterior clinoid processes	6
5	Internal frontal – Sella	Internal cortical plate of frontal bone, along the cribiform plate of the ethmoid, the superior surface of the sphenoid body, to tuberculum sellae	9
6	Sphenoethmoidale	From fronto-sphenoethmoidal suture to Basion, along the anterior border of the body and the greater wings of the sphenoid bone and the exocranial surface of basioccipital	5
7	Orbit	Anterior border of the zygomatic bone, terminating at Orbitale	6
8	Zygomaticomaxillary	From the posterior margin of frontal process of the zygomatic bone to the zygomatic process of the maxilla	9
9	Maxilla 1	From PNS anteriorly along the nasal floor, around ANS, and inferiorly along the alveolar process to supradentale	14
10	Maxilla 2	From PNS, along the outline of the palate, to the cervix of the maxillary incisors	8
11	PTM1	External surface of maxillary tuberosity	5
12	PTM2	Anterior surface of pterygoid process of sphenoid bone	5
13	Mandible	From infradentale, along the external outline of the mandible and around the condyle, to the anterior neck of the condyle	31
14	Symphysis	The lingual cortical plate of the symphysis	6

15	Anterior ramus	Anterior border of ramus from the level of the palate to the distal of the 1st mandiblular molar	4
16	Upper Soft	The contour of the soft tissue above stomion, from Glabella to Stomion Upper	25
17	Lower Soft	The contour of the soft tissue below stomion, from Stomion Lower to Menton Soft	23

Table 4: Percent variance described by the first principal components in shapespace, regarding hard tissue and facial profile

	Hard Tissue	Facial profile
	%Variance	%Variance
PC1	21.3%*	36.8%*
PC2	11.4%*	27.4%*
PC3	7.1%*	9.2%*
PC4	6.3%*	7.0%*
PC5	5.6%*	4.9%*
PC6	4.4%*	3.2%
PC7	4.0%*	2.5%
PC8	3.7%*	2.0%
PC9	3.6%*	1.4%
PC10	3.4%*	1.1%
Sum	70.9%	95.5%

**: statistically meaningful PCs*

Figures

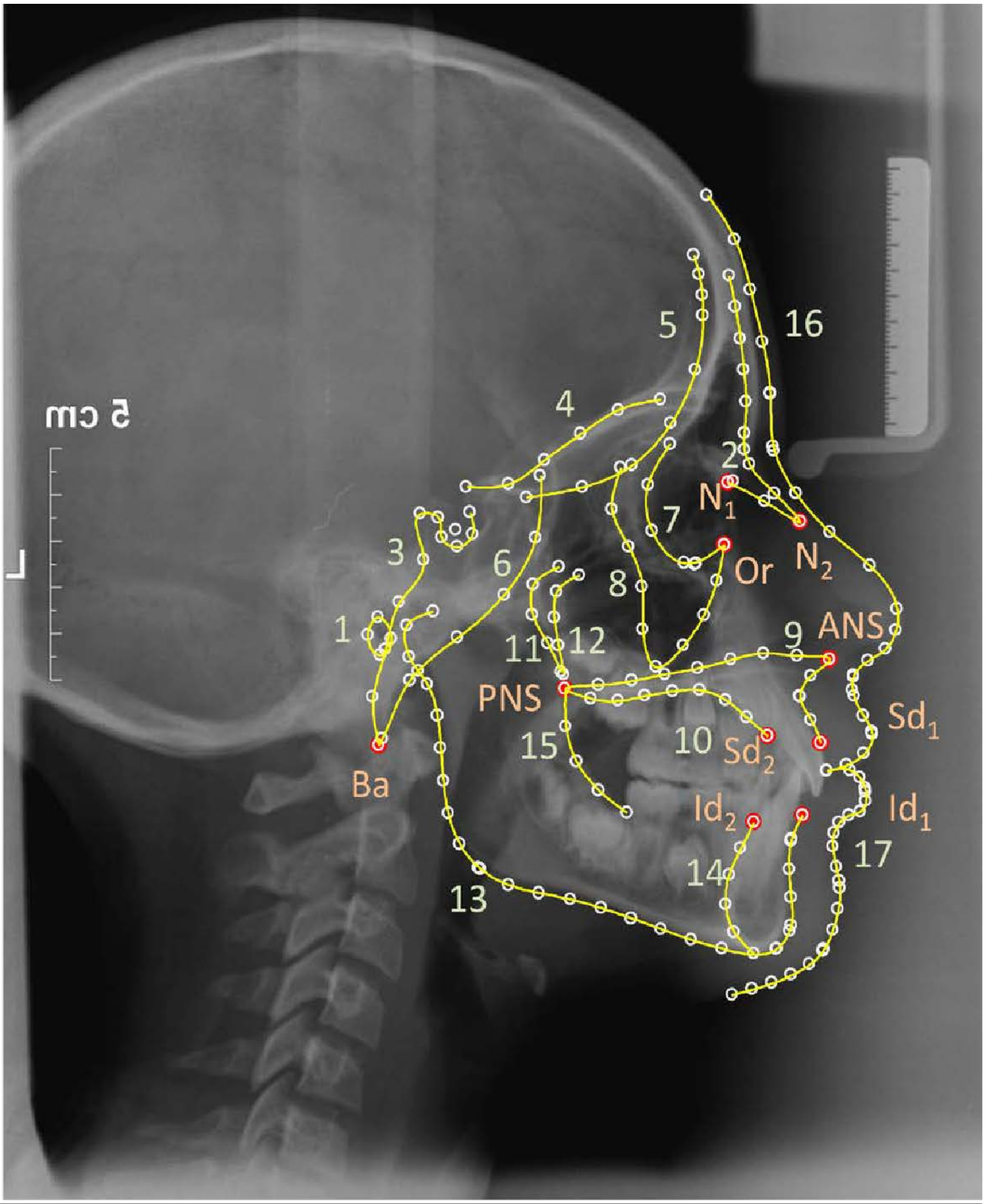


Figure 1: Graphical depiction of craniofacial complex with 17 curves (Table 3) and 10 fixed landmarks (red points): basion (Ba), orbitale (Or), posterior nasal spine (PNS), anterior nasal spine (ANS), supradentale labial (Sd1), supradentale palatal (Sd2), infradentale labial (Id1), infradentale lingual (Id2), the most posterior point of the frontonasal suture (N1), the tip of nasal bone (N2).

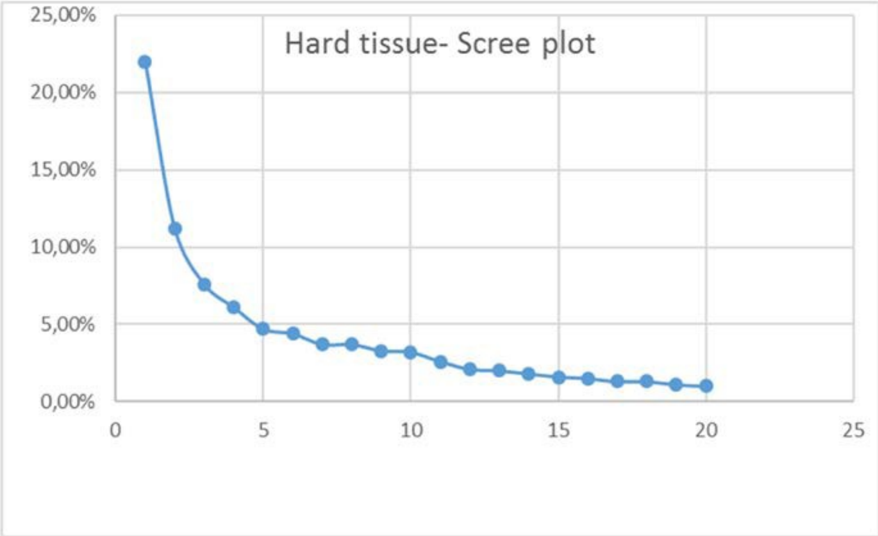


Figure 2: Scree plots showing the meaningful PCs for pre-treatment extraction and non-extraction cases concerning hard tissue and facial profile.

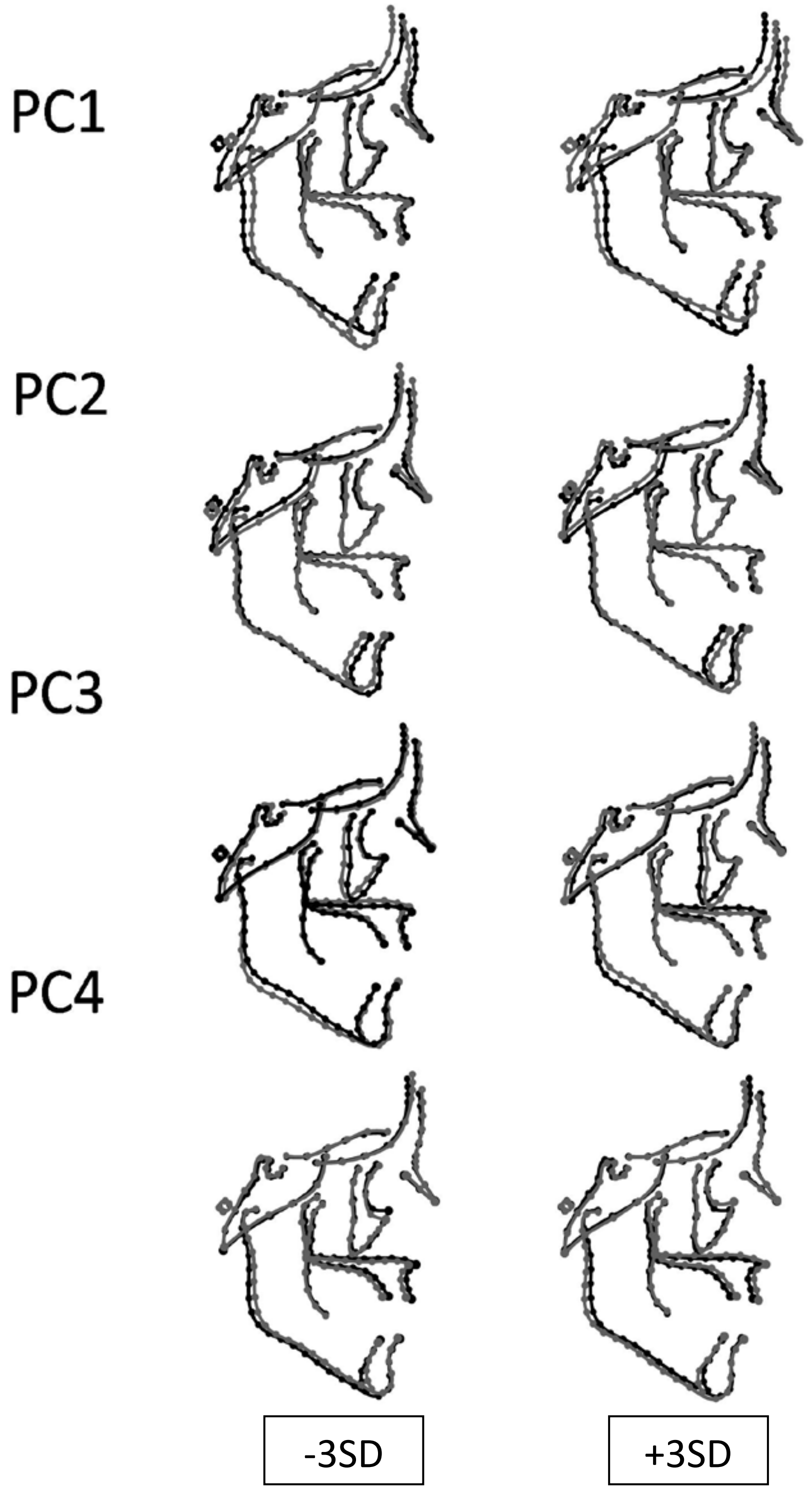
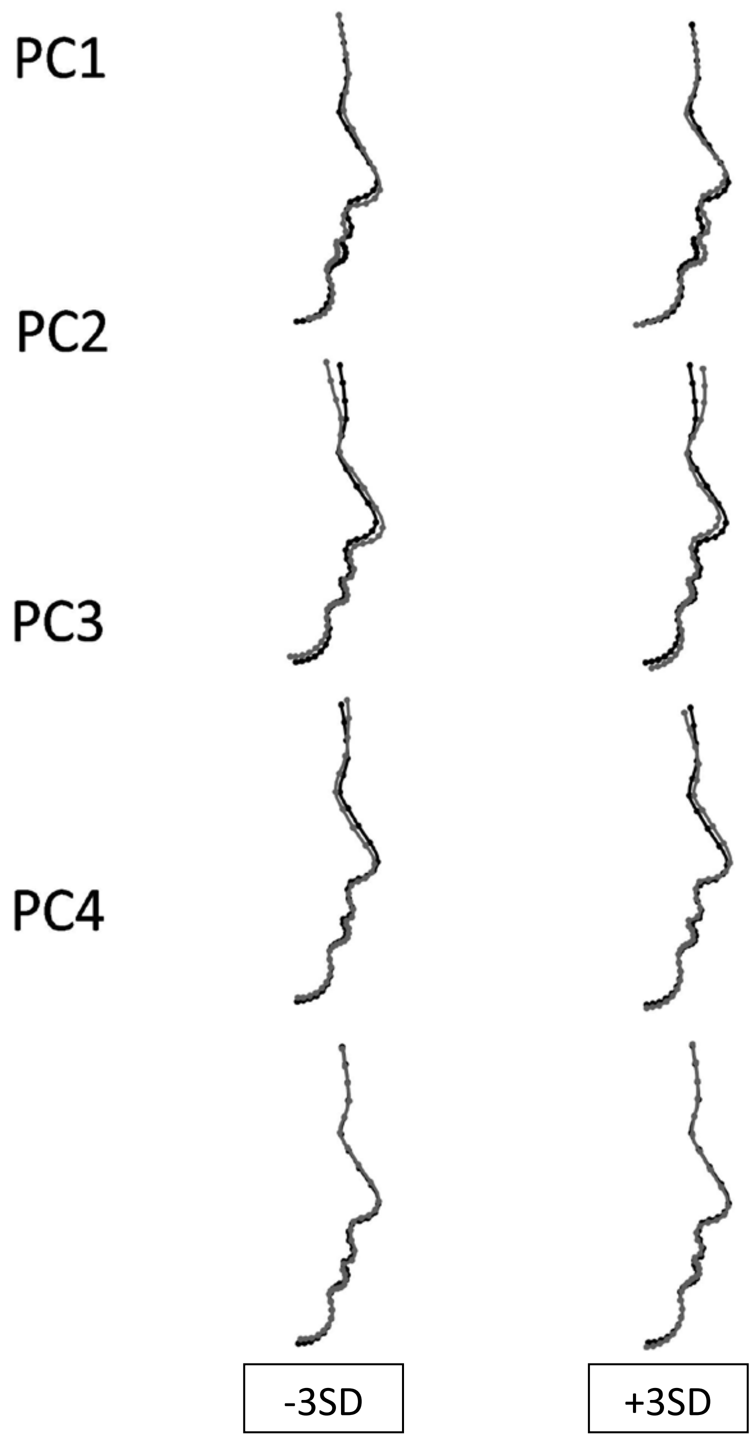
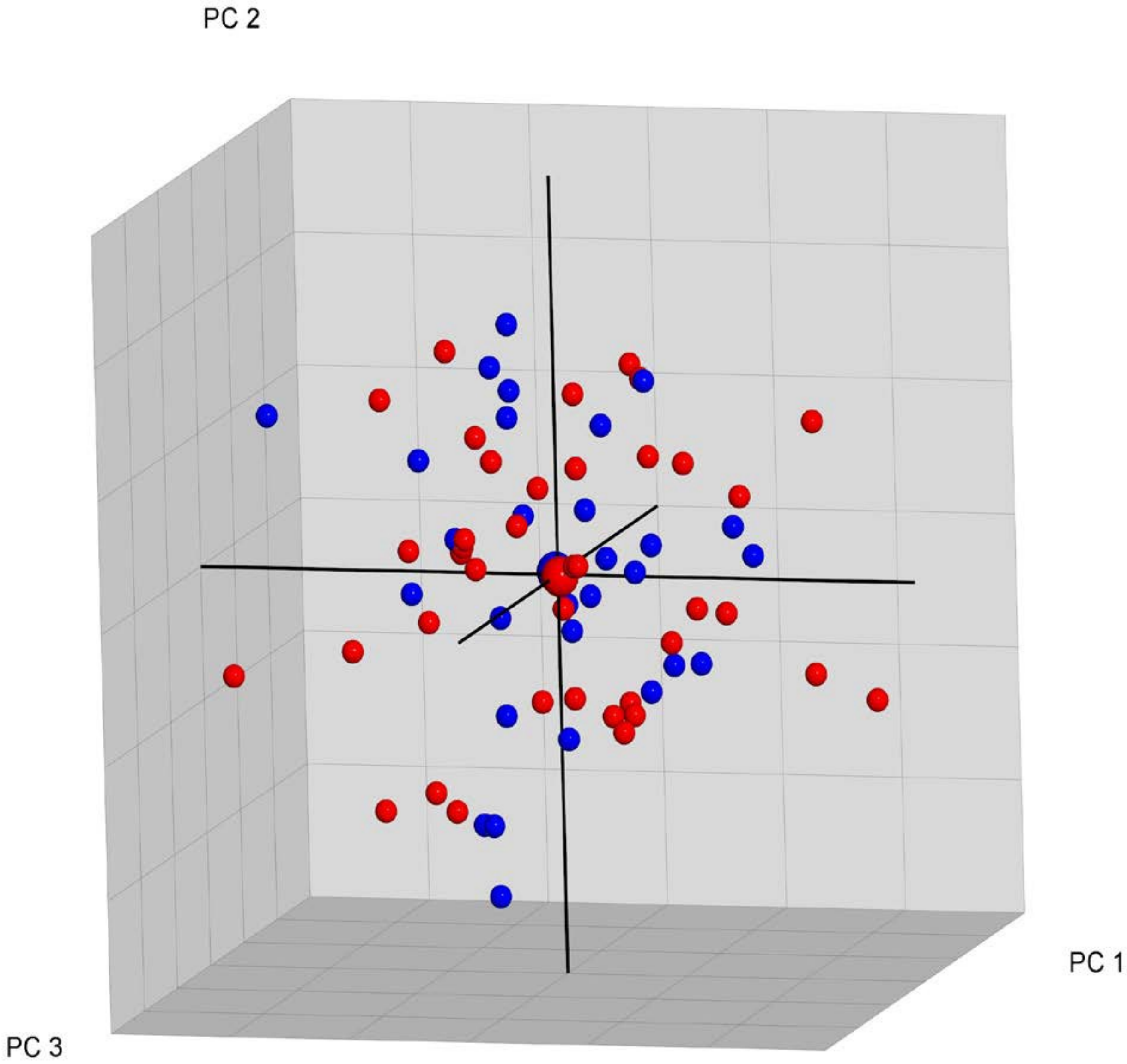


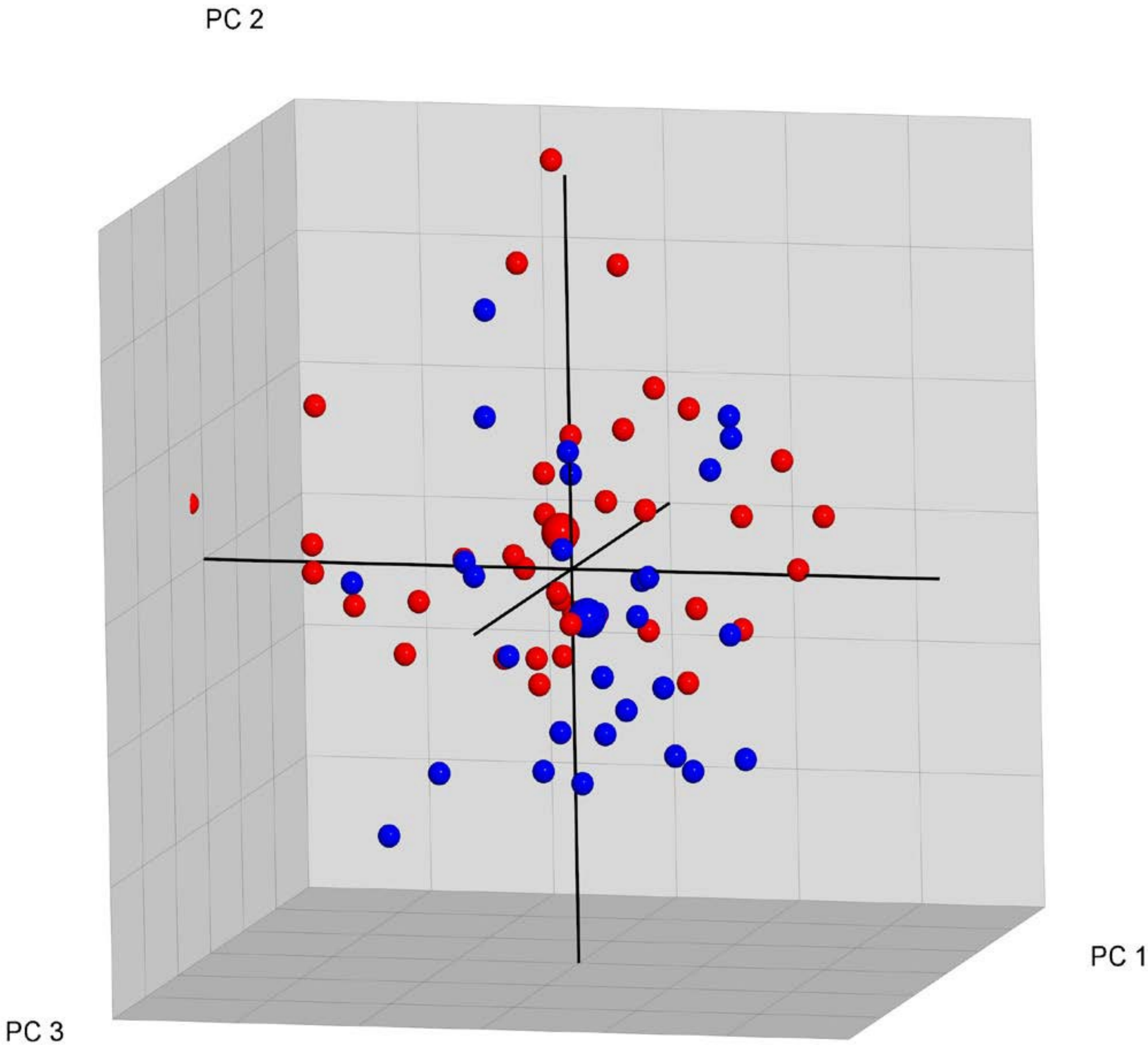
Figure 3: Variation of each one of the meaningful PCs for hard tissue profile at a range of +/- 3SD. Black: shape consensus, Grey: +/- 3SD form.



<u>Figure 4</u>: Variation of each one of the meaningful PCs for facial profile at a range of +/- 3SD. Black: shape consensus, Grey: +/- 3SD form.



<u>Figure 5</u>: Plot showing hard tissue distribution of the sample, concerning gender, in shape-space. No sexual dimorphism is observed. Blue: Males; Red: Females.



<u>Figure 6</u>: Plot showing soft tissue distribution of the sample, concerning gender, in shape-space. Sexual dimorphism is observed. Blue: Males; Red: Females.

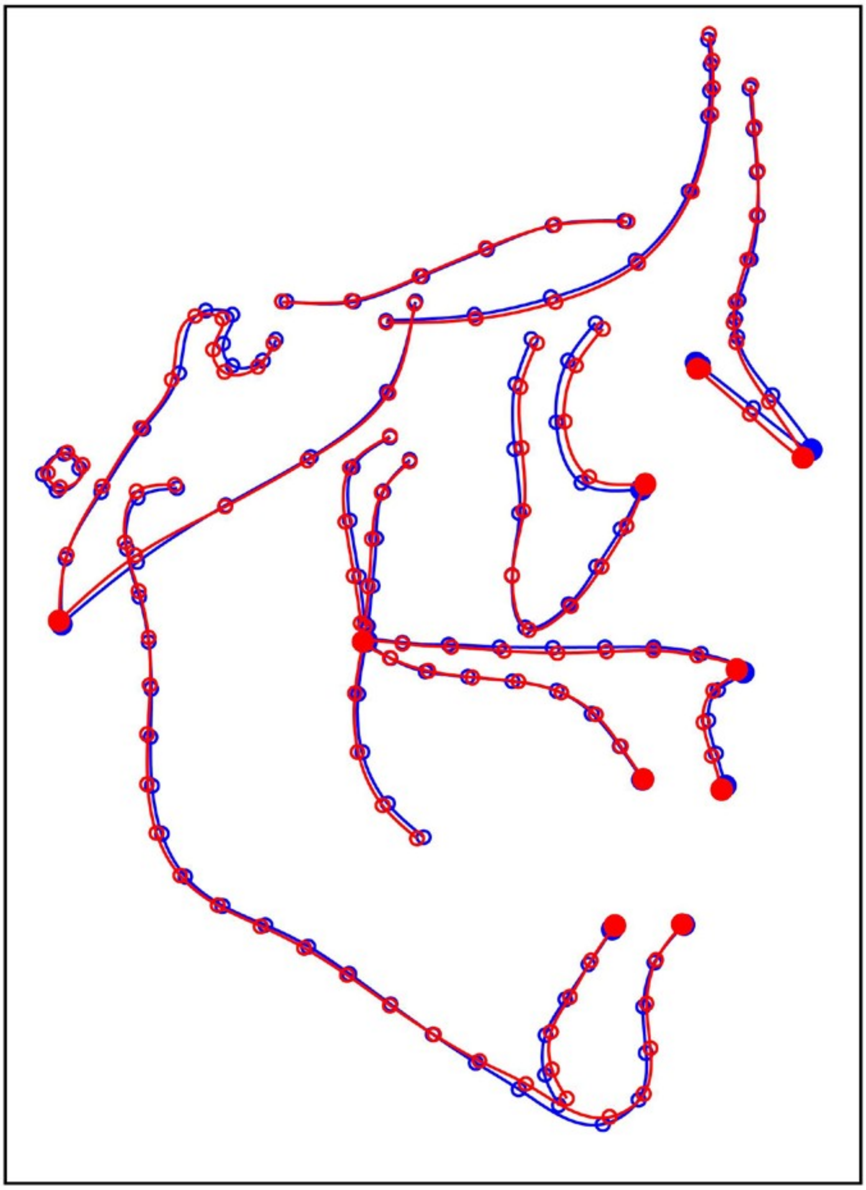
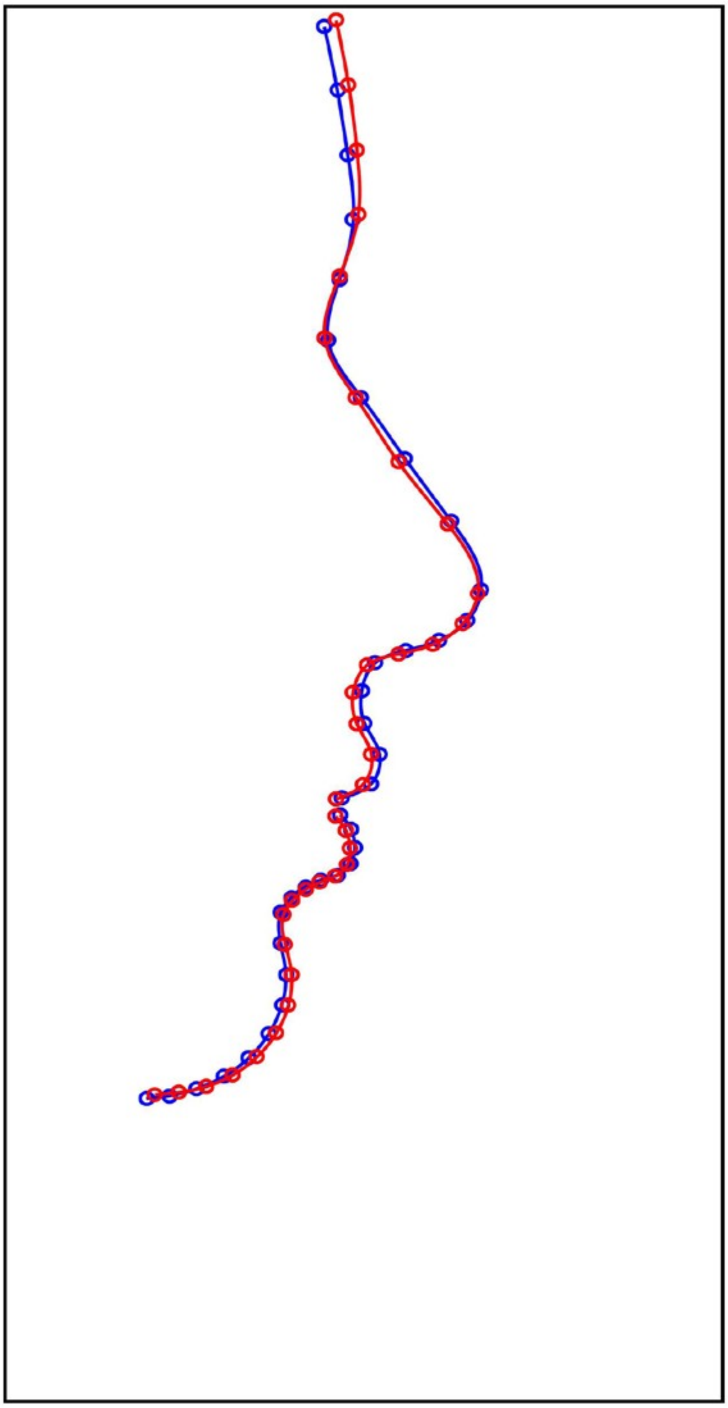


Figure 7: Comparison of hard tissue shape consensus between males and females at pre-treatment stage. Blue: Males; Red: Females.



<u>Figure 8</u>: Comparison of facial profile shape consensus between males and females at pre-treatment stage. Blue: Males; Red: Females.

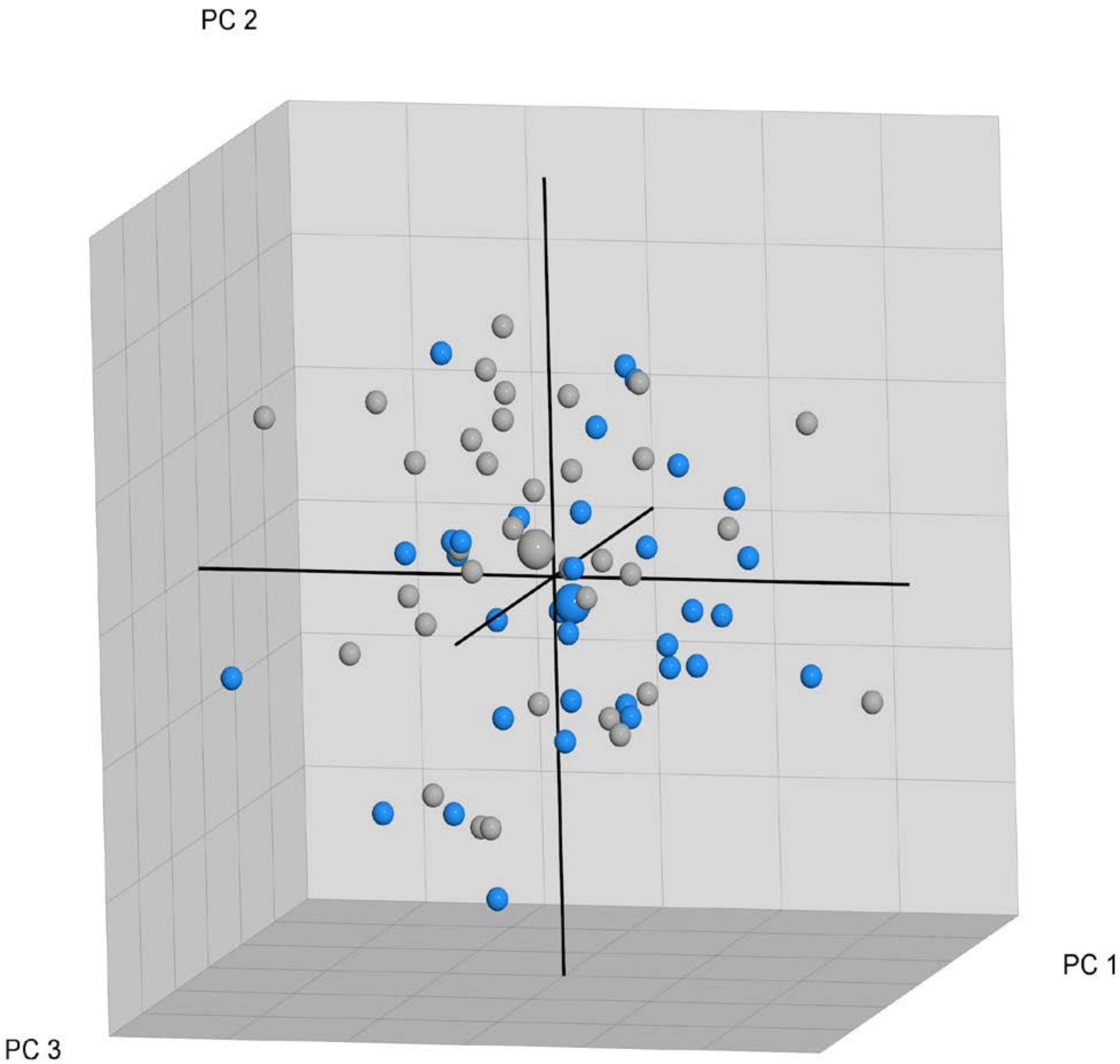


Figure 9: Plot showing hard tissue distribution of the sample (extraction and non-extraction pre-treatment cases) in shape-space. No statistically significant difference was observed. Small spheres: individuals; Big spheres: Group Means; Blue: Pre-treatment non-extraction cases; Grey: Pre-treatment extraction cases.

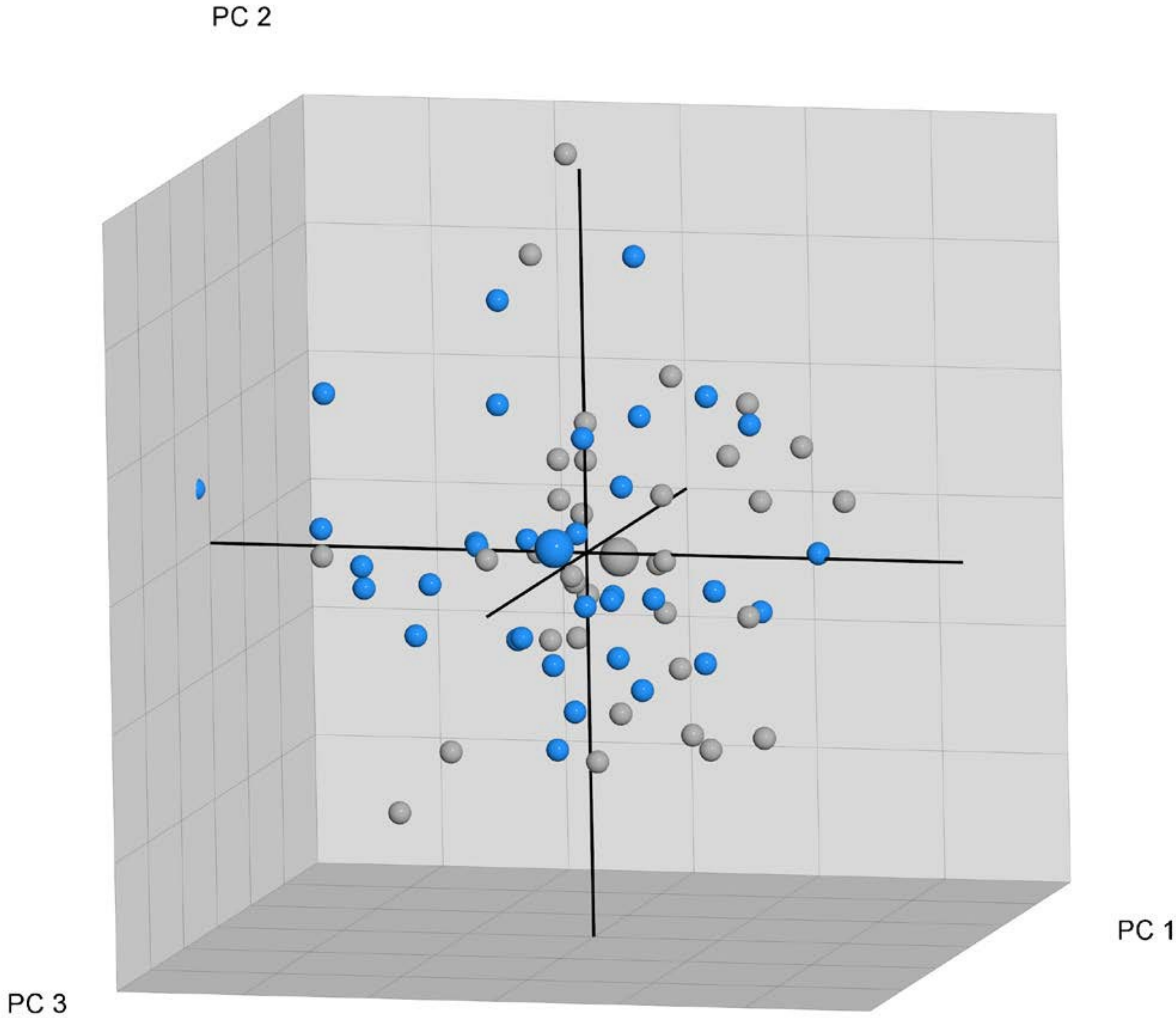
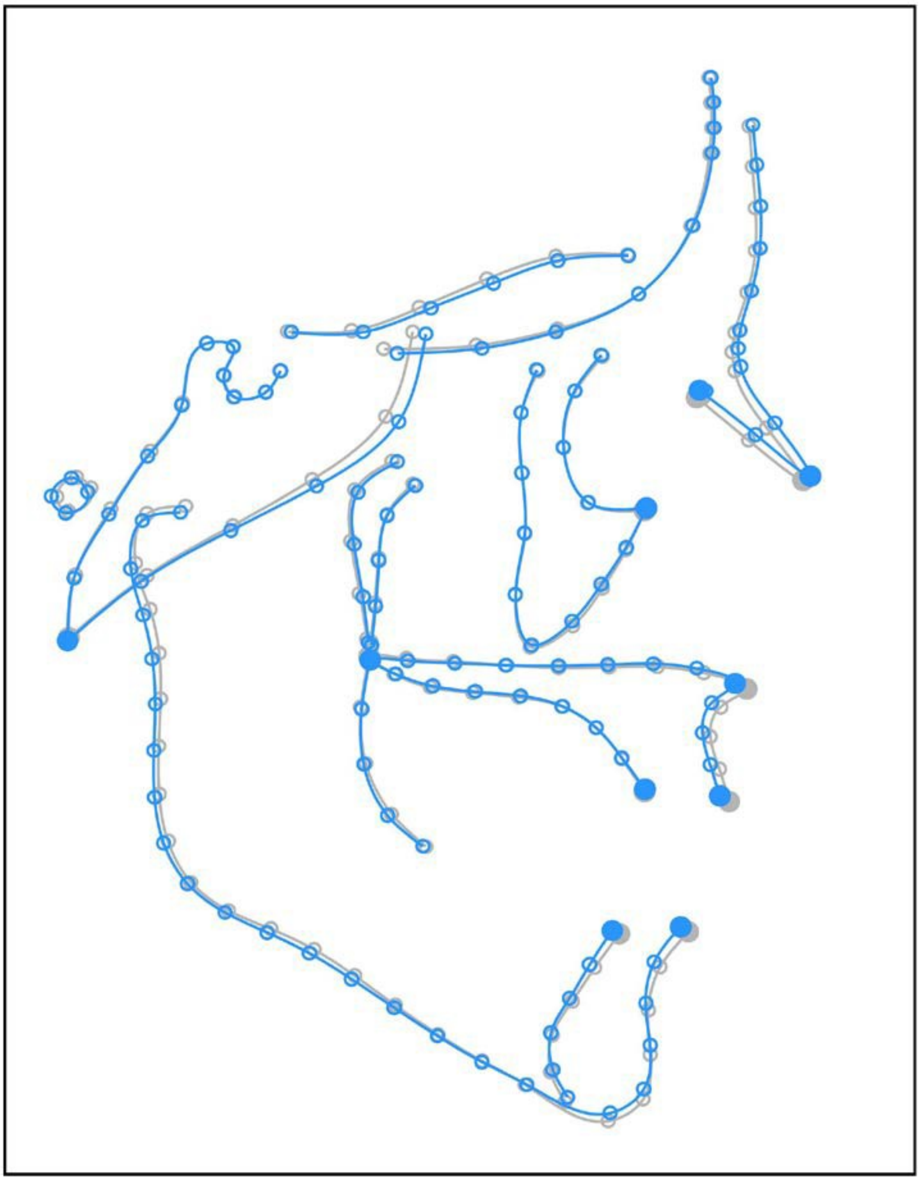
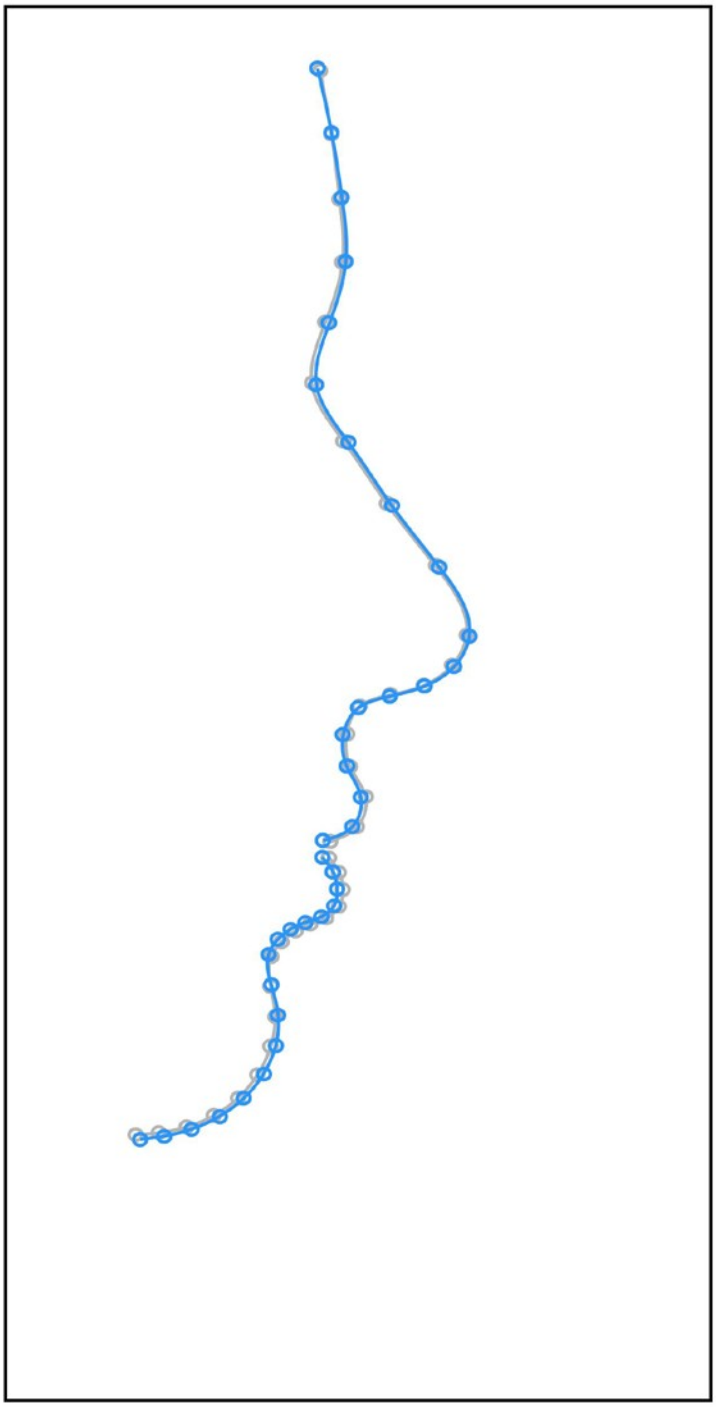


Figure 10: Plot showing distribution of the sample concerning facial profile (extraction and non-extraction pre-treatment cases) in shape-space. No statistically significant difference was observed. Small spheres: individuals; Big spheres: Group Means; Blue: Pre-treatment non-extraction cases; Grey: Pre-treatment extraction cases.



<u>Figures 11</u>: Hard tissue shape consensus exhibiting no difference between non-extraction and extraction pre-treatment groups. Blue: Pre-treatment non-extraction cases; Grey: Pre-treatment extraction cases.



<u>Figure 12</u>: Facial profile shape consensus exhibiting no difference between non-extraction and extraction pre-treatment groups. Blue: Pre-treatment non-extraction cases; Grey: Pre-treatment extraction cases.

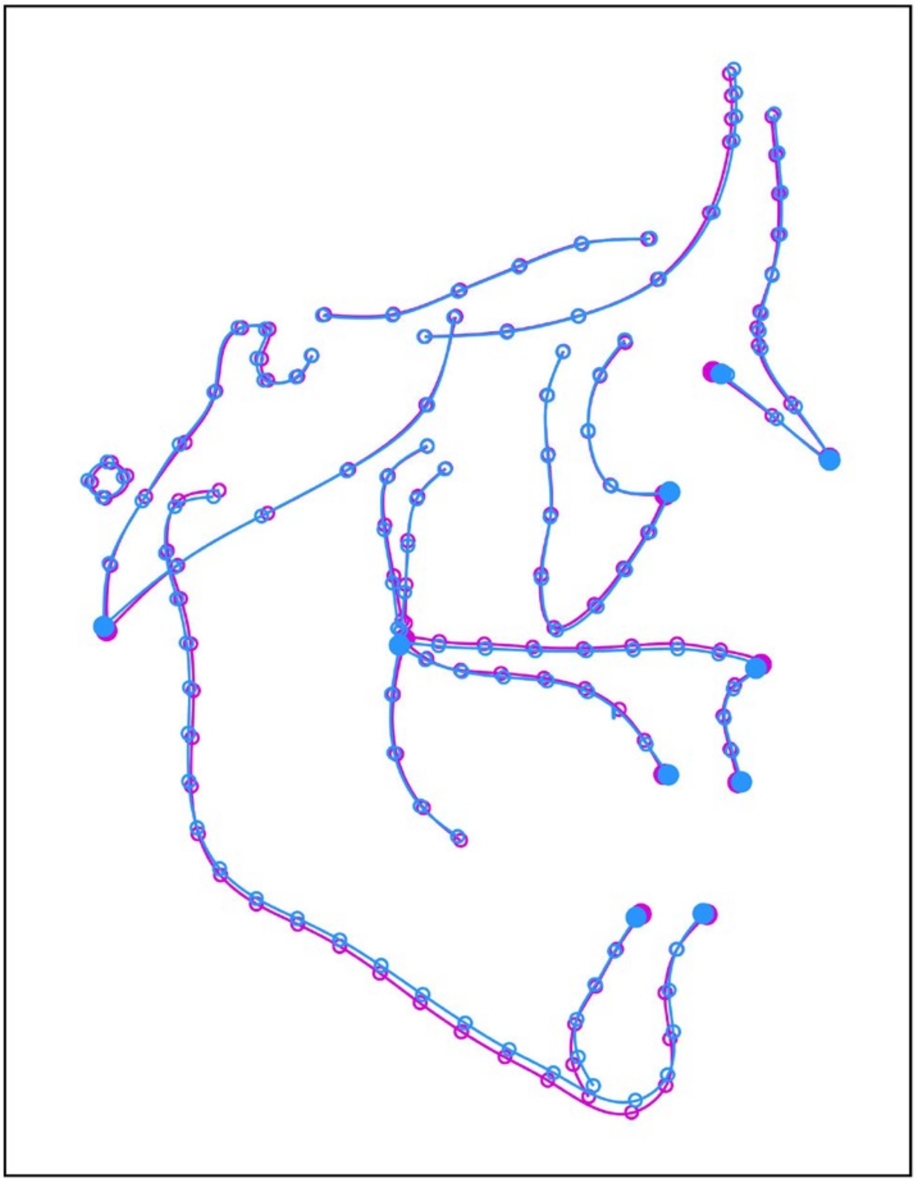


Figure 13: Comparison of hard tissue shape consensus between non-extraction pretreatment and post-treatment groups. Blue: Pre-treatment non-extraction cases; Purple: Post-treatment non-extraction cases.

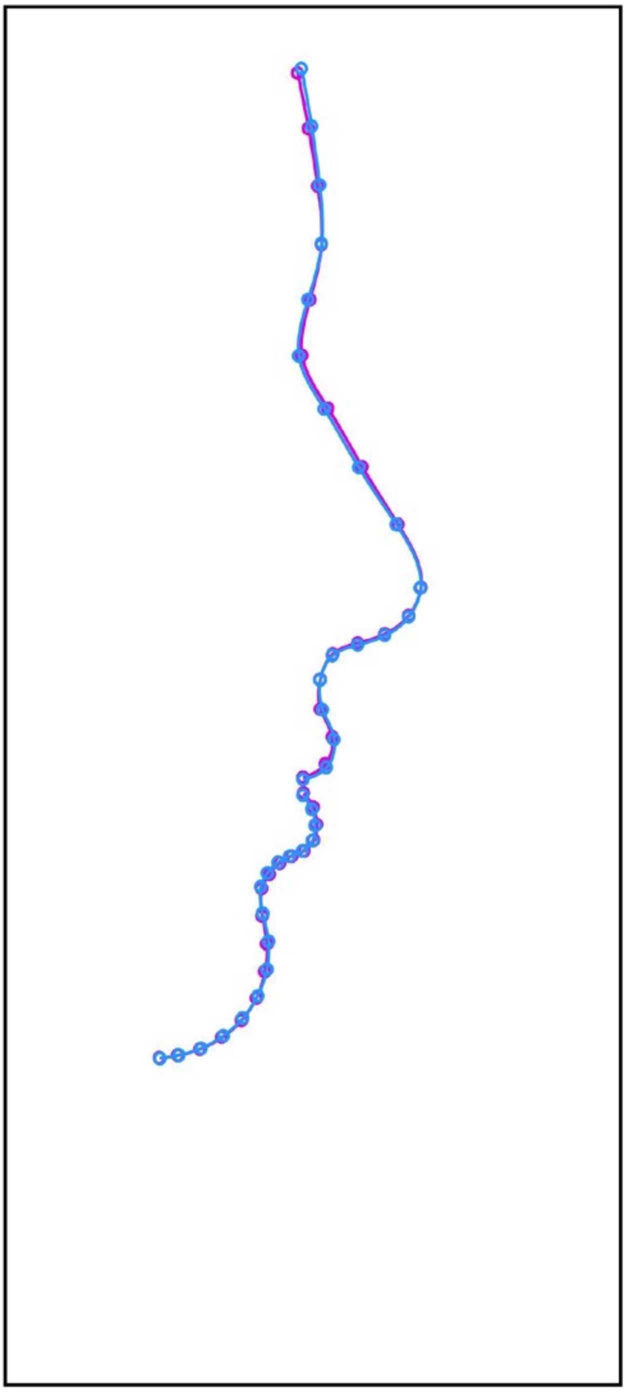


Figure 14: Comparison of soft tissue shape consensus between non-extraction pre-treatment and post-treatment groups. Blue: Pre-treatment non-extraction cases; Purple: Post-treatment non-extraction cases.

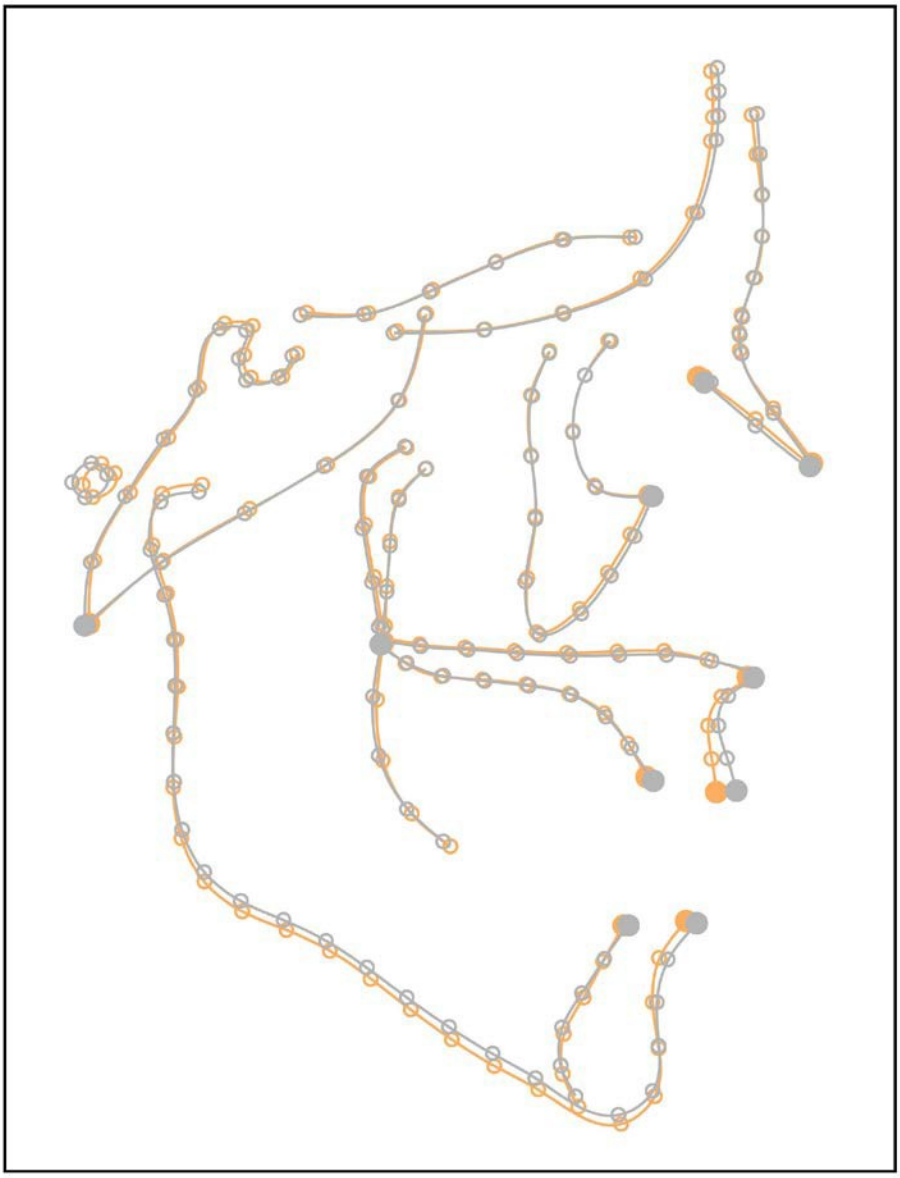
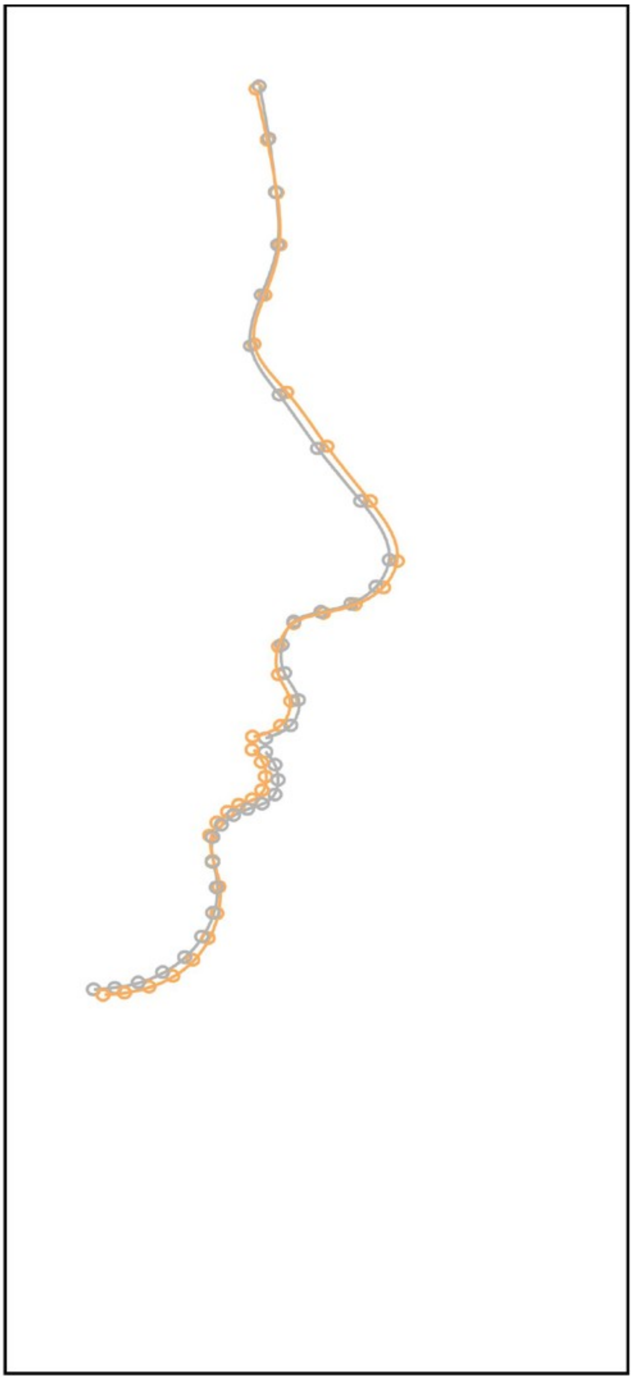


Figure 15: Comparison of hard tissue shape consensus between extraction pre-treatment and post-treatment groups. Grey: Pre-treatment extraction cases; Orange: Post-treatment extraction cases.



<u>Figure 16</u>: Comparison of soft tissue shape consensus between extraction pre-treatment and post-treatment groups. Grey: Pre-treatment extraction cases; Orange: Post-treatment extraction cases.

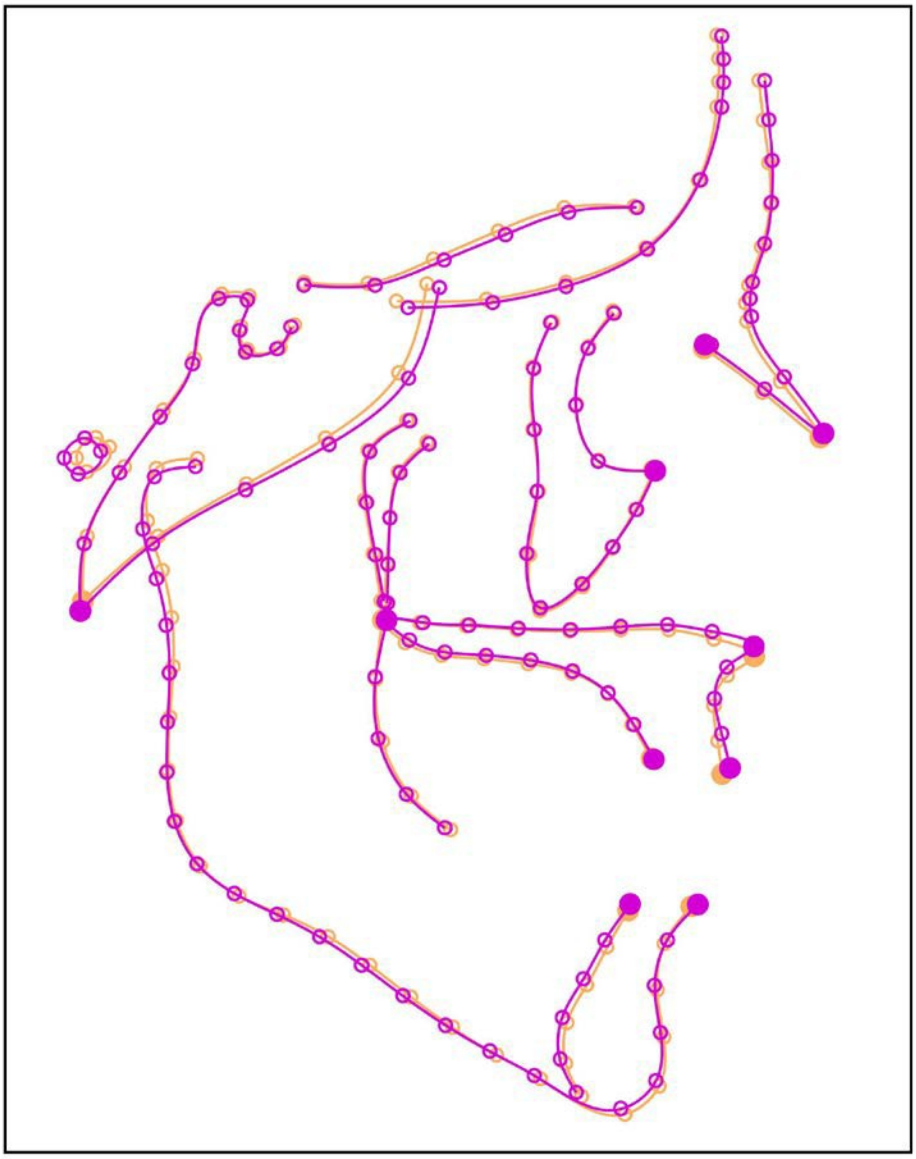


Figure 17: Comparison of hard tissue shape consensus between extraction and non-extraction post-treatment groups. Purple: Post-treatment non-extraction cases; Orange: Post-treatment extraction cases.

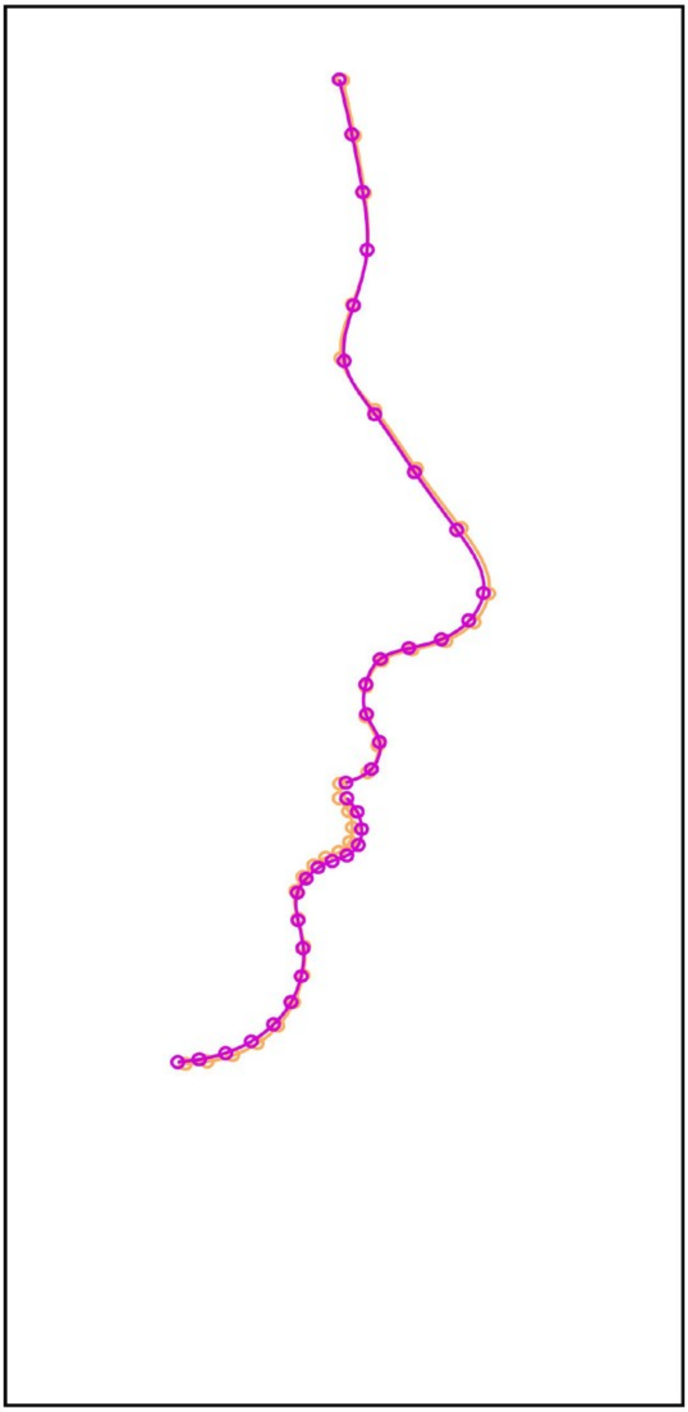
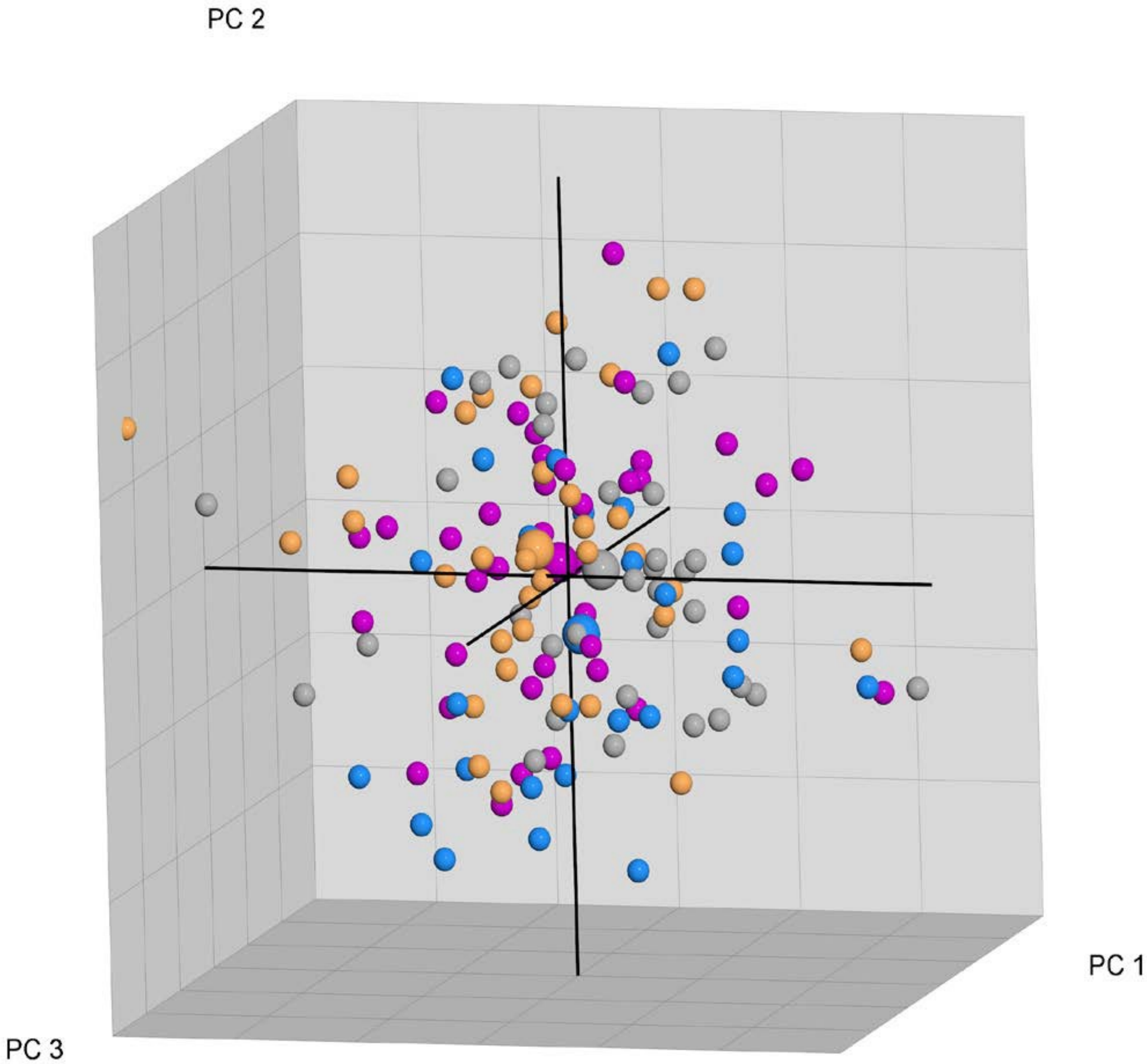
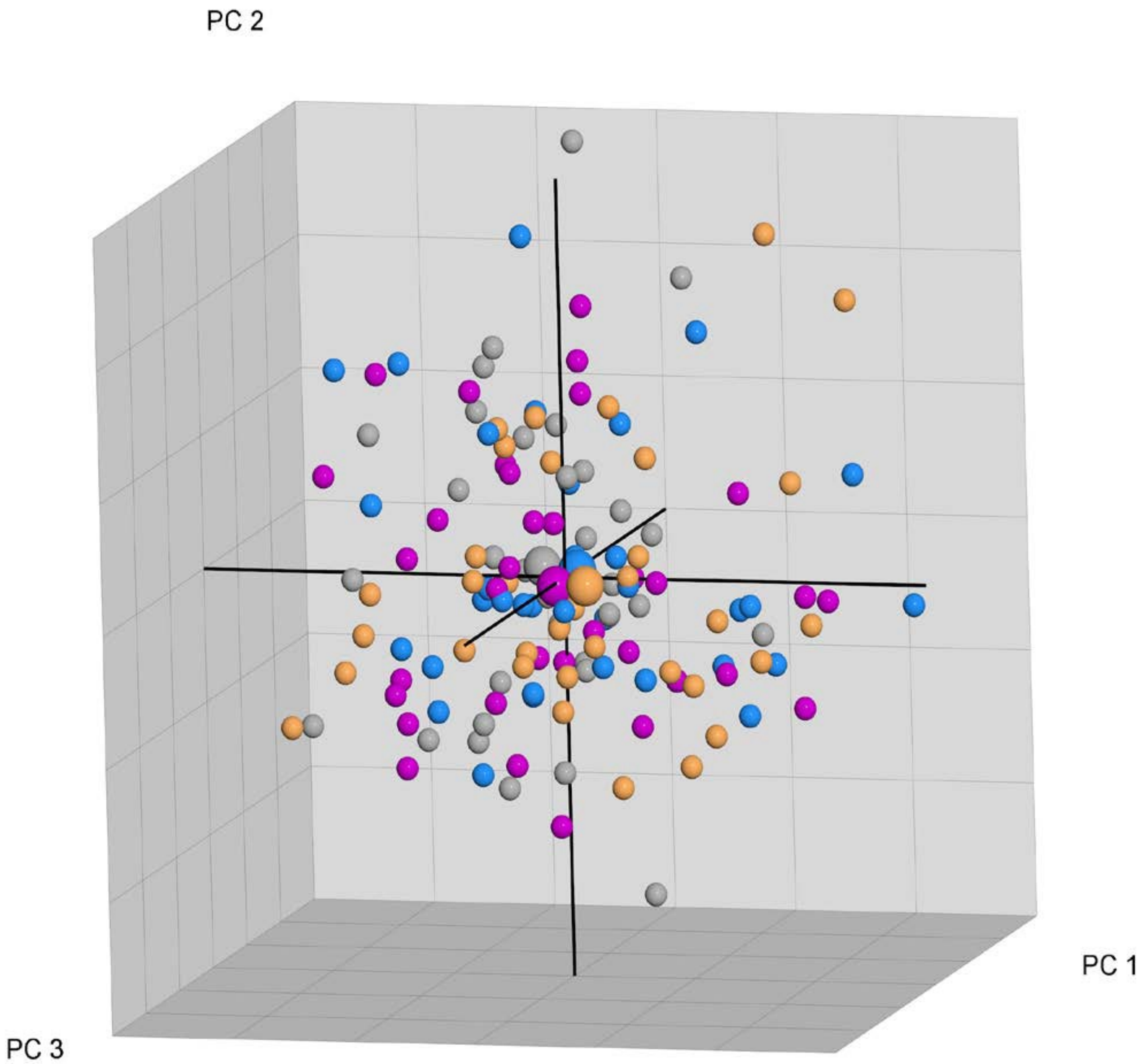


Figure 18: Comparison of soft tissue shape consensus between extraction and non-extraction post-treatment groups. Purple: Post-treatment non-extraction cases; Orange: Post-treatment extraction cases.



<u>Figure 19</u>: Plot showing hard tissue distribution of the sample (extraction and non-extraction pre-treatment and post-treatment cases) in shape-space. Small spheres: individuals; Big spheres: Group Means; Blue: Pre-treatment non-extraction cases; Purple: Post-treatment non-extraction cases; Grey: Pre-treatment extraction cases; Orange: Post-treatment extraction cases.



<u>Figure 20</u>: Plot showing distribution of the sample concerning facial profile (extraction and non-extraction pre-treatment and post-treatment cases) in shape-space. Small spheres: individuals; Big spheres: Group Means; Blue: Pre-treatment non-extraction cases; Purple: Post-treatment non-extraction cases; Grey: Pre-treatment extraction cases; Orange: Post-treatment extraction cases.

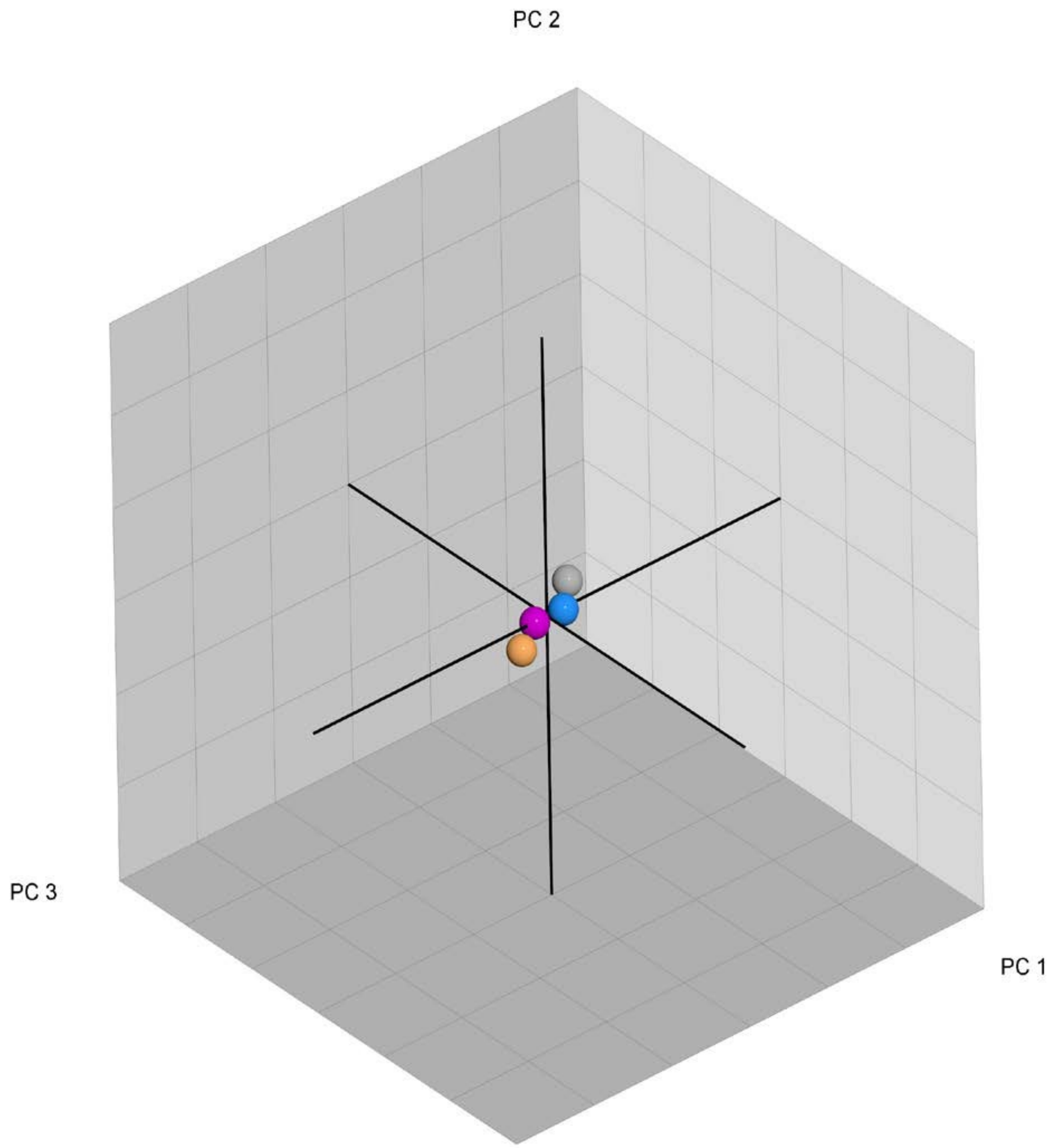


Figure 21: Plot presenting pre-treatment and post-treatment group means. Blue: Pre-treatment non-extraction group mean; Purple: Post-treatment non-extraction group mean; Grey: Pre-treatment extraction group mean; Orange: Post-treatment extraction group mean

Appendix - Sample Description

Non-Extraction cases					
	Code	Gender	Start date	End date	Date of birth
1.	AB1	M	10/6/2002	31/1/2004	6/12/1986
2.	AP1	F	21/10/2010	10/12/2012	9/5/1999
3.	AR1	M	27/8/2001	3/12/2002	1/4/1988
4.	AT1	M	10/12/2002	7/6/2004	13/9/1990
5.	BK2	F	14/9/2000	12/10/2003	15/7/1986
6.	BR1	F	31/5/2001	22/10/2002	19/10/1988
7.	BT1	M	27/7/2002	28/1/2004	23/11/1989
8.	DC1	F	1/10/2002	21/3/2004	2/4/1991
9.	EK1	F	30/5/2000	17/3/2002	16/12/1989
10.	EL1	F	11/8/2002	23/9/2004	13/7/1989
11.	GJ1	F	6/12/2001	1/4/2003	3/1/1990
12.	GJ2	M	17/10/1999	1/3/2001	14/2/1984
13.	GK1	F	24/10/2001	12/1/2003	18/6/1989
14.	HC1	M	16/8/2000	20/12/2001	23/4/1985
15.	JE1	M	14/12/2003	28/3/2005	6/4/1991
16.	KX2	F	22/10/2010	12/3/2012	18/3/1985
17.	MK1	F	9/11/2002	29/8/2004	10/8/1990
18.	MM1	F	9/11/2002	2/8/2005	28/2/1990
19.	PC1	F	4/1/2003	20/5/2004	15/7/1991
20.	RH1	F	8/11/1998	7/9/2000	21/6/1986
21.	RK1	F	30/9/2003	6/1/2005	5/9/1989
22.	SJ1	F	7/9/1999	16/10/2000	25/6/1986
23.	SJ2	M	24/10/2003	20/1/2005	8/9/1990
24.	SL1	F	4/2/2002	1/12/2002	21/3/1989
25.	TA1	M	24/1/2012	12/10/2015	31/5/2001
26.	TD1	M	26/2/2000	17/3/2002	14/4/1987
27.	TK2	F	9/11/2009	13/1/2012	8/7/1986
28.	WJ1	F	5/3/1998	4/4/2001	16/5/1987
29.	WJ2	M	4/12/2000	27/3/2002	27/3/1984
30.	WJ4	M	5/11/2001	10/12/2002	7/11/1986
31.	WL1	F	21/10/2003	12/9/2004	9/9/1990
32.	WZ1	M	13/8/2001	11/2/2003	17/3/1987
33.	XP1	M	17/10/2011	2/7/2013	23/3/1993
34.	ZA1	M	6/10/2002	15/6/2004	21/10/1986

Extraction cases					
	Code	Gender	Start date	End date	Date of birth
1.	BJ1	F	30/3/2002	5/4/2004	25/5/1989
2.	BK1	F	5/11/2000	11/2/2003	28/6/1987
3.	BV1	F	18/9/2000	15/12/2003	25/8/1975
4.	CC1	F	17/10/1999	4/9/2002	17/6/1985
5.	CL1	F	5/3/2001	4/11/2002	12/10/1988
6.	CM1	F	6/2/2002	22/11/2003	4/1/1991
7.	CT1	M	17/8/2000	12/4/2003	8/9/1984
8.	DD1	F	4/9/2000	30/7/2002	17/3/1975
9.	EF2	F	25/9/2007	4/3/2011	23/10/1995
10.	EM2	F	9/9/2005	27/4/2009	4/8/1994
11.	EV2	F	24/10/2005	1/11/2010	10/8/1994
12.	GH1	F	28/11/1999	10/6/2001	10/11/1985
13.	GL1	F	20/10/1999	21/3/2002	11/9/1986
14.	GM1	M	27/11/2000	9/5/2003	7/5/1987
15.	GS1	M	10/11/2008	17/1/2013	10/9/1991
16.	HM1	M	27/7/2002	17/3/2004	4/7/1988
17.	HN1	M	9/10/2003	28/3/2005	20/5/1991
18.	IL1	M	18/2/2010	22/3/2013	30/11/1994
19.	KC1	F	5/10/2002	17/3/2004	8/2/1990
20.	KC2	M	5/11/2000	3/6/2002	18/9/1987
21.	LJ1	F	1/7/2001	12/2/2002	3/11/1988
22.	MG1	F	25/11/2011	8/7/2015	3/5/2001
23.	MK1	M	7/7/2006	5/8/2008	5/4/1990
24.	MT1	M	7/7/2006	15/12/2010	19/6/1990
25.	RB1	M	4/6/2003	14/12/2004	6/4/1990
26.	SA1	M	24/6/2009	9/7/2014	14/1/1999
27.	SC1	F	1/10/2000	20/8/2002	22/3/1987
28.	SR1	M	22/10/2002	8/11/2004	5/8/1989
29.	TJ1	M	18/7/1999	4/11/2001	19/2/1983
30.	TL1	M	15/10/2001	17/2/2004	6/8/1988
31.	WC1	F	22/8/2001	17/8/2003	23/8/1988
32.	WK1	M	13/12/2000	14/3/2004	6/10/1985
33.	WS1	F	1/10/2002	1/11/2004	9/10/1991
34.	WS2	F	10/10/1999	25/5/2003	23/2/1989

Matching						
Extraction Cases			Non-Extraction Cases			Difference
CODE	GENDER	AGE (start)	CODE	GENDER	AGE (start)	(years)
SA1	M	10,38	TA1	M	10,65	**-0,27**
MG1	F	10,56	EK1	F	10,45	**0,11**
WS2	F	10,63	WJ1	F	10,80	**-0,18**
WS1	F	10,98	AP1	F	11,45	**0,47**
CM1	F	11,09	PC1	F	11,47	**-0,38**
EM2	F	11,10	DC1	F	11,49	**-0,39**
EV2	F	11,21	GJ1	F	11,92	**0,72**
EF2	F	11,92	MK1	F	12,25	**-0,33**
HN1	M	12,39	AT1	M	12,24	**0,15**
CL1	F	12,39	GK1	F	12,35	**0,04**
KC1	F	12,65	RH1	F	12,38	**0,27**
LJ1	F	12,66	BR1	F	12,61	**0,04**
BJ1	F	12,85	MM1	F	12,70	**0,15**
WC1	F	13,00	SL1	F	12,88	**0,12**
GL1	F	13,11	EL1	F	13,08	**0,03**
KC2	M	13,13	BT1	M	12,67	**0,46**
RB1	M	13,16	JE1	M	12,69	**0,47**
TL1	M	13,19	TD1	M	12,87	**0,32**
SR1	M	13,21	SJ2	M	13,13	**0,09**
BK1	F	13,36	WL1	F	13,11	**0,24**
SC1	F	13,53	SJ1	F	13,20	**0,33**
GM1	M	13,56	AR1	M	13,40	**0,16**
GH1	F	14,05	RK1	F	14,07	**-0,02**
HM1	M	14,06	WZ1	M	14,41	**-0,35**
CC1	F	14,33	BK2	F	14,17	**0,16**
WK1	M	15,19	WJ4	M	15,00	**0,19**
IL1	M	15,22	HC1	M	15,32	**-0,10**
CT1	M	15,94	AB1	M	15,50	**0,44**
MT1	M	16,05	GJ2	M	15,67	**0,38**
TJ1	M	16,41	ZA1	M	15,95	**0,46**
GS1	M	17,17	WJ2	M	16,68	**0,49**
MK1	M	18,60	XP1	M	18,56	**0,04**
BV1	F	25,07	TK2	F	23,34	**1,73**
DD1	F	25,47	KX2	F	25,60	**-0,13**