Three-dimensional evaluation of changes in condylar morphology and position in patients undergoing orthognathic surgery.

Irene Méndez-Manjón

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Three-dimensional evaluation of changes in condylar morphology and position in patients undergoing orthognathic surgery.

Irene Méndez-Manjón

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A mis padres
Margarita y José Manuel.

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Preliminary remarks

The present PhD Thesis is a compendium of four publications broadening the knowledge of the effects of orthognathic surgery on the temporomandibular joint.

Original published versions of the articles as they appear in their respective journals are included in appendix 1.

Complete results with figures and tables are available in the corresponding original article.

Each publication’s individual reference list can be consulted separately in journal PDF format in appendix 1.

List of papers

Paper I

Early changes in condylar position after mandibular advancement: a three-dimensional analysis.

Méndez-Manjón I, Guijarro-Martínez R, Valls-Ontañón A, Hernández-Alfaro F.

Int J Oral Maxillofac Surg. 2016 Jun;45(6):787-92. doi: 10.1016/j.ijom.2016.01.002.

Impact Factor: 1.56 (According to JCR)

Paper II

Cranial base superimposition of cone-beam computed tomography images: A voxel-based protocol validation.

Luiz Haas Jr O; Guijarro- Martínez R; Sousa-Gil A; **Méndez- Manjón I;** Valls-Ontañón A; de Oliveira B; Hernández-Alfaro F.

Under review in: J Craniomax Surg

Impact Factor: 1.59 (According to JCR)

Paper III:

Semi-automated method for three-dimensional condylar reconstruction: A Hounsfield-unit based protocol.

Méndez-Manjón I; Haas Jr OL; Guijarro-Martínez R; Belle de Oliveira R; Valls-Ontañón; Hernández-Alfaro F.

Under review in: Oral Surg Oral Med Oral Path Oral Radiol

Impact Factor: 1.26 (According to JCR)

Paper IV:

Minimally invasive intraoral condylectomy: proof of concept report.

Hernández-Alfaro F, **Méndez-Manjón I**, Valls-Ontañón A, Guijarro-Martínez R.

Int J Oral Maxillofac Surg. 2016 Sep;45(9):1108-14. doi: 10.1016/j.ijom.2016.04.001.

Impact Factor: 1.56 (According to JCR)

List of abbreviations

ANOVA:	Analysis of variance
ATM:	Articulación temporomandibular
BSSO:	Bilateral sagittal split osteotomy
CBCT:	Cone-beam computed tomography
CI:	Confidence interval
CT:	Computed tomography
DICOM:	Digital Imaging and Communications in Medicine
e.g:	In example
HU:	Hounsfield Units
ICC:	Intraclass correlation coefficient
FH:	Frankfort horizontal
FOV:	Field of view
Min:	Minimum
Max:	maximum
MRI:	Magnetic resonance imaging
N:	Sample size
NHP:	Natural head position
SARPE:	Surgically Assisted Rapid Palatal Expansion
TMD:	Temporomandibular disorder
TMJ:	Temporomandibular joint
VAS:	Visual analogue scale
2D:	Two-dimensional
3D:	Three-dimensional

1. SUMMARY (IN SPANISH)

1.1 INTRODUCCIÓN

En la actualidad existe un creciente interés por el estudio de la articulación temporomandibular en el contexto de la ortodoncia y la cirugía ortognática. Este hecho está fundamentalmente motivado por el conocimiento de los posibles cambios posicionales y morfológicos que ocurren en la articulación temporomandibular (ATM) tras la realización de cirugía ortognática. (1–13)

El estudio de la frecuencia y magnitud de estos cambios adquiere un papel esencial ya que ha sido demostrado que pueden promover inestabilidad postoperatoria y con ello recidiva (14–17), disfunción temporomandibular(18,19) y reabsorción condilar progresiva (8,20–27)

En este sentido, la realización de estudios prospectivos que nos permitan conocer qué magnitud de cambio es clínicamente relevante, en términos de sintomatología articular y estabilidad de tratamiento, es fundamental. A pesar de la continua preocupación por esclarecer los posibles efectos beneficiosos/perjudiciales que la cirugía ortognática produce sobre la ATM, es una hipótesis todavía sin resolver.

Mientras algunos autores describen un empeoramiento en la sintomatología articular en pacientes con historia de disfunción temporomandibular (28), las recientes revisiones sistemáticas concluyen que este tipo de pacientes refieren con mayor frecuencia una mejoría en la sintomatología tras la cirugía que un empeoramiento.(29–31)

Este hecho parece ser frecuentemente observado en relación al dolor. La mayoría de los estudios encuentran mejoría tanto en el dolor miofascial como en la artralgia tras la corrección de la discrepancia esquelética de base.(30–35)

Sin embargo, la importancia del estudio de la articulación temporomandibular en pacientes sometidos a cirugía ortognática no se circunscribe únicamente a la sintomatología. Los posibles cambios posicionales tras la cirugía ortognática pueden derivar no sólo en inestabilidad postoperatoria y sensibilidad muscular(6) sino, en reabsorción condilar progresiva y recidiva. (8,20,21,36), Algunos autores, han mostrado que si estos cambios posicionales son lo suficientemente pequeños, se produce un remodelado y adaptación fisiológica sin consecuencias patológicas para la articulación.(7,37,38)

Desafortunadamente, hoy en día no existe evidencia disponible que nos permita identificar cuál es el límite de variación posicional que derivará en remodelado fisiológico o, por el contrario, en una reabsorción condilar progresiva. Por ello, estudiar prospectivamente los cambios posicionales y morfológicos del cóndilo es fundamental para mejorar el pronóstico a largo plazo de nuestros pacientes.

Para responder a esta pregunta clínica de manera amplia es necesario abordarla desde el punto de vista de cambio posicional y volumétrico.

El primero, permitiría identificar qué tipo de cambio posicional y en qué magnitud podríamos esperar un perjuicio para la funcionalidad articular y la estabilidad del tratamiento. En relación a ello, el desplazamiento mediolateral del cóndilo ha sido descrito como el más perjudicial por su potencial de comprimir el disco articular.(14,20,21) Sin embargo, no conocemos la magnitud máxima de desplazamiento al que la articulación se puede adaptar.

En segundo lugar, el estudio de la morfología y volumen condilar permitirá definir el límite entre el remodelado fisiológico y la reabsorción condilar progresiva. En esta dirección, el estudio morfológico de la articulación permitirá además identificar posibles factores de riesgo preoperatorios como un volumen condilar pequeño (37), osteoartrosis o una inclinación posterior del cuello del cóndilo(8).

La inclusión del estudio morfológico en nuestro protocolo habitual de seguimiento en los pacientes de cirugía ortognática nos permitiría además identificar procesos de reabsorción de forma temprana y reducir sus consecuencias de recidiva tardía(23).

Del mismo modo, el análisis morfológico de la articulación previo al tratamiento permite al clínico la identificación de deformidades del desarrollo como hiperplasias condilares que deben ser tratadas concomitantemente. (39)

Desde la introducción de la tomografía computerizada de haz cónico (CBCT), disponemos de una herramienta que, junto a un software de planificación apropiado, supone un instrumento sin precedentes en el diagnóstico y plan de tratamiento en cirugía ortognática. (40,41) Este método diagnóstico nos permite además analizar tridimensionalmente la articulación, realizar mediciones lineales precisas y superponer la situación pre y postoperatoria.(7,42,43)

En la aplicación concreta del estudio de la articulación temporomandibular, el CBCT ha sido probado como una opción fiable con una precisión mayor en la identificación de lesiones óseas condilares que la radiografía panorámica o la tomografía computerizada multicorte.(44–47)

Los modelos trimensionales obtenidos a partir de la información del CBCT proporcionan información diagnóstica adicional de la morfología y localización exacta de la lesión ósea en el cóndilo. Basado en ello, varios autores han descrito su aplicación en el estudio de una gran variedad de patologías como osteoartritis(48,49), trauma(44), erosiones(46), osteofitos(45) y anomalías del desarrollo (39,44,50).

La posibilidad de superponer estas reconstrucciones tridimensionales nos permite no sólo estudiar el volumen sino también los cambios en la posición condilar tras la cirugía. Esta posibilidad elimina la necesidad de realizar mediciones lineales en los cortes 2D del CT, que tiene el inconveniente inherente de identificación de puntos de referencia(51) en una estructura no fija como es el cóndilo.

A pesar de los citados beneficios de la superposición de reconstrucciones tridimensionales, todavía existen algunas limitaciones en cuanto a su aplicación. La primera de ellas es la necesidad de establecer un protocolo de superposición que elimine al máximo posible el número de intervenciones que realiza el operador. Con ello, aumentará no sólo la rapidez del procedimiento sino también la eficacia y fiabilidad del mismo al reducir la posibilidad de introducción de errores en pasos acumulativos. En este sentido, hoy en día sabemos que los métodos semiautomáticos, basados en el registro por voxel, ofrecen superposiciones más precisas con respecto a los métodos clásicamente usados basados como el registro de puntos o superficies de referencia.(52–55)

La segunda limitación es la dificultad de segmentación inherente que representa el cóndilo debido a su menor densidad en comparación el resto de la mandíbula y a la cercana relación con el disco articular.(56)

Con el fin de responder a esta necesidad, todas estas limitaciones en relación al estudio radiológico del cóndilo han sido respondidas en la presente tesis doctoral. De este modo, su aplicación permitirá la continuidad a largo plazo de esta área de estudio.

1.2. RESUMEN DE OBJETIVOS Y PLAN DE TRABAJO

En respuesta a la necesidad de estudiar los cambios posicionales y morfológicos postoperatorios que se producen en la ATM tras cirugía ortognática se planteó la presente tesis con el siguiente plan de trabajo:

1. Como punto de partida, se quiso estudiar qué cambios se producen en la ATM cuando se realiza una cirugía de avance mandibular aislada. De este primer trabajo se pudo concluir que se producían cambios estadísticamente significativos de posición condilar tras el avance mandibular mediante osteotomía sagital de rama. Estos primeros resultados basados en observaciones a corto plazo nos confirmaron la necesidad de profundizar en esta área de la investigación. De este modo, se planteó estudiar si estos cambios producían repercusiones clínicamente relevantes a largo plazo.

   En el momento de la realización del trabajo de campo de este estudio en el año 2013 se aplicó una de las técnicas de superposición tridimensional más descritas en aquel momento basada en el registro por superficie. Se eligió para este propósito la base craneal como estructura anatómica estable.

Sin embargo, comenzaban a publicarse artículos que mostraban que aquellas técnicas de superposición que no estaban basadas en la determinación de un punto o una superficie de referencia, proporcionaban resultados más precisos.

2. Debido a la aplicabilidad que la superposición tridimensional tiene en el campo de la cirugía ortognática y concretamente en los cambios posicionales del cóndilo, se consideró importante realizar un estudio de validación de superposición tridimensional basada en el registro por voxel que fuera aplicable en nuestra línea de investigación. El objetivo de ello era definir un método de superposición preciso que fuera fácilmente aplicable en el estudio de los cambios de posición de la ATM y del resultado de la cirugía ortognática a largo plazo. Los buenos resultados extraídos de este protocolo en términos de precisión y rapidez de la superposición permitirán su aplicación futura no sólo en el estudio de la ATM a largo plazo, sino también en el estudio de cualquier estructura del área cráneo-facial.

   Gracias a ello, aseguramos que eliminamos al máximo el posible sesgo de los resultados derivado de la imprecisión de los protocolos de superposición.

3. Tras la realización del primer estudio observamos la extrema dificultad que supone la segmentación para la obtención de la

reconstrucción 3D mediante el delineado manual en cada uno de los cortes bidimensionales. Esta dificultad es más acusada en el caso del cóndilo articular respecto al resto de estructuras del área cráneo-facial debido fundamentalmente a dos características: la menor densidad respecto al resto de la mandíbula y la cercanía con el disco articular. En relación a este hecho, algunos autores han intentado describir protocolos automatizados de segmentación condilar que reduzcan la dependencia del operador y aumenten la fidelidad de la reconstrucción tridimensional. De forma similar al caso de la superposición tridimensional, se asumió que la realización de un estudio de validación de segmentación condilar basado en unidades Hounsfied (HU) podría dar respuesta a esta necesidad. De esta manera, se llevó a cabo el tercer estudio cuyo objetivo era determinar la precisión y la reproducibilidad del protocolo de segmentación semiautomática basado en HU que proponemos. Para definir la precisión y la reproducibilidad del protocolo, el estudio fue realizado por dos investigadores independientes cuyas mediciones fueron repetidas en dos tiempos diferentes (separados 4 semanas). Los resultados reflejaron una alta reproducibilidad tanto intra como interexaminador, confirmando la conveniencia del uso de este protocolo en el estudio de la morfología y posición condilar.

La presente validación aporta tanto a la comunidad científica como al clínico la posibilidad de obtener reconstrucciones tridimensionales del cóndilo muy fieles a la realidad anatómica, usando un sólo software y reduciendo considerablemente el tiempo de procesamiento.

Su utilidad no se limita exclusivamente al estudio de posición y volumen condilar sino que permite estudiar cualquier defecto estructural del cóndilo, anomalías del crecimiento tales como hiperplasias condilares o procesos degenerativos.

La obtención de una reconstrucción tridimensional fidedigna del cóndilo es fundamental no sólo a nivel científico en la realización de estudios morfológicos condilares sino a nivel clínico. Son múltiples los beneficios que tiene para el clínico tener en sus manos una herramienta de estudio fácil y sencilla como la descrita.

Con la posibilidad de la reconstrucción tridimensional pudimos diagnosticar y planificar tridimensionalmente 7 casos de hiperplasia condilar en pacientes que eran subsidiarios de recibir cirugía ortognática. Gracias a ello fue posible la definición de un nuevo abordaje quirúrgico mínimamente invasivo para las hiperplasias y tumoraciones benignas condilares por vía intraoral.

4. El objetivo del cuarto artículo fue definir un nuevo abordaje quirúrgico que, gracias a la planificación tridimensional, permitió la exéresis quirúrgica de hiperplasias y tumoraciones benignas condilares por vía intraoral en 7 pacientes consecutivos. Este tipo de abordaje supone una gran reducción tanto de la morbilidad para el paciente como del tiempo

quirúrgico. Es fundamental destacar que este tipo de abordaje quirúrgico no sería posible sin la aplicación de métodos de reconstrucción y planificación tridimensional.

5. Como continuación de esta vía de investigación y en aplicación del aprendizaje adquirido se aplicarán los protocolos presentados en el estudio de los cambios posicionales y morfológicos del cóndilo en pacientes de cirugía bimaxilar a largo plazo. Con ello pretendemos definir si estos cambios son estables en el tiempo y si producen efectos perjudiciales como la reabsorción condilar progresiva y recidiva de la deformidad dentofacial.

   El estudio del volumen condilar a largo plazo nos permitirá también conocer qué límite de remodelado vs reabsorción condilar se relaciona con una recidiva del tratamiento realizado.

   Como se deduce de estos objetivos, la presente tesis doctoral supone una unidad de conocimiento integrada compuesta por cuatro trabajos de valor científico independiente.

1.3. RESUMEN DE METODOLOGÍA, RESULTADOS Y CONCLUSIONES DE LAS PUBLICACIONES

1.3.1 Artículo primero:

El primer artículo se publicó en el International Journal of Oral and Maxillofacial Surgery[*]. Esta revista es la publicación oficial de la IAOMS (International Association of Oral and Maxillofacial Surgeons).

Con el objetivo de evaluar tridimensionalmente los cambios de posición que se producían en el cóndilo tras cirugía de avance mandibular, se realizó un análisis prospectivo de 22 pacientes consecutivos. Para ser incluidos en el estudio, los pacientes debían ser mayores de 18 años, presentar clase II esquelética subsidiaria de corrección quirúrgica, no presentar historia de disfunción temporomandibular y dar su conformidad por escrito.

Aquellos pacientes que requiriesen de alguna otra cirugía concomitante (Lefort I, SARPE, mentoplastia…), o presentasen asimetrías, anomalías congénitas o historia de trauma fueron excluidos.

Con el objetivo de conocer si alguna variable relacionada con el procedimiento quirúrgico y/o las características del paciente influían en el resultado, se recogieron las siguientes variables: Edad en el momento de la cirugía, sexo, cantidad de avance

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[*] *Referencia Completa: Méndez-Manjón I, Guijarro-Martínez R, Valls-Ontañón A, Hernández-Alfaro F. Early changes in condylar position after mandibular advancement: a three-dimensional analysis. Int J Oral Maxillofac Surg. 2016 Jun;45(6):787-92. doi: 10.1016/j.ijom.2016.01.002.*

mandibular (mm), y tipo de rotación del plano oclusal (horario/antihorario).

Se obtuvieron las reconstrucciones tridimensionales del cráneo a partir de los datos del CBCT preoperatorio y del postoperatorio a las dos semanas. Para ello se procedió a la segmentación automática que fue posteriormente optimizada mediante segmentación manual, eliminando así los posibles artefactos.

Posteriormente las dos reconstrucciones fueron superpuestas utilizando la base craneal como estructura anatómica de referencia, por considerar que se mantiene sin cambios tras la cirugía.

Se definieron 5 puntos por cóndilo (anterior, posterior, superior medial y lateral) que nos permitiesen evaluar el cambio en las tres dimensiones del espacio. Este cambio fue cuantificado utilizando un mapa de color. Para cada punto se registró el valor más alto de la escala de color asumiendo la "peor" situación posible.

Los principales resultados de este estudio pueden resumirse en los siguientes:

- Tras la cirugía de avance mandibular mediante osteotomía sagital de rama bilateral se producen cambios estadísticamente significativos en la posición condilar. ($P<0.05$)

- Se encontró una correlación positiva entre la cantidad de avance mandibular (>6 mm/ < 6 mm) y los cambios de posición del cóndilo. Esta correlación alcanzó la significancia estadística para el cóndilo izquierdo ($P<0.01$)
- Se observó que el área donde se produjo mayor cambio fue en el punto posterior, donde se observaron desplazamientos mayores a 1 mm en el cóndilo derecho en el 36 % de los pacientes y en el cóndilo izquierdo en el 32 % de los casos. El segundo punto de mayor desplazamiento fue el punto lateral (torque mediolateral). Para el resto de puntos sólo el 15-20 % de los pacientes presentaban cambios mayores de 1mm. Sin embargo, no se obtuvieron diferencias estadísticamente significativas ni entre los puntos ni entre los cóndilos contralaterales.

Con ello se concluyó que tras la cirugía de avance mandibular ocurre un desplazamiento estadísticamente significativo del cóndilo articular. Sin embargo, es necesaria la evaluación de estos cambios a largo plazo para evaluar la capacidad de adaptación que la articulación temporomandibular tiene a los citados cambios.

1.3.2 Artículo segundo

Con el fin de definir un protocolo de superposición preciso que superase los métodos clásicos operador-dependientes se realizó este segundo trabajo. El estudio está en revisión en el Journal of Cranio-Maxillofacial Surgery[**].

Con el objetivo de evaluar la precisión, reproducibilidad y eficiencia del protocolo propuesto, se seleccionaron 25 CBCT de pacientes que fueran portadores de implantes. El motivo es que el ápice del implante sería utilizado para medir la precisión de translación de la superposición. Estos 25 escáneres CBCT fueron duplicados y guardados de forma independiente. Con ello se crearon dos bases DICOM independientes: la original (Volumen Base) y el Duplicado (2º Volumen) que permitirían la superposición.

Se excluyeron aquellos pacientes que presentaban alguna condición médica que pudiera afectar la estructura ósea o tejido blando. Aquellos escáneres cuya calidad no permitiese la aplicación de los requerimientos del protocolo también fueron excluidos.

Los archivos DICOM “Original” y “Duplicado” fueron importados en el software Dolphin Imaging 3D®. Cada par de secuencias DICOM fueron grabados de forma independiente como dos estudios diferentes para cada paciente.

[**] Cranial base superimposition of cone-beam computed tomography images: A voxel-based protocol validation.Luiz Haas Jr O; Guijarro- Martínez R; Sousa-Gil A; **Méndez- Manjón I;** Valls-Ontañón A; de Oliveira B; Hernández-Alfaro F.
Under review in: J Craniomax Surg

La orientación craneal inicial de los 50 volúmenes (25 volúmenes iniciales más 25 volúmenes duplicados) fueron alterados aleatoriamente por el investigador 1. Este paso fue realizado porque ambos volúmenes (Original + Duplicado) tenían las mismas coordenadas inicialmente.

Posteriormente se aplicó el proceso de superposición propuesto.

Este proceso consta de tres fases:

1- Superposición inicial basada en 5 puntos anatómicos de referencia.
2- Optimización de la superposición mediante la técnica automática de "Registro por Voxel" usando la base craneal como superficie de referencia.
3- Exportación de las coordenadas finales de cada volumen (Pitch, Roll and Yaw / XYZ). Se asume que una superposición precisa requiere que ambos volúmenes (Original/duplicado) presenten las mismas coordenadas tras la superposición.

Precisión de Rotación: Fue calculada mediante la diferencia media absoluta (en grados) entre la Orientación del volumen Original y el duplicado tras la Superposición.

Precisión de Traslación: Se utilizaron puntos de referencia estandarizados en los ápices de los implantes para medir la precisión de traslación.

Esta precisión de traslación se calculó mediante la diferencia de medias ponderada entre los puntos de referencia del volumen original y el Duplicado.

Reproducibilidad: De los 25 pares de CBCT superpuestos, se eligieron los 5 con mejor precisión translacional y los 5 peores para el re-análisis por el operador 1 y el primer análisis por el operador 2.

Un mes después de los cálculos iniciales, se alteró nuevamente la orientación y se procedió a repetir el protocolo de superposición en los 10 CBCT seleccionados.
Estos resultados fueron analizados mediante el Coeficiente de Correlación Intraclase. (CCI)

Eficiencia: Para analizar la efiencia, se registró el tiempo necesario para realizar todo el protocolo propuesto.

Los principales resultados de este estudio pueden resumirse en los siguientes:

1- El tiempo medio necesario para completar el protocolo fue de 198 segundos.
2- El protocolo tuvo una precisión rotacional de 0,10 º-0,19º y una precisión translacional de 0,20-0,24 mm.
3- La reproducibilidad intraobservador e interobservador fue de 0.921-1 respectivamente.

Los resultados de este estudio sugieren que el protocolo descrito es preciso, reproducible y eficiente. La validación de este método permite su aplicación en el análisis de los resultados de tratamiento en cirugía ortognática eliminando los posibles sesgos derivados del proceso de superposición. El hecho de utilizar un sólo software lo convierte en un protocolo fácil de usar tanto en el ámbito académico como clínico.

1.3.3 Artículo Tercero

Una vez definimos un protocolo de superposición tridimensional preciso para el estudio de los cambios que se producen tras cirugía ortognática, era necesario definir un método de reconstrucción tridimensional del cóndilo articular que fuera fiable. Este artículo está en revisión en el Oral Surg Oral Med Oral Path Oral Radiol[***].

Como se ha comentado en la introducción, el cóndilo articular presenta una dificultad de segmentación superior a otras áreas anatómicas del área craneofacial. Los principales motivos son su baja densidad y su cercana relación con el disco articular. En este sentido, la comunidad científica parece estar de acuerdo en que aquellos protocolos más automatizados que reducen la

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[***] Semi-automated method for Three-Dimensional Condylar reconstruction: A Hounsfield-unit based protocol.
Méndez-Manjón I; Haas Jr OL; Guijarro-Martínez R; Belle de Oliveira R; Hernández-Alfaro F.
Under review in: Oral Surg Oral Med Oral Path Oral Radiol

intervención del operador parecen proporcionar una mayor precisión.

Con el objetivo de definir un protocolo de segmentación condilar semiautomático y más eficiente a los descritos hasta el momento se elaboró la presente validación.

Para ello, se utilizaron los estudios de CBCT preoperatorios de 10 pacientes de la base de datos del Instituto Maxilofacial (Centro Médico Teknon. Barcelona).

En primer lugar, se aplicó en todos los casos un protocolo estandarizado de orientación de la cabeza en Dolphin Imaging 3D®.

Posteriormente, tras definir el volumen de interés, se aplicó el intervalo Hounsfield propuesto para la reconstrucción automática de la superficie condilar (> 80 HU).

Una vez obtenida la reconstrucción automática, el contorno condilar fue optimizado manualmente mediante delineado tridimensional.

Todo el proceso fue repetido dos veces por dos investigadores independientes. El investigador 1 no tenía experiencia en el delineado manual del cóndilo mientras el investigador 2 contaba con amplia experiencia en el proceso.

Tras aplicar las unidades Hounsfield propuestas para el cóndilo, se registró el volumen craneal total como método de validación del mismo. Si tras aplicar el intervalo Hounsfield el volumen total del cráneo era el mismo, nos estaría indicando que el posible error del proceso ocurriría en el momento de la optimización manual y no en la segmentación automática basada en unidades Hounsfield.

Las mediciones del volumen condilar se tomaron como medida de conformidad entre ambos observadores, así como las unidades Hounsfield media total del cóndilo.

Adicionalmente, se estudió la posible relación entre las unidades Hounsfield medias obtenidas para el cóndilo con las unidades Hounsfield craneales.

Para analizar la eficiencia del proceso se registró el tiempo total empleado en todo el proceso.

Los principales resultados fueron los siguientes:

- La reproducibilidad del volumen condilar fue excelente para las mediciones intra-examinador (CV=3,65%, ICC=0,97) y buena para las mediciones inter-examinador (CV=3,65%, ICC= 0,89).
- El coeficiente de variación y el Coeficiente de Correlación Intra-clase fue de 0 y 1 respectivamente para el volumen craneal intra-observador. Esto quiere

decir, que el pequeño error obtenido ocurre durante el proceso de optimización manual y no en el momento de aplicar la segmentación automática por unidad Hounsfield.

- El tiempo medio de procesamiento fue 6,78 ± 3,42 min in T1 y 6,29 ± 2,69 min en T2 para el operador 1. Para el operador 2 el tiempo medio fue de 6,29± 2,69 min en T1 y 5,88 ± 2,33 min en T2.
- El coeficiente de correlación no lineal de Spearman (r= 0,0552) mostró una relación directa y de magnitud moderada entre las HU craneales y condilares.

A partir de estos resultados pudo concluirse que este método proporciona una herramienta precisa y reproducible de reconstrucción 3D del cóndilo mandibular a partir de la información del CBCT. La implementación de este protocolo permite el seguimiento de los cambios morfológicos y volumétricos del cóndilo y por lo tanto, permitirá identificar procesos de reabsorción condilar en estadios tempranos.

El hecho de utilizar el mismo software que se utiliza para la planificación de la cirugía ortognática y la marcada reducción de tiempo de procesamiento, lo convierte en un método altamente eficiente.

1.3.4 Artículo cuarto.

Finalmente, el cuarto artículo perteneciente a esta línea de investigación fue publicado en el International Journal of Oral en Maxillofacial Surgery[****].

Como se ha mencionado anteriormente, la posibilidad de la reconstrucción tridimensional ofrece una herramienta sin precedentes en el estudio de la morfología condilar. Entre los beneficios que podemos extraer de ello están la detección más precisa de procesos erosivos del cóndilo, así como anomalías del desarrollo tales como las hiperplasias condilares.

Gracias a la posibilidad de la obtención de un modelo tridimensional preciso fue posible definir un abordaje de tratamiento de las hiperplasias condilares por vía intraoral y sin necesidad de coronoidectomía. La definición de esta técnica fue el objeto de este último artículo.

Se presenta un análisis exhaustivo de la experiencia preliminar de los autores con siete casos consecutivos como prueba de la viabilidad, eficiencia y seguridad de esta técnica.

La viabilidad de esta nueva técnica de abordaje intraoral pasa obligatoriamente por la necesidad de una correcta planificación tridimensional que describimos a continuación:

[****] Referencia completa: Hernández-Alfaro F, Méndez-Manjón I, Valls-Ontañón A, Guijarro-Martínez R. Minimally invasive intraoral condylectomy: proof of concept report. Int J Oral Maxillofac Surg. 2016 Sep;45(9):1108-14. doi: 10.1016/j.ijom.2016.04.001.

- Escáner CBCT del paciente en posición de máxima apertura para evaluar la morfología condilar y la translación en máxima apertura interincisal.
- Obtención de la reconstrucción tridimensional a partir de los datos del CBCT.
- Planificación de la ostectomía:
    Condilectomía alta: Cóndilo de anatomía normal
    Condilectomía baja: Tumores benignos

La realización del CBCT con el paciente en máxima apertura permitió evaluar si el abordaje intraoral era posible y si la coronoides suponía una interferencia para el acceso quirúrgico.

Protocolo quirúrgico descrito:

Incisión de 2 cm a nivel del borde anterior de la rama ascendente de la mandíbula.

Disección subperióstica hacia el proceso coronoideo y posteriormente hacia la escotadura sigmoidea.

Se diseccionó el tendón temporal en el borde anterior, lateral y medial de la rama. La inserción temporal en la coronoides por encima del nivel de la escotadura se preservó completamente.

Se realizó la coronoidectomía cuando suponía una interferencia para el acceso quirúrgico a la hiperplasia condilar.

Para la ostectomía se utilizó un aditamento customizado extralargo piezoeléctrico que permitía alcanzar la lesión sin dañar el tejido blando adyacente. El fragmento condilar se estabilizó con un tornillo temporal y alambre para permitir la disección del tejido blando con facilidad.

El dolor postoperatorio fue evaluado mediante escala visual analógica (VAS).

Los resultados obtenidos fueron los siguientes:

- El cóndilo afectado fue el izquierdo en todos los pacientes excepto uno.
- De los 7 casos presentados, 2 fueron hiperplasias condilares tipo 1 y 5 fueron hiperplasias tipo 2 (osteocondroma) según la clasificación de Wolford.[*****]
- Los dos primeros pacientes fueron operados con la ayuda de endoscopio.
- La coronoidectomía sólo fue necesaria en 2 de los 7 casos.
- El tiempo quirúrgico medio fue de 16. 9 minutos.
- El dolor posteoperatorio medio fue de 1 en la escala VAS (rango 0-2)
- Se produjo una marcada mejoría en la asimetría de los pacientes que fueron posteriormente operados de cirugía ortognática siguiendo el protocolo de “cirugía tardía” (después de la preparación ortodóncica)

[*****] Wolford LM, Movahed R, Perez DE. A classification system for conditions causing condylar hyperplasia. J Oral Maxillofac Surg; 2014 Mar; 72(3):567–95.

- No hubo ninguna recurrencia durante el periodo de seguimiento (Media: 8.7 meses)

En conclusión, comparado con el acceso preauricular convencional, un acceso intraoral al cóndilo mandibular tiene el potencial de minimizar la incidencia de complicaciones neurovasculares y salivares, elimina las cicatrices faciales y la necesidad de abrir la cápsula articular.

Esto conlleva una reducción significativa de la morbilidad para el paciente. Tras la experiencia mostrada, mediante el uso de una planificación tridimensional precisa, esta técnica podría convertirse en el tratamiento de elección de la mayoría de las hiperplasias condilares.

2. INTRODUCTION

Introduction

2.1 IMPORTANCE OF THE STUDY OF THE TEMPOROMANDIBULAR JOINT IN THE CONTEXT OF ORTHOGNATHIC SURGERY.

The combined orthodontics-orthognathic surgery approach is a widely validated procedure in adult patients with severe skeletal dysplasia. Its aim is to obtain an adequate skeletal relation improving facial harmony and occlusion.

However, while orthognathic surgery will correct the underlying skeletal discrepancy, there is constant concern about its potential beneficial/deleterious effect on the temporomandibular joint (TMJ).

The study of the changes that occur in the TMJ has become one of the main concerns in the field of orthognathic surgery. This is due not only to the possible influence of surgery on joint symptomatology but also on the role that these changes could play in relapse after treatment. (8,14,57,58)

In this sense, although a good occlusion is achievable after the combined treatment of orthognathic surgery and orthodontics, controlling the position of the condyle during and after surgery is difficult. (13,59) There are many factors that can affect the position of the condyle after surgery, such as the rotational movement of the distal segment,(6,60) tensional balance of the muscles, method of fixation,(61,62) intermaxillary immobilization, amount and direction of movement(63,64) and surgeon experience. The importance of studying these changes derives from the fact that it has been demonstrated that they can cause postoperative instability, relapse,(14,15) temporomandibular disorder,(18,19) and progressive condylar resorption (PCR).(8,18,20–23,33,65–70)

Because of the great impact that these factors have on the result of treatment, it is essential to carry out prospective studies that enable us to discern the magnitude of change that is actually clinically relevant. It has been suggested that, if the magnitude of these changes is sufficiently small, adaptive remodeling can ensue without any damage to the TMJ. (7,37,38)

However, unfortunately, the adaptation limit of the TMJ without undesirable effects remains undefined.

The most feared undesirable effect is PCR.(8,20,21,36,69) This can be the cause of late relapse and, in some cases, need for retreatment. It is for this reason that the study of condylar changes after orthognathic surgery should not be limited only to the condyle-disc position or relation but also include morphological and volumetric changes. The monitoring of volumetric condylar changes in patients subjected to orthognathic surgery would allow early detection of possible processes of condylar resorption and allow us to anticipate consequent relapse.(71)

This monitoring will be particularly important in those cases with a greater risk of PCR – i.e. women aged 20-30 years, high mandibular angle, pre-existing TMJ dysfunction, large surgical mandibular advancement, counter-clockwise rotation,(17) and small preoperative condylar volume.(23)

Other important reasons why the study of the TMJ has acquired a leading role in the field of orthognathic surgery is that dentofacial deformities that require surgical treatment often coexist with temporomandibular disorders (TMD).(72–75)

A higher prevalence of TMD has been identified in patients with underlying malocclusion, especially in the context of mandibular hypoplasia and Angle class II malocclusion.(34,76)

Consequently, there is ongoing investigation to test the hypothesis that orthognathic surgery can give way to an improvement in patients with a history of TMD. While some authors describe a worsening in joint symptomatology in patients with a history of TMD,(28) recent systematic reviews conclude that this type of patient more often refers postoperative improvement in symptomatology rather than worsening. (29–32) This fact seems to be a common finding in relation to pain. Most studies find improvement both in myofascial pain and arthralgia after correction of the underlying skeletal discrepancy. (30–35,59)

Some authors also found better mandibular dynamics and condylar disc-relation after treatment.(77,78)

In this line, Dervis et al.(79) prospectively studied the influence of orthognathic surgery on patients with TMD compared to a control group. After two years of exhaustive monitoring, they concluded that surgical correction of dentofacial deformities has a beneficial effect on both signs and symptoms relating to TMJ pain and dysfunction. They also observed that preoperatively symptomatic Class I and Class III patients improved more than Class II patients after treatment. This greater susceptibility to TMD and condylar resorption in patients with mandibular retrognathia has been corroborated by other studies.(76,80)

It must be emphasized that the absence of conclusive results in reference to the relationship between TMD and orthognathic surgery derives from the lack of randomized, prospective, and multi-center studies with a long period of follow-up. In addition, the great heterogeneity that exists in the scientific literature regarding the diagnosis, classification, and treatment of TMD contributes as well.

Most clinical studies focus on the monitoring of a specific subgroup of patients, which makes it difficult to obtain a common conclusion. In this sense, it seems that if we can expect a detrimental effect in the TMJ after orthognathic surgery, it is in the subgroup of patients with high-angle, class II occlusion, undergoing counter-clockwise rotation or large mandibular advancement procedures.(81) Thus, the study of the TMJ in the context of orthognathic surgery requires the standardization of diagnostic imaging, which allows the study of the positional, morphological, and volumetric changes of the condyle in a reproducible way. Concomitantly, there is a need for consensus on the diagnostic criteria of TMD and their subsequent application in prospective, randomized, multicentric studies in order to allow definitive conclusions to be drawn.

2.2 CONVENIENCE OF CBCT FOR TMJ ANALYSIS IN ORTHOGNATHIC SURGERY: Advantages and limitations of 3D virtual models and superimposition techniques.

The introduction of cone beam computed tomography (CBCT) imaging has provided an accurate tool to evaluate condylar position.(7,37,42) Lateral X-ray films have important limitations in terms of precision and the assessment of mediolateral movements. Conversely, CBCT enables a comprehensive 3D evaluation of the TMJ, provides highly accurate linear measurements,(37) and permits the superimposition of pre- and postoperative situations.(82) The reconstructed 3D models also allow for a better assessment of condylar position within the glenoid fossa.(44,83–85)

The possibility of superimposing 3D virtual models allows the quantification of roll, jaw, and pitch movements as well as postoperative condylar volumetric changes, which could not have been performed with 2D radiographs.(71,86–88)

CBCT has proven to be a reliable option for studying condylar bone lesions, with superior reliability and greater accuracy than panoramic radiography and multislice CT.(44–47,89) 3D models from CBCT data provide additional diagnostic information on morphology and exact location of the bony lesion in the condyle.

In this context, several authors described its application in the study of an extensive variety of TMD such as osteoarthritis,(48,49,90) trauma,(44) erosions,(46,91,92) osteophytes,(45) and developmental abnormalities.(39,44)

The possibility of using the same CBCT to plan our surgeries and to follow the changes in condylar morphology is a great possibility that reduces the number of imaging tests required in each patient.

Despite the cited benefits of the superimposition of 3D reconstructions, there are still some limitations in terms of their application. The first limitation is the need to establish a protocol of superimposition that minimizes the number of interventions carried out by the operator. With this, not only will the speed of the procedure increase but also its efficiency. In this sense, today we know that semiautomatic methods, based on voxel registration, offer superimpositions that are more precise in relation to the methods classically used that are based on the registration of points or reference surfaces.(52–54) The second limitation is the inherent difficulty of condylar segmentation due to its lesser density in comparison with the rest of the jaw and to its close relationship to the joint disc. (56) These limitations have been addressed in the present thesis. The application of the proposed methodology will allow long-term continuity of this area of study.

3. AIMS

3.1 GENERAL AIM

To apply CBCT to evaluate the changes in condylar position and morphology in patients undergoing orthognathic surgery.

3.2 SECONDARY AIMS

Paper I

To perform a 3D assessment of positional changes of the mandibular condyle after bilateral sagittal split osteotomy (BSSO).

Paper II

To evaluate the accuracy of voxel-based superimposition of CBCT datasets with a protocol developed for an orthognathic surgery virtual planning software. The secondary objectives were to analyze the reproducibility and efficiency of this protocol.

Paper III

To validate a semi-automated segmentation method for 3D reconstruction of the mandibular condyle from CBCT data and its use for the volumetric analysis of the condyle.

Paper IV

To describe a minimally invasive surgical protocol for intraoral condylectomy based on precise 3D treatment planning.

4. RESULTS OF EACH PAPER

In the following section, results of each paper are presented. Complete results with figures and tables can be consulted in each complete PDF version.

Paper I

Early changes in condylar position after mandibular advancement: a three-dimensional analysis.
Méndez-Manjón I, Guijarro-Martínez R, Valls-Ontañón A, Hernández-Alfaro F.
Int J Oral Maxillofac Surg. 2016 Jun;45(6):787-92. doi: 10.1016/j.ijom.2016.01.002.

- The overall displacement of the condyles after mandibular advancement was statistically significant (P<0.05)
- The mean mandibular advancement was 6.7 +- 1.6 mm.
- A clockwise rotation was performed in 59.1 % of the patients (n =13) and a counter-clockwise rotation in 40.9 % (n=9)
- The greatest positional changes occurred in the posterior point, where displacement was greater than 1 mm in the right condyle for 36 % of patients an in the left condyle for 32 % of patients. The second greatest displacement corresponded to the lateral point. For the remaining studied point, only 15-20 % of the patients showed displacement beyond 1 mm. Nevertheless, this difference was not statistically significant between measured points or between contralateral condyles.
- Demographic variables (age and sex) showed no statistically significant influence on changes in condylar position.

- Occlusal plane rotation and the amount of mandibular advancement did show a statistically significant correlation in condylar position.
- When a clockwise rotation was performed, condylar displacement was greater in the right condyle (P<0.05). Conversely, when a counter-clockwise rotation was done, the left condyle showed greater displacement (P<0.05).
- Postoperatively, all patients were symptom-free in terms of TMJ pathology and no pathological changes were visible on the CBCT scan.

Paper II

Cranial base superimposition of cone-beam computed tomography images: A voxel-based protocol validation.
Luiz Haas Jr O; Guijarro- Martínez R; Sousa-Gil A; **Méndez- Manjón I;** Valls-Ontañón A; de Oliveira B; Hernández-Alfaro F.
Under review in: J Craniomax Surg

- **Rotational and translational accuracy:** The protocol described in this study had a mean rotational accuracy of 0.12° (SD=0.06; 0.03– 0.33) along the P axis, 0.10° (SD=0.06; 0.01–0.23) along the R axis, and 0.19° (SD=0.16; 0.00–0.58) along the Y' axis. Translational accuracy was 0.24 mm (SD=0.11; 0.06–0.48) in the transverse, 0.23 mm (SD=0.10; 0.05–0.51) in the vertical, and 0.20 mm (SD=0.10; 0.04–0.46) in the sagittal axis.
- **Reproducibility:** The tested protocol exhibited excellent reproducibility, with an ICC of 1 for all rotational and translational parameters on intra-observer analysis and an

ICC range of 0.921–1 for inter-observer analysis. P-values were statistically significant for all correlation coefficients.

- **Efficiency:** The mean time spent on the three steps of the superimposition protocol was 198 seconds (range 119–329 seconds).
- The validation of this method enables unbiased analysis of surgical outcomes based on a single, user-friendly software product that is widely available in academic and clinical settings.

Paper III

Semi-automated method for Three-Dimensional Condylar reconstruction: A Hounsfield-unit based protocol.
Méndez-Manjón I; Haas Jr OL; Guijarro-Martínez R; Belle de Oliveira R; Hernández-Alfaro F.
Under review in: Oral Surg Oral Med Oral Path Oral Radiol

- The mean time needed for the segmentation process for Operator 1 was 6.78 ± 3.42 minutes at T1 and 6.29 ± 2.69 minutes at T2. The mean time for Operator 2 was 6.29± 2.69 minutes at T1 and 5.88 ± 2.33 minutes at T2.
- The overall mean condylar volume was 1481.95 mm^3 for observer 1 and 1889.38 mm^3 for observer 2. The overall mean Hounsfield units of the condyle was 341.79 for observer 1 and 329.88 for observer 2.
- The reproducibility of the condylar volume measurements was excellent for intra-examiner parameters (CV= 3.65%,

ICC= 0.97) and good for inter-examiner parameters (CV= 7.15%, ICC= 0.89).

- The reproducibility of the mean Hounsfield Units was excellent for both intraexaminer (CV=2.54%, ICC=0.99) and inter-examiner parameters (CV=4.98%; ICC=0.96)
- The Coefficient of Variation and the ICC was 0 and 1 respectively for the cranial volume in the intra-observer measurements. This means that the error in condylar segmentation occurs during the manual refinement process and not at the time of applying the Hounsfield interval.

Paper IV

Minimally invasive intraoral condylectomy: proof of concept report.
Hernández-Alfaro F, **Méndez-Manjón I**, Valls-Ontañón A, Guijarro-Martínez R.
Int J Oral Maxillofac Surg. 2016 Sep;45(9):1108-14. doi: 10.1016/j.ijom.2016.04.001.

- A proof-of-concept evaluation was performed of a novel minimally invasive technique for condylectomy performed through an intraoral approach. Based on precise 3D virtual planning to define intraoperative references, this technique provides an excellent access for total or partial condylectomy through a limited intraoral incision.
- Active condylar growth was detected in all cases. The affected joint was the left side in all patients except one. The underlying cause of the abnormal condylar growth was Wolford[*****] CH type 1 in two cases and CH type 2 in the other five.
- The average duration of surgery from incision to last suture was 16.9 min (range 14–25 min).
- The average postsurgical pain on the VAS was 1 (range 0–2).
- Orthodontic treatment to prepare for subsequent orthognathic surgery was initiated between 1 and 2 weeks after surgery.

[*****] Wolford LM, Movahed R, Perez DE. A classification system for conditions causing condylar hyperplasia. J Oral Maxillofac Surg; 2014 Mar; 72(3):567–95.

- The timing of surgery was scheduled according to a “surgery late” protocol (conventional full orthodontic preparation) in three cases and “surgery early” in one.
- No recurrence of facial asymmetry was observed over an average follow-up of 8.7 months (range 2–16 months).

5. GENERAL DISCUSSION

The potential connection between orthognathic surgery and secondary TMJ changes continues to be a topic of debate for maxillofacial surgeons and orthodontists. This concern is based on two main facts:

- The difficulty in controlling condylar position during and after surgery(13,59)
- The high prevalence of TMD in patients who need to undergo orthognathic surgery. (73,75,93,94)

For this reason, the starting point of the present PhD thesis was to investigate whether orthognathic surgery produced significant changes in condylar position. At the time of carrying out the thesis project, various study groups had not yet found any statistically significant changes in condylar position after orthognathic surgery.(42,67,95) However, it must be pointed out that these evaluations were often based on two-dimensional imaging methods such as lateral cephalograms,(95) where condylar changes cannot be assessed three-dimensionally. The study of changes in condylar position in 3D is crucial given the fact that mediolateral movement or torque has been described as one of the most detrimental for the TMJ.(21,96) The evaluation of this type of movement in lateral radiographs is not possible; hence, several researchers have advocated for the need to apply CBCT technology and 3D superimposition techniques in future investigations.(7,37,42,68,82) In this context, our first study was designed applying the methodology previously recommended in the literature.

As a starting point, a sample of patients without underlying TMJ pathology and who would undergo mandibular advancement surgery was chosen. To have a comprehensive 3D evaluation of the TMJ, CBCT technology and 3D superimposition of the virtual models was employed.

The results of this first study (Paper I) suggest that statistically significant displacement of the condyles occurs after BSSO for mandibular advancement ($P<0.01$).(97) These first results were in agreement with those observed in other studies that applied CBCT to the study of the TMJ.(6,82,98)

The analysis of the changes of condylar position through 3D superimposition allowed us to evaluate not only the magnitude of the change but also the areas of greatest displacement. In this way, it was observed that the posterior and lateral aspects of the condyle tended to vary more than the other points studied. This finding were in agreement with the results presented by Carvalho et al. Using 3D superimposition, these authors also found that the posterior condylar region was the area that exhibited the greatest changes with remodeling at the one-year follow-up.(82)

It is important to highlight that, even though we found a statistically significant displacement of the condyle after mandibular advancement, the overall changes were below 1 mm in 75 % of patients. This finding is also in agreement with the results presented by Carvalho et al., who reported that the mean change in condylar position was below 1 mm, and only four patients showed changes beyond 2 mm.(82) Interestingly, although their sample was clinically symmetrical, displacement was usually unilateral. These results differ from those of the present study, in which positive correlation of both condyles could be established.

In addition to the evaluation of the occurrence of condylar changes after mandibular advancement, a second aim of this first study was to assess the potential influence of several factors in condylar position. Patient-related variables such as age and sex did not show any statistically significant influence on postsurgical changes. However, the amount of mandibular advancement and the type of rotation did show a relevant association. Regarding the amount of mandibular advancement, this was found to be positively correlated with the amount of condylar displacement, reaching significance for the left side ($P<0.01$). This finding was also previously demonstrated in the study by Harris et al., who found that large mandibular advancements were correlated with condylar angulation and supero-inferior changes of condylar position.(61) Secondly, in the present study it was observed that the type of rotation influenced the pattern of postoperative change. When a clockwise rotation was performed, greater changes occurred in the right condyle; by contrast, when a counter-clockwise rotation was performed, the greatest change happened in the left condyle. There appears to be no other reference to such a preliminary finding in the scientific literature. Although this requires further investigation, the surgeon’s position during surgery could play a role (in the setting of the study’s institution, the operator stands on the right of the surgical table).

Although the results of this first study suggest that we can expect significant changes in condylar position after mandibular advancement surgery, these results apply to the postoperative situation and therefore require long-term corroboration. It is fundamental to investigate the capacity of the TMJ to adapt to these positional changes without leading to joint damage such as postoperative instability, relapse,(14,15) TMD,(18,19) and Progressive Condylar Resorption (PCR).(8,20–23)

Once the need for long-term evaluation of positional and morphological changes of the condyle during orthognathic surgery had been confirmed, the methodological limitations we had to deal with at that time needed to be addressed specifically.

METHODOLOGICAL LIMITATIONS IN THE STUDY OF THE TMJ IN ORTHOGNATHIC SURGERY

At the time this PhD thesis was written, long-term evaluation of the TMJ in patients undergoing orthognathic surgery was hindered by the following limitations (which each gave way to a respective investigation and subsequent paper):

- The imprecision of superimposition protocols based on the identification of reference points or surfaces (Paper II).

- The difficulty of 3D reconstruction of the condyle through the techniques of manual outlining (Paper III).

In other words, there was a need to develop semi-automated protocols that minimize the number of interventions by the observer and thereby increase precision, reproducibility, and efficiency.

The aim of papers II and III was, therefore, to provide a response to these needs.

In Paper I we applied the most widespread methods of 3D superimposition: landmark-based (99,100) and surface-based registration.(53,55) However, these methods are influenced, respectively, by some quality limitation inherent to their dependence on identification and selection of anatomic landmarks(51,99,100), and to the precision of virtual model surface segmentation.(55,101) In response to this, some authors have stated that superimpositions based on voxel registration provide the best results in terms of precision because they are observer-independent.(52–54,102,103)

In this context, the objective of the Paper II was to find the accuracy of voxel-based superimposition of CBCT datasets with a protocol developed specifically for an orthognathic surgery virtual planning software that is widely available in academic and clinical settings (Dolphin Imaging 3D® version 11.8). The secondary objectives were to analyze the reproducibility and efficiency of this protocol. Results showed that the proposed protocol had a rotational accuracy of 0.10°–019° and a translational accuracy of 0.20–0.24mm. These results are better than those previously reported, in which accuracy was around 0.3 mm,(52) 0.4 mm,(104) and 0.25-0.5 mm(54), and precision was lower, with standard deviations of 0.12 mm(52) and 0.14 mm(104). Furthermore, linear (translational) measurements obtained at the maxilla and mandible provided additional evidence of this accuracy in regions distant from the cranial base-center of rotation. This means that a single software product can be used for image superimposition and analysis of surgical results in other anatomic regions such as the mandible. It is important to note that the excellent quality of this protocol was also reproducible (intra-observer ICC=100% and inter-observer ICC>92%). Reproducibility is due to the fact that superimposition was performed on the cranial base, a fixed structure that completes growth during childhood (105) and has a large voxel area.(52,54,55) Additionally, to date, this protocol showed the shortest superimposition time reported in the literature that has demonstrated its efficiency.

The validation of this method enables unbiased analysis of surgical outcomes based on a single, user-friendly software that is widely available in academic and clinical settings. Its application in future studies of condylar position changes will allow investigatiors to overcome the limitations which we found in our first study. On the one hand, it will ensure great precision in the superimposition process and, on the other, it will allow us to define the change in condylar position for the axes Pitch, Roll, and Yaw (P, R, Y). This possibility offers us a wider and more precise analysis of positional change.

In our Paper I (97), the color map offered by the software (Simplant O & O, Materialise Dental SL) needed to be used for change analysis after superimposition. The main limitation of this is that the system cannot distinguish between the value 0 and 0.5 mm in the green range of the color map; consequently, it assumes that the value 0 (in other words, no positional change) is impossible. This means that the maximum possible error (the highest value of the numerical range and thus the greatest changes in condylar position) was considered systematically.

Through the application of this new superimposition system we were able to eliminate the need to analyze changes at a point or specific area through color mapping. Rather, positional change analysis is possible through the resulting vector (P,R,Y) of the superimposition of the preoperative, postoperative, and follow-up 3D models.

The next methodological objective we had to achieve to ensure a precise long-term study not only of condylar position but also of morphology, was the obtention of a precise method for 3D reconstruction of the condyle. At the time this thesis protocol was designed, most proposed protocols in the literature on 3D rendering of condylar surface were based on the manual outlining of the condylar contour in 2D-cross sections of the CBCT scan.(56,88,106) However, this technique is highly observer-dependent, usually requires the use of different software to process the data, and is very time-consuming. In addition, the condylar region has inherent difficulties in manual outlining in comparison to other areas of the skull due to its low density and close relation to the discus articularis.(56) In fact, it has been shown that the condyle and the medial side of the mandible are the areas most susceptible to observer experience(56).

Thus, in the same way as it occurred with the system of superimposition, we needed to develop a precise and reproducible protocol that was observer-independent. Accordingly, the aim of the Paper III was to define and validate a fast, semi-automated method for 3D condylar rendering using the same software we used for superimposition (Dolphin Imaging 3D version 11.8 software). Should we be successful, we would be able to complete the whole process of the evaluation of condylar position and morphology using a single software, thereby providing the scientific community with a highly efficient and easy to use protocol.

Semi-automated 3D reconstruction is based on the application of a Hounsfield interval specifically defined for the condyle and its later manual optimization. This interval was defined on the basis of a previous study that showed that morphological evaluation of the condyle using 3D reconstruction from CBCT was most accurate when performed at density levels below those recommended for osseous examination.(107)

An excellent intra-examiner (CV= 3.65%, ICC= 0.97) and good inter-examiner reproducibility (CV= 7.15%, ICC= 0.89) was found for condylar volume measurements with an average time below 6 minutes of image processing. This implies a reduction to half the time of image processing compared to the fastest segmentation protocol published to date.(86)

In our study, the total skull volume when applying the Hounsfield unit range for the condyle was used to test the method. The CV and the ICC were 0 and 1 respectively for the cranial volume in intra-observer measurements. This means that the error in condylar segmentation occurs during the manual refinement process and not at the time of applying the Hounsfield unit range selected in the software. These results corroborate the fact that the more observer-dependent a process is, the greater the error accumulation that we can expect. Therefore, methods that reduce or eliminate the number of manual interactions(71,86) seem not only to reduce processing time but also increase the reliability of the method.

In conclusion, the present protocol is an accurate and reproducible tool for clinicians interested in condylar volume, who will be able to identify PCR in its early stages. This, together with the application of the described superimposition protocol, will allow the comprehensive evaluation of positional and morphological changes of the condyle after orthognathic surgery using one single software.

The possibility of obtaining precise 3D reconstructions of the condyle offers multiple applications in TMJ diagnosis. Its functions are not limited to the study of the resorption processes that affect the condyle, since it has been indicated as the imaging modality of choice for evaluating the osseous components of the TMJ,(44) with greater diagnostic accuracy than panoramic radiography and spiral tomography.(44–47,89)

Several authors described the application of CBCT in the study of an extensive variety of TMD such as osteoarthritis,(48,49) trauma,(44) erosions,(46) osteophytes,(45) and developmental abnormalities. The fourth article(39) comprised in the present PhD thesis is an example of this. Thanks to 3D reconstruction, the precise definition of the morphology and localization of condylar hyperplasia in patients with significant facial asymmetry was possible. The 3D virtual model of the patient in maximum mouth opening enabled the determination of whether the amount of condylar translation in maximum opening would be clearly sufficient to enable surgical resection through an intraoral approach. In addition, the anatomical relationship to the coronoid process was evaluated to determine if it would cause an interference with surgical access.

Based on this precise 3D planning, a novel technique for minimally invasive intraoral condylectomy could be described. This novel, minimally invasive concept, in comparison to the conventional pre-auricular approach, minimizes the incidence of neurovascular and salivary complications, avoids the creation of facial scars, and preserves the integrity of the articular capsule, thereby reducing the risk of fibro-osseous TMJ ankyloses.(108–110) Additional benefits of proposed 3D virtual planning for intraoral condylectomy include the determination of the prospective level and orientation of the ostectomy and the potential need of concomitant coronoidectomy. In fact, as corroborated with CBCT imaging in maximum mouth opening, full condylar translation provides an adequate obstacle-free route to the condyle without interference to the coronoid in most cases.

In conclusion, the results of this proof-of-concept evaluation suggest that this technique allows reliable and accurate condylar resection with minimal morbidity to the patient. This alternative approach could become the treatment of choice for most condylar hyperplastic conditions.

After completing this PhD thesis, it seems clear that reconstruction and 3D superimposition should be established as the method of choice in the study of the bony components of TMJ. This will allow complete analysis of the TMJ in the context of orthognathic surgery and morphological anomalies, whether these be congenital or the consequence of applied treatment (i.e. progressive condylar resorption)

The main methodological limitations that this study of the condylar joint confronted at the start of this PhD thesis have been resolved, allowing this line of research to continue. The effort to define protocols that are easy to implement and employ a single software also enables them to be applied by clinicians in their daily practice and not only in the context of research. In this way, we offer a great tool for the clinic both in the analysis of treatment outcomes of orthognathic surgery and in this surgery’s potential long-term effects on the TMJ.

6 .CONCLUSIONS

- Statistically significant changes of condylar position occur after mandibular advancement. This displacement shows a positive correlation with the magnitude of advancement, and the region of greatest changes tends to be located in the posterior aspect of the condyle (Paper I)
- The proposed voxel-based protocol for three-dimensional superimposition of cone-beam computed tomography images is accurate, precise, reproducible and efficient. The validation of this method will enable unbiased analysis of surgical outcomes. (Paper II)
- The validated semi-automated method for 3D reconstruction of the mandibular condyle is accurate and reproducible. The implementation of this protocol allows to monitor the morphological changes of the bone tissues using an imaging segmentation based on the Hounsfield-unit system. (Paper III)
- Precise 3D reconstruction of the mandibular condyle and 3D surgical planning validates the reliability and accuracy of a minimally invasive intraoral approach for condylar resection. This alternative approach could become the treatment of choice for most condylar hyperplastic conditions. (Paper IV)

7. FUTURE PERSPECTIVES

Having overcome the methodological limitations that the study of the TMJ in the context of orthognathic surgery faces, we intend to apply this new methodology for the long-term follow-up of these patients.

As described in this PhD thesis, when positional changes of the condyle exceed the adaptive capacity of the joint, undesirable effects such as progressive condylar resorption may occur. To corroborate or refute this hypothesis, we have designed a prospective long-term study in patients undergoing bimaxillary surgery. The aim is to study the positional and morphological condylar changes in the long-term and to investigate if their certain movements or preoperative characteristics entail a high risk of condylar resorption and therefore, relapse.

Additionally, we aim to determine the threshold value of condylar remodelling that produces relapse and therefore, could be defined as “resorption”. In other words, we will try to define the difference between physiological remodelling and resorption, which has not been described three-dimensionally in the scientific literature yet. For this purpose, a prospective radiological evaluation of 50 patients who underwent bimaxillary surgery (Lefort I osteotomy and Bilateral Sagittal Split Osteotomy) at the Institute of Maxillofacial Surgery of the Teknon Medical Center (Barcelona, Spain) is being performed. The usual imaging protocol for orthognathic surgery cases is being followed: CBCT scans are taken pre, postoperatively (1 month after surgery) and at the 1 year follow-up. For each patient, the following variables are being recorded: 1) Age at the time of surgery; 2) Sex; 3) Amount of mandibular advancement (mm) / mandibular setback; 4) Type of occlusal plane rotation (clockwise vs. counterclockwise).

5) Preoperative mandibular plane angle (Sn-MeGo) 6) TMJ signs and symptoms after surgery. Subsequently, a volumetric study of the mandibular condyles is being performed in the preoperative, postoperative and 1-year follow-up. To obtain reconstructions of the mandibular condyle, a semi-automatic segmentation method based on Hounsfield units, previously validated by the present working group, is being applied using the planning software Dolphin Imaging 3D version 11.8 software (Dolphin Imaging & Management Solutions, Chatsworth, California, USA). For each 3D reconstruction, the condylar volume and mean Hounsfield units of each condyle are being recorded. In addition, a cephalometric study is being implemented to study the relationship between volume change and treatment recurrence. With this ongoing line of research, we intend to broaden our knowledge on what happens in the TMJ in the different surgical scenarios. We hope our work aids the clinician to identify potential risk factors and to detect early stages of deleterious adverse effects.

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APPENDIX 1

Original published versions of the articles as they appear in their respective journals

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Early changes in condylar position after mandibular advancement: a three-dimensional analysis

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I. Méndez-Manjón R. Guijarro-Martínez, A. Valls-Ontañón, F. Hernández-Alfaro: Early changes in condylar position after mandibular advancement: a three-dimensional analysis. Int. J. Oral Maxillofac. Surg. 2016; 45: 787–792.

Abstract. The aim of this study was to perform a three-dimensional (3D) assessment of positional changes of the mandibular condyle after bilateral sagittal split osteotomy (BSSO). A prospective evaluation of 22 skeletal class II patients who underwent a BSSO for mandibular advancement was performed. Pre- and postoperative cone beam computed tomography scans were taken. Using the cranial base as a stable reference, the pre- and postoperative 3D skull models were superimposed virtually. Positional changes of the condyles were assessed with a 3D colour mapping system (SimPlant O&O). A Brunner–Langer statistical test was applied to test the null hypothesis that the condylar position remains stable after BSSO. The level of significance was set at 0.05. The mean mandibular advancement in the studied sample was 6.7 ± 1.6 mm. Overall, the condylar positional changes after BSSO for mandibular advancement were statistically significant ($P < 0.05$). A positive correlation was found between the displacement of the left condyle and the amount of mandibular advancement ($P < 0.01$). The results of this study suggest that statistically significant changes of condylar position occur after mandibular advancement. Long-term evaluation is needed to assess the capacity of the temporomandibular joint to adapt to these changes.

Key words: temporomandibular joint; bilateral sagittal split osteotomy; retrognathia; three-dimensional analysis.

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Significant skeletal dysplasia in non-growing patients is efficiently managed with orthognathic surgery and orthodontics. In the particular case of mandibular hypoplasia, the bilateral sagittal split osteotomy (BSSO) is the most common surgical technique for mandibular advancement.[1–7]

A higher prevalence of temporomandibular joint disorders (TMD) has been identified in patients with underlying malocclusion,[8] especially in the context of mandibular hypoplasia and Angle class II malocclusion. While orthognathic surgery will correct a skeletal base discrepancy, there is ongoing concern about its potential beneficial/deleterious effects on the temporomandibular joint (TMJ).

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Although many studies have reported an improvement in TMD symptoms after orthognathic surgery,[4,7–10] others have detected postoperative worsening of these symptoms.[5,11] In a systematic review on the influence of orthognathic surgery on TMD, Abrahamsson et al. concluded that there is insufficient scientific evidence to assess TMD before and after surgery and that well-designed studies are needed in this regard.[11]

In this context, the investigation of possible changes in condylar position and in the disc–condyle relationship after orthognathic surgery is particularly relevant. There is currently no consensus in relation to this. Several study groups have claimed that no statistically significant changes in condylar position occur after surgery.[4,6,7,10,12–14] Conversely, Bailey et al. detected condylar position changes after surgery in 5–10% of the patients who underwent surgical advancement of the mandible.[15] The percentage of observable TMJ changes after BSSO was substantially higher in the study by Saka et al., especially when a splint was not used (54%).[16] It has been suggested that if these changes are small enough, they could allow adaptive remodelling without any TMJ damage.[7,17] It seems that physiological adaptation may fit small changes in condylar position, but that this process requires a long time.[7]

At any rate, if positional changes do occur, their significance is poorly understood. Positional modifications could promote relapse, TMJ problems, or condylar resorption.[3–8,10,11,13–22] Regarding the latter, Arnett et al. showed that posteriorization and medial or lateral torquing during orthognathic surgery could cause morphological changes and lead to progressive condylar resoption.[18,19] In order to minimize this possible movement of the condyles, some authors have advocated the use of different condylar positioning devices during surgery.[2,3] However, these devices have not been proven to improve condylar positioning when compared to a control group.[2,3] Consequently, there is currently no scientific evidence to support their use in orthognathic surgery.

The introduction of cone beam computed tomography (CBCT) imaging has provided an accurate tool to evaluate condylar position.[7,14,17,23] X-ray films have important limitations in terms of precision and the assessment of mediolateral movements. Conversely, CBCT enables a comprehensive three-dimensional (3D) evaluation of the TMJ, provides highly accurate linear measurements,[17] and permits superimposition of pre- and postoperative situations.[20]

The aim of the present study was to apply CBCT technology to evaluate postoperative changes in the TMJ condyle after BSSO for mandibular advancement. In addition, the potential effect of several patient-related and process-related variables on condylar displacement was assessed.

Patients and methods

A prospective radiological evaluation of 22 consecutive patients who underwent BSSO for mandibular advancement at a maxillofacial surgery institute in Barcelona, Spain was performed. The usual imaging protocol for orthognathic surgery cases was followed: CBCT scans were taken pre- and postoperatively (15 days after surgery). This study followed the Declaration of Helsinki on medical protocol and ethics and was approved by the necessary ethics committees.

Patients were selected on the basis of the following inclusion criteria: age ≥18 years, skeletal class II profile in need of surgical correction, no history of TMD, and signed informed consent. Exclusion criteria were skeletal dysplasia requiring additional surgical procedures (i.e., maxillary Le Fort I osteotomy, surgically assisted rapid palatal expansion, etc.), asymmetry, congenital anomalies, history of trauma, and absence of or disagreement with informed consent.

For each patient, the following variables were recorded: age at the time of surgery, sex, amount of mandibular advancement (mm), and type of occlusal plane rotation (clockwise vs. counter-clockwise).

All patients were operated on under general anaesthesia and controlled hypotension. The mandibular advancement procedure was performed according to the standardized BSSO technique defined by Trauner and Obwegeser[24] and incorporating the modifications of Hunsuck[25] and Dal Pont.[26] The proximal (condyle-bearing) fragments were repositioned into the uppermost-anterior part of the fossa with a bidirectional manoeuvre. One single straight miniplate with two screws on each side was used to achieve fixation of the fragments. Patients left the operating room without any rigid intermaxillary fixation apart from two guiding elastics. At 15 days postoperative, a clinical examination of the TMJ was performed. At this time point, patients initiated active physiotherapy and were instructed to do maximum mouth opening exercises with the aim of gaining normal joint function.

CBCT scans were taken with an i-CAT Vision device (Imaging Sciences International, Hatfield, PA, USA). Standard scanning conditions for orthognathic surgery patients were ensured: patient breathing quietly, sitting upright, with the clinical Frankfort horizontal plane parallel to the floor, and biting on a wax-bite in centric occlusion. Preliminary data were saved in DICOM format. For image processing, a computer with the following characteristics was used: Pentium 4 Processor, 3.8 GHz, W/SP5 Windows XP Professional, 120 GB of memory, 2 GB of RAM, and a screen of 20 inches minimum. i-CAT Vision (version 1.8.0.5; Imaging Sciences International) and SimPlant O&O (Materialise Dental SL) software programs were installed on this computer for image viewing and processing, respectively.

A 3D simulation of the pre- and postoperative anatomy was performed. An appropriate mask and region of interest were defined for this purpose. Through automatic segmentation, a preview image was obtained. This was later optimized by manual segmentation, eliminating possible artefacts.

Once the 3D reconstructions of the pre- and postoperative conditions had been obtained, they were superimposed virtually in order to evaluate possible changes in condylar position in all three planes of space. Superimpositions were done using the cranial base as a stable anatomical reference, since it is assumed to remain unchanged after surgery. The software allowed for proper adjustment of the superimposed images in the three views (sagittal, coronal, and axial) in every single slice (Fig. 1). Once the correct superimposition had been obtained, the relationship was saved as the 'home position', such that the program would always connect the two 3D reconstructions in the same relationship. Following this methodology, the program created a coded overlay colour map that enabled visual analysis and objective quantification of the changes in three dimensions (Fig. 2).

The 3D analysis of condylar position was systematized as follows: five points were defined on each condyle; these points were named anterior, posterior, superior, medial, and lateral (Fig. 3).

Positional changes were evaluated separately for each point. Because each colour indicates an interval of change in the colour map, it was decided that the highest value of each corresponding interval would be recorded. This methodology assumed that the value '0' is not possible and ensured that the highest possible change – in other words, the 'worst possible

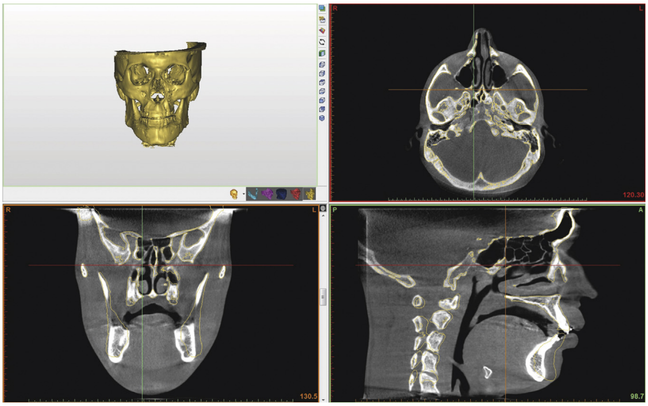

Fig. 1. Superimposition of the pre- and postoperative conditions. The cranial base was used as a stable reference area to superimpose the two images and was adjusted in the sagittal, coronal, and axial planes.

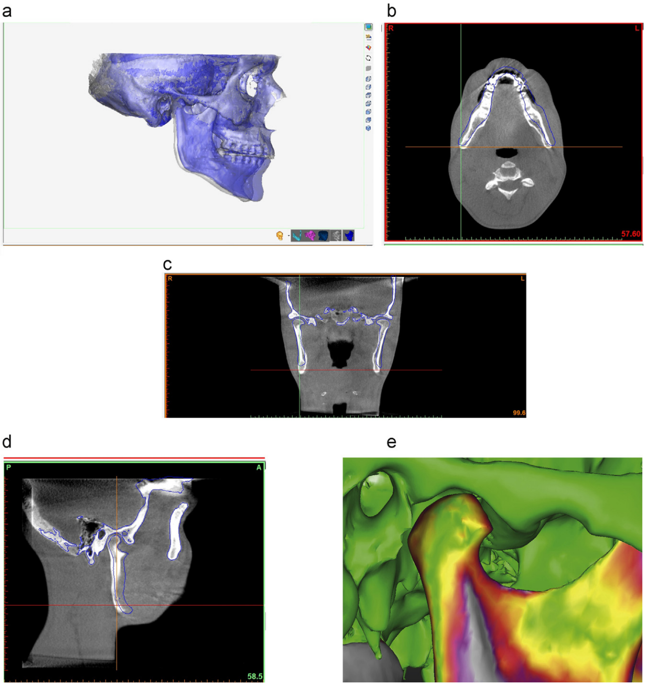

Fig. 2. Preoperative (grey) and postoperative (blue) superimposition. (A) 3D superimposition. (B) Mandibular advancement in axial view. (C) Mandibular condyle and mandibular ramus position in coronal view. (D) Mandibular counter-clockwise rotation in sagittal view. (E) Coded overlay colour map of the pre- and postoperative conditions. Green areas denote no change (0–0.5 mm), whereas yellow (0.5–1 mm), orange (1–1.5 mm), red (1.5–2 mm), and purple (2–2.5 mm) areas denote changes between the two situations. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

situation' – was assumed systematically for each point.

The data analysis was performed using SPSS for Windows version 15.0.1 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for the quantitative analysis. Following a Shapiro–Wilk test in which a normal distribution was ruled out, a non-parametric Brunner–Langer test was performed to test the null hypothesis that the condylar position remains stable after BSSO for mandibular advancement. Spearman's correlation coefficient was used to test the correlation between the changes in condylar position and the amount of advancement, age, and sex, and also between contralateral condyles. The level of significance was set at 0.05.

Results

The study sample ($N = 22$) comprised 14 women (63.6%) and eight men (36.4%); their mean age at the time of surgery was 34.3 years (range 19–59 years). The mean mandibular advancement was 6.7 ± 1.6 mm. A clockwise rotation was performed in 59.1% of the patients ($n = 13$) and a counter-clockwise rotation in 40.9% ($n = 9$).

Table 1 displays the mean positional changes that occurred for both condyles. The overall displacement reached statistical significance ($P < 0.05$).

The descriptive analysis revealed that the greatest positional changes occurred in the posterior point, where displacement was greater than 1 mm in the right condyle for 36% of patients and in the left condyle for 32% of patients. The second greatest displacement corresponded to the lateral point. For the remaining studied points, only 15–20% of the patients showed displacements beyond 1 mm. Nevertheless, this difference was not statistically significant between measured points or between contralateral condyles.

Spearman's correlation coefficient confirmed a positive correlation in the posterior and lateral points between the two condyles that turned out to be statistically significant ($P < 0.05$ and $P < 0.01$, respectively). However, the concordance was low for the posterior point (kappa index, $I_\kappa = 0.277$) and moderate for the lateral point ($I_\kappa = 0.489$).

Demographic variables (age and sex) showed no statistically significant influence on changes in condylar position. Conversely, occlusal plane rotation and the amount of mandibular advancement did show a statistically significant correlation with changes in condylar position.

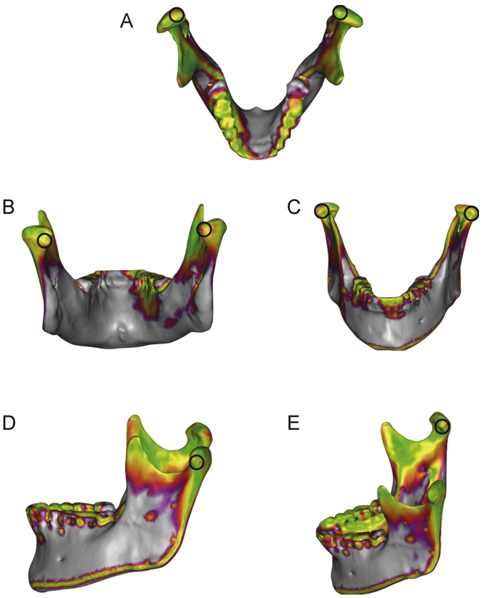

Fig. 3. Regions of interest taken to systematize the condylar position. For each point, the highest value of the colour interval was recorded. (A) Superior point: the most superior point from a craniocaudal view. (B) Posterior point: the most posterior point from the posterior view of the 3D reconstruction. (C) Anterior point: the most anterior point from the anterior view of the 3D reconstruction. (D) Lateral point: the most external point from the lateral view. (E) Medial point: the most external point from the medial view.

In particular, a direct positive correlation was found between condylar displacement and the amount of mandibular advancement. Interestingly, this relationship was statistically significant for the left condyle ($P < 0.01$) but not for the right condyle ($P = 0.053$) (Table 2). Finally, a statistically significant association between the type of occlusal plane change and the movement of the condyles was found. When a clockwise rotation of the maxillomandibular complex was performed, condylar displacement was greater in the right condyle ($P < 0.05$). Conversely, when a counter-clockwise rotation was done, the left condyle showed greater displacement ($P < 0.05$).

Postoperatively, all patients were symptom-free in terms of TMJ pathology and no pathological changes were visible in the CBCT scan.

Table 1. Changes in the different points on the left condyle and right condyle; mean and standard deviation values (SD).[a]

	Number	Mean	SD	Median
Left condyle				
Superior	22	1.07	0.62	1.00
Anterior	22	0.95	0.46	1.00
Posterior	22	1.02	0.63	0.75
Medial	22	0.84	0.61	0.50
Lateral	22	0.95	0.57	1.00
Right condyle				
Superior	22	0.86	0.49	0.50
Anterior	22	0.91	0.53	0.75
Posterior	22	1.09	0.65	1.00
Medial	22	0.77	0.43	0.50
Lateral	22	1.16	0.61	1.00

[a] Data are expressed in millimetres.

Table 2. Descriptive analysis of the amount of mandibular advancement.[a]

	Amount of mandibular advancement		
	Total	<6 mm	>6 mm
Right condyle			
Number	22	9	13
Mean	0.96	0.89	1.01
SD	0.24	0.24	0.24
Minimum	0.60	0.60	0.70
Maximum	1.40	1.30	1.40
Median	1.00	0.90	1.00
Left condyle			
Number	22	9	13
Mean	0.97	0.82	1.06
SD	0.36	0.26	0.40
Minimum	0.50	0.50	0.50
Maximum	1.98	1.30	1.98
Median	0.90	0.70	1.00

SD, standard deviation.

[a] Data are expressed in millimetres.Mean changes in the right and left condyles related to the amount of mandibular advancement.

Discussion

The potential connection between orthognathic surgery and secondary TMJ changes continues to be a topic of debate for maxillofacial surgeons and orthodontists. Whereas postoperative improvements in TMJ symptoms[4,8–10] and better mandibular dynamics[2,8,9] have been reported by some study groups, it has also been suggested that positional modifications of the condyle–fossa relationship can promote postoperative occlusal instability and relapse,[3,21] TMD,[5,16] or progressive condylar resorption.[18,19]

Although some study groups have not found any statistically significant changes in condylar position after orthognathic surgery,[10,13,14,23] it must be pointed out that these evaluations were often based on two-dimensional imaging methods such as lateral cephalograms,[10] where condylar changes cannot be assessed three-dimensionally. In this context, several researchers have stated the need to apply CBCT technology and 3D superimposition techniques in future investigations.[7,14,15,17,23,27]

The present study is an example of such a recommended methodology. Primary CBCT data were processed in order to perform a virtual superimposition of the 3D reconstructions of the pre- and immediate postoperative (15 days postoperative) condylar situations. Although the whole process is technically demanding and quite time-consuming (120 min are needed for the complete evaluation of one single case), it is believed that this methodology enables a detailed analysis of positional changes of the TMJ.

Globally, statistically significant changes in condylar position were found after BSSO for mandibular advancement ($P < 0.01$). These findings are in agreement with those of other studies.[22,28] In the present sample, the posterior and lateral aspects of the condyle tended to vary more than the other points evaluated. Using 3D superimposition, Carvalho et al. found that the posterior condylar region was the area that exhibited the greatest changes with remodelling at the 1-year follow-up.[27]

From the methodological point of view, it is important to point out that due to the system's inability to distinguish between 0 and 0.5 mm in the green range of the colour map, it was assumed that the 0 value (in other words, no positional change) is not possible. The maximum possible error (the highest value of the numerical range and thus the greatest possible change in condylar position) was considered systematically. Nevertheless, the overall changes were below 1 mm in 75% of patients. This finding is also in agreement with the results presented by Carvalho et al., who reported that the mean change in condylar position was smaller than 1 mm (left, 0.98 ± 1.46 mm; right, 0.81 ± 1.40 mm); only four patients showed changes above 2 mm.[27] Interestingly, although their sample was clinically symmetrical, displacement was usually unilateral. These results differ from those of the present study, in which a positive correlation between the displacements of both condyles could be established. Chen et al. did not find any significant differences between the right and left condylar changes either.[22]

At any rate, long-term prospective studies are necessary to ascertain whether postoperative condylar displacement is permanent or not. With a long-term follow-up period of 18.36 ± 4.01 months, Kim et al. demonstrated that the condyle moved slightly backwards to its preoperative position,[7] suggesting that the TMJ can adapt to small positional changes over time.[7,17,21] Early postoperative conditions such as intra-articular oedema or stretching of the masticatory muscles and temporomandibular ligaments may explain short-term positional changes,[22] which might recover over time. Another factor capable of playing a role in early condylar displacement may be the presence of a bony interference in the osteotomy gap. This has been related to mediolateral torquing of the condyles,[22,29] which is probably the most harmful type of condylar displacement due to its potential for disc compression and the subsequent risk of condylar resorption.[3,18,19] Conversely, small positional changes may lead to physiological remodelling and joint adaptation without secondary TMJ damage.[7] Indeed, based on a 3D superimposition methodology, Carvalho et al. reported visible morphological changes and remodelling of the posterior aspect of the condyle at 1 year after BSSO, but no resulting TMD symptomatology.[27]

Another important aspect that requires further clarification is the potential relationship between postoperative condylar displacement and surgical relapse. In this regard, Gerressen et al. suggested that intraoperative distraction of the condyle from the fossa was related to early relapse.[3] Conversely, in their study comparing a group with stable postoperative results and a group with relapse, Zafar et al. did not find any statistically significant changes in condylar displacement.[30] They concluded that small positional changes of the condyle were not related to skeletal relapse.

In addition to the evaluation of the occurrence of condylar changes after mandibular advancement, a second aim of the present investigation was to assess the potential influence of several factors on condylar position. Patient-related variables such as age and sex did not show any statistically significant influence on postsurgical changes. However, other factors did show a relevant association. First, the amount of mandibular advancement was found to be positively correlated with the amount of condylar displacement on the left side ($P < 0.01$). The influence of this factor has been reported previously by Harris et al., who demonstrated that the amount of mandibular advancement was correlated with condylar angulation and supero-inferior changes in condylar position.[28] Second, this study also found a statistically significant association between occlusal plane changes and condylar displacement. Interestingly, the type of rotation influenced the pattern of postoperative change. When a clockwise rotation was introduced, greater changes occurred in the right condyle; by contrast, when a counter-clockwise rotation was performed, the greater change happened in the left condyle. There appears to be no other reference to such a preliminary finding in the scientific literature. Although this requires further investigation, the surgeon's position during surgery could play a role (in the setting of the study institution, the operator stands on the right of the surgical table). Most studies evaluating the influence of maxillomandibular complex rotation on the TMJ have focused on joint symptomatology. Frey et al. reported that large mandibular advancements (>7 mm) with counter-clockwise rotation were related to greater muscle tenderness and joint symptoms.[5] Nevertheless, these symptoms tended to decline over time and thus might be clinically significant only in the short term.[5]

In conclusion, the results of this study suggest that statistically significant displacement of the condyles occurs after BSSO for mandibular advancement. This displacement shows a positive correlation with the magnitude of advancement, and the region of greatest change tends to be located in the posterior aspect of the condyle. These findings apply to the immediate postoperative situation and require further corroboration in the long term. Similarly, the capacity of the TMJ to adapt to these positional changes and the possible influence of these displacements on skeletal relapse are relevant issues that must be evaluated in future studies.

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None.

Competing interests

The authors declare no conflicts of interest.

Ethical approval

This study was approved by the Ethics Committee of the Teknon Medical Centre and the Ethics Committee of the Universitat Internacional de Catalunya.

Patient consent

Not required.

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Cranial base superimposition of cone-beam computed tomography images: A voxel-based protocol validation

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Abstract

The primary objective of the present study was to find the accuracy of voxel-based superimposition of cone-beam computed tomography (CBCT) datasets with a protocol developed for an orthognathic surgery virtual planning software. The secondary objectives were to analyze reproducibility and efficiency of this protocol. Twenty-five CBCT datasets of patients with dental implants present were selected. Each Base Volume dataset was duplicated to create a second volume. Subsequently, both volumes were superimposed with a voxel-based protocol consisting of 3 successive steps: 1) "Side-by-side Superimposition"; 2) "Overlay Superimposition"; 3) "Export Orientation to 2nd Volume". The protocol's accuracy was evaluated by measuring the mean distance between the apex of each dental implant on the Base Volume and second volume datasets. Efficiency was given by the mean time needed to complete all superimposition steps. Reproducibility was analyzed by calculating the intraclass correlation coefficients. Mean time needed to complete the protocol was 198 seconds. The protocol had a rotational accuracy of 0.10°–019° and a translational accuracy of 0.20–0.24mm. Intra-observer and inter-observer reproducibility were 1 and 0.921–1, respectively. Results suggest the protocol is accurate, precise, reproducible, and efficient. The validation of this method enables unbiased analysis of surgical outcomes based on a single, user-friendly software product that is widely available in academic and clinical settings.

Keywords: Superimposition; Voxel-based; Anterior cranial base; Orthodonthics; Oral and maxillofacial surgery; Orthognathic surgery.

Introduction

Image superimposition has become a valuable tool for Orthodontists and Oral and Maxillofacial Surgeons to analyze the outcomes of their interventions, both from the standpoint of procedural accuracy and in terms of long-term stability (*Nada et al., 2011*)

Several protocols for superimposition of computed tomography (CT) imaging datasets have been reported in the scientific literature. The most widespread methods are landmark-based (*Lagravère et al., 2011; Lascal et al., 2004*), surface-based (*Gkantidis et al., 2015; Almukhtar et al., 2014*), and voxel-based (*Nada et al., 2011; Almukhtar et al., 2014; Wiessheimer et al., 2015; Terajima et al., 2008; Cevidanes et al.; 2005; Cevidanes et al., 2009; Cevidanes et al., 2007; Swennen et al., 2009*). The first two are affected by some quality limitations inherent to their dependence on identification and selection of anatomic landmarks (*Lagravère et al., 2011; Lascal et al., 2004; Lou et al., 2007; Lagravère and Major, 2005*) and to the precision of virtual model surface segmentation (*Gkantidis et al., 2015*), respectively. Thus, these image superimposition methods are operator-dependent, i.e., non-automated (*Gkantidis et al., 2015; Cevidanes et al., 2007*). The voxel-based method currently provides the best results in terms of accuracy and precision (*Almukhtar et al., 2014*) due to its observer-independent and semi-automated nature (*Nada et al., 2011, Almukhtar et al., 2014, Wiessheimer et al., 2015*). It is also widely acknowledged that the anatomic area that provides the most accurate results for superimposition of CT images is the anterior cranial base (*Nada et al., 2011*), regardless of whether the superimposition method is landmark-based or voxel-based (*Gkantidis et al., 2015*).

Since the introduction of voxel-based superimposition by Cevidanes et al. in 2005, different protocols have been assessed to reduce the number of steps and software products required for superposition, thus expediting and improving the efficiency of the process (*Nada et al., 2011; Choi and Mah, 2010*). However, CT image superimposition alone does not provide an objective result for analysis of surgical interventions; this usually requires sequential use of two software products, one to perform superimposition and one for objective analysis.

Within this context, the primary objective of the present study was to find the accuracy of voxel-based superimposition of cone-beam computed tomography (CBCT) datasets with a protocol developed specifically for an orthognathic surgery virtual planning software that is widely available in academic and clinical settings. The secondary objectives were to analyze reproducibility and efficiency of this protocol.

Materials and methods

Sample selection

A sample of 25 full-face CBCT's (glabella to hyoid) of patients with dental implants was randomly selected from the imaging database of the Institute of Maxillofacial Surgery (Teknon Medical Center, Barcelona, Spain). All patients provided written informed consent for the use of their CBCT scans and the Teknon Medical Center ethical committee approved the study (CIR-ECL-2012-03)

All 25 CBCT scans were duplicated and saved independently. This created two isolated DICOM (Digital Imaging and Communication in Medicine) datasets, the original one (Base Volume) and a duplicate (2nd Volume), thus enabling superimposition.

Inclusion criteria

CBCT scans were selected on the basis of a history of dental implant rehabilitation with at least one dental implant, image acquisition in centric occlusion or maximal intercuspation.

Exclusion criteria

Patients with any medical condition that could affect the skeletal or soft-tissue structure of the skull were excluded from this study. Similarly, CBCT datasets whose quality was inconsistent with the protocol's requirements were excluded from further evaluation.

Image acquisition

CBCT scans were performed using a standardized scanning protocol (i-CAT^{TM}, Imaging Sciences International, Inc., Hatfield, PA) between July and October 2015. Patients were instructed to sit upright and position themselves in natural head position looking forward as they were seeing themselves. They were instructed to place the mandible in maximum intercuspation or centric relation with the help of a thin wax bite. They were asked to rest the tongue in a relaxed position, breathe lightly, and avoid any other motor reaction. Vertical scanning was performed in “extended field” modus (field of view (FOV) 17 cm diameter, 22 cm height; scan time 2x20 sec; voxel size 0.4 mm) at 120 kV (according to DICOM field 0018,0060 kVp) and 48 mA (according to DICOM field 0018,1151 X-ray tube current).

The original and duplicate DICOM datasets were exported to the Dolphin Imaging 3D® version 11.8 software (Dolphin Imaging & Management Solutions, Chatsworth, California, USA). Files were automatically recognized by the program, and each pair of DICOM sequences was saved independently (as 2 different studies) for each corresponding patient.

Virtual head orientation

The baseline head orientation of all 50 full-face datasets (25 Base Volumes plus 25 2^{nd} Volumes) was randomly altered by investigator 1 (OLHJ) along the following axes of rotation: pitch (P), roll (R), and yaw (Y’). The software's embedded “Orientation Calibration” tool was used for this purpose. This preliminary step was undertaken because the Base Volume and 2^{nd} Volume had the same original positions as a result of setting the scanner coordinates at zero, P: 0°, R: 0°; and Y’: 0° (Fig. 1).

Image superimposition protocol

The duplicate CBCT ($2^{nd\ Volume}$) was selected and superimposed onto its original CBCT (Base Volume) following a specific protocol entailing three steps:

Step one (landmark-based superimposition)

Using the “Side-by-Side Superimposition” tool in the software, the two CBCT datasets were superimposed based on five fixed anatomic landmarks on the skull in three dimensions. These landmarks were defined as follows: 1) Most medial point on the right frontozygomatic suture; 2) Central point on the frontonasal suture; 3) Most medial point on the left frontozygomatic suture; 4) Point on the zygomaticomaxillary suture overlying the right orbital rim; 5) Point on the zygomaticomaxillary suture overlying the left orbital rim. (Fig. 2).

Step two (voxel-based superimposition on the cranial base)

During this stage, three-dimensional (3D) superimposition was refined using the “Overlay Superimposition” tool. This tool allows an automatic voxel-based superimposition (“Auto

Superimposition”) on a selected anatomic area of the skull along the axial, sagittal and coronal planes. With the software’s “Superimpose on a sub-region of the volumes” option, the cranial base was delimited along these three planes of space, with emphasis on the sphenoid bone (Fig. 3).

- In the axial plane, the region with the largest anatomic surface area was selected. This region consisted of the wings of the sphenoid bone, the sphenoid sinus, and the body of the sphenoid bone.
- In the sagittal plane, the midline was selected. This region comprised the body of the sphenoid, the sphenoidal sinus, and the sella turcica.
- In the coronal plane, the anatomic area that visually corresponded to the wings of the sphenoid, sphenoidal sinus, body of the sphenoid, and pterygoid processes of the sphenoid was selected.

At this point, the "Superimpose now!" instruction was given to the software, thus completing cranial base superimposition. The quality of the resulting superimposition was visually improved as compared to the outcome of the first step (landmark-based superimposition). No manual adjustments were performed (Fig. 4).

Step three (head orientation export)

Using the “Export Orientation to 2nd Volume” tool, the head orientation of the 2nd Volume was altered in accordance with the 3D position of the skull after superimposition on the Base Volume. The Dolphin Imaging 3D® software presents this tool when the “Analysis/Verify Result” function is used to verify the outcome of the superimposition process. As the name implies, protocol quality is analyzed at this stage of the process.

It is assumed that an accurate superimposition requires that the Base Volume and 2nd Volume have the same coordinates on the pitch, roll, and yaw axes (Fig. 5).

Analysis of accuracy, reproducibility, and efficiency

Rotational accuracy

The accuracy of superimposition was assessed by angular measurements on the P, R, and Y’ axes. The rotational difference in head orientation between the Base Volume and 2nd Volume after superimposition and orientation exportation with the “Export Orientation to 2nd Volume” command was calculated.

In addition, the software's "Orientation Calibration" tool was applied. This tool enables 3D visualization of rotational changes in skull position along the P, R, and Y' axes on the "Rotational Changes from Initial Orientation" menu (Fig. 5).

Rotational accuracy was calculated as the absolute mean difference (in degrees) between the Base Volume and 2nd Volume head orientations after image superimposition.

Translational accuracy

Once the third step (head orientation) has been completed, the Base Volume and 2nd Volume are presumed to have the same linear coordinates on the "x" (transverse value), "y" (vertical value) and "z" (sagittal value) axes. The "Digitize Measurement" tool of the software was then used to place standardized landmarks at the apex of the dental implants in the maxilla and mandible of each patient.

Linear values on the "x", "y" and "z" axes of the Base Volume and 2nd Volume were thus analyzed so that the accuracy of anatomic location of the reference landmarks would correspond to the translational accuracy of superimposition.

Translational accuracy was calculated as the weighted mean difference (in mm) between landmarks on the Base Volume and 2nd Volume.

The flowchart in Fig. 6 illustrates the sequence of the superimposition protocol.

Reproducibility

Among the 25 pairs of superimposed CBCT scans, the 5 with the best translational accuracy and the 5 with the worst translational accuracy were selected for reanalysis by investigator 1 (OLHJ) and first analysis by investigator 2 (APSG).

One month after the initial calculations, the head orientation of the 2nd Volumes was altered randomly so that investigator 1 and investigator 2 could run the superimposition protocol again on the 10 selected CBCT pairs and thus test protocol reproducibility. Results were analyzed by intraclass correlation coefficients (ICCs).

Efficiency

To measure the efficiency of the tested protocol, the time (in seconds) required to complete all three steps of the image superimposition process (landmark-based superimposition, voxel-based superimposition, and orientation export) was analyzed.

Statistical analysis

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS) for Windows, version 22.0 (IBM Corp., Armonk, NY, USA).

Sample characteristics were demonstrated individually and summarized in means and range or percentage. Rotational accuracy and efficiency were analyzed by means, standard deviation and range. Translational accuracy was evaluated by weighted mean, standard deviation and range. Intraclass correlation coefficients (ICCs) were obtained in 10 superimposed CBCTs (5 best translational accuracy and 5 worst translational accuracy) to reproducibility analysis.

Results

The analyzed sample of 25 CBCT scans comprised 10 (40%) male and 15 (60%) female patients. The mean age at the time of image acquisition was 57 years (40-78). In all, these patients had received 188 dental implants, 105 (55.8%) in the maxilla and 83 (44.2%) in the mandible (Table 1).

Rotational and translational accuracy

The protocol described in this study had a mean rotational accuracy of 0.12° (SD=0.06; 0.03–0.33) along the P axis, 0.10° (SD=0.06; 0.01–0.23) along the R axis, and 0.19° (SD=0.16; 0.00–0.58) along the Y' axis. Translational accuracy was 0.24 mm (SD=0.11; 0.06–0.48) in the transverse, 0.23 mm (SD=0.10; 0.05–0.51) in the vertical, and 0.20 mm (SD=0.10; 0.04–0.46) in the sagittal axis (Table 1).

A box plot of accuracy measurements revealed outliers in only two cases (patients 10 and 20) for rotational measurements and three cases (patients 8, 10, and 24) for translational measurements (Fig. 7 and Fig. 8).

Reproducibility

Superimposition accuracy parameters for investigator 1 after one month were as follows: 0.17° (SD=0.11; 0.06–0.42) along the P axis, 0.19° (SD=0.14; 0.02–0.48) along the R axis, 0.15° (SD=0.16; 0.01–0.46) along the Y' axis, 0.23 mm (SD=0.13; 0.04–0.45) in the transverse axis, 0.18 mm (SD=0.10; 0.02–0.34) in the vertical axis, and 0.19 mm (SD=0.07; 0.06–0.35) in the sagittal axis. Parameters for investigator 2 were as follows: 0.20° (SD=0.07; 0.09–0.29) along the P axis, 0.21° (SD=0.13; 0.06–0.51) along the R axis, 0.15° (SD=0.10; 0.01–0.28) along the Y' axis, 0.35 mm (SD=0.14; 0.07–0.65) in the transverse axis, 0.21 mm (SD=0.07; 0.03–0.28) in the vertical axis, and 0.16 mm (SD=0.07; 0.05–0.34) in the sagittal axis (Table 2).

The tested protocol exhibited excellent reproducibility, with an ICC of 1 for all rotational and translational parameters on intra-observer analysis and an ICC range of 0.921–1 for inter-observer analysis. P-values were statistically significant for all correlation coefficients (Table 3).

Efficiency

The mean time spent on the three steps of the superimposition protocol was 198 seconds (range 119–329 seconds). There was no correlation between protocol time and number of dental implants present on the scan, nor between protocol time and accuracy of superimposition (Table 1).

Discussion

The superimposition accuracy was tested in a widespread software for orthognathic surgery planning at clinical and academic research settings. Although image superimposition has become a popular method to evaluate treatment outcome and stability, to the best of our knowledge the superimposition algorithm of the aforementioned software has not been validated specifically. Prior to any clinical application, the gold-standard of each treatment planning software's tools is absolutely mandatory for accurate interpretation of results.

In general, superimposition protocols tend to be complex, time-consuming and often require more than one software package. The protocol tested in this study was developed so as to apply the features of the Dolphin Imaging 3D® software imaging superimposition tool in the user-friendliest way possible. It was thus structured into three successive steps: step one, "Side by Side Superimposition"; step two, "Overlay Superimposition"; and step three, "Analysis/Verify Result". Step one was performed solely because it is required for the software to recognize the images for superimposition. The five anatomic landmarks selected for the protocol were chosen on the basis that they are all fixed structures that remain unchanged after orthognathic surgery. The software itself implies that, the better the accuracy of landmark selection at this stage, the better the final accuracy of superimposition. However, if the software did not require this step, the protocol would begin directly with step two, since the scientific literature has clearly established that voxel-based image superimposition is more accurate and reproducible than landmark-based methods (*Nada et al., 2011; Almukhtar et al., 2014; Wiessheimer et al., 2015; Terajima et al., 2008; Cevidanes et al.; 2005; Cevidanes et al., 2009; Cevidanes et al., 2007*).

Accordingly, step two is the most critical point in the protocol, as it is this step that confers quality to the superimposition procedure. It is important to note that the excellent quality of this protocol was also reproducible (intra-observer ICC=100% and inter-observer ICC>92%). Reproducibility is due to the fact that superimposition was performed on the cranial base, a fixed structure that completes growth during childhood (*Cevidanes et al., 2009*) and has a large voxel area (*Nada et al., 2011; Gkantidis et al., 2015; Wiessheimer et al., 2015*). The selection of different anatomic structures of the sphenoid bone was only possible because the chosen software allows multiplanar (axial, sagittal, and coronal) area selection, which also made it easier to avoid marking regions concomitant with structures that undergo changes after orthognathic surgery such as the maxilla and mandible (Fig. 3 and Fig. 4). Although the software permits voxel-based superimposition on volumes, it is precisely this concomitance of fixed anatomic structures and anatomic structures that undergo changes after orthognathic surgery what calls for a voxel-based protocol on a single cranial region rather than on the entire CBCT volume.

Step three of the protocol represents the time point at which the quality of superimposition can be checked visually and the superimposed 2nd Volume head orientation can be saved with the “Export Orientation to 2nd Volume” tool. This step justifies the use of duplicate CBCT’s to find the gold-standard for image superimposition accuracy and to validate the protocol, as patient head orientation is the same on the original CBCT scan and on its duplicate. This ensures that, at the time of DICOM file export for later analysis, the baseline head orientation (0°) on the P, R and Y’ axes as determined by the software – center of rotation – will be exactly the same on the Base Volume and 2nd Volume.

To test the accuracy of the image superimposition protocol described in this study, two forms of accuracy were assessed: rotational and translational. The first was based on head orientation, assessed by angular measurements along the P, R, and Y’ axes. This was accomplished by altering the head orientations of the Base Volume and second volume randomly along all three axes of rotation. Knowing that the original images as acquired from the CBCT scanner were identical in terms of head orientation, the investigators could calculate the difference between P, R, and Y’ in the Base Volume and 2nd Volume (Table 1, Fig. 5 and Fig. 7) after superimposition and application of the “Export Orientation to

2nd Volume” command, enabling analysis of rotational accuracy.

In addition, rotational accuracy results may be considered an automatic output of the software, as they were not observer-dependent. Thus, the protocol described herein can be considered accurate, with a mean difference between Base Volume and 2nd Volume head orientations <0.19° on all three axes of rotation (P: 0.12°; R: 0.10°; Y’: 0.19°). Similarly, the protocol can be considered precise because it yielded standard deviations ≤0.06° on P and R (P: SD=0.06°; R: SD=0.06°; Y’: SD=0.16°), a near-negligible range of variation between measurements (P: 0.03–0.33°; R: 0.01–0.23°; Y’: 0.00–0.58°), and only two outliers (Table 1, Fig. 7). To our knowledge are no published studies that include rotational analyses of image superimposition accuracy in the literature.

The second method used for accuracy analysis involved measurement of weighted mean linear differences along the transverse (x), vertical (y), and sagittal (z) axes. For this purpose, after step three, the “Digitize Measurement” tool was used to place landmarks on the apex of each dental implant present on the Base Volume and 2nd Volume. It was assumed that the difference (in mm) between these points along the “x”, “y”, and “z” axes would represent the translational accuracy of the image superimposition process. The use of control CBCT scans of dental implant patients, which enables streamlined, standardized placement of these landmarks, is justified as a means of attenuating any potential bias during landmark selection by the observer (*Gkantidis et al., 2015; Lou et al., 2007; Lagravère and Major, 2005*).

Taking into account the results, the translational accuracy for image superimposition can be assumed to have been satisfactory. This measurement ranged from 0.24 to 0.20 mm (transverse, 0.24 mm; vertical, 0.23 mm; sagittal, 0.20 mm). Regarding precision, superimpositions had a standard deviation approximately of 0.10 mm on all three axes (transverse: SD=0.11mm, 0.06–0.48 mm; vertical: SD=0.10 mm, 0.05–0.51 mm; sagittal: SD=0.10 mm, 0.04–0.46 mm), and only three outliers (Table 1, Fig. 8). These results are superior to those reported in previous studies in which accuracy was around of 0.3 mm (*Nada et al., 2011*), 0.4 mm (*Lee et al., 2012*), and 0.25–0.5 mm (*Weissheimer et al., 2015*), and precision was lower with standard deviations of 0.12 mm (*Nada et al., 2011*) and 0.14mm (*Lee et al., 2012*). Compared to our study, Almukhtar et al. (*Almukhtar et al., 2014*) reported higher accuracy (0.05 mm) but lower precision (SD=0.20 mm), which denotes a lack of standardization in superimpositions. In turn, Gknatidis et al. (*Gknatidis et al., 2015*), reported lower accuracy for superimposition on the anterior cranial base (0.35–0.52 mm) than with a combination of anterior cranial base and foramen magnum (0.07–0.11 mm), but the superimposition method was surface-based.

The combined analysis of rotational and translational accuracy measurements leads to several interpretations. The first is that both correlate, so that the roll axis is most accurate and precise, and superimposition along the "z" plane is also more accurate than along the "x" and "y" planes, i.e., translational accuracy performed as expected in relation to rotational accuracy (Fig. 5, Table 1, Fig. 7, Fig. 8). The second finding is that, in view of this correlation, the method used for analysis of translational accuracy was satisfactory, and it was able to minimize landmark selection bias. The third and most important interpretation concerns the now-validated use of this image superimposition protocol for treatment outcome evaluation in future studies, particularly in orthognathic surgery settings. Voxel-based superimposition of CBCT images on the cranial base with Dolphin 3D Imaging® software can be considered accurate as demonstrated by rotational measurements. Furthermore, linear (translational) measurements obtained at the maxilla and mandible provide additional evidence of this accuracy in regions distant from the cranial base – center of rotation. In short, this means that a single software product can be used to perform image superimposition and analysis of surgical goals in other anatomic regions of the face, such as the maxilla and mandible.

Corroborating the accuracy and precision of the tested protocol, analysis of superimposition reproducibility yielded excellent results for all intra-observer (ICC=1) and inter-observer (ICC=0.921–1) measurements. Only for translational accuracy on the transverse axis (x) was the confidence interval in the satisfactory to excellent range (0.716–0.980) (Table 3). Reproducibility was also demonstrated by the accuracy obtained by investigator 1 after a 30-day "washout" period and by investigator 2. In the 10 retested cases, both observers obtained a rotational accuracy of 0.15–0.21° and a translational accuracy of 0.16–0.35 mm (Table 2). Therefore, the initial results obtained for the 25-case sample were highly similar to those obtained at the second time point of assessment. These analyses show that the tested protocol is reproducible, as previously demonstrated for other protocols of voxel-based image superimposition on the cranial base (*Nada et al., 2011; Cevidanes et al., 2009; Cevidane et al., 2007*), and that landmark selection bias was indeed minimized.

Having established the efficacy of the protocol, the authors believe it is also efficient, as demonstrated by the satisfactory results in terms of time spent on completing the three-step image superposition process and by the fact that objective analyses can be conducted within the same computer program. This is particularly evident when comparing the time needed to complete this protocol (198 seconds, i.e. approximately 3 minutes) versus those reported in other studies: 45–60 minutes (*Cevidanes et al., 2005*), 30–40 minutes (*Nada et al., 2011*), and 25 minutes (*Gkantidis et al., 2015*). In addition, these alternative protocols required at least two software products to complete the respective methods. Weissheimer et al. (*Weissheimer et al., 2015*) reported the shortest time spent on a superimposition procedure itself (10–15 seconds), but the software employed does not allow for all objective analyses. Another important point regarding the efficiency of the tested protocol is that no correlation between quality of image superimposition and time spent on the protocol was found whatsoever. Similarly, no correlation between quality and the number of dental implants present was detected either. Thus, this protocol is far more dependent on the agility of the operator or on the computing power of the workstation than on the data processing capacity of the software program.

The confirmation of an accurate value for imaging superimposition purposes is important for investigators conducting research at an academic setting that involves treatment outcome analysis. In addition, and more importantly, it gives clinicians outside an academic setting the opportunity to analyze treatment outcomes with a simple, user-friendly protocol entailing one single software. Our next research step after to find the gold-standard value and to validate internally the software is to use this protocol in an orthognathic surgery prospective sample to test the superimposition accuracy in different CBCT's moments and analyze this sample to surgical accuracy and long-term stability.

Conclusion

In conclusion, the results of this study suggest that the software provides an accurate and precise gold-standard value for CBCT image superimposition, beyond that the protocol tested is reproducible and efficient.

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Conflict of interest: The authors declare that they have no conflict of interest.

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Captions to illustrations

Figure 1. Randomized head orientation in the "Orientation Calibration" tool. Red rectangle: angles in the pitch, roll, and yaw axes.

Figure 2. Protocol step one: selection of five anatomic landmarks (red arrows) using the "Side by Side Superimposition" method.

Figure 3. Protocol step two: voxel-based image superimposition on the cranial base using the "Overlay Superimposition" method and the "Superimpose on a sub-region of the volumes" tool. Red rectangle: structures of the sphenoid bone outlined manually by the observer (axial, sagittal, and coronal views). Images before superimposition.

Figure 4. Protocol step two: voxel-based image superimposition on the cranial base using the "Overlay Superimposition" method and the "Superimpose on a sub-region of the volumes" tool. Rotational (pitch, roll, yaw) and translation (x, y, z) orientations in Dolphin Imaging 3D software. Images after superimposition (red arrow).

Figure 5. Protocol step three: head orientation export. **A** – "Analysis/Verify Result". The 2nd Volume takes on the position of the Base Volume after application of the "Export Orientation to 2nd Volume…" command (red arrow). **B** – Head orientation of Base Volume (P: 6.35; R: 1.34; Y: 5.97). **C** – Head orientation of 2nd Volume before image superimposition (P: 1.68; R: 1.66; Y: 12.34). **D** – Head orientation of 2nd Volume after image superimposition (P: 6.38; R: 1.39; Y: 6.04).

Figure 6. Flowchart of image superimposition protocol.

Figure 7. Box plot of rotational accuracy. Only two outliers were found.

Figure 8. Box plot of translational accuracy. Only three outliers were found.

Table 1. Descriptive data, protocol time and superimposition accuracy.

	Age	Gender	Dental implants	Protocol time (s)	Rotational accuracy (degrees)	Translational accuracy (mm)
1*	54	Female	2 (2Mx)	175	P:0.11, R:0.22, Y':0.22	x:0.10, y:0.17, z:0.13
2	52	Female	12 (6Mx, 6Md)	181	P:0.12, R:0.12, Y':0.07	x:0.14, y:0.12, z:0.30
3#	51	Female	5 (3Mx, 2Md)	172	P:0.05, R:0.02, Y':0.13	x:0.25, y:0.37, z:0.30
4	60	Male	16 (8Mx, 8Md)	230	P:0.12, R:0.05, Y':0.06	x:0.14, y:0.36, z:0.22
5#	78	Female	10 (3Mx, 7Md)	178	P:0.05, R:0.14, Y':0.32	x:0.37, y:0.18, z:0.31
6	57	Male	4 (2Mx, 2Md)	190	P:0.08, R:0.12, Y':0.02	x:0.29, y:0.13, z:0.17
7	66	Male	2 (2Mx)	183	P:0.05, R:0.12, Y':0.36	x:0.48, y:0.09, z:0.02
8#	52	Male	7 (7Md)	198	P:0.31, R:0.14, Y':0.06	x:0.22, y:0.37, z:0.46
9*	57	Female	4 (4Mx)	119	P:0.01, R:0.08, Y':0.10	x:0.06, y:0.14, z:0.14
10#	63	Female	4 (4Mx)	211	P:0.33, R:0.01, Y':0.00	x:0.40, y:0.51, z:0.04
11	41	Female	18 (9Mx, 9Md)	164	P:0.20, R:0.02, Y':0.27	x:0.27, y:0.27, z:0.21
12	66	Female	6 (3Mx, 3Md)	178	P:0.05, R:0.12, Y':0.15	x:0.21, y:0.21, z:0.20
13	48	Female	9 (5Mx, 4Md)	245	P:0.09, R:0.16, Y':0.08	x:0.24, y:0.26, z:0.32
14	72	Male	5 (3Mx, 2Md)	329	P:0.26, R:0.08, Y':0.07	x:0.14, y:0.22, z:0.12
15*	52	Male	15 (7Mx, 8Md)	183	P:0.16, R:0.09, Y':0.05	x:0.10, y:0.05, z:0.14
16	58	Female	11 (9Mx, 2Md)	206	P:0.16, R:0.02, Y':0.54	x:0.46, y:0.23, z:0.17
17	50	Female	7 (4Mx, 3Md)	234	P:0.30, R:0.04, Y':0.50	x:0.38, y:0.14, z:0.20
18	72	Male	4 (1Mx, 3Md)	176	P:0.01, R:0.03, Y':0.31	x:0.04, y:0.23, z:0.25
19	40	Male	4 (2Mx, 2Md)	221	P:0.05, R:0.18, Y':0.20	x:0.23, y:0.22, z:0.09
20#	61	Female	4 (3Mx, 1Md)	183	P:0.17, R:0.23, Y':0.58	x:0.36, y:0.31, z:0.24
21	58	Female	11 (8Mx, 3Md)	165	P:0.05, R:0.11, Y':0.22	x:0.36, y:0.25, z:0.09
22	48	Female	14 (9Mx, 5Md)	217	P:0.12, R:0.01, Y':0.09	x:0.26, y:0.27, z:0.08
23*	68	Male	7 (5Mx, 2Md)	206	P:0.06, R:0.13, Y':0.05	x:0.17, y:0.23, z:0.12
24	57	Male	5 (3Mx, 2Md)	230	P:0.15, R:0.11, Y':0.18	x:0.27, y:0.12, z:0.45
25*	48	Female	2 (2Md)	166	P:0.03, R:0.05, Y':0.07	x:0.11, y:0.05, z:0.18
Sample Average	**57**	**25 Female 15(60%) Male 10(40%)**	**188 Mx 105(55,8%) Md 83(44,2%)**	**198 39SD (119-329)**	**P:0.12, R:0.10, Y':0.19 P:0.06SD (0.03-0.33) R:0.06SD (0.01-0.23) Y':0.16SD (0.00-0.58)**	**x:0.24, y:0.23, z:0.20 x:0.11SD (0.06-0.48) y:0.10SD (0.05-0.51) z:0.10SD (0.04-0.46)**

Legend: * – Five best translational accuracy; # – Five worst translational accuracy; Mx – Maxilla; Md – Mandible; s – seconds; SD – standard deviation; P – pitch; R – roll; Y' – yaw; mm – millimeters; x – transversal; y – vertical; z – sagittal.

Table 2. Observer $1^{\text{one month}}$ superimposition accuracy and Observer 2 superimposition accuracy.
Legend: * – Five best translational accuracy; $^{\#}$ – Five worst translational accuracy; SD – standard deviation; P – pitch; R – roll; Y' – yaw;

	Observer 1 (OLHJ) **one month**		**Observer 2 (APSG)**	
Patient	Rotational accuracy (degrees)	Translational accuracy (mm)	Rotational accuracy (degrees)	Translational accuracy (mm)
1^{*}	P:0.29, R:0.04, Y':0.14	x:0.04, y:0.25, z:0.12	P:0.09, R:0.29, Y':0.01	x:0.39, y:0.07, z:0.05
$3^{\#}$	P:0.14, R:0.23, Y':0.01	x:0.16, y:0.10, z:0.27	P:0.18, R:0.15, Y':0.04	x:0.34, y:0.14, z:0.18
$5^{\#}$	P:0.06, R:0.02, Y':0.26	x:0.45, y:0.34, z:0.11	P:0.29, R:0.10, Y':0.16	x:0.32, y:0.23, z:0.16
$8^{\#}$	P:0.18, R:0.23, Y':0.05	x:0.13, y:0.21, z:0.23	P:0.26, R:0.06, Y':0.22	x:0.65, y:0.27, z:0.25
9^{*}	P:0.42, R:0.30, Y':0.08	x:0.32, y:0.08, z:0.35	P:0.28, R:0.51, Y':0.07	x:0.28, y:0.05, z:0.07
$10^{\#}$	P:0.11, R:0.21, Y':0.09	x:0.06, y:0.07, z:0.13	P:0.18, R:0.21, Y':0.28	x:0.27, y:0.28, z:0.27
15^{*}	P:0.19, R:0.48, Y':0.16	x:0.30, y:0.21, z:0.16	P:0.10, R:0.30, Y':0.23	x:0.31, y:0.25, z:0.10
$20^{\#}$	P:0.11, R:0.16, Y':0.46	x:0.19, y:0.14, z:0.28	P:0.15, R:0.19, Y':0.17	x:0.07, y:0.27, z:0.11
23^{*}	P:0.06, R:0.21, Y':0.12	x:0.08, y:0.07, z:0.20	P:0.20, R:0.14, Y':0.05	x:0.41, y:0.23, z:0.16
25^{*}	P:0.11, R:0.03, Y':0.09	x:0.19, y:0.02, z:0.06	P:0.24, R:0.16, Y':0.24	x:0.52, y:0.03, z:0.34
Sample Average	**P:0.17, R:0.19, Y':0.15** **P:0.11SD (0.06-0.42)** **R:0.14SD (0.02-0.48)** **Y':0.13SD (0.01-0.46)**	**x:0.23, y:0.18, z:0.19** **x:0.13SD (0.04-0.45)** **y:0.10SD (0.02-0.34)** **z:0.07SD (0.06-0.35)**	**P:0.20, R:0.21, Y':0.15** **P:0.07SD (0.09-0.29)** **R:0.13SD (0.06-0.51)** **Y':0.10SD (0.01-0.28)**	**x:0.35, y:0.21, z:0.16** **x:0.14SD (0.07-0.65)** **y:0.07SD (0.03-0.28)** **z:0.07SD (0.05-0.34)**

mm – millimeters; x – transversal; y – vertical; z – sagittal;

Table 3. Intra-observer and inter-observer superimposition reproducibility.

		Observer 1 X Observer 1$^{\text{one month}}$ ICC (CI 95%)	**P-value**	**Observer 1 X Observer 2 ICC (CI 95%)**	**P-value**
Rotation	**P**	1 (1 – 1)	<0.001	0.999 (0.997 – 1)	<0.001
	R	1 (1 – 1)	<0.001	0.993 (0.971 – 0.998)	<0.001
	Y'	1 (1 – 1)	<0.001	1 (0.998 – 1)	<0.001
Translation	**x**	1 (1 – 1)	<0.001	0.921 (0.716 – 0.980)	<0.001
	y	1 (1 – 0.999)	<0.001	0.999 (0.994 – 1)	<0.001
	z	1 (1 – 1)	<0.001	0.988 (0.975 – 0.998)	<0.001

Legend: $^{\text{one month}}$ – Observer 1 reanalysis after one month; ICC – Intraclass Correlation Coefficient; CI – Confidence interval; P – pitch; R – roll; Y' – yaw; x – transversal; y – vertical; z – sagittal;

Figure 1.

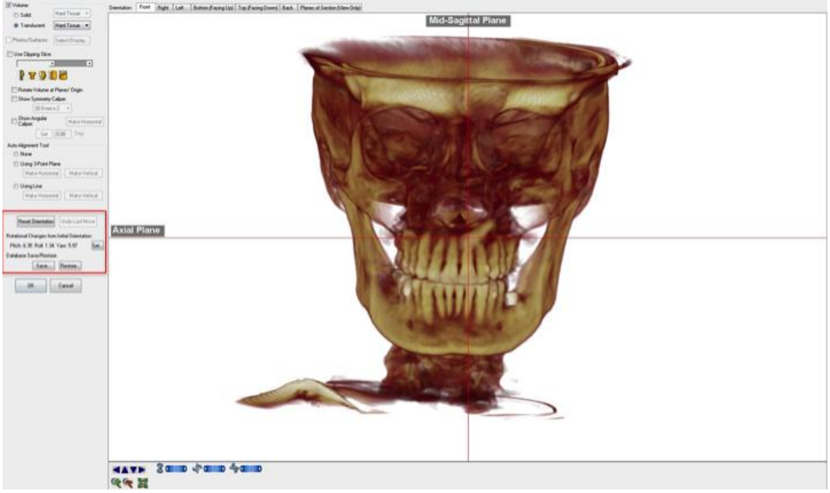


Figure 2.

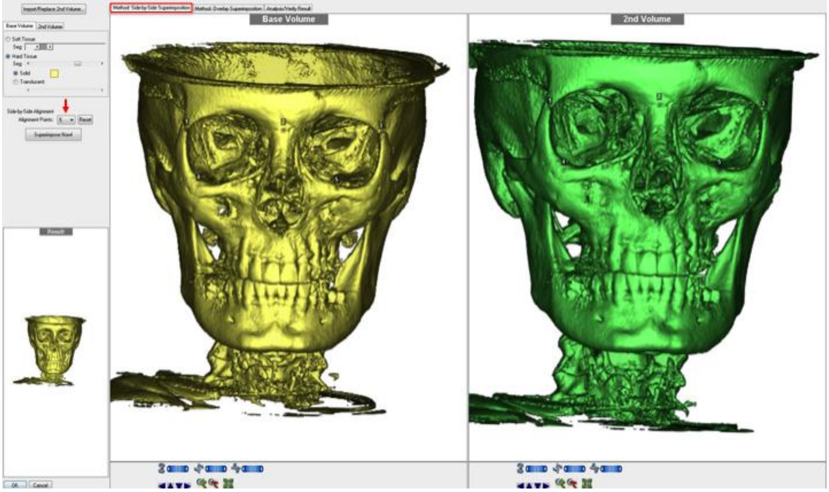
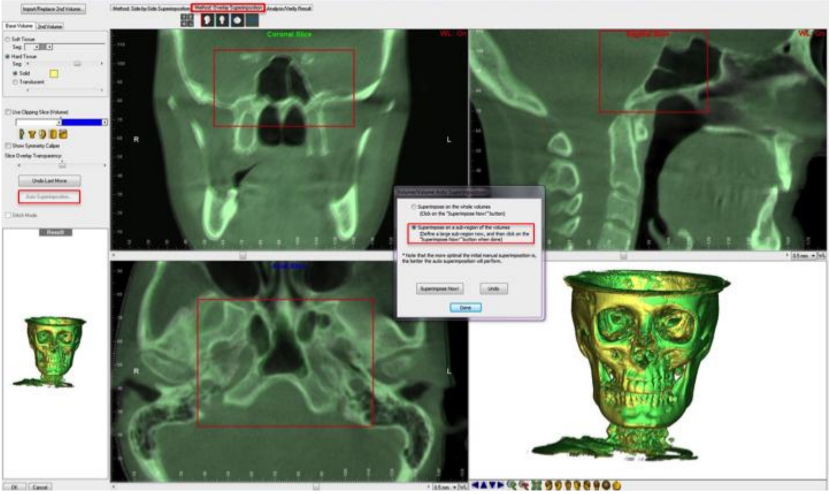


Figure 3.

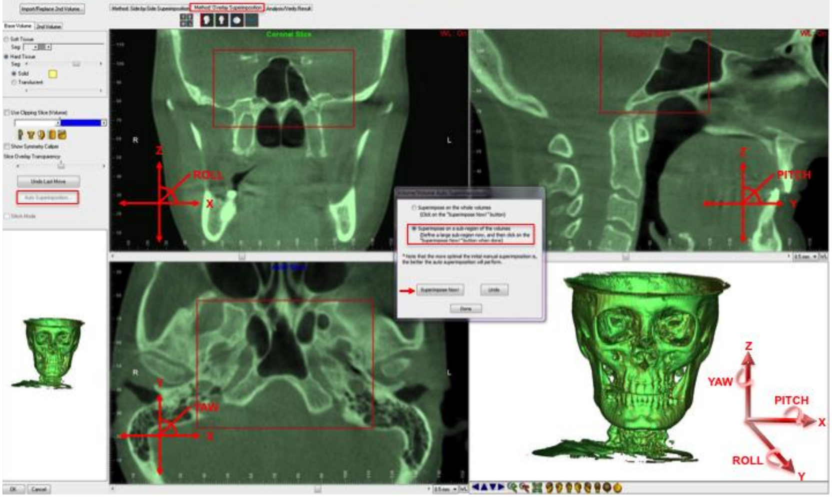


○ Superimpose on the whole volumes
(Click on the "Superimpose Now!" button)

● Superimpose on a sub-region of the volumes
(Define a large sub-region now, and then click on the "Superimpose Now!" button when done)

* Note that the more optimal the initial manual superimposition is, the better the auto superimposition will perform.

Figure 4



○ Superimpose on the whole volumes
(Click on the "Superimpose Now!" button)

● Superimpose on a sub-region of the volumes
(Define a large sub-region now, and then click on the "Superimpose Now!" button when done)

* Note that the more optimal the initial manual superimposition is, the better the auto superimposition will perform.

Figure 5

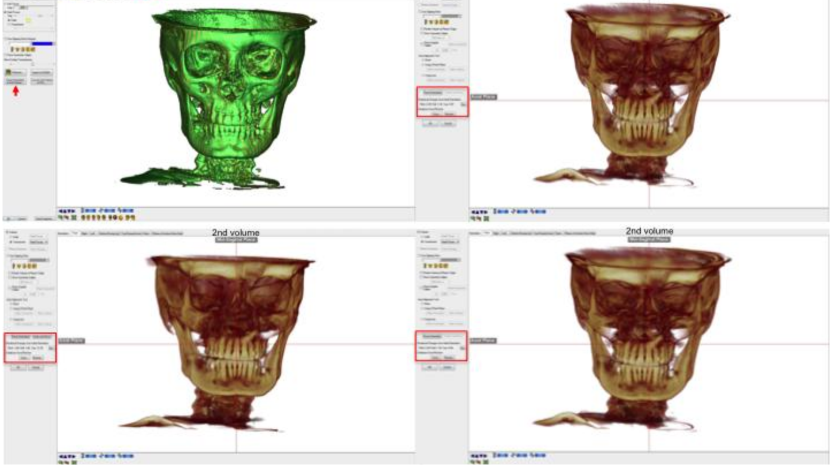


Figure 6

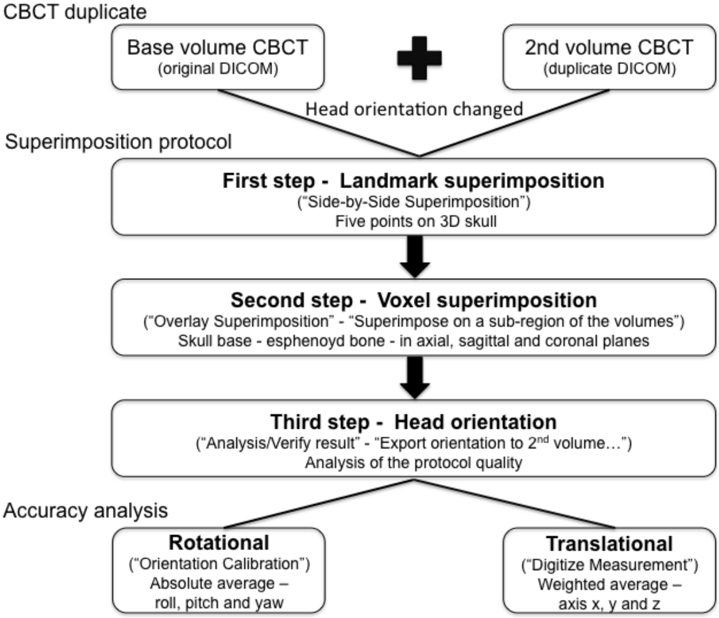


Figure 7

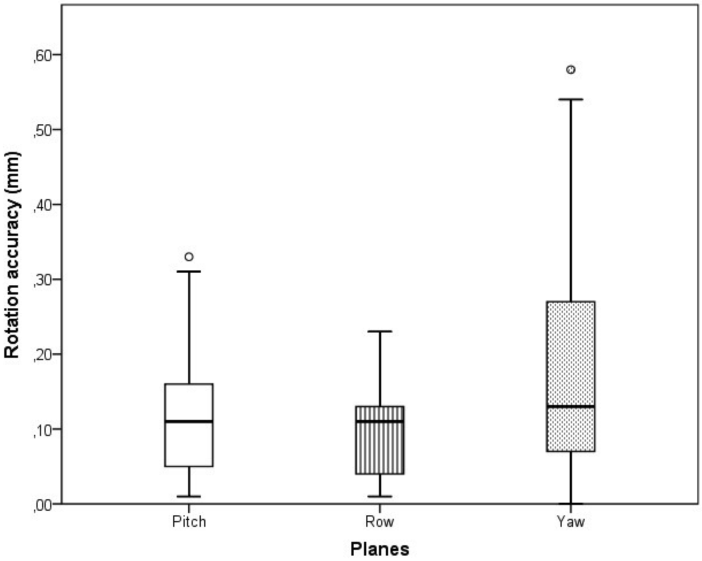
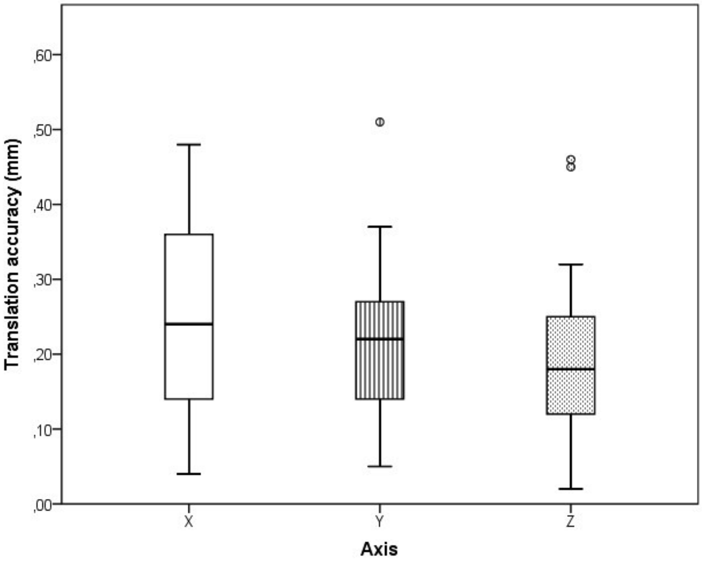


Figure 8



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Title: Semi-automated three-dimensional condylar reconstruction: a Hounsfield unit-based protocol

Article Type: Original Research Article

Keywords: orthognathic surgery, 3D reconstruction, TMJ, progressive condylar resorption

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Abstract: Objective: To validate a semi-automated segmentation method for 3D reconstruction of the mandibular condyle from CBCT data and demonstrate its use for volumetric analysis of the condyle.
Study design: Ten CBCT datasets were used to validate the proposed semi-automatic method for 3D rendering of mandibular condyles. First, a standardized orientation protocol of the skull was applied in all cases. After defining the volume of interest, a Hounsfield-unit range was set in the software (80-11717) to allow automatic reconstruction of the condyle surface. The condylar contour was later optimized manually. The whole process was repeated twice by two independent observers. Volumetric measurements of the condyle were used as a measure of conformity between the two observers.
Results: The reproducibility of the condylar volume reconstruction was excellent for intra-examiner measurements (CV=3.65%, ICC=0.97) and good for inter-examiner measurements (CV=7.15%, ICC=0.89). The overall mean time for the segmentation process was 6.31 +- 2.78 sec.
Conclusion:
This method provides an accurate and reproducible tool for 3D reconstruction of the mandibular condyle using CBCT data. Implementation of this protocol allows follow-up of morphological changes in bone tissues using an imaging segmentation method based on Hounsfield units.

***Statement of Clinical Relevance (max 40 words)**

CLINICAL RELEVANCE

The present protocol provides an accurate and reproducible tool for follow-up of condylar volume, thus enabling detection of progressive condylar resorption in the early stages. The use of a single software for orthognathic surgery planning, Hounsfield unit-based image segmentation, and condylar volume analysis saves time and facilitates postoperative assessment.

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Semi-automated three-dimensional condylar reconstruction: a Hounsfield unit-based protocol.

Running title: Semi-automated method for 3D condylar reconstruction

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Abstract

Objective: To validate a semi-automated segmentation method for three-dimensional (3D) reconstruction of the mandibular condyle from CBCT data and illustrate its application in volumetric analysis of the condyle.

Study design: Ten CBCT datasets were used to validate the proposed semi-automatic method for 3D rendering of mandibular condyles. First, a standardized orientation protocol of the skull was applied. After defining the volume of interest, a Hounsfield-unit range was set in the software (80-11717) to allow for automatic reconstruction of the condyle's surface. Subsequently, condylar contour was optimized manually. The whole process was repeated twice by two independent investigators. Volumetric measurements of the condyle were used as a measure of conformity between both investigators.

Results: The reproducibility of condylar volume reconstruction was excellent for intra-examiner measurements (CV=3.65%, ICC=0.97) and good for inter-examiner measurements (CV=7.15%, ICC=0.89). The overall mean time required for the segmentation process was 6.31 +- 2.78 min.

Conclusion: The proposed protocol provides an accurate and reproducible tool for 3D reconstruction of the mandibular condyle using CBCT data. Its implementation will enable adequate follow-up of morphological changes in bone tissue with a Hounsfield unit-based imaging segmentation method.

Clinical application: The present protocol provides an accurate and reproducible tool for the follow-up of condylar volume, thus enabling early detection of progressive condylar resorption. The use of a single software for orthognathic surgery planning, Hounsfield unit-based image segmentation, and condylar volume analysis saves time and facilitates postoperative assessment.

Keywords: TMJ, 3D imaging, condylar resorption, orthognathic surgery, condyle, three-dimensional.

Introduction

Positional and morphological changes of the mandibular condyles are frequently reported after orthognathic surgery procedures[1–7]. At any rate, when positional changes do occur, their clinical significance is poorly understood. In this regard, several studies have demonstrated that the temporomandibular joints (TMJ) can adapt to small positional changes by undergoing physiological remodelling without secondary TMJ damage[1,8,9]. However, other investigations have evidenced that positional changes of the condyle can promote postoperative occlusal instability and relapse[10,11], temporomandibular disorders (TMD)[6,12], and progressive condylar resorption (PCR)[13–18].

In particular, the commonly reported association between PCR and late postoperative relapse [16,18–21] calls for the definition of an effective protocol to evaluate condylar morphology after orthognathic surgery.

Cone-beam computed tomography (CBCT) has become the imaging modality of choice for diagnosis and treatment planning in orthognathic surgery and orthodontics.[22–24]. It is an excellent low radiation dose alternative to conventional CT imaging[25], with several other advantages. In particular, the possibility to build three-dimensional (3D) virtual models with registration and to perform 3D superimposition has led to a definitive change in treatment planning and long-term evaluation in orthognathic surgery[26]. CBCT is also becoming the imaging modality of choice for the osseous components of the TMJ[27]. It has been shown that CBCT provides greater diagnostic accuracy than panoramic radiography and spiral tomography in the detection of condylar cortical erosion and osteophytes.[28,29,30]

The prospect of using the same CBCT-based protocol to plan orthognathic surgery treatment and to study subsequent changes in condylar morphology over time would provide the invaluable advantage of reducing the number of imaging tests needed in each patient.

Despite the superior reliability of CBCT for the study of condylar morphology, some drawbacks persist. Segmentation and 3D rendering of the condyles are inherently difficult due to the low bone density of this region in comparison to the rest of the mandible and its close relation to the articular disc.[31] In this context, several protocols have been proposed to establish a reproducible method for 3D rendering of the condylar surface[32–35]. Nevertheless, most of these proposed protocols are based on manual outlining of the condylar contour in two-dimensional (2D) cross-sections of the CBCT scan, a highly observer-dependent procedure. In fact, research has shown that the condyle and lingual aspect of the mandible are the most susceptible areas to observer experience[31]. Moreover, this technique usually requires the use of additional software for data processing and is very time-consuming.

Recently, a semi-automated protocol for condyle rendering has been proposed to overcome the aforementioned limitations.[35] This protocol is based on 3D region-growing and local thresholding algorithms that require that the observer indicates a seed point every five slides. Thus, although both the process of manual outlining and processing time are substantially reduced, the observer's judgment still plays an important role.

The purpose of the present study is to validate a fast, semi-automated approach to 3D rendering of the condyles using one single software. This protocol is applicable to the analysis of condylar morphology changes over time as well as to orthognathic surgery planning.

Subjects and Methods

The Declaration of Helsinki guidelines were followed in all study phases. Approval from the Ethics Committee of the Universitat Internacional de Catalunya (Barcelona, Spain) and Teknon Medical Center (Barcelona, Spain) were obtained (reference number CIR-ECL-2012-03).

Subjects

The preoperative CBCT datasets of 10 adult Caucasian patients were randomly selected from the database of the Institute of Maxillofacial Surgery (Teknon Medical Center, Barcelona, Spain). Scans were obtained with an iCAT-Q Vision device, version 1.8.0.5 (Imaging Sciences International, Hatfield, Pennsylvania). The institution's standard scanning conditions for orthognathic surgery patients were ensured: patient breathing quietly, sitting upright, with the clinical Frankfurt horizontal (FH) plane parallel to the floor, and the condyles in centric relation with the help of a wax wafer.[36] Preliminary data were saved in DICOM format. Image viewing and processing were carried out in a workstation (Intel® Pentium 4 processor, 3.80 GHz, 120 GB hard drive, 2 GB RAM, operating system Microsoft Windows® XP Professional SP5, minimum screen size 20 inches) running ICAT-Q Vision Imaging Sciences 1.8.0.5 and Dolphin Imaging 3D version 11.8 software (Dolphin Imaging & Management Solutions, Chatsworth, California, USA).

Image processing

Head orientation

In order to systematize the position of the 3D virtual model of each patient, a standardized orientation protocol was applied to the pitch, roll, and yaw axes.

The pitch axis was oriented taking the FH plane as a reference, defined bilaterally by the right and left 3D porion and right and left orbitale landmarks, as described by Cevidanes et al[37] . The midsagittal plane (yaw) was defined by the crista galli and center of the magnum foramen. Finally, the roll axis was defined by the fronto-zygomatic sutures bilaterally (Fig. 1).

Semiautomatic segmentation

Using the previously oriented 3D virtual models, two independent observers segmented a total of 20 condyles in Dolphin Imaging 3D version 11.8 software. Observer 1 (OLH) had no experience with segmentation of condyles based on CBCT data, while observer 2 (IMM) had extensive experience on manual outlining-based segmentation of condyles. The overall segmentation process was repeated twice by each, with a 4-week interval between sessions.

Step 1: Determination of the volume of interest

In order to isolate the region of the mandibular condyle, the C-point was identified as the most caudal point of the sigmoid notch bilaterally, as described by Xi et al.[34]

A built-in software tool (head plane parallel to the FP that passes through the C-point) was used to isolate the volume of interest.

Step 2: Semiautomatic segmentation based on Hounsfield units

A Hounsfield unit (HU) range of 80-11717 HU was set in the software in order to standardize 3D rendering of the condyles for volumetric evaluation (Fig. 2). This tool creates a color map based on the available HU range of the software, which allows the operator to distinguish the boundaries of the surface outline of the condyle. The observer reduced the window until no green color could be observed (in other words, until all the area corresponded to >80 HU). Finally, the reconstruction was edited using the "sculpting" tool to eliminate any data outside the area of interest (Fig. 3). Subsequently, the volume of the resulting reconstruction and the mean HU were obtained. After applying the HU range to segment the condyle, the total volume of the skull was also obtained to test the method.

Statistical analysis

Condylar volumes and mean HU for each segmented condyle were calculated within the two groups (Investigator 1. and Investigator 2). Statistical analysis was carried out in IBM SPSS Statistics for Windows (IBM Corp; Armonk, NY, USA). The level of significance was set at 5% ($\alpha = 0.05$).

For a paired-samples t-test, considering a medium effect size (0.5) for detection, the achieved power was 0.56 for a confidence level of 95%. The intraclass correlation coefficient (ICC) was calculated using the volumetric measurements as a measure of conformity between both observers. An ICC

<0.51 was considered as poor, 0.51-0.70 as moderate, 0.71-0.90 as good, and >0.90 as excellent.

Results

The study group consisted of 10 patients (5 males and 5 females). A total of 20 condyles were segmented in each group. Variances and ICCs of volumetric measurement error were calculated. The mean duration of the segmentation process for observer 1 was 6.78 ± 3.42 minutes at T1 and 6.29 ± 2.69 minutes at T2. The mean time for the observer 2 was 6.29 ± 2.69 minutes at T1 and 5.88 ± 2.33 minutes at T2.

The mean overall condylar volume was found to be 1481.95 mm^3 by observer 1 and 1889.38 mm^3 by observer 2. The mean overall HU level of the condyle was 341.79 for observer 1 and 329.88 for observer 2.

Reproducibility of condylar volume measurements was excellent for intra-examiner parameters (CV=3.65%, ICC=0.97) and good for inter-examiner parameters (CV=7.15%, ICC=0.89). Reproducibility of the mean HU was excellent for both intra-examiner (CV=2.54%, ICC=0.99) and inter-examiner parameters (CV=4.98%; ICC=0.96) (Table 1).

The CV and ICC were 0 and 1 respectively for the cranial volume in the intra-observer measurements.

Dahlberg’s error (D) and CV were recalculated for low-density (<320 HU) and high-density (>320 HU) condyles. Working with low density condyles did not seem to increase the error between examiners with this segmentation method (Table 2).

A direct, moderate magnitude relationship between cranial density and condylar density was observed (r= 0.552, P=0,098).

Discussion

CBCT has proven its reliability in the assessment of condylar lesions, with greater reliability and accuracy than panoramic radiography and multislice CT.[27–30] Three-dimensional models from CBCT data provide additional diagnostic information on morphology and exact location of the bony lesion in the condyle.

In this context, several authors have described its application in the study of an extensive variety of TMDs, such as osteoarthritis[32,33], trauma[27], erosions[29], osteophytes[28], and developmental abnormalities[27,38]. In the field of orthognathic surgery, superimposition of 3D reconstructions from CBCT data allows not only the evaluation of changes in condylar morphology[39,40] and volume, but also of potential positional changes of the condyle during the postoperative period.[4,41,9,42] This eliminates the need to perform linear measurements in 2D slices from CT scans, which have the inherent drawback of landmark identification in a non-fixed structure such as the condyle.

This 3D analysis of the condylar morphology and surface offers the clinician the possibility of detecting early signs of progressive condylar resorption and anticipating the possible consequences of late relapse. In this sense, Xi et al. (2015)[18] showed that, in 3D analyses, patients with a reduction of condylar volume greater than 17% developed significant relapse in the horizontal and vertical direction. Although these data are based on a small sample, they pave the way for a new line of research that would allow establishment of thresholds to distinguish condylar remodeling from condylar resorption during postoperative follow-up.

The preoperative analysis of condylar morphology through 3D reconstructions also gives clinicians the opportunity to identify possible risk factors or developmental deformities, such as condylar hyperplasia, at the start of treatment.[38] Some conditions, such as small preoperative condylar volume[18], osteoarthrosis, and posterior inclination of the condylar neck, have been associated with a higher risk of PCR.[21] Moreover, it has been shown that patients with a class II skeletal structure have a significantly smaller preoperative condylar volume than class I and class III patients[43]. Given current knowledge of these prognostic factors, long-term morphological changes should be included in the usual assessment protocol.

Considering that several studies have reported condylar remodeling and resorption after orthognathic surgery,[15, 21,44,45,] the establishment of a rapid, user-friendly protocol for the evaluation of condylar morphology is crucial. Different segmentation protocols have been proposed to obtain adequate 3D reconstructions of the condylar surface.[32–35] However, some of the proposed methods are based on manual outlining of the condylar contour in 2D cross-sections, which is highly observer-dependent and time-consuming[33,46]. In fact, the condyle has been referred to as one of the more difficult areas to segment, due to its low density in comparison to the rest of the mandible and the difficulty of isolating it from the articular disc[31].

These early methods, besides the aforementioned drawbacks, required the use of several software products, which further hinders or even prevents the generalized use by all clinicians without the help of a specialized technician. In the present validation study, results obtained by an experienced observer in manual outlining segmentation were compared to those of an inexperienced observer. Good inter-examiner reproducibility was observed (CV=7.15%, ICC=0.89), illustrating the fact that this method can be applied easily by clinicians without the need for a specialized technician.

As mentioned, the significantly lower bone density of the condyle in comparison to the rest of the mandible is one of the main reasons for the difficulty of its segmentation[31]. In this sense, Schlueter et al.[47] performed a validation study with 50 dry human condyles to determine the ideal window for 3D reconstruction of the condyle by CBCT. They found that morphological evaluation of the condyle using CBCT-based 3D reconstructions was most accurate when performed at density levels below those recommended for osseous examination. Based on these findings, we set our HU range in the software below osseous levels. Later, the refinement process was performed, obtaining an excellent intra-examiner (CV=3.65%, ICC=0.97) and good inter-examiner (CV=7.15%, ICC=0.89) reproducibility for condylar volume examination.

Additionally, we observed that, by applying this HU-based segmentation method, the higher susceptibility to segmentation error due to low condylar density could be eliminated. When analyzing the error between examiners for low- and high-density condyles, there was no greater tendency to error when working with low-density bone.

Based on the discussed limitations and the importance of establishing a user-friendly, rapid method accessible to all clinicians involved in condylar morphology analysis, some researchers have made important efforts towards developing efficient techniques. The protocol proposed by Xi et al.[35] , based on 3D region-growing and local thresholding algorithms, reduced time and operator dependence significantly, thereby increasing the method's efficiency. However, their method implies the selection of one seed point every five slides, such that the observer's judgment still plays a fundamental role. Our proposed protocol gives clinicians the opportunity to monitor condylar morphology of orthognathic surgical patients over time in the same software environment used for planning. This makes the suggested method more convenient and effective for the clinician, reducing costs, time, and obviating the need for a dedicated technician.

As noted, excellent intra-examiner and good inter-examiner reproducibility were obtained for condylar volume measurements with an average image processing time of less than 6 minutes – less than half the time required by the fastest segmentation protocol published to date.[35]

In our study, the total volume of the skull after applying the HU range for the condyle was used to test the method. The CV and ICC were 0 and 1 respectively for cranial volume in intra-observer measurements. This means that the error in condylar segmentation occurs during the manual refinement process, not at the time of applying the HU range selected in the software. These results corroborate the fact that, the greater the observer dependence of the process, the greater error accumulation can be expected. Therefore, methods that reduce or eliminate the number of manual interactions[34,35] seem not only to shorten processing time but also to increase the reliability of the method.

In conclusion, the proposed protocol showed excellent intra-observer and good inter-observer reproducibility for 3D assessment of condylar volume. The marked reduction of processing time achieved and the use of one single software to plan and monitor cases over time make the method highly efficient.

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None.

Competing interests

The authors declare no conflicts of interest.

Ethical approval

This study was approved by the Ethics Committees of Teknon Medical Centre and Universitat Internacional de Catalunya.

Patient consent

Not required.

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Tables

	INTRA-OBSERVER			INTER-OBSERVER		
	D	CV (%)	ICC	D	CV (%)	ICC
Cranial volume	0	0	1	16.614.4	2.69	0.983
Condylar volume (mm^3)	55.6	3.65	0.970	109.6	7.15	0.892
Hounsfield units (HU)	8.49	2.54	0.990	16.7	4.98	0.965

Table 1: Intra-observer and inter-observer Dahlberg's D, coefficient of variation (CV), and intraclass correlation coefficients.

SESSION	PARAMETER	N	D	CV (%)
1	Condylar volume (mm^3), low-density group (< 320 HU)	10	98.8	6.35
	Condylar volume (mm^3), high-density group (<320 HU)	10	145.3	9.69
2	Condylar volume (mm^3), low-density group (<320 HU)	10	78.5	5.03
	Condylar volume (mm^3), high-density group (<320 HU)	10	109.1	7.18

Table 2. Inter-examiner differences (1 and 2) between the two-time points of assessment and measurements of condylar volume in two groups of condyles, according to degree of density (low/high). Dahlberg's D and coefficient of variation (CV).

Captions to Illustrations

Figure 1. Head orientation. **A.** Frankfurt horizontal plane for pitch orientation. **B.** Frankfurt horizontal plane for roll orientation. **C.** Yaw orientation was defined by the crista galli and center of the magnum foramen.

Figure 2. Case 2, CBCT. **A.** Axial view of condyles. **B.** Axial view of condyles with Hounsfield scale. **C.** Coronal view of condyles. **D.** Coronal view of condyles with Hounsfield scale. **E.** Sagittal view of condyles. **F.** Sagittal view of condyles with Hounsfield scale.

Figure 3. Semi-automated protocol for condyle segmentation and specific Hounsfield unit scale. **A.** Condyle without automated segmentation by Hounsfield units. **B.** Condyle with automated segmentation by Hounsfield units. **C.** Manual segmentation of the condyle for refinement. **D.** Segmented condyle with confirmation of Hounsfield units.

Figure 1
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Figure 2
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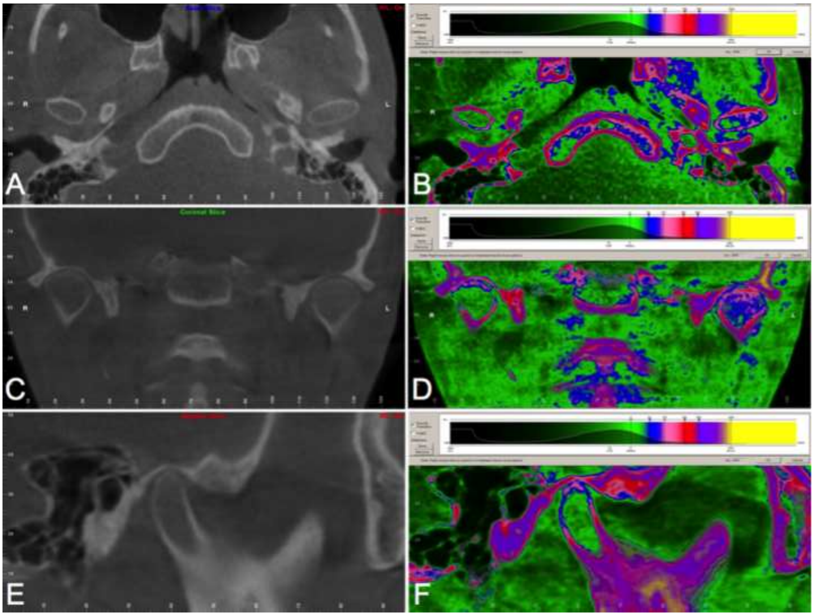
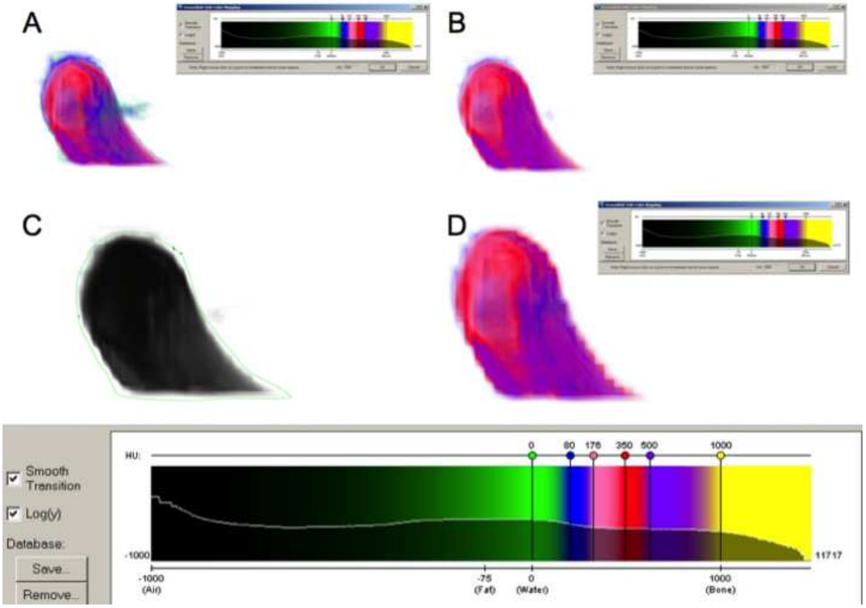


Figure 3



☑ Smooth Transition

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TMJ Disorders

Minimally invasive intraoral condylectomy: proof of concept report

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Abstract. A significant proportion of facial asymmetry cases are caused by abnormal growth of the mandibular condyles. Surgical management is generally based on a condylectomy performed through a pre-auricular transcutaneous access. However, this approach entails potential neurovascular, salivary, and aesthetic complications. In this study, a proof-of-concept evaluation was performed of a novel minimally invasive technique for condylectomy performed through an intraoral approach. Based on precise three-dimensional virtual planning to define intraoperative references, this technique provides an excellent access for total or partial condylectomy through a limited intraoral incision. Piezoelectric surgery with customized attachments enables the safe, accurate execution of the condylectomy. In addition, experience gained in seven consecutive cases suggests that the need for coronoidectomy can be obviated, surgical time is reduced to an average of 16.9 min, and postoperative morbidity is minimal. This alternative intraoral approach could become the treatment of choice for most condylar hyperplastic conditions.

Key words: temporomandibular joint; condylar osteochondroma; condylar hyperplasia; endoscope; intraoral; computer-assisted.

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Generically, condylar hyperplasia (CH) refers to any condition capable of enlarging the mandibular condyle, thereby affecting the size and morphology of the mandible, altering the occlusion, and indirectly affecting the maxilla.[1] A symmetric or most often asymmetric dentofacial deformity can develop as a result. Treatment entails temporomandibular joint (TMJ) surgery to address the underlying pathological condition in the condyle and subsequent or concomitant orthognathic surgery to restore facial harmony and re-establish a functional occlusion.

The conventional approach to the mandibular condyle consists of an extraoral access through a pre-auricular incision.[2–8] This extraoral approach provides excellent visualization of the condyle, condylar neck, and glenoid fossa. Moreover, additional anatomical exposure can be gained by temporal extension, zygomatic arch sectioning, or combination with a submandibular approach.[2,9,10] Due to the proximity to vital anatomical structures, this approach entails a risk of neurovascular complications or salivary fistulae.[5,11–15] It is technically complex, time-consuming, and requires a certain degree of surgical expertise. In addition, the use of an external transcutaneous incision can result in unaesthetic scarring.[11,15]

As an alternative to this extraoral approach, an intraoral access to the condyle is possible.[11,13,15,16] This intraoral approach minimizes the risk of facial nerve injury and salivary fistulae, and visible facial scars are avoided completely.[11,13,15–17] Hence, a rapid postoperative recovery and high patient satisfaction are to be expected. Despite these advantages, the popularity of this approach, as reported in the scientific literature, is

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comparatively low. This is probably due to the lack of a comprehensive description of the surgical technique and the absence of precise treatment planning criteria.

A minimally invasive surgical protocol for intraoral condylectomy is described herein. This novel technique is based on precise three-dimensional (3D) treatment planning and piezoelectric surgical resection of the condylar process using customized attachments. A comprehensive analysis of the authors' preliminary experience with seven consecutive cases is presented as a proof-of-concept demonstration of the feasibility, efficiency, and safety of this technique.

Patients and methods

All patients with facial asymmetry due to abnormal condylar growth, who underwent condylectomy via an intraoral approach at a specialized centre for the treatment of dentofacial deformities, were evaluated prospectively. The Declaration of Helsinki guidelines on medical protocol and ethics were followed at all stages of treatment. The performance of this study did not alter the ethically approved protocol for the diagnosis and treatment of facial asymmetry at the study centre and hence was exempt from the requirement for further ethical approval.

Diagnostic workup and treatment planning

After a detailed interview and thorough clinical assessment, the imaging protocol for facial asymmetry at the study institution was followed. This protocol includes: (1) technetium 99m (^{99m}Tc) scintigraphy, in order to investigate active condylar growth, and (2) cone beam computed tomography (CBCT) (i-CAT version 17–19; Imaging Sciences International, Hatfield, PA, USA) in maximum mouth opening position, in order to evaluate the condylar morphology and the translation in maximum inter-incisal opening. The study centre's standardized scanning protocol for dentofacial deformity patients was used. This protocol comprises vertical (sitting upright) scanning in the 'extended field' mode (field of view (FOV) 17 cm diameter and 22 cm height, scan time 7 s, voxel size 0.4 mm) at 120 kV and 5 mA. Patients were instructed to sit upright and position themselves in natural head position (NHP).

Primary CBCT images were stored as 576 DICOM (Digital Imaging and Communications in Medicine) data files. These were segmented manually and processed using third-party software (SimPlant Pro OMS; Materialise Dental, Leuven, Belgium). A 3D skull model reconstruction was obtained (Fig. 1). The prospective level and orientation of the ostectomy were planned according to the underlying diagnosis and the adjacent anatomical structures, respectively (Fig. 2). A high condylectomy was planned for an anatomically normal condyle, whereas a low condylectomy (at the junction of the condylar head and neck and preserving the condylar neck) was planned for benign tumours. Scanning in maximum mouth opening enabled the surgeon to determine whether the amount of condylar translation in maximum opening would be clearly sufficient to enable the planned resection through an intraoral approach. In addition, the anatomical relationship to the coronoid process was evaluated in terms of potential interference with the surgical access.

Surgical technique

Under general anaesthesia and nasotracheal intubation, maximum mouth opening was forced with a Molt mouth gag fitted with silicone tubing to avoid dental injuries.

A 2-cm vertical incision was made along the anterior border of the ascending mandibular ramus. This incision is similar to that used for a sagittal split osteotomy. Sub-periosteal dissection proceeded cranially towards the coronoid process and then deeply towards the sigmoid notch. The temporalis tendon was dissected from the anterior, lateral, and medial border of the ramus up to the level of the sigmoid notch (Fig. 3). The superior temporalis attachment on the coronoid process above the level of the mandibular notch was preserved completely. If required, a coronoidectomy was performed at this stage using a piezoelectric microsaw (Implant Center 2; Satelec-Acteon Group, Tuttlingen, Germany).

The sub-periosteal dissection along the condylar neck and head was continued up to the inferior joint space, such that the

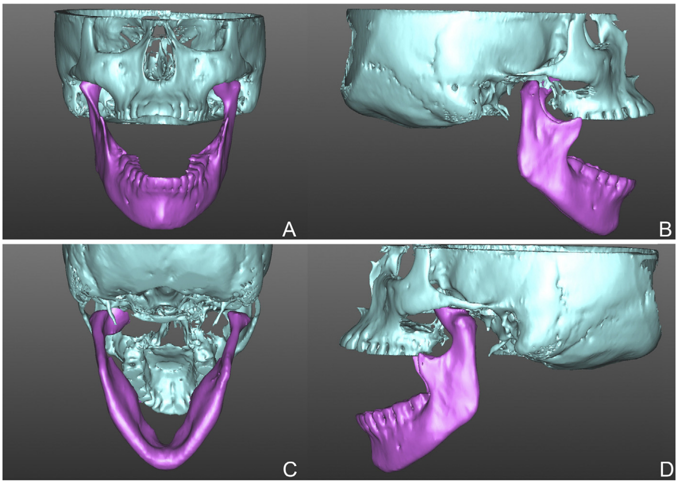

Fig. 1. Three-dimensional skull model in maximum mouth opening. Frontal (A), right profile (B), inferior (C), and left profile (D) views.

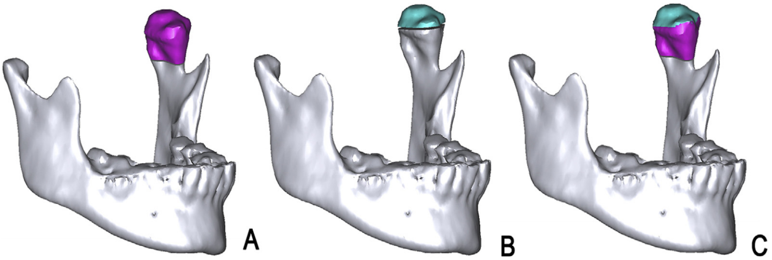

Fig. 2. Treatment planning of the prospective level and orientation of the ostectomy. A low condylectomy (A), high condylectomy (B), and superimposition of both treatment plans (C) are shown. A low condylectomy (A) was performed in this patient.

disc was not disrupted. The same microsaw was used to execute a condylectomy at the planned level and with the anticipated angulation. A specific extra-long customized instrument with a short angulated tip was used for this purpose (Fig. 4). This device enables the surgeon to reach the condylar neck from an intraoral access comfortably while minimizing the soft tissue dissection and allowing a steady execution of the ostectomy. The articular capsule and lateral pterygoid muscle were dissected off the condylar head and neck. At this point, stabilization of the condylar fragment with a temporary screw and wire can facilitate the soft tissue dissection (Fig. 5). After intraoral delivery of the osteotomized fragment, a tension-free watertight soft tissue closure was performed with resorbable 4–0 polyglactin (Vicryl; Ethicon, Somerville, NJ, USA) (Fig. 6). No drainage tubes were left in place.

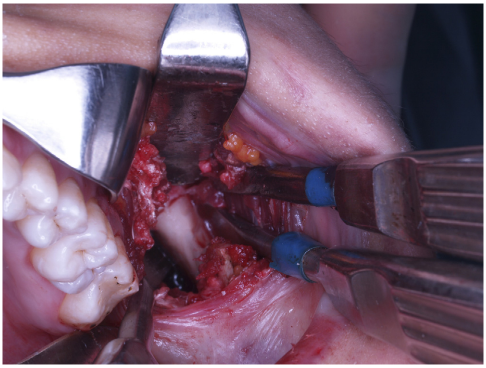

Fig. 3. Sub-periosteal dissection. The temporalis tendon is dissected off the anterior, lateral, and medial borders of the ramus up to the level of the sigmoid notch, with preservation of the superior temporalis attachment on the coronoid process above the level of the mandibular notch.

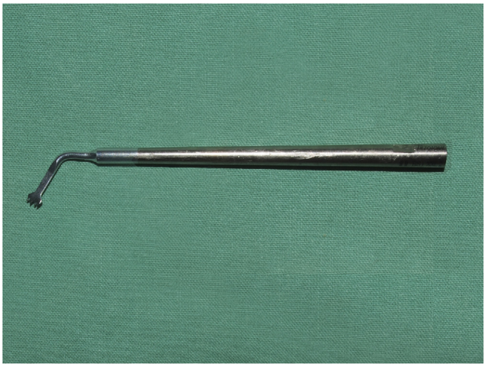

Fig. 4. Extra-long piezoelectric surgery instrument.

Endoscopic assistance may be used throughout the surgical intervention to improve illumination and visualization of the surgical field.

Patients were discharged from the hospital the following day. Average postoperative pain was evaluated on a visual analogue scale (VAS), with a range of 0 (no pain) to 10 (worst pain imaginable). Active physiotherapy was started 3–4 days after surgery to accelerate functional recovery and prevent joint ankylosis.

A complete case example is shown in Fig. 7.

Results

From August 2014 to January 2016, seven patients underwent an intraoral condylectomy at the study centre due to progressive facial asymmetry. The patient demographic characteristics, clinical findings, surgical procedure, pathology results, and postoperative pain levels are summarized in Table 1. Active condylar growth was detected in all cases. The affected joint was on the left side in all patients except one. The underlying cause of the abnormal condylar growth was Wolford CH type 1 in two cases and CH type 2 in the other five.[1]

Chronologically, the first two cases were operated on under endoscopic assistance, and a coronoidectomy was performed in both. In the remaining cases, direct illumination of the surgical field with a headlight was deemed sufficient, and resection of the coronoid process was

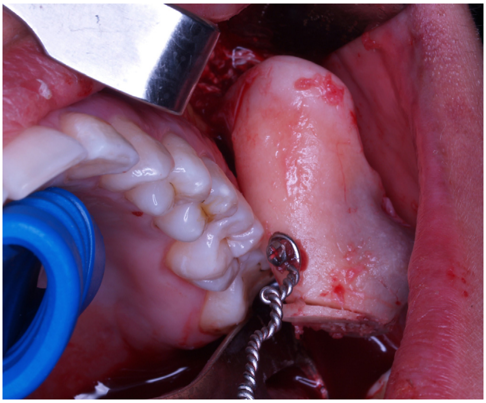

Fig. 5. Temporary stabilization of the condylar fragment with a screw and wire.

obviated. The average duration of surgery from incision to last suture was 16.9 min (range 14–25 min). A progressive reduction in the operation time was observed chronologically from case 1 to case 7.

Postoperative swelling was minimal in all cases. No other complications occurred. The average postsurgical pain on the VAS was 1 (range 0–2). The facial asymmetry was improved markedly immediately after surgery, and a normal, painless maximum mouth opening could be achieved within 48 h with active physiotherapy.

Orthodontic treatment to prepare for subsequent orthognathic surgery was initiated between 1 and 2 weeks after surgery. To date, four patients have undergone orthognathic surgery. The timing of surgery was scheduled according to a ‘surgery late’ protocol (conventional full orthodontic preparation) in three cases and

Table 1. Patient demographic characteristics, clinical findings, surgical procedure, pathology results, and postoperative pain level.

Patient	Age, years	Sex	Clinical findings	Affected side	Coronoidectomy	Endoscopic assistance	Duration of surgery (min)	Pathological findings	Postop. pain (VAS)
1	29	F	Progressive facial asymmetry Chin deviation to the right Ipsilateral and anterior open bite, contralateral crossbite Normal mouth opening	Left	Yes	Yes	25	CH 2	1
2	25	M	Progressive facial asymmetry Chin deviation to the right Ipsilateral open bite Normal mouth opening	Left	Yes	Yes	19	CH 2	2
3	32	F	Progressive facial asymmetry Chin deviation to the right Ipsilateral open bite, contralateral crossbite Normal mouth opening	Left	No	No	16	CH 1	0
4	22	F	Progressive facial asymmetry Chin deviation to the right Ipsilateral and anterior open bite, contralateral crossbite Normal mouth opening	Left	No	No	14	CH1	0
5	42	F	Progressive facial asymmetry Chin deviation to the right Ipsilateral and anterior open bite, contralateral crossbite Normal mouth opening	Left	No	No	15	CH 2	2
6	28	F	Progressive facial asymmetry Chin deviation to the left Contralateral crossbite Normal mouth opening	Right	No	No	15	CH 2	0
7	38	F	Progressive facial asymmetry Chin deviation to the right Ipsilateral open bite, contralateral crossbite Normal mouth opening	Left	No	No	14	CH 2	2

Postop., postoperative; VAS, visual analogue scale (range 0–10); F, female; M, male; CH 1, condylar hyperplasia type 1; CH 2, condylar hyperplasia type 2 (osteochondroma).

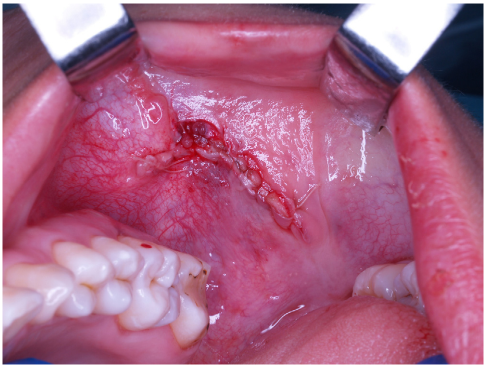

Fig. 6. Wound closure.

a 'surgery early' protocol in one.[18] No recurrence of facial asymmetry has been observed over an average follow-up of 8.7 months (range 2–16 months).

Discussion

In 2013, Wolford proposed a classification system for CH covering all conditions that lead to excessive growth and enlargement of the mandibular condyle and which are therefore potential causes of alterations in the bony architecture of the mandible, malocclusion, and dentofacial deformity.[1] This classification is comprehensive but simple and reflects well the clinical and imaging characteristics, occurrence rate, natural progression, histological particularities, and recommended treatment. In brief, CH type 1 refers to accelerated

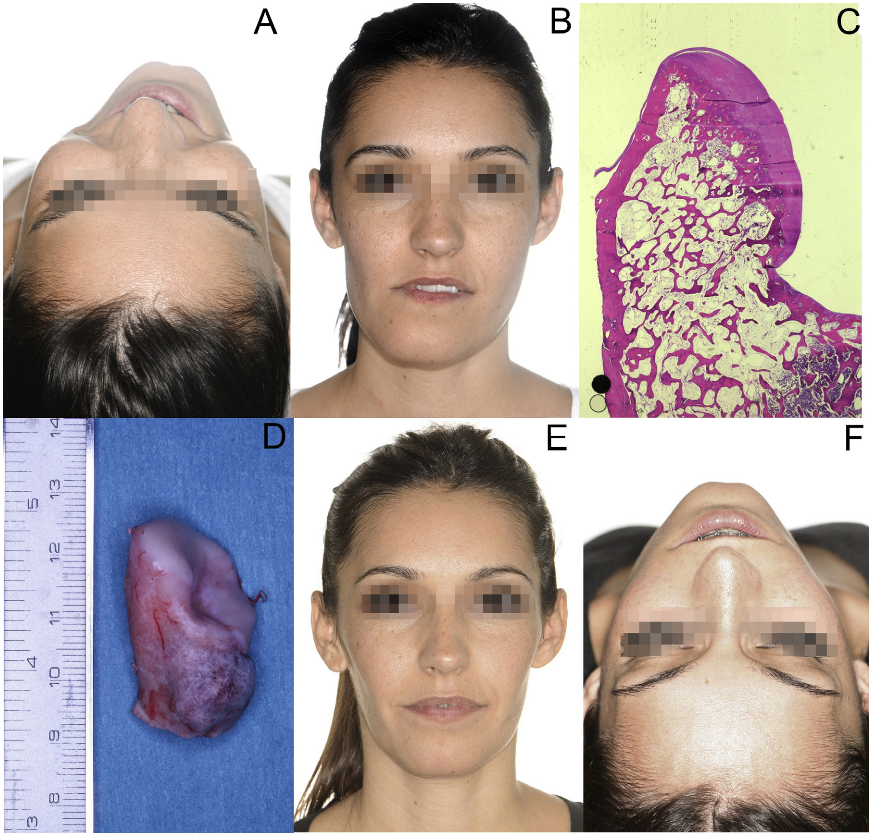

Fig. 7. Facial and pathology images of the patient shown in Figs 1–6. (A) and (B) are preoperative images. (C) and (D) show the pathological analysis, which was compatible with condylar osteochondroma. (E) and (F) show the patient at 3 weeks after surgery.

and prolonged 'normal' growth, CH type 2 corresponds to osteochondroma, CH type 3 includes other types of benign condylar tumours, and CH type 4 comprises malignant condylar tumours.

At the authors' institution, the treatment protocol for facial asymmetry due to CH includes interruption of abnormal condylar growth with a condylectomy and second-stage correction of facial asymmetry with orthognathic surgery. If the patient has completed growth and systemic conditions allow, first-stage surgery is performed as soon as the diagnosis of excessive condylar growth is established. Although it is to be expected that the sooner the condylar growth is normalized the less facial deformity will develop and thus the easier secondary corrective orthognathic surgery will be, in adolescents it seems reasonable to wait for complete contralateral mandibular growth.

The conventional and most common surgical approach to the mandibular condyle is through a pre-auricular incision.[2–8] This approach provides ample exposure of the TMJ hard and soft tissue components and can easily be extended to allow additional exposure of the adjacent anatomical structures.[2,9,10] However, visible unaesthetic facial scars, paresis of the temporal and zygomatic branches of the facial nerve, and salivary fistulae are significant potential complications.[5,11–15] As an alternative, access to the mandibular condyle from an intraoral approach is possible due to condylar translation in maximum mouth opening. This approach minimizes the incidence of neurovascular and salivary complications, avoids the creation of facial scars, and preserves the integrity of the articular capsule, thereby reducing the risk of fibro-osseous TMJ ankylosis.[11,13,15,16] Moreover, taking into account that osteochondromas grow anteromedially in most cases,[8,13] an intraoral approach provides a more direct path to the tumour with less tissue dissection.[11,13] Overall, these advantages result in minimal patient morbidity.[11,13,15,16]

The intraoral route to the mandibular condyle can be contextualized within the current trend for minimally invasive procedures that enable expedited postoperative recovery, and the preferential use of natural orifices for surgical access. It represents the maxillofacial counterpart to the so-called NOTES (natural orifice transluminal endoscopic surgery) in gastrointestinal surgery and interventional gastroenterology. This emerging field in which a scar-less access to the peritoneal cavity is gained via a hollow viscus (mouth, stomach, colon, anus, vagina, urethra, or cystic cavities) has already been used for a variety of diagnostic explorations of the peritoneal cavity, as well as complex organ resections.[19] Potential advantages include the lower anaesthesia requirements, faster recovery and shorter hospital stay, and avoidance of the potential complications of external wounds (including unaesthetic scars and infections).[20]

In this proof-of-concept evaluation of the feasibility of intraoral condylectomy, endoscopic assistance was used in only two cases. Although the spatial orientation and perception of depth can be somewhat difficult in inexperienced hands, the use of an endoscope improves illumination of the surgical field, provides a magnified visualization of the TMJ for the whole surgical team, and may be a useful adjunct, especially for young surgeons. Nevertheless, direct visualization from the surgeon's intraoral viewpoint is sufficient for a safe and accurate execution of the procedure.

The key issue in determining whether a mandibular condylectomy is feasible through an intraoral access is the degree of condylar translation with mouth opening. To this effect, CBCT scanning of the patient in maximum mouth opening was performed. It may be argued that condylar movement can be simulated with treatment planning software, but the authors believe that virtual simulation of condylar rotation and translation is too inaccurate unless sequential scanning at different degrees of mouth opening is performed; however, this practice would be contraindicated ethically.

Additional benefits of 3D virtual planning for the intraoral condylectomy include the determination of the prospective level and orientation of the ostectomy and the potential need for a concomitant coronoidectomy. Regarding the former, it must be noted that, in comparison to other surgical procedures in which 3D planning involves the fabrication of CAD/CAM surgical guides or splints, the authors' virtual planning protocol for intraoral condylectomy does not result in the production of any type of surgical guide. Therefore, the intraoperative design of the condylectomy is not exact but approximate. However, virtual simulation of the level and orientation of the bone cut according to the underlying diagnosis and adjacent anatomical structures helps the surgeon to anticipate each situation individually and precisely.

Although at the beginning of the authors' learning curve an additional coronoidectomy was performed, experience has shown that resection of the coronoid process may be unnecessary. As corroborated with CBCT imaging in maximum mouth opening, full condylar translation provides an adequate obstacle-free route to the condyle without interference from the coronoid in most cases. Furthermore, the anteromedial location of most osteochondromas[8,13] implies excellent exposure of the tumour without the need for coronoidectomy. Increasing surgical experience and the avoidance of coronoidectomy enabled the operative time to be reduced to an average of 16.9 min. Together with a minimally invasive surgical technique, the reduced theatre time was probably responsible for the patients' rapid and uneventful recovery and the low levels of postoperative pain.

It is a general perception that the type of condylectomy should be individualized according to the underlying diagnosis. While CH types 3 and 4 call for an individualized treatment plan according to tumour size and histology, most authors agree that the proliferative zone in CH type 1 can be eliminated adequately with a high condylectomy.[1] In CH type 2, the recommended height of the condylectomy continues to be the subject of debate. A review of the scientific literature found that most osteochondromas were managed with a total condylectomy,[8] but proponents of a more conservative approach refer to the benign nature of the lesion and avoiding TMJ reconstruction to justify a low condylectomy. In a retrospective cohort study of 37 osteochondroma cases with postoperative follow-up averaging 48 months (range 12–288 months), no recurrence occurred after a low condylectomy.[21] The surgical protocol developed by Wolford included ipsilateral reshaping of the condylar neck with disc repositioning and contralateral disc repositioning – when displaced – via a pre-auricular access, and concomitant orthognathic surgery.[21] In the present study, the selected level of resection for the two CH type 2 cases was a low condylectomy. No additional TMJ procedures were performed. Ongoing follow-up will confirm whether the positive results obtained are maintained in the longer term.

In conclusion, compared to the conventional pre-auricular access, an intraoral approach to the mandibular condyle has the potential to minimize the incidence of neurovascular and salivary complications, avoid creating facial scars and opening the articular capsule, and reduce patient morbidity. A minimally invasive protocol for intraoral condylectomy based on precise 3D treatment planning, a reduced incision, and customized piezoelectric surgical instruments has been described herein. The results of the proof-of-concept evaluation suggest that this technique allows reliable and accurate condylar resection and is technically simple and fast, and that patient morbidity is minimal. This alternative approach could become the treatment of choice for most condylar hyperplastic conditions.

Funding

None.

Competing interests

None.

Ethical approval

Exempt.

Patient consent

Patient consent was obtained to publish the clinical photographs.

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APPENDIX 2

Approval of the PhD Thesis Project by the UIC.

Universitat Internacional de Catalunya | Escola de Doctorat

Barcelona, 25 de noviembre de 2013

Sra. Irene Méndez Manjón
Urbanización San Sadurniño c/ as lameiriñas nº47
15894, Teo, A Coruña

Estimada Sra.

Por la presente, le comunico que la Comisión Académica del Doctorado en Ciencias de la Salud, en la su sesión del 12 de noviembre de 2013, y una vez estudiada su solicitud ha acordado:

Se acuerda admitir a la Sra. Irene Méndez Manjón al Periodo de Investigación del Doctorado en Odontologia.

Se acuerda aprobar el Proyecto de Tesis titulado "Evaluación tridimensional de los cambios en la morfología y posición condilar en pacientes sometidos a cirugía ortognática", y nombrar al Dr. Federico Hernández Alfaro como Director de la Tesis.

Adicionalmente, se le informa que la normativa de la UIC establece que debe obtener una evaluación favorable del Comité de Ética en la Investigación, antes de la puesta en marcha de la investigación. Deberá aportar este informe cuando lo obtenga.

Aprovecho la oportunidad para saludarla cordialmente,

Jaime Oliver Serrano
Secretario Comisión Académica
Doctorado en Ciencias de la Salud

Universitat Internacional de Catalunya
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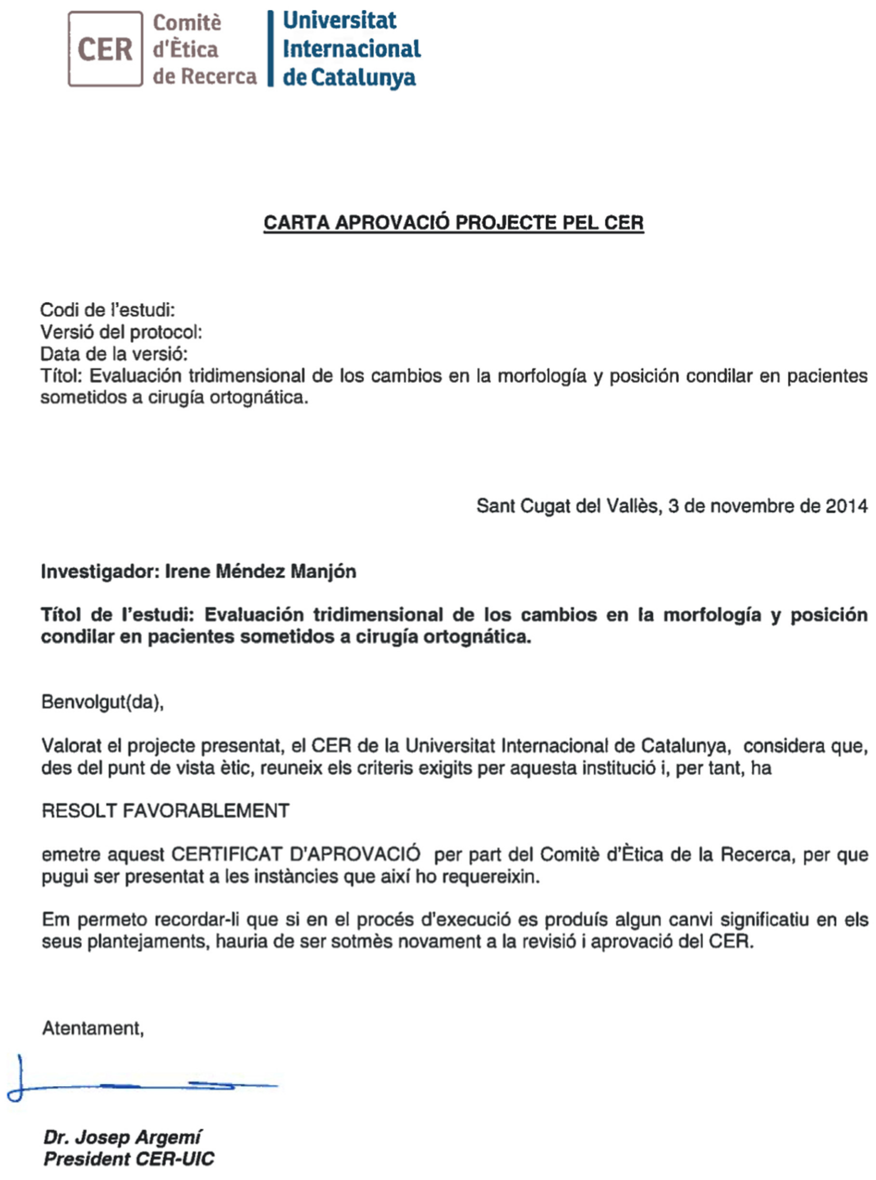
Approval of the PhD Thesis project by the Ethics in Research Committee (Comité d'Ética de Recerca, CER).



CER Comitè d'Ètica de Recerca
Universitat Internacional de Catalunya

CARTA APROVACIÓ PROJECTE PEL CER

Codi de l'estudi:
Versió del protocol:
Data de la versió:
Títol: Evaluación tridimensional de los cambios en la morfología y posición condilar en pacientes sometidos a cirugía ortognática.

Sant Cugat del Vallès, 3 de novembre de 2014

Investigador: Irene Méndez Manjón

Títol de l'estudi: Evaluación tridimensional de los cambios en la morfología y posición condilar en pacientes sometidos a cirugía ortognática.

Benvolgut(da),

Valorat el projecte presentat, el CER de la Universitat Internacional de Catalunya, considera que, des del punt de vista ètic, reuneix els criteris exigits per aquesta institució i, per tant, ha

RESOLT FAVORABLEMENT

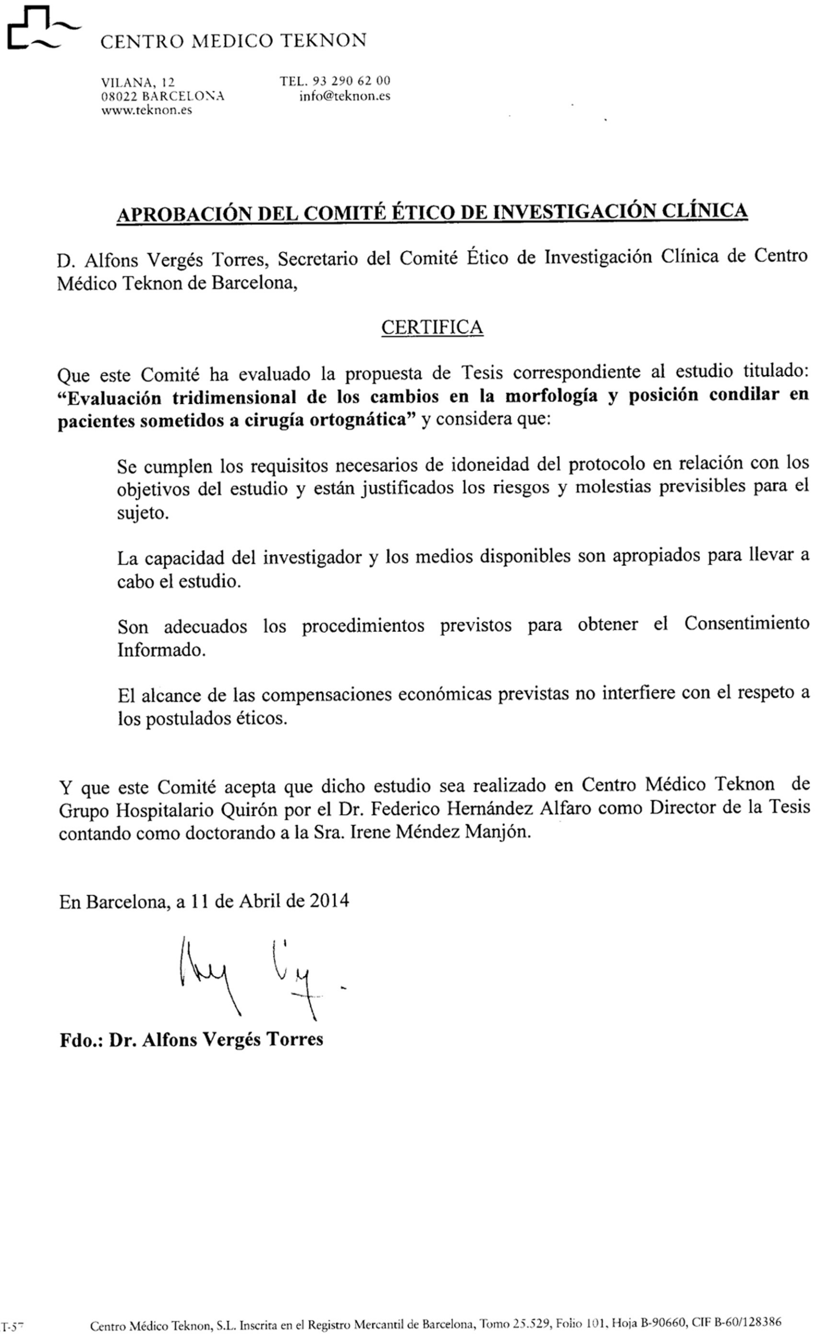
emetre aquest CERTIFICAT D'APROVACIÓ per part del Comitè d'Ètica de la Recerca, per que pugui ser presentat a les instàncies que així ho requereixin.

Em permeto recordar-li que si en el procés d'execució es produís algun canvi significatiu en els seus plantejaments, hauria de ser sotmès novament a la revisió i aprovació del CER.

Atentament,

Dr. Josep Argemí
President CER-UIC

Approval of the PhD Thesis project by the Teknon Medical Center Ethics Committee of Clinical Investigation (Comité Ético de Investigación Clínica, CEIC).



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TEL. 93 290 62 00
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APROBACIÓN DEL COMITÉ ÉTICO DE INVESTIGACIÓN CLÍNICA

D. Alfons Vergés Torres, Secretario del Comité Ético de Investigación Clínica de Centro Médico Teknon de Barcelona,

CERTIFICA

Que este Comité ha evaluado la propuesta de Tesis correspondiente al estudio titulado: **“Evaluación tridimensional de los cambios en la morfología y posición condilar en pacientes sometidos a cirugía ortognática”** y considera que:

> Se cumplen los requisitos necesarios de idoneidad del protocolo en relación con los objetivos del estudio y están justificados los riesgos y molestias previsibles para el sujeto.
>
> La capacidad del investigador y los medios disponibles son apropiados para llevar a cabo el estudio.
>
> Son adecuados los procedimientos previstos para obtener el Consentimiento Informado.
>
> El alcance de las compensaciones económicas previstas no interfiere con el respeto a los postulados éticos.

Y que este Comité acepta que dicho estudio sea realizado en Centro Médico Teknon de Grupo Hospitalario Quirón por el Dr. Federico Hernández Alfaro como Director de la Tesis contando como doctorando a la Sra. Irene Méndez Manjón.

En Barcelona, a 11 de Abril de 2014

Fdo.: Dr. Alfons Vergés Torres

CMT-57 Centro Médico Teknon, S.L. Inscrita en el Registro Mercantil de Barcelona, Tomo 25.529, Folio 101, Hoja B-90660, CIF B-60/128386

Approval of Dr. Raquel Guijarro Martínez as Codirector.

uic Universitat Internacional de Catalunya | Escola de Doctorat

IRENE MÉNDEZ MANJÓN
URB. SAN SADURNIÑO C/AS LAMEIRIÑAS Nº
15894 TEO (A CORUÑA)

Estimada Sra. Méndez

Con la presente, le comunico que la Comisión Académica del Doctorado en Ciencias de la Salud, en su sesión del pasado 8 de julio, y una vez estudiada su solicitud acordó aprobar la inclusión de la Dra. Raquel Guijarro Martínez como Codirectora de su tesis.

Para cualquier cuestión que quieran comentar no duden en ponerse en contacto con nosotros.

Atentamente

Empar Lorda

Empar Lorda
Secretaria de la Comisión Académica Doctorado en Salud
Escuela de Doctorado
Universitat Internacional de Catalunya

Barcelona, 17 de julio de 2014