厚生労働科学研究費補助金

（第３次対がん総合戦略研究事業）

医科歯科連携のチーム医療における オーラルケア法の開発

平成24年度　総括研究報告書

研究代表者　別所　和久

平成 25 年（2013 年）５月

目　　次

Ⅰ．総括研究報告

厚生労働科学研究費補助金（第３次対がん総合戦略研究事業）
総括研究年度終了報告書

医科歯科連携のチーム医療におけるオーラルケア法の開発

研究代表者　別所　和久　京都大学・医学研究科・教授

研究要旨

平成24年度診療報酬改定において、がん患者等の周術期の口腔機能を管理する観点から、「周術期口腔機能管理料」が新設された。がん患者にとって、現在のシステムでは口腔を清潔に保つことは困難であり、いわゆる「要介護性歯科疾患」を発症する可能性が高い。つまり、歯の寿命の延長が歯周病やう蝕の多発、疼痛・咀嚼機能の低下、さらには、病巣感染による全身疾患の起炎菌としての危険性が一層増大し、口腔の機能と清潔度ががん患者の生命予後をも左右すると考えられる。このような背景から、がん患者のQOLの飛躍的向上に寄与するための施策が重要となってきた。オーラルケアと肺炎予防に関する先行研究では、「週１回の歯科衛生士の口腔ケアの介入により肺炎が予防できること（米山ら，Lancet354, 1999）」は報告されているが、医科・歯科・介護スタッフが連携してオーラルケアを行ない全身への影響を評価した研究はない。また、客観的（普遍的）な口腔細菌の検査法も確立されていない。さらに、病院や施設においてオーラルケアを毎日提供するためのマネジメント法も確立されていない。本研究では、(1)オーラルケアを通して肺炎を予防した施設をモデルに「オーラルケア・マネジメント・マニュアル」を作成する。(2)普遍的な口腔細菌の検査法を確立し、近隣のオーラルケアを行っていない施設において口腔・全身の状態を調査・比較する。(3)近隣のオーラルケアを行なっていない施設にオーラルケア・マネジメントを介入し、有効性を確認する。(4)介護力に違いのある病院や施設を全国的に選択して、オーラルケア・マネジメントの実践が有病者や高齢者の口腔と全身に与える影響を検討する。(5)有効なオーラルケア・マネジメント法を確立して啓発する。研究の最終ゴールは、がん患者の有効なオーラルケア・マネジメント法を確立し、がん患者のQOLの飛躍的向上に寄与することである。

研究分担者氏名・所属研究機関名及び所属研究機関における職名

- ●別所和久　京都大学医学研究科　教授
- ●石井孝典　公益財団法人ライオン歯科衛生研究所　理事
- ●武井典子　公益財団法人ライオン歯科衛生研究所　副主席研究員
- ●石川正夫　公益財団法人ライオン歯科衛生研究所　研究員
- ●中山健夫　京都大学医学研究科　教授
- ●堀　信介　京都大学医学研究科　非常勤講師
- ●高橋　克　京都大学医学研究科　准教授
- ●家森正志　京都大学医学研究科　助教

A．研究目的

平成24年度診療報酬改定において、がん患者等の周術期の口腔機能を管理する観点から、歯科衛生士が月に数回の専門的口腔清掃を行うよりも口腔ケア・マネジメントを行った方が、施設全体の口腔環境が改善するという報告（菊谷ら，2008.）が根拠となり、「周術期口腔機能管理料」が新設された。一方、申請者らは、某病院の関連施設において歯科医師・歯科衛生士が摂食・嚥下機能訓練を含むオーラルケアを多職種と連携・実践することで、肺炎による入院患者数・在院日数が半減し、医療費を73%削減できることを確認した。

そこで、肺炎予防の効果が認められた「オーラルケア・マネジメント法」を基に、それぞれの職種の専門性を考慮した具体的な方法をマニュアル化して、近隣の施設でその普遍性を実証することが急務である。また、有効なオーラルケア法を確立するためには、細菌学的な評価も重要となるが、含嗽ができない場合に行われる従来のスワブによる採取法は、採取者や圧によりバラツキが生じ、客観的な指標とするには課題がある。これを解決するための新たな採取法を含む検査法を開発する必要がある。

申請者らは、2000年より、オーラルケア・マネジメントの重要性に気づき「高齢者オーラルケア分類表（武井ら，2003.）」を開発した。オーラルケアを介護度と口腔状態から９つのカテゴリーに分類してオーダーメードのオーラルケア法を身近な介護者に理解しやすく提案・実践・細菌学的な評価を繰り返してきた。さらに、近年では、機能的ケアを付加した「高齢者の総合的な口腔機能評価と管理のシステム（武井ら，2009.）」を開発して評価を継続している。これらをベースに、摂食・嚥下機能訓練法および多職種連携の具体的方法を追加することにある。

以上の特色を生かして、本研究の目的は、がん患者等の有効なオーラルケア・マネジメント法を確立し、がん患者等のQOLの飛躍的向上に寄与することである。

B．研究方法

有効なオーラルケア・マネジメント・マニュアルの開発と評価法の検討

(1)摂食・嚥下訓練を含むオーラルケア・マネジメント・マニュアルの開発

①肺炎予防の効果が認められた「オーラルケア･マネジメント法」を参考に、医師･歯科医師･看護師･歯科衛生士･栄養士･介護スタッフ等に分け、その役割と具体的な方法をマニュアル化する。

②口腔清掃法は、「高齢者オーラケア分類表」の介護度（自立･部分介助･要介護）と口腔状態（多数歯・中・少数歯・無歯顎）から９つのカテゴリーに分類してオーラルケア用具と具体的な方法をマニュアル化する。

③機能的なオーラルケア法は、口腔機能を口のまわり（口唇･頬）、入口（咀嚼機能）、奥（嚥下機能）、口腔全体の環境（唾液湿潤度等）の４つのカテゴリーに分類して客観的な検査を実施して、摂食・嚥下機能訓練も含めて口腔機能向上方法をマニュアル化する。

(2)オーラルケア・マネジメントの有効性を確認するための口腔内微生物・機能の客観的検査法の開発

過去の研究から、申請者らは以下の客観的な検査法を開発して評価を行なっている。

①唾液湿潤度の測定
②総菌数の測定
③唾液吐出液から濁度とアンモニアの測定
④カンジダ菌の測定
⑤口腔機能の嚥下機能に関する検査
⑥咀嚼能力に関する検査

(3)近隣のオーラルケアを行っていない施設に

おける口腔および全身の状態の調査・比較

某病院の関連施設（特別養護老人ホームA、50床）において摂食・嚥下訓練を含むオーラルケアを医科・歯科・介護スタッフと連携して実践し、肺炎による入院患者数・在院日数が半減し、医療費を73%削減できることを確認してきた。さらに、近隣にも特別養護老人ホームB（80床）があり、現在はオーラルケアを積極的に実践していない。そこで、特別養護老人ホームAおよびBの(2)の客観的な検査結果と肺炎による入院患者数・在院日数・医療費を比較検討する。

未実施施設でオーラルケア・マネジメント介入・有効性の確認

(1)未実施の施設にオーラルケア・マネジメントを介入・有効性の再確認

特別養護老人ホームBに「オーラルケア・マネジメント」を(1)のマニュアルに基づき、介入してその有効性を確認する。

オーラルケア・マネジメントによる要介護度・医療費の低減の実証

(1)オーラルケア・マネジメントの有効性の検証とマニュアルの強化

介護力に違いのある病院や施設を全国的に選択して、オーラルケア・マネジメントの実践が有病者や高齢者の口腔と全身にどのような影響を与えるかを検討する。具体的には、研究分担者らの京都大学関連病院（26施設）および関連施設（特別養護老人ホーム等）に幅広く実施を呼びかけ、個々人および家族の同意を得て、長期的に実施・評価する。

(2)有効なオーラルケア・マネジメント・マニュアルをテキストとした実務研修の全国展開

①オーラルケア・マネジメント・マニュアルのテキストを作成する。

②京都大学関連病院を核に全国的に展開する。

今回の有効なマニュアルを全国に広げるために、執筆・講演活動を積極的に行なう。

（倫理面への配慮）

1．インフォームド・コンセント

本研究は、疫学に関する倫理指針（平成19年8月16日）に準拠して実施され、調査の趣旨に賛同した者のみが対象となる。調査への賛同は、同意書を書面にて入手する。なお、各々の研究施設毎に医の倫理委員会の承認を得た後に、当該施設における研究は開始するものとする。

2．個人情報の保護

1）氏名など個人が同定できる調査項目は集計ファイルとは別の独立したファイルとし厳重に保管管理する。

2）データ解析等では、被検者識別コードを用いて個人が特定されないようにする。

3）結果の公表は、個人を同定できない統計解析結果の形で行う。

4）データは研究終了時点で廃棄する。

具体的には、オーラルケア・マネジメントを行う病院および施設の対象者については、本人および家族に十分な説明を行い、書面にて了解が得られた施設入所者および病院入院患者のみに行なう。事前に健診、検査、調査を行い、その後、その結果に基づくオーラルケアプランおよびマネジメントにおいて、本人または身近な介護者が毎日、オーラルケアを行い、口腔環境（口腔内微生物、唾液湿潤度）および口腔機能の検査を行うこと、それらは苦痛を伴うことなく、安全で、全身のためにも大切なことを十分に説明する。

C．研究結果

本年度は、当初の研究計画に沿い、有効なオーラルケア・マネジメントの開発とその応用による周術期口腔機能管理マニュアルの作成に取り組んだ。オーラルケア・マネジメントの実質的手法に関しては、歯科系医療従事者単独、病院看護師単独で作成した出版物は存在するものの、最も必要とされる多職種がそれぞれの立場から、協働する全医療関係者を対象として作成したマニュアルは、未だ存在しない。周術期には、主治医、麻酔科医、看護師、理学療法士、管理栄養士、薬剤師、歯科医師、歯科衛生士、歯科技工士、医療事務職員など、さまざまな職種が患者に関与する。これらの全医療従事者によるチーム医療、多職種協働で口腔機能管理を行うためには、それぞれの専門性を十分に発揮し、継続的で有効な口腔機能管理ができるように連携することが大切である。周術期に質の高い口腔機能管理を行うためには、現存する口腔内疾患やその時点で行われている器質的・機能的オーラルケアについての的確な評価および今後に起こりうるリスク評価を行い→その結果に基づいた口腔機能管理計画を策定し→策定した計画を実施→当初の計画に基づき実施した効果の再評価→再評価結果に基づく計画修正というPDCAサイクル（Plan: 計画→ Do: 実行→ Check: 確認→ Act: 改善）を回す必要がある。

そこで、今回の周術期口腔機能管理マニュアル作成には、当科が介入して開発した当科関連病院で先行実施しているオーラルケア・マネジメント法（既に出版済）を基本とした。マニュアル作成に際しては、京大病院歯科口腔外科スタッフに加え、化学療法部、放射線治療科、呼吸器内科、薬剤部、看護部、医療事務職員など、さまざまな職種の協力を得、特に全身麻酔下での手術患者、化学療法・放射線治療・緩和治療を受ける患者を対象の中心とした。このマニュアルに関しては、既に出版準備を終えており、本年２月中旬には出版予定である。今回、口腔機能管理分野において、現時点で一番後れを取っている評価法についても合わせて検討を加えた。種々の評価手法について検討し、様々な患者にも対応出来る評価法を目標として、当院内で臨床研究を既に開始している。マニュアルには、各がん治療種別に項目を設け、評価後に行う口腔疾患の治療、器質的オーラルケア（口腔清掃、口腔疾患の症状緩和・予防など）、機能的オーラルケア（摂食機能訓練、構音機能訓練、開口訓練など）に関し、それらの必要性、手法、効果の評価法などに至るまで盛り込んでいる。そのため、口腔内のことに今まで注目していなかった歯科系以外の医療従事者が、初めて口腔機能管理に取り組む際にでも活用できるよう、視覚に訴える平易なマニュアルとした。また、歯科口腔外科のない病院も含めた種々の環境の病院においても活用してもらえるように、参考資料として、診療情報提供書、周術期口腔機能管理計画書、周術期口腔機能管理報告書、同意書、患者への報告書、看護師用評価表、患者説明用リーフレット、周術期患者への説明用パンレット、化学療法・放射線治療患者への説明用パンフレット、各科外来掲示用ポスターを付した。

この周術期口腔機能管理マニュアルの各がん治療種別に設けた項目内には、それぞれ入院前から退院後に至るまでの口腔機能管理の流れを、１）入院前または入院時のオリエンテーション、２）治療前・術前の口腔機能管理、３）治療中・術後入院中の口腔機能管理、４）治療後、退院後の口腔機能管理の４期に分類し、各々の段階についての要点を詳細に記載した。

また、現在、口腔機能管理の有効性を正当に評価し得る口腔微生物・口腔機能の客観的検査法の確立にも取り組んでいる。その中の

ひとつである口腔内総菌数は、日内変動や採取部位、被検部位の乾燥度、採取方法などにより、口腔清掃状態を判定するに十分な真の口腔内総菌数を表す菌採取採取が困難である。現在行われている手法では、総菌数測定値は不安定で口腔清掃状態を表すには至っていない。総菌数測定値を口腔清掃度評価に用いることを可能にするためには、試料採取条件を規格化し、正確に患者の口腔内清掃状態を反映させる指標とする必要がある。さらに、検査を行うスタッフ間の手技の差や同じスタッフでも採取する度にその結果が不安定にならないよう、試料採取を視野の確保が容易で操作しやすい部位を選択することなどの配慮も必要になる。今後、採取部位や口腔乾燥度などと採取される菌数との関連を検討し、規格化した総菌数測定手法を確立する予定である。既に、測定手法の規格化を目指し、パイロットスタディーとしてのデータの収集は終えており、今後、新たな菌採取器具、採取菌測定手法、測定器具などの規格化を行うことまで考えている。

D．健康危険情報

なし

E．研究発表

1．論文発表

Yamazaki T, Yamori M, Asai K, Nakano-Araki I, Yamaguchi A, Takahashi K, Sekine A, Matsuda F, Kosugi S, Nakayama T and Bessho K. Mastication and risk for diabetes in a Japanese population: a cross-sectional study. *PLoS ONE*, 2013 in press

Yamamoto K, Sumi E, Yamazaki T, Asai K, Yamori M, Teramukai S, Bessho K, Yokode M, Fukushima M. A pragmatic method for electronic medical record-based observational studies: developing an electronic medical records retrieval system for clinical research. *BMJ Open*, 2012, in press

Huang B, Takahashi K, Sakata-Goto T, Kiso H, Togo Y, Saito K, Tsukamoto H, Sugai M, Akira S, Shimizu A, Bessho K. "Phenotypes of CCAAT/enhancer-binding protein beta deficiency: hyperdontia and elongated coronoid process", *Oral Dis.*, 2012, in press

Hussain A, Bessho K, Takahashi K, Tabata Y. "Magnesium calcium phosphate / β-tricalcium phosphate incorporation into gelatin scaffold, in vitro comparative study". *J Tissue Eng Regen M.* 2012, in press

別所和久、これからはじめる周術期口腔機能管理マニュアル（別所和久　監修）永末書店、京都、1-111

Huang B, Takahashi K, Yamazaki T, Saito K, Yamori M, Asai K, Yoshikawa Y, Kamioka H, Yamashiro T, Bessho K. "Assessing anteroposterior basal bone discrepancy with the Dental Aesthetic Index". *Angle Orthod*, 83, 527-532, 2013

Takahashi K, Kiso H, Saito K, Togo Y, Tsukamoto H, Huang B and Bessho K. (2013) Feasibility of gene therapy for tooth regeneration by stimulation of a third dentition: Gene Therapy-Tools and Potential Applications, In Tech, Rijeka, Croatia, 30, 727-744

Nakao K, Okubo Y, Yasoda A, Koyama N, Osawa K, Isobe Y, Kondo E, Fujii T, Miura M, Nakao K, Bessho K. The Effects of C-type Natriuretic Peptide on Craniofacial Skeletogenesis. *J Dent Res*, 92, 58-64, 2013

Koyama N, Miura M, Nakao K, Kondo E,

Fujii T, Taura D, Kanamoto N, Sone M, Yasoda A, Arai H, Bessho K, Nakao K. "Human Induced Pluripotent Stem Cells Differentiated into Chondrogenic Lineage Via Generation of Mesenchymal Progenitor Cells". *Stem Cells Dev.* 22, 102-113, 2013

Yamazaki T, Yamori M, Ishizaki T, Asai K, Goto K, Takahashi K, Nakayama T, Bessho K. "Increased incidence of osteonecrosis of the jaw after tooth extraction in patients treated with bisphosphonates: A cohort study". *Int J Oral Maxillofac Surg.* 41, 1397-1403, 2012

Sakata-Goto T, Takahashi K, Kiso H, Huang B, Tsukamoto H, Takemoto M, Hayashi T, Sugai M, Nakamura T, Yokota Y, Shimizu A, Slavkin H, Bessho K. "Id2 controls chondrogenesis acting downstream of BMP signaling during maxillary morphogenesis", *Bone.* 50, 69-78, 2012

Hussain A, Bessho K, Takahashi K, Tabata Y. "Magnesium calcium phosphate as a novel component enhances mechanical/physical properties of gelatin scaffold and osteogenic differentiation of bone marrow mesechymal stem cells". *Tissue Eng Part A.* 18, 768-774, 2012

Yamazaki T, Yamori M, Yamamoto K, Saito K, Asai K, Sumi E, Goto K, Takahashi K, Nakayama T, Bessho K. "Risk of osteomyelitis of jaw induced by oral bisphosphonates in patients taking medications for osteoporosis: a hospital-based cohort study in Japan". *Bone*, 51, 882-887, 2012

Curtin CM, Cunniffe GM, Lyons FG, Bessho K, Dickson GR, Duffy GP, O'Brien FJ. "Innovative collagen nano-hydroxyapatite scaffolds offer a highly efficient non-viral gene delivery platform for stem cell-mediated bone formation". *Adv Mater.* 24, 749-54, 2012

Fujimura K, Bessho K. "Rigid Fixation of Intraoral Vertico-Sagittal Ramus Osteotomy for Mandibular Prognathism". *J Oral Maxillofac Surg.* 70, 1170-1173, 2012

2．学会発表

山崎亨、家森正志、浅井啓太、高橋克、別所和久：歯周病および食習慣がメタボリックシンドロームに与える影響について、第66回　日本口腔科学会、広島、2012/5/17-18

山崎亨、家森正志、浅井啓太、高橋克、別所和久：咀嚼能率とメタボリックシンドロームの関連について、第66回　日本口腔科学会、広島、2012/5/17-18

浅井啓太、家森正志、山崎亨、高橋克、別所和久：ながはま0次予防コホート事業における喪失歯数と動脈硬化に関する検討、第66回　日本口腔科学会、広島、2012/5/17-18

東郷由弥子、高橋克、喜早ほのか、Boyen Haung、斎藤和幸、喜早ほのか、塚本容子、別所和久：CEBP/ß 遺伝子欠損マウスを用いた筋突起過長に関する形態学的解析、第66回　日本口腔科学会、広島、2012/5/17-18

斎藤和幸、高橋克、喜早ほのか、東郷由弥子、塚本容子、別所和久：歯牙再生に向けたBMP7を用いた歯の大きさの制御、第11回　日本再生医療学会総会、横浜、2012/6/12-14

磯部悠、家森正志、喜早ほのか、田村佳代、高橋克、別所和久：顎変形症患者におけるセファロメトリーによる形態学的評価と中

枢気道抵抗の関係についての横断的研究、第22回日本顎変形症学会総会、福岡、2012/6/18-19

喜早ほのか、家森正志、小林友里恵、磯部悠、田村佳代、高橋克、別所和久：顎変形症患者における術前の顎顔面形態と中枢気道抵抗に関する検討、第43回　日本口腔外科学会近畿地方会、大阪、2012/6/23

山崎亨、家森正志、浅井啓太、斉藤和幸、後藤和久、高橋克、別所和久：骨粗鬆症治療薬内服患者における経口ビスフォスフォネート製剤による顎骨骨髄炎の発生リスクに関して：コホート研究、第30回日本骨代謝学会学術集会、東京、2011/7/19-21

斎藤和幸、高橋克、喜早ほのか、東郷由弥子、塚本容子、別所和久：BMP7、USAG-1の発現量減少は下顎切歯体積を増大させる、第19回ＢＭＰ研究会、東京、2012/7/22

Asai K, Yamori M, Yamazaki T, Hamada A, Taguchi T, Mori M, Takahashi K, Sekine A, Kosugi S, Matsuda F, Nakayama T, Jayattisa R, Yamori Y and Bessho K. The relationship between oral health and risk factors of hypertension ; Comparison with Australian Aboriginnals, Sri-lankan and Japanese. ISH2012, Sydney 2012/10/1-4

浅井啓太、家森正志、山崎亨、後藤和久、高橋克、別所和久：根尖性歯周炎モデルにおけるビスフォスフォネート関連顎骨骨髄炎発症に関する検討、第57回　日本口腔外科学会総会、横浜、2012/10/19-21

塚本容子、高橋克、東郷由弥子、喜早ほのか、斎藤和幸、Boyen Haung、別所和久：CEBP/ß遺伝子欠損マウスを用いた過剰歯に関する形態学的解析、第57回　日本口腔外科学会総会、横浜、2012/10/19-21

福本幸恵、高橋克、別所和久：線維性異形成症部に生じた下顎骨骨折の治療経験、第57回　日本口腔外科学会総会、横浜、2012/10/19-21

東郷由弥子、高橋克、喜早ほのか、斉藤和幸、塚本容子、高藤洋之、藤村和磨、別所和久：非症候群性の多発性過剰歯を認めた２症例、第24回　日本口腔科学会近畿地方会、大津、2012/11/17

喜早ほのか・高橋克・磯部悠・斎藤和幸・東郷由弥子・池野正幸・小山典昭・別所和久：線維性異形成症のヒト疾患特異的iPS細胞樹立に向けた病変部におけるGNAS1遺伝子変異の検討、第24回　日本口腔科学会近畿地方会、大津、2012/11/17

Ｆ．知的財産権の出願・登録状況（予定を含む）

１．特許出願

なし

２．実用新案登録

なし

３．その他

なし

Ⅱ．研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
別所和久	これからはじめる周術期口腔機能管理マニュアル	別所和久	これからはじめる周術期口腔機能管理マニュアル	永末書店	京都	2013	1-111

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Yamazaki T, Yamori M, Asai K, Nakano-Araki I, Yamaguchi A, Takahashi K, Sekine A, Matsuda F, Kosugi S, Nakayama T, Bessho K	Mastication and risk for diabetes in a Japanese population: a cross-sectional study	PLoS ONE			In press
Yamamoto K, Sumi E, Yamazaki T, Asai K, Yamori M, Teramukai S, Bessho K, Yokode M, Fukushima M	Phenotypes of CCAAT/enhancer-binding protein beta deficiency: hyperdontia and elongated coronoid process	BMJ Open			In press
Huang B, Takahashi K, Sakata-Goto T, Kiso H, Togo Y, Saito K, Tsukamoto H, Sugai M, Akira S Shimizu A, Bessho K	Phenotypes of CCAAT/enhancer-binding protein beta deficiency: hyperdontia and elongated coronoid process	Oral Dis			In press
Hussain A, Bessho K, Takahashi K, Tabata Y	Magnesium calcium phosphate / β -tricalcium phosphate incorporation into gelatin scaffold, in vitro comparative study	J Tissue Eng Regen M			In press
Huang B, Takahashi K, Yamazaki T, Saito K, Yamori M, Asai K, Yoshikawa Y, Kamioka H, Yamashiro T, Bessho K	Assessing anteroposterior basal bone discrepancy with the Dental Aesthetic Index	Angle Orthod	83	527-532	2013
Nakao K, Okubo Y, Yasoda A, Koyama N, Osawa K, Isobe Y, Kondo E, Fujii T, Miura M, Nakao K, Bessho K	The Effects of C-type Natriuretic Peptide on Craniofacial Skeletogenesis	J Dent Res	92	58-64	2013
Koyama N, Miura M, Nakao K, Kondo E, Fujii T, Taura D, Kanamoto N, Sone M, Yasoda A, Arai H, Bessho K, Nakao K	Human Induced Pluripotent Stem Cells Differentiated into Chondrogenic Lineage Via Generation of Mesenchymal Progenitor Cells	Stem Cells Dev	22	102-113	2013

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Yamazaki T, Yamori M, Ishizaki T, Asai K, Goto K, Takahashi K, Nakayama T, Bessho K	Increased incidence of osteonecrosis of the jaw after tooth extraction in patients treated with bisphosphonates: A cohort study	Int J Oral Maxillofac Surg	41	1397-1403	2012
Sakata-Goto T, Takahashi K, Kiso H, Huang B, Tsukamoto H, Takemoto M, Hayashi T, Sugai M, Nakamura T, Yokota Y, Shimizu A, Slavkin H, Bessho K	Id2 controls chondrogenesis acting downstream of BMP signaling during maxillary morphogenesis	Bone	50	69-78	2012
Hussain A, Bessho K, Takahashi K, Tabata Y	Magnesium calcium phosphate as a novel component enhances mechanical/physical properties of gelatin scaffold and osteogenic differentiation of bone marrow mesechymal stem cells	Tissue Eng Part A	18	768-774	2012
Yamazaki T, Yamori M, Yamamoto K, Saito K, Asai K, Sumi E, Goto, K, Takahashi K, Nakayama T, Bessho K	Risk of osteomyelitis of jaw induced by oral bisphosphonates in patients taking medications for osteoporosis: a hospital-based cohort study in Japan	Bone	51	882-887	2012
Curtin CM, Cunniffe GM, Lyons FG, Bessho K, Dickson GR, Duffy GP, O'Brien FJ	Innovative collagen nano-hydroxyapatite scaffolds offer a highly efficient non-viral gene delivery platform for stem cell-mediated bone formation	Adv Mater	24	749-754	2012
Fujimura K, Bessho K	Rigid Fixation of Intraoral Vertico-Sagittal Ramus Osteotomy for Mandibular Prognathism	J Oral Maxillofac Surg	70	1170-1173	2012

Ⅲ. 研究成果の刊行物・別刷

Original Article

Assessing anteroposterior basal bone discrepancy with the Dental Aesthetic Index

Boyen Huang[a]; Katsu Takahashi[b]; Toru Yamazaki[c]; Kazuyuki Saito[c]; Masashi Yamori[d]; Keita Asai[c]; Yusuke Yoshikawa[e]; Hiroshi Kamioka[f]; Takashi Yamashiro[g]; Kazuhisa Bessho[h]

ABSTRACT

Objective: To investigate dental appearance and cephalometric features, using a sample of orthognathic and/or orthodontic patients. A special interest was to identify the relationship of the Dental Aesthetic Index (DAI) with anteroposterior basal bone discrepancy (APBBD) and cephalometric indicators.

Materials and Methods: A full sample of 159 patients in two Japanese hospitals was used. Each patient was assessed with a preorthodontic dental cast and cephalometric radiography.

Results: Malocclusion with APBBD was more prevalent among high DAI subjects ($P = .034$, OR = 1.04, 95% CI: 1.00–1.08), Class III malocclusion patients ($P = .048$, OR = 2.32, 95% CI: 1.01–5.34) and male patients ($P = .008$, OR = 2.96, 95% CI: 1.33–6.61). Participants scoring 88 points (the highest score in this sample) of the DAI had 16.84 times the risk of APBBD of those who scored 17 points (the lowest score in this sample). Patients with APBBD presented with a greater adjusted ANB angle ($t = -8.10$, $P < .001$) and a larger adjusted A-B/NF appraisal ($t = -9.65$, $P < .001$). The SNA angle ($P < .001$), the SNB angle ($P = .002$), the adjusted ANB angle ($P = .001$), and the adjusted A-B/NF appraisal ($P = .035$) were associated with DAI scores in cubic regression models.

Conclusion: This study has demonstrated a relationship between the DAI and APBBD. Feasibility of using the adjusted ANB angle and the adjusted A-B/NF appraisal to assess severity of APBBD has been confirmed. The DAI may provide a supportive method to evaluate orthognathic needs. Future investigations are indicated. (*Angle Orthod.* 2013;83:527–532.)

KEY WORDS: Dental Aesthetic Index; Jaw disharmony; ANB angle

INTRODUCTION

Various diagnostic methods for orthodontic and/or orthognathic needs, mainly involving cephalometric analysis[1–3] and three-dimensional analysis,[4,5] have been introduced from the last century. Among those, the ANB angle[1–3,6,7] and the A-B/NF appraisal (also known as the anteroposterior distance of the jaws)[7–9] are two of the popular criteria to distinguish between dental displacement with and without anteroposterior basal bone discrepancy (APBBD). The ANB angle is formed with the vertex at point N (nasion, the most anterior aspect of the frontonasal suture, located by visual inspection on the

[a] Associate Professor of Paediatric Dentistry, School of Medicine and Dentistry, James Cook University, Cairns, Australia.
[b] Senior Lecturer, Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan.
[c] PhD student, Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan.
[d] Assistant Professor, Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan.
[e] PhD student, Department of Orthodontics and Dentofacial Orthopedics, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan.
[f] Associate Professor, Department of Orthodontics and Dentofacial Orthopedics, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan.
[g] Professor, Department of Orthodontics and Dentofacial Orthopedics, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan.
[h] Professor, Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan.

Corresponding author: Dr Boyen Huang, Associate Professor, School of Medicine and Dentistry, James Cook University, PO Box 6811, Cairns QLD 4870, Australia
(e-mail: boyen.huang@jcu.edu.au)

Accepted: September 2012. Submitted: May 2012.
Published Online: October 18, 2012

tracing) and two sides respectively extending to A-point (the deepest point on the contour of the premaxilla) as well as B-point (the deepest point on the contour of the mandible).[6] Taking point S (sella, canter of the pituitary fossa located by visual inspection on the tracing) into account, the SNA and the SNB angles were also commonly used to assess positions of the upper and the lower jaws, respectively.[1–3,6,7] The difference between the SNA and the SNB angles is equivalent to the ANB angle.[1] Of further note, the A-B/NF appraisal represents the distance between the orthogonal projections from A-point and B-point onto the nasal floor plane.[7,8] This indicator is similar to the Wits appraisal.[1,7] Nevertheless, identifying the anatomic landmarks largely relies on the aid of cephalometric radiography which entails radiation exposure and usage of special equipment.[10] A similar concern has also been raised for application of three-dimensional analysis.[4] These compromised establishing the prevalence of APBBD from a large sample.

On the other hand, the Dental Aesthetic Index (DAI) has been suggested to assess dental appearance using objective measures of occlusal conditions since decades ago.[11] A higher DAI score indicated a severer impairment in the dental profile.[11] Without the need of using special equipment and the risk of radiation exposure, "the DAI can serve the dental epidemiologist as an index of severity and need for orthodontic treatment."[12] An adequate validity of this approach has been reported by population-based studies of malocclusion.[13,14] In addition, literature has demonstrated a better interexaminer consistency provided by the DAI than other approaches.[15] The DAI has also displayed a correlation with the Index of Orthodontic Treatment Need,[14,16] although some papers suggested a higher differentiability[17] and sensitivity[18] of the former over the latter. To the best of our knowledge, however, application of the DAI on assessing jaw deformity has involved cleft lip and palate only.[19,20] A relationship between the DAI and orthognathic needs has never been reported.

Therefore, this study aimed to carry out an investigation in dental appearance and cephalometric features, using a sample of orthognathic and/or orthodontic patients in Japan. A special interest was to identify the association of the DAI with cephalometric indicators such as the SNA angle, the SNB angle, the ANB angle as well as the A-B/NF appraisal, and occurrence of APBBD.

MATERIALS AND METHODS

This study was conjunctly conducted at two university hospitals in western Japan. Appropriate research ethics approval has been obtained from the Human Research Ethics Committees of Kyoto University and Okayama University, respectively. The size of the sample was calculated for satisfactory precision of a logistic regression model and a curve estimation model. Firstly, we estimated 100 subjects was the minimal number of subjects, using the reported proportion of APBBD at 40.3% in malocclusion,[21] for reporting four independent variables including DAI, age, sex, and occlusion type in a logistic regression model.[22] Secondly, to separately estimate the relationship between DAI and cephalometric indicators in a linear, a quadratic, and a cubic regression model, 120 subjects as the minimal number of subjects were estimated to report 95% confidence limits for the regression coefficients with an anticipated squared multiple correlation coefficient (R^2) at 0.25.[23] When calculating the sample size required, a cubic regression model was estimated as a linear regression model with three predictor variables. Since 100 and 120 subjects were respectively needed in a logistic and a cubic regression model, the minimal sample size required was decided to be 120 to meet criteria for both models. Formulae for estimations of the models have been reported earlier.[22,23] A possible negative response rate of 20% further raised the estimation to 150 subjects. All patient records dated from October 2009 to September 2011 (24 months) at the two hospitals were thereby screened and selected to contribute to a sufficient number of orthodontic and/or orthognathic cases. To avoid unnecessary radiation exposure, nonpatient individuals were not included in this study. An opt-out consent option has been provided to all patients approached and their legal guardians in cases younger than 18 years of age.[24] A pilot study has been carried out and the results confirmed that the protocol was feasible.

To be eligible for inclusion, a subject needed to have a preorthodontic dental cast and lateral cephalometric radiograph available in either of the two hospitals. Casts and radiographs were assessed by two examiners. Interexaminer reliability was measured with Cohen kappa coefficient and Pearson product moment correlation coefficient in categorical and continuous variables, respectively.[25] From the dental cast, data collected included missing teeth, crowding, spacing, diastema, largest anterior irregularity, overjet, open bite, and molar relation. Calculating with predetermined weights, the DAI score was generated from the data above.[11] In addition, occlusal type based on Angle's classification of malocclusion was recorded.[26] On the other hand, point N, point S, A-point, B-point, and the nasal floor plane were identified from the tracing of the lateral cephalometric radiograph. Thus, the ANB, the SNA as well as the SNB angles and the A-B/NF appraisal were generated and calculated. Using these indicators was due to their clinical relevance for assessing needs and outcomes of orthognathic surgery.[27–29] Based on predetermined clinical and radiographic criteria,[7] malocclusion and/or APBBD were diagnosed by two senior clinicians and then subjects were classified as the

cases (with APBBD) or the controls (without APBBD). Of further note, participants' age and sex were gathered from the patient records.

Data entry and statistical analysis were carried out with IBM SPSS Statistics (version 20, IBM Corporation, Somers, NY). Data analysis included descriptive statistics. The absolute value of the ANB angle has been applied to denote severity of APBBD.[30] When generating absolute values, the two indicators containing negative values (the ANB angle and the A-B/NF appraisal) were adjusted according to the following methods in order to preserve deviation distances from the mean of the general population. The means of the ANB angle and the A-B/NF appraisal in the general population are 3.7° and 6.1 mm, respectively.[9] Thus, 3.7 and 6.1 were separately subtracted from the original values of the ANB angle and the A-B/NF appraisal before calculation of the absolute values. Means of the adjusted ANB angle and the adjusted A-B/NF appraisal were compared between APBBD and non-APBBD subjects with an independent samples *t*-test.[25] A multivariate binary logistic regression method was used to examine the relationship between APBBD and age, sex, occlusal type as well as the DAI.[25] The reference indicators of categorical variables used in the logistic regression model were female and Class I occlusion for sex and occlusal type, separately. Furthermore, a curve estimation method including a linear, a quadratic and a cubic regression model was applied to assess the contribution of the DAI to cephalometric indicators such as the SNA angle, the SNB angle, the adjusted ANB angle, and the adjusted A-B/NF appraisal.[25] The level of two-sided significance was set at 5%.

RESULTS

One hundred ninety-eight orthodontic and/or orthognathic patients were identified from the records of the two hospitals. Among these, 15 patients opted not to participate, providing a response rate of 92.4%. Excluding 12 cases without a valid cephalometric radiograph, eight cases in lack of a preorthodontic dental cast and four cases with incomplete data of cephalometric measurements, a total of 159 subjects were included in this sample. The participants' age ranged from 10 to 54 years (21.6 ± 7.6). One hundred seventeen subjects (73.6%) were female. The patients' SNA, SNB, and ANB angles ranged from 68.1° to 98.8° (80.2 ± 4.1), from 64.9° to 92.9° (78.3 ± 4.8), and from −10.6° to 11.4° (1.9 ± 3.8), respectively. The distance of A-B/NF appraisal ranged between −13.0 and 27.5 mm (4.7 ± 6.7). Forty-nine cases were diagnosed with APBBD (30.8%). The number of subjects with Class I, Class II, and Class III malocclusion were 58 (36.5%), 40 (25.2%), and 61 (38.3%), respectively. In addition, DAI scores calculated according to outcomes of dental casts ranged from 17 to 88 (38.2 ± 10.5). Results of Cohen kappa coefficients and Pearson product moment correlation coefficients indicated a good interexaminer agreement. Kappa values ranged from 0.86 to 1.00 and Pearson coefficients ranged from 0.83 to 0.98. Patients with APBBD presented with a greater adjusted ANB angle ($t = -8.10$, $P < .001$) and a larger adjusted A-B/NF appraisal ($t = -9.65$, $P < .001$). Table 1 shows the frequency distribution of participants' age, sex, occlusal type, DAI scores, and occurrence with APBBD.

Those subjects who reported a higher DAI score ($P = .034$, OR = 1.04, 95% CI: 1.00–1.08), who were male ($P = .008$, OR = 2.96, 95% CI: 1.33–6.61), or who had Class III malocclusion ($P = .048$, OR = 2.32, 95% CI: 1.01–5.34), were more likely to sustain APBBD over nonskeletal related malocclusion (Table 1). Age was not associated with the occurrence of APBBD ($P = .172$). The result of the logistic regression model displayed a model chi-square at 30.57 ($df = 5$, $P < .001$), a correct percentage at 76.7% and a Hosmer-Lemeshow Goodness of fit at 7.01 ($df = 8$, $P = .535$). When assessing with a cubic regression model, the SNA angle ($R^2 = 0.110$, $P < .001$), the SNB angle ($R^2 = 0.090$, $P = .002$), the adjusted ANB angle ($R^2 = 0.098$, $P = .001$), and the adjusted A-B/NF appraisal ($R^2 = 0.054$, $P = .035$) were all associated with DAI scores. Table 2 showed regression relationships between the above indicators and DAI scores.

DISCUSSION

This study has suggested for the first time a relationship between high DAI scores and occurrence of APBBD. An odds ratio of the effect of DAI scores at 1.04 indicated that an increase of one DAI score raised 1.04 times the risk of APBBD. Thus, patients scoring 88 points (the highest score in this sample) of the DAI had 16.84 times the risk of APBBD of those who scored 17 points (the lowest score in this sample). The binary logistic regression model displayed a good model chi-square, an appropriate correct percentage, and an excellent Hosmer-Lemeshow goodness of fit. All of these indicated a properly explanatory power of the logistic regression model.[31] Hence, the DAI could assist to identify patients of APBBD when cephalometric radiography and three-dimensional analysis are not available. Even though, this study does not recommend using the DAI in full substitution for cephalometric radiography and three-dimensional analysis. Future investigation is indicated.

The results of the independent samples *t*-test confirmed the relationship between APBBD and the adjusted cephalometric indicators such as the adjusted ANB angle and the adjusted A-B/NF appraisal. As original values of the ANB angle and the A-B/NF appraisal have been used

Table 1. Frequency Distribution of Anteroposterior Basal Bone Discrepancy (APBBD) by DAI Score, Age, Sex, and Occlusal Type in the Sample of the Study (n = 159)

	With APBBD	Without APBBD	All	OR (95% CI)	*P* Value
Mean of DAI scores	41.0 ± 15.5	36.9 ± 6.9	38.2 ± 10.5	1.04 (1.00–1.08)	.034*
Mean of age	22.3 ± 7.3	21.2 ± 7.8	21.6 ± 7.6	1.04 (0.99–1.09)	.172
Sex					
Female	27 (23.1%)	90 (76.9%)	117 (73.6%)	1	
Male	22 (52.4%)	20 (47.6%)	42 (26.4%)	2.96 (1.33–6.61)	.008*
Occlusal type					
Class I	14 (24.1%)	44 (75.9%)	58 (36.5%)	1	
Class II	5 (12.5%)	35 (87.5%)	40 (25.2%)	0.39 (0.12–1.29)	.122
Class III	30 (49.2%)	31 (50.8%)	61 (38.3%)	2.32 (1.01–5.34)	.048*

* $P < .05$.

for diagnosis of APBBD, this demonstrated that the adjusted indicators are still able to differentiate malocclusion with and without APBBD. The outcomes agreed with a previous study which used the absolute value to assess the sagittal base relationship.[30] The ANB angle could be calculated by subtracting the SNB angle from the SNA angle[32] or by subtracting the SNA angle from the SNB angle.[28] Similarly, the A-B/NF appraisal could be measured from the projection of A-point to that of B-point, and vice versa.[7] Therefore, it would be appropriate to use the formulae with adjusted absolute values of the ANB angle and the A-B/NF appraisal to represent the magnitude of APBBD for a statistical purpose.

The low R^2 value found in the cubic regression models assessing the relationship between the DAI score and the cephalometric indicators suggested a poor prediction.[25] This could result from a small sample size in this study as the R^2 value used for estimating the minimal number of subjects has been decided as 0.25.[23] Nevertheless, the cubic regression relationships between the DAI score and the indicators including SNA angle, the SNB angle, the adjusted ANB angle, and the adjusted A-B/NF appraisal could confirm the association between DAI scores and APBBD as demonstrated by the logistic regression model earlier in this article.

Class III malocclusion was a predisposing factor of APBBD in this study. This could be due to a severer jaw disharmony of Class III malocclusion generally found in the Japanese population over other ethnic backgrounds.[33,34] Since patients' occlusal status regarding Angle's classification of malocclusion can be identified with a dental cast,[26] the enhancing effect of Class III malocclusion observed in this sample would not compromise future application of the model. On the other hand, the higher risk of APBBD among the male subjects found in this study agreed with a previous study.[35] Nevertheless, literature suggested distinct appearance motives between male and female orthognathic patients,[36] which influenced their decisions to seek orthodontic/orthognathic management.[37] Since subjects of this study were recruited from hospital patient pools, sampling bias resulting from

Table 2. Regression Relationships Between Cephalometric Indicators (y) and DAI Scores (x), $y = a_0 + a_1x + a_2x^2 + a_3x^3$

Equation	R^2 Value	*F* Value	*P* Value	a_0 Value	a_1 Value	a_2 Value	a_3 Value
y = SNA angle							
Linear	0.020	3.173	.077	82.306	−0.056		
Quadratic	0.023	1.855	.160	80.217	0.044	−0.001	
Cubic	0.110	6.383	<.001*	109.187	−2.006	0.043	−0.0003
y = SNB angle							
Linear	<0.001	0.014	.905	78.492	−0.004		
Quadratic	0.002	0.127	.881	80.115	−0.082	0.001	
Cubic	0.090	5.115	.002*	114.065	−2.483	0.053	−0.0003
y = Adjusted ANB angle							
Linear	0.057	9.495	.002*	0.488	0.067		
Quadratic	0.070	5.892	.003*	3.368	−0.070	0.001	
Cubic	0.098	5.631	.001*	14.941	−0.889	0.019	−0.0001
y = Adjusted A-B/NF appraisal							
Linear	0.006	0.991	.321	3.717	0.035		
Quadratic	0.007	0.544	.582	2.709	0.083	−0.001	
Cubic	0.054	2.944	.035*	26.370	−1.591	0.036	−0.0002

* $P < .05$.

sex-differentiated appearance motives might also contribute to the larger likelihood of APBBD seen in men. This was a research limitation of the study.

Without a need of radiation exposure and special equipment, the DAI may provide a supportive method to evaluate orthognathic needs of APBBD. This would be especially workable when conducting large-scale epidemiological studies and/or screening patients at rural/remote areas. Further investigations are indicated.

CONCLUSION

- This study has demonstrated a relationship between the DAI and APBBD. Feasibility of using the adjusted ANB angle and the adjusted A-B/NF appraisal to assess severity of APBBD has been confirmed. In addition, a higher risk of APBBD was reported in Class III malocclusion and/or male patients.

REFERENCES

1. Jacobson A. The "Wits" appraisal of jaw disharmony. *Am J Orthod.* 1975;67:125–138.
2. Steiner CC. Cephalometrics in clinical practice. *Angle Orthod.* 1959;29:8–29.
3. Downs WB. Variations in facial relationships: their significance in treatment and prognosis. *Am J Orthod.* 1948;34: 812–840.
4. Shimomatsu K, Nozoe E, Ishihata K, Okawachi T, Nakamura N. Three-dimensional analyses of facial soft tissue configuration of Japanese females with jaw deformity—a trial of polygonal view of facial soft tissue deformity in orthognathic patients. *J Craniomaxillofac Surg.* 2012;40: 559–567.
5. Kobayashi T, Ueda K, Honma K, Sasakura H, Hanada K, Nakajima T. Three-dimensional analysis of facial morphology before and after orthognathic surgery. *J Craniomaxillofac Surg.* 1990;18:68–73.
6. Hussels W, Nanda RS. Analysis of factors affecting angle ANB. *Am J Orthod.* 1984;85:411–423.
7. Wellens H. Improving the concordance between various anteroposterior cephalometric measurements using Procrustes analysis. *Eur J Orthod.* 2009;31:503–515.
8. Ferrazzini G. Critical evaluation of the ANB angle. *Am J Orthod.* 1976;69:620–626.
9. Liu CA, Chang CH. A supernumerary tooth in mandibular anterior region—case report. *Chin Dent J.* 2006;25:143–151.
10. Looe HK, Eenboom F, Chofor N, et al. Dose-area product measurements and determination of conversion coefficients for the estimation of effective dose in dental lateral cephalometric radiology. *Radiat Prot Dosimetry.* 2007;124: 181–186.
11. Cons N, Jenny J, Kohout F. *DAI—the Dental Aesthetic Index.* Iowa City, Iowa: College of Dentistry, University of Iowa; 1986.
12. Cons NC, Jenny J, Kohout FJ, Yupin S, Jotikastira D. Utility of the dental aesthetic index in industrialized and developing countries. *J Public Health Dent.* 1989;49:163–166.
13. Page LAF, Thomson WM, Quick AN. Changes in malocclusion over time in New Zealand adolescents. *Aust Orthod J.* 2011;27:169–175.
14. Cardoso CF, Drummond AF, Lages EMB, Pretti H, Ferreira EF, Abreu MHNG. The Dental Aesthetic Index and dental health component of the Index of Orthodontic Treatment Need as tools in epidemiological studies. *Int J Environ Res Public Health.* 2011;8:3277–3286.
15. Danyluk K, Lavelle C, Hassard T. Potential application of the dental aesthetic index to prioritize the orthodontic service needs in a publicly funded dental program. *Am J Orthod Dentofacial Orthop.* 1999;116:279–286.
16. Liu Z, McGrath C, Hägg U. Associations between orthodontic treatment need and oral health-related quality of life among young adults: does it depend on how you assess them? *Community Dent Oral Epidemiol.* 2011;39:137–144.
17. Jenny J, Cons NC. Comparing and contrasting two orthodontic indices, the Index of Orthodontic Treatment Need and the Dental Aesthetic Index. *Am J Orthod Dentofacial Orthop.* 1996;110:410–416.
18. Shelton AT, Hobson RS, Slater D. A preliminary evaluation of pre-treatment hypodontia patients using the Dental Aesthetic Index. How does it compare with other commonly used indices? *Eur J Orthod.* 2008;30:244–248.
19. Vettore MV, Sousa Campos AE. Malocclusion characteristics of patients with cleft lip and/or palate. *Eur J Orthod.* 2011;33:311–317.
20. Hongal SG, Ankola A, Nagesh L. Malocclusion and treatment needs of cleft lip and/or palate subjects aged between 12 and 18 years visiting KLE's Hospital, Belgaum, India. *Oral Health Prev Dent.* 2010;8:237–242.
21. Saleh F. Prevalence of malocclusion in a sample of Lebanese schoolchildren: an epidemiological study. *East Mediterr Health J.* 1999;5:337–343.
22. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol.* 1996;49: 1373–1379.
23. Knofczynski GT, Mundfrom D. Sample sizes when using multiple linear regression for prediction. *Educ Psychol Meas.* 2008;68:431–442.
24. Junghans C, Feder G, Hemingway H, Timmis A, Jones M. Recruiting patients to medical research: double blind randomised trial of "opt-in" versus "opt-out" strategies. *BMJ.* 2005; 331:940.
25. Altman D. *Practical Statistics for Medical Research.* London, UK: Chapman and Hall; 1991.
26. Angle EH. *Treatment of Malocclusion of the Teeth and Fractures of the Maxillae: Angle's System.* 6th ed. Philadelphia, Pa: S. S. White Dental Manufacturing Company; 1900.
27. Potts B, Fields HW, Shanker S, Vig KWL, Beck FM. Dental and skeletal outcomes for Class II surgical-orthodontic treatment: a comparison between novice and experienced clinicians. *Am J Orthod Dentofacial Orthop.* 2011;139: 305–315.
28. Tsang ST, McFadden LR, Wiltshire WA, Pershad N, Baker AB. Profile changes in orthodontic patients treated with mandibular advancement surgery. *Am J Orthod Dentofacial Orthop.* 2009; 135:66–72.
29. Michiels LY, Tourne LP. Nasion true vertical: a proposed method for testing the clinical validity of cephalometric measurements applied to a new cephalometric reference line. *Int J Adult Orthod Orthognath Surg.* 1990;5:43–52.
30. Sadat-Khonsari R, Dathe H, Knösel M, Hahn W, Kubein-Meesenburg D, Bauss O. Geometric influence of the sagittal and vertical apical base relationship on the ANB angle [in English, German]. *J Orofac Orthop.* 2009;70: 152–158.
31. Hosmer DW, Lemeshow S. *Applied Logistic Regression.* 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc; 2000:392.

32. Root TL. Level anchorage system treatment of Class III malocclusions. *Am J Orthod Dentofacial Orthop.* 1991;100: 562–571.
33. Bukhary M. Comparative cephalometric study of Class III malocclusion in Saudi and Japanese adult females. *J Oral Sci.* 2005;47:83–90.
34. Ishii N, Deguchi T, Hunt NP. Craniofacial differences between Japanese and British Caucasian females with a skeletal Class III malocclusion. *Eur J Orthod.* 2002;24:493–499.
35. Baccetti T, Reyes BC, McNamara JA. Gender differences in Class III malocclusion. *Angle Orthod.* 2005;75:510–520.
36. Øland J, Jensen J, Papadopoulos MA, Melsen B. Does skeletal facial profile influence preoperative motives and postoperative satisfaction? A prospective study of 66 surgical-orthodontic patients. *J Oral Maxillofac Surg.* 2011;69:2025–2032.
37. Williams AC, Shah H, Sandy JR, Travess HC. Patients' motivations for treatment and their experiences of orthodontic preparation for orthognathic surgery. *J Orthod.* 2005;32:191–202.