Efficiency of conventional and computer-assisted implant planning and placement in partially edentulous patients using single splints.

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Eficiencia de la planificación y colocación de implantes convencional y asistida por ordenador en pacientes edéntulos parciales usando férula única.

Tesis Doctoral Europea

Departamento de Cirugía Oral y Maxilofacial

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A todos mis maestros,

por hacer el más generoso gesto: Enseñar.

En especial,

A Raquel, por ser la mejor compañera de clase que se pueda desear.

A mi hermano, que me enseña a ser sensible.

A mis padres, que me han enseñado el significado de la generosidad.

A Nicolás, que me está enseñando a ser padre.

To all my teachers,

for doing the most generous act: Teaching.

Specially,

To Raquel, for being the best classmate anyone could wish.

To my brother, who teaches me how to be affectionate.

To my parents, who have taught me the meaning of generosity.

To Nicolás, who is teaching me how to be a father.

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Preliminary remarks

The present investigation has tried to analyze and compare two implant planning and placement treatment concepts from a holistic approach. Conventional and, more frequently, computer-assisted implant planning and placement protocols have been repeatedly investigated in terms of implant placement accuracy. However, the implant placement precision is only one of the relevant aspects when evaluating an implant planning and placement procedure. Other aspects such as treatment's predictability, complications or unexpected events derived, treatment outcomes, patients' perception, influence on the patient's quality of life, or time and economic costs derived, are identically relevant when assessing the treatment's value. Therefore, the aim of this study was to investigate all of these parameters in order to quantify the treatments' efficiency. For that purpose, the investigation, as well as the way the materials and methods, results and discussion are presented, were categorized into 4 research areas:

- **Clinician-related variables**
- **Patient-related variables**
- **Time and costs**
- **Accuracy**

With the intention to favor the manuscript reading and allow an easier understanding of the different study areas, the investigation categories have been coded in colors to allow the reader to jump from the material and methods section of a particular research topic to the results and thereafter to the discussion section without mixing information from other topics evaluated. In the digital version hyperlinks have been added at the end of each section with that purpose. Due to the wide array of topics assessed, the authors recommend this method of reading the manuscript in order to properly follow the investigation's outcome.

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1. Resumen

Introducción

La colocación de implantes dentales para rehabilitar pacientes con edentulismos parciales o totales se considera un procedimiento rutinario con excelentes porcentajes de éxito a largo plazo(1, 2). La alta predictibilidad de estos resultados se basa en una secuencia de tratamiento protocolizada, que comprende una fase de diagnóstico y planificación, una fase quirúrgica y una fase restauradora.

La fase de diagnóstico preoperatorio implica un detallado análisis protésico, clínico y radiográfico. En este momento, se realiza un set-up protésico que permite predecir el contorno de la futura reconstrucción protésica con el fin de determinar la posición ideal del implante. Este set-up se transforma en una férula radiológica que el paciente porta durante el examen radiográfico. La imagen resultante incorpora la referencia protésica a la imagen radiográfica y permite, conjuntamente con la información obtenida de la exploración clínica, el estudio de la disponibilidad ósea, la identificación de estructuras anatómicas relevantes, y la determinación de la posición y dimensiones del implante a colocar. Posteriormente, el clínico intenta transferir la posición planeada al escenario clínico con la ayuda de una férula quirúrgica convencional, que transfiere la información protésica al campo operatorio.

La capacidad de las radiografías bidimensionales para permitir la planificación y colocación de implantes está ampliamente reconocida(3). No obstante, la incorporación de la técnica de imagen tridimensional (3D) al campo de la Odontología ha mejorado el potencial diagnóstico y ha abierto nuevas perspectivas de tratamiento(4-7). En el campo de la Implantología, ha llevado al desarrollo de protocolos de planificación y colocación de implantes asistida por ordenador (PCIAO). Estos procedimientos implican la determinación 3D de la posición del implante en un software de planificación virtual y la producción de una férula quirúrgica que guía completamente la osteotomía y inserción del implante.

Debido a la visualización 3D y las herramientas de planificación virtual, se asume que los protocolos de PCIAO aportan un mejor potencial diagnóstico y una planificación preoperatoria más detallada. La colocación totalmente guiada del implante debería conllevar una implantación más precisa. Debido a está anticipada mayor precisión, se ha defendido la posibilidad de llevar a cabo cirugías de colocación de implantes sin elevar un colgajo(8-10). Este procedimiento podría acortar los tiempos quirúrgicos y suavizar los periodos postoperatorios de los pacientes(11-13). De la misma manera, la gran precisión de estos protocolos debería permitir al técnico de laboratorio confeccionar preoperatoriamente una prótesis implantosoportada que podría instalarse inmediatamente tras la cirugía y permitir al paciente una función inmediata(14). Desde el punto de vista del clínico, los protocolos PCIAO podrían resultar en procedimientos menos estresantes debido a la mayor información preoperatoria y al fresado e inserción guiada de los implantes. Por último, estos protocolos podrían ejercer una influencia positiva en la percepción del paciente hacia el tratamiento ya que el carácter innovador del procedimiento y la rapidez y menor invasividad quirúrgica, podrían ser factores que actuaran como herramientas de marketing.

A pesar de estas esperadas ventajas, los protocolos de PCIAO pueden conllevar también desventajas como los mayores costes asociados debido a la inversión inicial en el software de planificación, los kits de instrumentos quirúrgicos específicos y los costes derivados de la producción de la férula quirúrgica. Además, han sido descritos complicaciones quirúrgicas y protésicas inherentes a la técnica que podrían suponer una mayor complejidad de ejecución comparado con las técnicas convencionales(15).

En cualquier caso, muchos de los beneficios y deficiencias teóricas de los protocolos de PCIAO no han sido objetivados hasta la fecha(15). Sorprendentemente, esto también es cierto para los protocolos convencionales; no existe prácticamente evidencia científica de la precisión o la relación coste-beneficio de los protocolos de colocación convencional de implantes. En este contexto, se ha desarrollado un estudio para realizar una comparación integral objetiva de ambas estrategias de tratamiento: convencional y asistida por ordenador. Para ello, la eficiencia, o en otras palabras, el ratio de trabajo útil generado por un proceso contrastado con el total de energía invertido en él(16), se consideró el parámetro optimo de comparación. En nuestro marco,

"trabajo útil" comprende todos los parámetros positivos derivados de cada protocolo, mientras que "energía total" corresponde a los costes económicos, procesales o biológicos derivados. Por otro lado, la PCIAO es un concepto muy amplio que engloba un extenso abanico de procedimientos clínicos. Conocemos que determinados factores intrínsecos a la técnica de PCIAO influyen sustancialmente en el resultado final del tratamiento. Por ejemplo, el tipo de soporte de las férulas, la naturaleza y número de férulas usadas o la inserción guiada del implante tienen una influencia significativa en la precisión del procedimiento(17, 18). Por otro lado, la técnica de abordaje al campo operatorio, con o sin colgajo, influye también en el periodo postoperatorio experimentado por el paciente(19). Es por ello, que es imprescindible definir la naturaleza exacta del protocolo a evaluar para obtener resultados representativos. Esta investigación pretende comparar la eficiencia de los protocolos de planificación y colocación de implantes convencionales con los protocolos de PCIAO que conlleven ferula única, dentosoportada, con colgajo y con inserción guiada del implante.

Objetivos e Hipótesis

Objetivo general:

Comparar la eficiencia de la planificación y colocación de implantes convencional con la asistida por ordenador en protocolos que conlleven ferula única, dentosoportada, con colgajo y con inserción guiada del implante.

Objetivos específicos:

- Evaluar el potencial diagnóstico de los diferentes protocolos.
- Determinar las complicaciones y eventos inesperados aparecidos durante las cirugías.
- Evaluar las complicaciones biológicas o mecánicas de los implantes y reconstrucciones realizadas.
- Investigar la percepción del paciente hacia los diferentes protocolos, antes y después del tratamiento.
- Estudiar el periodo intraoperatorio y postoperatorio experimentado por los pacientes.
- Analizar los costes y tiempos derivados de cada paso del tratamiento.
- Evaluar la precisión para transferir la posición del implante planeada a la posición clínica final.

Cada parámetro se evaluará de manera independiente para el protocolo convencional y los 2 protocolos asistidos por ordenador.

Hipótesis Nula (H_0)

Los protocolos de planificación y colocación de implantes convencionales son tan eficientes como los protocolos PCIAO cuando se evalúan procedimientos con férula única, dentosoportada, con colgajo y con inserción guiada del implante. Ambos protocolos presentan similares:

- Potencial diagnóstico
- Porcentaje de complicaciones o eventos inesperados durante la cirugía implantológica.

- Número de complicaciones mecánicas o biológicas de los implantes o reconstrucciones protésicas.
- Percepción del tratamiento por parte del paciente, antes o después de recibir el mismo.
- Periodos intraoperatorios o postoperatorios experimentados por los pacientes.
- Tiempos y costes derivados de cada paso del tratamiento.
- Precisión para transferir la posición del implante planeada a la posición clínica final.

Hipótesis alternativa (H_1)

Los protocolos de planificación y colocación de implantes convencionales son menos eficientes que los protocolos PCIAO cuando se evalúan procedimientos con férula única, dento-retenida, con colgajo y con inserción guiada del implante. Los protocolos PCIAO presentan:

- Mejor potencial diagnóstico.
- Menor porcentaje de complicaciones o eventos inesperados durante la cirugía implantológica.
- Menor número de complicaciones mecánicas o biológicas de los implantes o reconstrucciones protésicas.
- Mejor percepción del tratamiento por parte del paciente, antes o después de recibir el mismo.
- Mejores periodos intraoperatorios o postoperatorios experimentados por los pacientes.
- Menores tiempos y costes derivados de cada paso del tratamiento.
- Mayor precisión para transferir la posición del implante planeada a la posición clínica final.

Metodología y Resultados.

Diseño: Ensayo clínico controlado randomizado con 3 grupos:

- Grupo Control: Planificación y colocación de implantes convencional: estudio radiográfico bidimensional utilizando férula radiológica, planificación de la posición del implante en negatoscopio, producción de férula quirúrgica por el técnico de laboratorio, colocación de implantes convencional.
- Grupo Test 1: Planificación y colocación de implantes asistida por ordenador siguiendo el protocolo Simplant (SimPlant, Materalise, Leuven, Belgium): estudio radiográfico tridimensional utilizando férula radiológica, planificación de la posición del implante con el software Simplant (Materalise, Leuven, Belgium), producción de férula quirúrgica por Materialise (Materalise, Leuven, Belgium), colocación de implantes utilizado férula quirúrgica guiada.
- Grupo Test 2: Planificación y colocación de implantes asistida por ordenador siguiendo protocolo SwissMeda (SwissMeda, Zürich, Switzerland): estudio radiográfico tridimensional sin férula radiológica, escaneado óptico de encerado diagnóstico y superimposición al estudio radiológico en software SMOP (SMOP, SwissMeda, Zürich, Switzerland), planificación de la posición del implantes con el software SMOP (SMOP, SwissMeda, Zürich, Switzerland), producción de férula quirúrgica por impresión 3D, colocación de implantes utilizando férula quirúrgica guiada.

Muestra: 75 edéntulos parciales buscando rehabilitación protética implantosoportada (25 participantes por grupo).

Criterios de inclusión:

- Pacientes parcialmente edéntulos buscando una rehabilitación protésica implanto-soportada.
- El edentulismo de los pacientes debe permitir un asentamiento de la férula quirúrgica dentosoportado para asegurar la estabilidad durante el fresado y colocación del implante.

Evaluaciones y resultados

Debido a la diversidad de factores analizados para cada protocolo, se decidió categorizar las evaluaciones y resultados en grupos con el fin de facilitar la comprensión lectora del documento. Las variables fueron agrupadas en:

- Variables relacionadas con el clínico
- Variables relacionadas con el paciente
- Análisis de tiempos y costes
- Análisis de precisión

Variables relacionadas con el clínico

Predictibilidad del plan quirúrgico

Para evaluar el potencial diagnóstico de los diferentes protocolos de tratamiento se les pidió a los operadores que predijeran el tipo de anatomía ósea de la zona a implantar, así como el tipo y dimensiones del implante y materiales necesarios para la regeneración ósea si esta fuese necesaria. Posteriormente se recogieron los parámetros reales durante la cirugía de colocación de implantes y se compararon ambos resultados. Para determinar el potencial predictivo de los diferentes protocolos se realizaron test Kappa.

Los resultados demostraron que los protocolos donde la planificación se realizaba mediante un examen radiográfico tridimensional y un software de planificación virtual ofrecían mayor predictibilidad a la hora de conocer el tipo de defecto óseo esperado y el tipo y cantidad de material necesario para llevar a cabo la regeneración ósea. También permitieron predecir con mayor exactitud la longitud final del implante. Los resultados sugieren que la evaluación radiográfica tridimensional permite una mejor visualización del volumen óseo disponible y una mayor predictibilidad del plan quirúrgico.

Complicaciones y eventos inesperados intraoperatorios

Se recogieron todos las complicaciones quirúrgicas o cambios en el protocolo de tratamiento que aparecieron durante las cirugías de colocación de implantes.

Cualquier problema relacionado con las férulas también fue reflejado, así como los tiempos necesarios para solucionar el problema.

Los resultados se analizaron con estadística descriptiva y las diferencias entre grupos se evaluaron mediante tests de Chi cuadrado para variables cualitativas y mediante tests de Kruskal-Wallis para variables continuas. Para los tests post-hoc, se aplicó el test de Mann-Whitney con la corrección de Bonferroni ($p<0.016 = 0.05/3$).

El porcentaje de complicaciones y eventos inesperados fue alto para los 3 grupos. Las incidencias pudieron categorizarse en incidencias relacionadas con las férulas quirúrgicas y cambios voluntarios en el protocolo quirúrgico para ajustar posiciones subóptimas de implantes. Los protocolos convencionales tuvieron menos incidencias relacionadas con las férulas que los protocolos asistidos por ordenador. Las incidencias relacionadas con las férulas en los protocolos de PCIAO se debían mayormente a desajustes entre la férula y los dientes del paciente. Basados en la alta incidencia de modificaciones intraoperatorias del protocolo quirúrgico, se concluyo que la confianza ciega en la férula quirúrgica podría conllevar el posicionamiento de los implantes en localizaciones subóptimas. Una estricta monitorización de cada paso quirúrgico para comprobar la idoneidad de la posición del implante es recomendable en ambos protocolos, tanto convencional como asistido por ordenador.

Implantes y reconstrucciones protésicas

Se recogieron todas las incidencias biológicas y mecánicas relacionadas con los implantes o reconstrucciones protésicas desde la colocación de los implantes hasta la entrega de la reconstrucción final.

Los resultados se analizaron con estadística descriptiva y las diferencias entre grupos se evaluaron mediante tests de Chi cuadrado para variables cualitativas y mediante tests de Kruskal-Wallis para variables continuas. Para los tests post-hoc, se aplicó el test de Mann-Whitney con la corrección de Bonferroni ($p<0.016 = 0.05/3$).

Todos los implantes pudieron ser colocados en una posición compatible con la oseointegración y con la obtención de una rehabilitación protésica que cumpliera

todos los requisitos funcionales, higiénicos y estéticos independientemente del protocolo terapéutico utilizado.

Variables relacionadas con el paciente

Percepción del tratamiento por parte del paciente

Con la intención de sondear la percepción de los pacientes hacia los diferentes protocolos de planificación y colocación de implantes, antes de empezar el tratamiento se realizó la siguiente pregunta de respuesta múltiple: "¿Qué tipo de tratamiento preferiría recibir?" Las posibles respuestas fueron: Protocolo convencional, protocolo asistido por ordenador o sin preferencia. Para homogeneizar la información preoperatoria emitida, los pacientes recibieron un documento de información donde se describían de una manera estandarizada los funcionamientos de los protocolos convencionales y de los asistidos por ordenador (apéndice I). La misma pregunta fue contestada por los pacientes en el postoperatorio inmediato tras la colocación de implantes.

Las frecuencias de respuesta se categorizaron según grupo de estudio.

Los pacientes manifestaron una mejor percepción de tratamiento con los protocolos asistidos por ordenador antes y después del tratamiento.

Confort intraoperatorio y morbilidad postoperatoria

Para evaluar el confort intraoperatorio experimentado por los pacientes se pidió que rellenaran un cuestionario en el postoperatorio inmediato. En él se preguntaba acerca de la duración de tratamiento y grado de confort y dolor percibidos durante el procedimiento quirúrgico.

Durante los primeros 7 días postoperatorios, los pacientes cumplimentaron otro cuestionario para evaluar el grado de afectación de su calidad de vida provocado por la cirugía. Para cuantificar sus respuestas se utilizaron escalas analógicas visuales de 100mm. Los parámetros estudiados fueron:

- Masticación
- Apertura bucal

- Habla
- Sueño
- Trabajo
- Actividades diarias
- Interacción social
- Actividades favoritas

También se recogieron las evaluaciones de los signos y síntomas experimentados por los pacientes:

- Inflamación
- Hematoma
- Sangrado
- Nausea
- Mal sabor
- Dolor medio
- Dolor máximo
- Influencia general en sus actividades diarias
- Número de analgésicos consumidos

Las diferencias entre las medianas se analizaron mediante un test de Kruskal-Wallis. Para los test post-hoc, se aplicó el test de Mann-Whitney con la corrección de Bonferroni ($p<0.016 = 0.05/3$). Las diferencias entre medias se analizaron mediante un análisis de varianza (ANOVA) y un test post-hoc de Bonferroni (Sheffé). Al evaluar otros factores predictores, se consideró una regresión lineal múltiple.

Para evaluar la evolución de los resultados en el tiempo, se emplearon tests ANOVA de medidas repetidas combinados con la corrección para valores p de Greenhouse-Geisser. Para evaluar cada periodo de tiempo de manera independiente, se emplearon tests de Kruskal-Wallis. Para los test post-hoc, se aplicó el test de Mann-Whitney con la corrección de Bonferroni ($p<0.016 = 0.05/3$).

No se encontraron diferencias estadísticamente significativas entre grupos para los parámetros de afectación de la calidad de vida intraoperatorios o postoperatorios.

Los pacientes presentaron niveles bajos de dolor y malestar intraoperatorios y la duración del tratamiento fue similar a su percepción. La cirugía influenció la calidad de vida de los pacientes especialmente durante los primeros 4 días. Para la mayoría de variables estudiadas los signos y síntomas fueron máximos durante el primer día postoperatorio y fueron reduciéndose progresivamente.

Análisis de tiempos y costes

Se recogieron todos los tiempos y costes derivados de cada paso terapéutico (planificación protésica, examen radiográfico, planificación quirúrgica, producción de la férula quirúrgica, cirugía de colocación de implantes). Los resultados se presentaron en tablas y gráficas categorizadas según grupo de estudio.

Los protocolos de PCIAO y convencionales requirieron tiempos similares para la toma de registros, examen radiográfico, y colocación de los implantes. No obstante los protocolos computadorizados requirieron mayores tiempos de planificación y mayores tiempos de espera para la producción de la férula quirúrgica. Los costes económicos fueron también mayores para los protocolos de PCIAO debido mayormente a los costes de producción de la férula quirúrgica, a la inversión inicial necesaria para la adquisición de la licencia del software de planificación y a los costes derivados de la adquisición de los juegos de instrumental quirúrgico necesarios para llevar a cabo la cirugía guiada.

Análisis de precisión

Para evaluar la precisión para transferir la posición planeada del implante a la posición clínica final se utilizó un software de fusión de imágenes (SMOP, SwissMeda, Zürich, Suiza) que solapaba la posición del implante planeada con la posición clínica final. Dicho software permite la fusión de ficheros DICOM y ficheros STL y analiza las desviaciones entre dos posiciones virtuales de implantes.

Se utilizó la férula quirúrgica como unidad de estudio por lo que sólo se consideró un único implante por paciente (el más mesial) para evaluar precisión.

Debido a que el protocolo convencional no incluía el estudio radiográfico tridimensional, la posición basal para este grupo se obtuvo mediante la planificación virtual de un implante en un fichero STL obtenido a partir del modelo de estudio inicial

con el encerado diagnóstico. El implanté se colocó siguiendo directrices protésicas con el objetivo de realizar una reconstrucción atornillada. En los grupos test, la posición basal se derivó de la posición del implante determinada durante la planificación virtual que a su vez se utilizó como referencia para la fabricación de la férula quirúrgica.

Para evitar tener que irradiar al paciente de nuevo al final del tratamiento, la posición del implante final se obtuvo mediante el escaneado óptico del modelo maestro con postes de escaneado. Este proceso produjo un modelo STL con la posición final del implante derivada del poste de impresión óptica.

La posición basal y la final se superpusieron mediante el software mencionado y se obtuvieron valores numéricos de las desviaciones entre la posición planeada y la final. Se eligieron 3 planos para evaluar desviaciones: plano oclusal, hombro del implante y ápice del implante. También se reflejaron discrepancias en la angulación y en la posición vertical del implante.

Se realizó un análisis descriptivo de los datos tanto para los valores globales, como para su fragmentación en vectores: mesio-distal y vestíbulo-oral. Para estudiar las diferencias de precisión entre grupos se utilizó un análisis de varianza con el test post hoc de Sheffé. Las variables de confusión fueron analizadas mediante regresión lineal múltiple. Para variables dicotómicas se empleo el test de Chi cuadrado.

Al comparar los dos grupos asistidos por ordenador, no se observaron diferencias para ningún parámetro de precisión evaluado. Cuando estos resultados se compararon con los obtenidos por el protocolo convencional, aparecieron diferencias estadísticamente significativas. La precisión global del protocolo convencional era más baja a nivel del hombro del implante, del ápice y de la angulación. No obstante, estas diferencias pueden achacarse más a un error metodológico que a la imprecisión de un tratamiento concreto. La determinación de la posición basal del implante en el grupo control resultó imprecisa. Ésta se realizó de manera virtual sobre un archivo STL del modelo de estudio con el encerado diagnóstico, sin incorporar ningún tipo de información ósea. La falta de parámetros radiográficos hizo que existiesen múltiples posiciones del implante compatibles con los parámetros protésicos determinados por la silueta generada por el encerado diagnóstico. Esto hizo que la posición determinada

fuera ambigua e impide la comparación con los otros 2 grupos de estudio. El único nivel en el que la comparación podría contemplarse sería a nivel occlusal, ya que la emergencia del eje del implante por el centro de la cara oclusal es un parámetro totalmente determinado por la prótesis. Corroborando la teoría del fallo metodológico, en este plano no existieron diferencias entre grupos. Es más, el hecho de que todos los implantes colocados con este protocolo pudieron ser restaurados con prótesis atornilladas que cumplían con los estándares de estética, función e higiene reafirman esta idea.

Conclusiones.

El exhaustivo estudio de los beneficios y costes derivados de los protocolos de planificación y colocación de implantes convencional y asistida por ordenador en casos con férula única, dentosoportada, con colgajo y con inserción guiada del implante ha desvelado diferencias entre grupos que otorgan a los protocolos de PCIAO un mayor potencial diagnóstico preoperatorio y una mejor percepción del tratamiento por parte del paciente, mientras que conllevan mayores gastos económicos y una mayor inversión en tiempo para llevarlos a cabo.

2. Introduction

The placement of dental implants to prosthetically restore partially and totally edentulous patients is considered to be a routine procedure with excellent long-term success rates(1, 2). Highly predictable results are obtained by the implementation of a protocolized treatment sequence, which involves a planning, surgical, and restorative phase.

The preoperative diagnostic phase implies a thorough prosthetic, clinical, and radiographic analysis. A prosthetic diagnostic set-up that predicts the contour of the prospective reconstruction is performed in order to optimize the determination of the ideal implant position. This set-up is then transformed into a radiographic splint that is worn by the patient during the radiographic examination. The resulting image incorporates the prosthetic reference into the radiographic dataset and enables, in conjunction with the information obtained from clinical examination, the study of the availability of bone, identification of relevant anatomic structures, and determination of the dimensions and position of the implants to be inserted. Subsequently, the operator attempts to transfer the planned position to the clinical scenario with the aid of a conventional surgical guide, which transfers the prosthetic information to the surgical field.

The adequacy of two-dimensional radiographs to provide the preoperative radiographic data required for implant placement planning is widely acknowledged(3). However, the incorporation of three-dimensional (3D) imaging to the field of Dentistry has significantly enhanced imaging potential and has opened new treatment perspectives(5-7). Particularly in Implant Dentistry, it has led to the development of computer-assisted implant planning and placement (CAIPP) protocols. These methodologies imply the 3D definition of implant position with virtual planning software and the subsequent production of surgical splints that fully guide implant osteotomy and placement.

Due to the 3D imaging and virtual planning tools, it is assumed that CAIPP protocols enable a more detailed diagnosis and preoperative planning. Fully guided implant osteotomy and insertion are expected to give way to a more accurate implantation procedure. As a result of this anticipated high accuracy, a flapless surgical approach has been advocated(8-10). This approach may speed the surgical procedure and grant a milder postoperative period for the patient(11, 12, 20). Similarly, the high precision to transfer the preoperatively planned implant position to the clinical scenario should allow the technician to preoperatively confection an implant-supported prosthesis that could be delivered immediately after surgery and allow immediate function(14). From the clinician's perspective, CAIPP protocols could result in less stressful procedures due to improved preoperative preparation and bur guidance. Finally, these protocols may have a positive influence in patients' perception of the treatment due to the innovativeness of the procedure and possibly faster and less invasive surgeries, factors that could act as a marketing tool.

Despite these expected advantages, CAIPP protocols may also entail some shortcomings such as increased economical costs due to the initial investment needed for the planning software, specific surgical kits, and splint-derived expenses. In addition, it has been pointed out that guided surgery may imply inherent surgical and prosthetic complications that could make these procedures more demanding than conventional approaches(15).

In any case, an evidence-based analysis of the aforementioned theoretical benefits and pitfalls of CAIPP protocols is lacking(15). Surprisingly, this is also true for conventional protocols; there is practically no scientific evidence on the accuracy or cost-benefit ratio of conventional implant placement protocols. In this context, an investigation was designed to perform a comprehensive comparison of both treatment strategies – conventional and computer-assisted – in an objective manner. To this effect, efficiency, that is, the ratio of the useful work performed by a process to the total energy expended in it(16), was considered an optimal parameter for comparison. In our setting, "useful work" comprised all positive outcomes derived from each protocol, while "total energy" corresponded to economical, procedural, and biological costs. However, CAIPP

is a broad concept that encloses a numerous array of clinical procedures. Several factors such as surgical splint support, nature and number of splints used, guided implant insertion or the capability to perform flapless surgeries, have proven to significantly influence the treatment outcome(15, 17, 18). Therefore, it is necessary to define the specific nature of the protocol to be evaluated. The aim of the present investigation was to compare the efficiency of conventional implant planning and placement protocols versus CAIPP protocols that involve tooth-supported, single-splint, guided implant insertion, open-flap procedures.

3. Aims

The aims of the investigation can be classified as follows:

3.1. General aim:

To compare the efficiency of conventional versus CAIPP protocols that involve tooth-supported, single-splint, guided implant insertion, open-flap procedures.

3.2. Specific aims:

1. To study the treatment's diagnostic potential.
2. To assess the complications and unexpected events encountered during implant surgery.
3. To identify failures of the implants and reconstructions placed.
4. To evaluate patients' treatment perception before and after the treatment.
5. To evaluate the intraoperative and postoperative periods experienced by the patients.
6. To analyze the time and costs derived from each treatment step.
7. To evaluate the accuracy to transfer the planned implant position to the final clinical position and the impact on the prosthetic outcome.

Each of these parameters will be tested separately for the conventional and CAIPP protocols.

4. Hypothesis

4.1 Null hypothesis (H_0)

Conventional implant planning and placement protocols are as efficient as CAIPP protocols when tooth-supported, single-splint, open-flap procedures are evaluated. Both protocols present comparable:

- Diagnostic potential.
- Rate of complications and unexpected events encountered during implant surgery.
- Number of biological and mechanical failures of implants and reconstructions placed.
- Patients' treatment perception before and after the treatment.
- Intraoperative and postoperative periods experienced by the patients.
- Time and costs derived from each treatment step.
- Accuracy when transfering the planned implant position to the final clinical position.

4.2 Alternative hypothesis (H_1)

Conventional implant planning and placement protocols are less efficient than CAIPP protocols when tooth-supported, single-splint, open-flap procedures are evaluated. CAIPP protocols present:

- Better diagnostic potential.
- Lower rate of complications and unexpected events encountered during implant surgery.
- Lower number of biological and mechanical failures of implants and reconstructions placed.
- Better patients' treatment perception before and after the treatment.

- Milder intraoperative and postoperative periods experienced by the patients.
- Less time and costs derived from each treatment step.
- Better accuracy to transfer the planned implant position to the final clinical position.

5. Materials and Methods

5.1. Study type:

The study was designed as a randomized clinical trial comparing three treatment groups: a control group represented by the conventional implant planning and placement protocol and two test groups represented by two different CAIPP protocols.

5.2. Patients:

The studied population included partially edentulous patients referred to the Department of Fixed and Removable Prosthodontics and Material Sciences of the Dental School of the University of Zürich for an implant-borne prosthetic restoration.

5.2.1. Inclusion criteria:

The following inclusion criteria were defined:

1. Adult patients (age 18 years or above).
2. Partial edentulism.
3. Informed written consent to participate in this investigation.

5.2.2. Exclusion criteria:

The following exclusion criteria were defined:

1. General contraindications for implant surgery
2. Remaining dentition that did not allow adequate stability for a tooth-supported radiologic template or surgical guide.

3. Changes in the residual dentition during the prosthetic treatment (full coverage reconstructions, orthodontic movements) that render the matching of the initial and final dental conditions impossible for the superimposition software.
4. Refusal to participate in this investigation.

5.2.3. Sample size calculation:

Sample size calculation was performed taking into consideration the following study outcomes: accuracy and costs. For both variables, a significance level of 95% and a power level of 80% were defined. The expected difference between groups in terms of accuracy was 1 mm with a standard deviation (SD) of 1 mm. For economical analysis a difference of 500 Swiss Francs (CHF) was considered relevant with a SD of 200 CHF.

Results of sample size calculation yielded 17 patients per group for accuracy and 15 per group for costs. Since an expected drop-out rate of 10% was determined, the final sample size comprised 25 patients per group.

5.2.4. Ethical approval and patient consent:

The study protocol was approved by the Ethics Review Board of the University of Zurich and of the International University of Catalonia, and was conducted in accordance with the Helsinki declaration.

All patients received detailed information on the study design and accepted to participate by signing an informed consent.

5.3. Materials:

Three treatment groups were studied: a conventional implant planning and placement protocol and two different CAIPP protocols. Two CAIPP protocols were analyzed and compared separately because they presented significant differences in terms of incorporation of the prosthetic reference to the implant planning software and in template design and production.

The conventional protocol consisted in implant planning based on a clinical evaluation combined with a 2D radiographic exam, and freehand implant placement supported by a conventional surgical splint.

In both computer-assisted protocols, a 3D radiographic exam was implemented and the implants were planned using a virtual planning software. The 3D-planned implants allowed for the production of a computer-assisted manufacturing (CAM) surgical splint that fully guided implant bed preparation and implant insertion.

5.4. Interventions:

5.4.1. Control group:

After a comprehensive anamnesis and clinical examination, preoperative pictures and alginate impressions were taken. The laboratory technician produced study plaster models that were mounted into a semiadjustable articulator. The ideal contour of the teeth to be replaced were modeled in wax, and an acrylic radiographic splint with radiopaque markers was confectioned. The radiographic template was tried in and adjusted, if necessary, to ensure a perfect fit before the radiographic examination. A panoramic X-ray was performed with the radiographic splint in place. The radiographic image with the prosthetic reference plus the study models and clinical pictures were used to plan the implant dimensions and positions. Based on the radiographic and clinical analysis, the clinician was asked to foresee specific surgically relevant aspects including intraoperative anatomy as well as materials and methods to be used during surgery. Implant brand selection (Dentsply-Astra (Mölndal, Sweden) or Straumann (Basel, Switzerland)) was randomized using a computer-generated list. The implant silhouettes were drawn on an acetate foil pasted over the X-ray on a light table. The radiographic splint was designed in a way that it could subsequently be used intrasurgically as a surgical splint reflecting the prospective prosthetic goal.

On the day of the surgical intervention, patients received oral analgesic and antibiotic prophylaxis (Diclofenac 50 mg and Amoxicillin 1500 mg) thirty minutes

before surgery. Following local anesthesia, a flap was elevated and the implant bed prepared according to the implant manufacturer's recommendations. The orientation of the osteotomy was strictly monitored intraoperatively using direction indicators, the surgical guide, and anatomical references (adjacent and opposing teeth). If needed, concomitant bone regeneration procedures were performed. Wounds were closed with non-resorbable interrupted sutures (Goretex, Arizona, USA). Postoperative medical instructions included the administration of antibiotics (Amoxicillin 750 mg every 8 hours during 4 days), anti-inflammatory/analgesic drugs (Diclofenac 50 mg every 8 hours on demand), and an antiseptic mouth rinse (0.12% Chlorhexidine 1 rinse every 12 hours during 15 days).

5.4.2. Test group 1:

Identical workup steps to those described for the conventional group were followed until the radiographic examination was reached. In test group 1 a cone-beam computed tomography (CBCT) was performed with the radiographic splint seated on the remaining dentition. The machine used was a 3D eXam CBCT machine (KaVo Dental GmbH, Biberach, Germany), which is a version of i-CAT Next Generation scanner (Imaging Sciences International, Hatfield, PA, USA). The CBCT scans were obtained with the following parameters: 120 kV acceleration voltage, 5 mA beam current, FOV diameter of 16 cm, FOV height of 6 cm, 600 projections, 360˚ rotation, voxel size of 0.25 mm and scan time of 26 seconds. The DICOM (Digital Imaging and Communications in Medicine) data thus generated were imported to an implant planning software (SimPlant, Materalise, Leuven, Belgium), where the implants were planned three-dimensionally according to prosthetic and anatomic parameters. In order to standardize time measurements, all plans were performed by a single investigator with extensive experience in CAIPP protocols and the specific planning software used, always in collaboration with the designated surgeon. Based on this planning, a single surgical guide was ordered online and subsequently produced via stereolithographic means by an external manufacturer (Materalise, Leuven, Belgium). A surface scan of the study model was performed (IScan D104, Imetric; Courgenay, Switzerland) and sent to the manufacturer to complete the surgical splint design. The delivered surgical guides

included metallic sleeves to allow for drilling and implant guidance based on a sleeve-in-sleeve concept. Two different guided implant systems were used (Straumann® Guided Surgery (Straumann, Basel, Switzerland) and Facilitate™ (Dentsply, Mölndal, Sweden)).

The preoperative protocol and flap design were identical to those employed for the control group. Implant bed preparation was fully guided by the surgical splint, but a strict implant osteotomy orientation monitoring was performed using implant direction indicators and adjacent anatomic references during the drilling sequence. Bone augmentation, wound suturing, and postoperative medication protocols were identical to the control group.

5.4.3. Test group 2:

Identical workup steps to those described for the conventional group were followed until the radiographic examination was reached. In test group 2, no radiographic splint was used; CBCT imaging was performed without any prosthetic reference. Alternatively, the study model with the prosthetic wax-up and the original model without the wax-up were optically scanned (IScan D104, Imetric; Courgenay, Switzerland) and the digital files thus generated (in surface tesselation language (STL) format) were matched to the radiographic CBCT data (in DICOM format) using another implant planning software (SMOP, SwissMeda, Zürich, Switzerland). The SMOP software allows the clinician to merge the silhouette of the dentition and soft tissues in the digitized models with the dentition and tissues in the radiographic image and to plan the implant positions according to the prosthetic set-up. All implants were planned by a single investigator and the designated surgeon in the same manner as in test group 1. According to the planned implant positions, a surgical guide design was generated by the software planning company (SwissMeda, Zürich, Switzerland) and printed in-house using a 3D printer (Objet Eden 260V, Stratasys; Eden Prarie, USA). This printed surgical guide incorporated no metallic sleeves in order to minimize the surgical guide-drill key tolerance (21).

The preoperative protocol and flap design were identical to those employed for the control group. Implant bed preparation was fully guided by the surgical splint, but a strict implant osteotomy orientation monitoring was performed using implant direction indicators and adjacent anatomic references during the drilling sequence. Bone augmentation, wound suturing, and postoperative medication protocols were identical to the control group.

5.5. Evaluations and statistics:

The comprehensive nature of the present comparison between conventional and CAIPP protocols required the evaluation of an array of diverse treatment traits. For structural purposes, the assessments have been categorized into clinician-related outcomes, patient-related outcomes, time and cost analysis, and accuracy evaluations.

5.5.1. Clinician-related outcomes:

5.5.1.1. Predictability of surgical planning:

The potential diagnostic benefits of 3D imaging and implant planning software were evaluated indirectly by studying the predictability of surgical planning. After completing the treatment plan, clinicians were asked to predict the bony morphology of the target implantation site and materials and time required for the specific surgical procedure. The following questions were posed:

1. "How would you classify the bone topography of the implant site?" Three possible options were available: Type 1: Implant fully embedded in bone; no need for regeneration procedures. Type 2: Implant fully embedded in bone but bone regeneration procedures are indicated to improve bone contour and thickness. Type 3: Implant with dehiscence or fenestration that needs bone regeneration procedures.
2. "If applicable, which materials will you need for the bone regeneration procedures?" Clinicians were expected to anticipate which bone substitute and barrier membrane were to be used.
3. "What implant type and dimensions will the planned implant have?"
4. "How much time will you plan for the total surgical appointment?"

Subsequently, the real bone morphology and materials used during the implant surgery, as well as the surgical appointment duration, were recorded and matched with the clinicians' predictions in order to evaluate the degree of agreement.

To compare the prediction potential between treatment groups, a Kappa evaluation of the strength of agreement was performed. To evaluate the degree of disagreement and its direction a Wilcoxon test was completed.

5.5.1.2. Intraoperative complications and unexpected events:

The rate and nature of complications and unexpected events was analyzed by registering the following parameters:

1. Deviations from the planned surgical protocol: Any intraoperative incidence causing a modification of the preoperative plan was recorded and categorized as follows:
    a. Technical problem: Any incidence due to the surgical guide or related instruments.
    b. Intraoperative surgical plan modification: Any intraoperative detection of implant malposition or lack of primary stability that required further actions to achieve an optimal position and stability or any deliberate change of the initial surgical plan (material, surgical procedure) decided intraoperatively by the clinician to optimize the implant outcome.
2. Time needed to solve the problems related to the surgical splint: The time required to solve the splint-related incidence was recorded in minutes.
3. Deviations from surgical splint guidance: Any clinical situation where the surgical splint could not be fully employed to guide the implant osteotomy and/or implant insertion was documented.

Descriptive statistics were used to study the sample sorted out by treatment group. Differences between groups were evaluated with the Chi-square test for qualitative variables and with the non-parametric Kruskal-Wallis test for quantitative continuous variables. For post-hoc tests, the Bonferroni corrected ($p<0.016 = 0.05/3$) Mann-Whitney test was used.

5.5.1.3. Implant and prosthetic outcome:

The biological and mechanical incidences related to the implants during the period comprised between the implant surgery and the prosthetic delivery were recorded. Any deviation from the initial prosthetic plan (screw-retained reconstruction) and its

probable etiology was also recorded. Furthermore, prosthetic reconstructions that hindered an acceptable esthetic, functional and hygienic result were registered.

Descriptive statistics were used to study the sample sorted out by treatment group. Differences between groups were evaluated with the Chi-square test for qualitative variables and with the non-parametric Kruskal-Wallis test for quantitative continuous variables. For post-hoc tests, the Bonferroni corrected ($p<0.016 = 0.05/3$) Mann-Whitney test was used.

5.5.2. Patient-related outcomes:

5.5.2.1. Treatment perception:

At the pre-treatment phase, patients' perception of the treatment to be delivered was evaluated with a multiple-choice question: "Which treatment protocol would you prefer to receive?" Available answers were: computer-assisted protocol, conventional protocol, and no preference. In order to homogenize the preoperative information transferred to the patient about the different treatment protocols and avoid any explanation bias, a Patient Study Information Document with standardized information on the three different treatment protocols was delivered (see appendix 1). Patients were asked to read this text and subsequently respond to the aforementioned multiple-choice question.

The same question was asked again at the immediate postoperative period.

Frequencies of answers for both questions were presented categorized according to treatment protocol.

5.5.2.2. Intraoperative comfort:

Patients' intraoperative comfort was evaluated with a questionnaire based partly on open-answer questions and partly on 100-mm visual analogue scales (VAS). This questionnaire was undertaken immediately after surgery and included the following items:

1. Perceived duration of the surgical procedure:
    a. VAS evaluation: A mark in the middle of the 100-mm VAS was used to represent patients' expected duration of the surgical procedure. Patients were asked to rate the duration as shorter than expected (mark on the 0-50 mm side) or longer than expected (mark on the 50-100 mm side).

b. Open answer question: Patients were asked to respond to the question: "How long do you think the surgery lasted?" The answer was recorded in minutes.

The real surgical procedure length was recorded to compare with the treatment duration perceived by the patient.

2. Perceived symptomatology:

A VAS evaluation was used to evaluate patients' perceived symptomatology at two time points:

a. Intraoperative period:
    i. Intraoperative comfort: "Was the surgery uncomfortable?" Patients were expected to rate the degree of discomfort experienced during surgery. The left end of the VAS represented "very comfortable" and the right end "very uncomfortable".
    ii. Intraoperative pain: "Was the surgery painful?" Patients were expected to rate the degree of pain experienced during surgery. The left end of the VAS represented "no pain" and the right end "extreme pain".
b. Immediate postoperative period: "How much pain are you feeling at this moment?" Patients were expected to rate the amount of pain experienced immediately after surgery. The left end of the VAS represented "no pain" and the right end "extreme pain".

Descriptive statistics robust summaries (median, minimum and maximum, and interquartile range (IQR)) were used for non-normally distributed data. Data that followed a normal distribution were described with mean and standard deviations (SD). Differences in medians between treatment groups were investigated by the non-parametric Kruskal- Wallis test. For post-hoc tests, the Bonferroni corrected ($p<0.016 = 0.05/3$) Mann-Whitney test was used. Differences in means between treatment groups were investigated by an analysis of variance (ANOVA) and a Bonferroni post-hoc test

(Scheffé). When additional predictors were evaluated, a multiple linear regression was considered.

5.5.2.3. Postoperative morbidity:

After surgery, a questionnaire evaluating the influence of the implant surgery on patients' quality of life in the early postoperative period was delivered. This questionnaire was to be fulfilled daily during the first 7 postoperative days. A 100-mm VAS was used to quantify the answers. The following questions were asked:

1. To what extent did the surgery influence the following activities?
    a. Mastication
    b. Mouth opening
    c. Speech
    d. Sleep
    e. Work
    f. Daily activities
    g. Social interaction
    h. Favorite activities
2. Please quantify the signs or symptoms you are suffering today.
    a. Swelling
    b. Hematoma
    c. Bleeding
    d. Nausea
    e. Bad taste
3. Please quantify the average pain suffered today.
4. Please quantify the maximal pain suffered today.
5. Please quantify the overall influence the surgery had on your daily activities.

Patients were also requested to register in the questionnaire the number of analgesic medication taken each postoperative day.

For a global comparison of outcome development with time, repeated measures ANOVA tests were applied together with the Greenhouse-Geisser correction

for the p values. Other predictors besides treatment group were taken into consideration for the repeated measures ANOVA models.

The Kruskal-Wallis test was used to investigate each time point separately in order to evaluate the differences between the three treatment groups. For post-hoc tests the Bonferroni corrected ($p<0.016 = 0.05/3$) Mann-Whitney test was used.

To evaluate the influence of other binary predictors a Mann-Whitney test for each time point was applied separately with a Bonferroni correction ($0.05/7 = 0.007$).

5.5.3. Time and costs:

Time and costs derived from each working step (prosthetic planning, radiographic imaging, surgical planning, surgical template production, and implant surgery) were recorded for each treatment protocol.

5.5.3.1. Time analysis:

Prosthetic planning:

1. Preliminary registrations (time derived from taking a maxillary and mandibular alginate impression and an intermaxillary bite registration): Time was started when the impression trays were tried in the patient's mouth and stopped when the register was finished.
2. Study cast fabrication and cast mounting on articulator: Time was started when the plaster was being weighed and stopped when the models were articulated.
3. Diagnostic wax-up production: Time was started when the heater touched the wax and stopped when the wax-up was finished.
4. Radiographic template production (only for control and test group 1): Time was started when the model undercuts were being blocked and stopped when the template was finished.
5. Cast optical scan (only for test groups 1 and 2): Time was started when the model was placed in the scanner and stopped when the scanning process was complete.

Radiographic imaging:

1. Radiographic exam (time needed to undergo the radiographic examination): Time was started when the patient was being prepared for examination and stopped when the patient left the Radiology Unit.

Surgical planning:

1. Start hardware (only for test groups 1 and 2): Time was started when computer was turned on and stopped when the planning software could be started.
2. Start software (only for test groups 1 and 2): Time was started when planning software icon was clicked and stopped when the software was functional.
3. Import DICOM data (only for test groups 1 and 2): Time was started when the "import DICOM file" tool was activated and stopped when the radiographic image was visible and the data ready to be worked with.
4. Prepare radiographic data (only for test groups 1 and 2): Time was started when the initial radiographic images were adjusted (viewing of the data, occlusal plane determination, brightness and contrast setting, image magnification etc.) and stopped when the data was prepared for virtual implant positioning.
5. Plan implant position and dimensions: In the control group, time was started when the transparent foil was placed over the OPG and stopped when the clinician finished drawing the implants and considered the implant surgery to be planned. For the test groups, time was started when the implant was selected from the virtual library and stopped when the final implant dimensions and positions were determined.
6. Export data (only for test groups 1 and 2): Time was started when the uploading process of the complete planning data was initiated and stopped when the planning software confirmed its successful reception.

Surgical template production:

1. Surgical template production: Time elapsed between the template order and its delivery.

Implant surgery:

1. Flap elevation: Time was started when the scalpel incised the tissues and stopped when the flap was fully elevated.
2. Study implant placement: Time was started when the initial bur contacted the bone and stopped when the study implant was seated and implant mount removed.
3. Guided bone regeneration (GBR) procedure(s): Time was started when the GBR technique was initiated and stopped when the first flap-closing suture was started.
4. Wound closure: Time was started when the first flap-closing suture was started and stopped when the last suture was completed.

Due to the non-normality of the data, descriptive statistics robust summaries (median, minimum and maximum, and interquartile range (IQR)) were used. Differences in medians between treatment groups were investigated by the non-parametric Kruskal- Wallis test. For post-hoc tests, the Bonferroni corrected ($p<0.016 = 0.05/3$) Mann-Whitney test was used.

5.5.3.2. Economical analysis:

Costs related to clinical procedures were calculated based on the Swiss Dental Association (SSO) tariff. In this rating system, every clinical procedure included has a number of tax points assigned, and each tax point is later multiplied by a numerical value. For the purpose of this study, a 3.10 CHF numerical tax point value was chosen based on the regulations by the Swiss National Social Insurance Law. For procedures that were not contemplated by the SSO tariff (e.g. virtual implant planning), time-dependent calculations were applied according to the SSO tariff system (position 4025): 9 tax points were charged for every 5 minutes of work, which multiplied by 3.10 CHF resulted in 335 CHF per hour. Costs for dental laboratory work were calculated based on the tariff of the Swiss Dental Laboratories Association (VZLS) using a 5.55 CHF multiplying numerical value.

Material costs were considered as billed by the companies or manufacturers. The costs derived from bone regeneration procedures or implants were excluded from further analysis because the aim was to evaluate the costs of the implant planning and placement protocols only.

The expenses due to the implant planning software license and computer-assisted implant placement surgical instruments were excluded from the economical analysis itself but were taken into consideration when interpreting the results.

5.5.4. Accuracy:

With the aim to evaluate the ability of each treatment protocol to transfer the planned implant position to the clinical reality, the preoperative implant planning position was matched to the final implant position by means of an image fusion software (SMOP, SwissMeda, Zürich, Switzerland). This program enables the matching of data derived from radiographs (DICOM file format) with surface data (STL file format) and analyzes position deviations between two virtual implant positions.

The surgical splint was considered the study unit for accuracy analysis. Accuracy was measured at a single implant per surgical splint because deviation errors within a splint are minimal (22), and analyzing every implant within a splint would lead to clustering bias. In cases where more than one implant was placed, accuracy was measured at the most mesial implant.

Since the baseline preoperative evaluation was different in the 3 studied groups, the methodology to determine the differences between the planned and the real implant positions was separately defined for each group:

- Control group:

  For study purposes, and since no 3D radiographic imaging was performed in this group, the baseline implant position was established by virtually planning an implant (SMOP, SwissMeda, Zürich, Switzerland) in an STL file of the study model with the wax-up. This preoperative virtual implant position was determined according to the wax-up's contour, following prosthetic-guided implant positioning guidelines with the aim to deliver a screw-retained implant restoration: In front teeth (incisors and canines) the screw access hole was intended to lay mesio-distally and apico-coronally centered in the palatal aspect of the crown, while in posterior teeth (premolars and molars) the access hole was planned in the center of the central fossa both mesio-distally and bucco-orally. In the vertical plane, the coronal level of the implant rough surface was placed 3 mm away from the cervical buccal margin of the wax-up. This distance would allow for the proper development of the

emergence profile of the restorations. The long axis of the implant was in line with the long axis of the prospective reconstruction.

- Test groups 1 and 2:

  For both test groups, the preoperative baseline implant position was given by the virtually planned implant position used as a reference to confection the surgical guide.

As an endpoint reference for all 3 groups, the real postoperative implant position was evaluated. With the aim to avoid additional radiation to the patient, rather than performing a second 3D radiographic exam, the master cast with the implant replica was optically scanned. Scanning posts were mounted on the implant replicas, and optical scans of the models taken. The STL file thus obtained was uploaded to the implant planning software (SMOP, SwissMeda, Zürich, Switzerland) and superimposed semi-automatically to the preoperative data by matching of the corresponding dental surfaces.

A virtual model of the scanning post was best-fitted to the scanned surface of the scanning post. Thereafter, the software determined the final implant position according to its relative position to the scanning post. Subsequently, numeric deviations were calculated between the planned and the final implant positions. Three planes were chosen to extract deviation coordinates: occlusal plane, implant shoulder, and implant apex. Additionally, angular and height deviations were calculated.

Descriptive statistics were calculated for global deviation values and their fragmented mesio-distal and bucco-oral vectors at each evaluation plane. Results were categorized per treatment group. In addition, discrepancies were graphically represented using a scatter plot with mesio-distal discrepancies in the x-axis and bucco-oral discrepancies on the y-axis.

To study global accuracy differences between study groups, an analysis of variance (ANOVA) was used with a Bonferroni post-hoc test (Scheffé). Possible confounding variables were analyzed using multiple linear regression with respect to treatment group. The confounding variables considered were implant location (maxilla

vs. mandible, incisor-canine region vs. premolar-molar region, left hemi-maxilla vs. right hemi-maxilla), splint support nature (partial edentulism Kennedy class I or II vs. Kennedy class III or IV) and implant dimensions (length and diameter).

The mesio-distal or bucco-oral distribution of the positioning errors were evaluated with a Chi-square test. A multiple logistic regression was considered when exploring for confounding variables. Odds ratios together with the corresponding 95% confidence intervals were computed.

6. Results

6.1. General:

During June 2010 and June 2013, 81 partially edentulous patients were included in the study (27 Control, 27 Test 1, 27 Test 2). Eight patients were excluded from the analysis due to incompleteness of the clinical record forms (1 Control, 3 Test 1, 4 Test 2). Seventy-tree implant planning and placement protocols were evaluated (26 Control, 24 Test 1, 23 Test 2). One hundred and one implants were placed (28 Control, 37 Test 1, 36 Test 2). Table 1 describes the sample's characteristics. Not every variable could be recorded for every patient due to partial incompleteness of some record forms. Therefor a description of the number of patients included in the analysis of each variable was reported for each study section.

Table 1. Study sample characteristics.

		Control	Test 1	Test 2
Number of patients		26	24	23
Number of guides		26	24	23
Number of implants		28	37	36
Age (mean (SD))		58.64 (14.31)	57.05 (11.18)	59.08 (14.04)
Sex (women)		16	12	14
Implant system	Straumann ®	21	5	15
	Astra ®	5	19	8
Partial edentulism	Kennedy class I and II	5	7	9
	Kennedy class III and IV	21	17	14
Study implant site location	Incisor (maxilla / mandible)	(1/0)	(2/0)	(3/0)
	Canine (maxilla / mandible)	(2/0)	(1/0)	(4/0)
	Premolar (maxilla / mandible)	(9/5)	(8/9)	(8/5)
	Molar (maxilla / mandible)	(4/5)	(0/4)	(0/3)
Number of surgical sites	1	24	18	19
	2	2	6	4
Concomitant GBR techniques	Yes	15	12	16
	No	11	12	7
Number of implants per patient	1	23	14	11
	2	3	7	9
	3	0	3	2
	4	0	0	1
Additional surgical procedures		None	1 Sinus lift	2 Sinus lift

6.2. Clinician-related outcomes:

6.2.1. Predictability of surgical planning:

The matched contrasts between predicted and true outcomes are presented in Tables 2 to 7. CAIPP protocols proved better prediction potential than conventional protocol for the following variables: Bone topography (Kappa value: Control: 0.15, Test 1: 0.53, Test 2: 0.67), need for simultaneous GBR procedures during implant placement (Kappa value: Control: 0.35, Test 1: 0.64, Test 2: 0.53), barrier membrane selection (Kappa value: Control: 0.12, Test 1: 0.57, Test 2: 0.41), and implant length (Kappa value: Control: 0.33, Test 1: 0.48, Test 2: 0.75).

Prediction values for implant type (Kappa value: Control: 0.76, Test 1: 0.74, Test 2: 0.72) and implant diameter (Kappa value: Control: 0.67, Test 1: 0.78, Test 2: 0.80) were high and constant between protocols.

The ability to predict the total surgical appointment time was similar for the three treatment protocols (Table 8).

Table 2. Bone topography prediction. Type 1: Implant fully embedded in bone; no need for regeneration procedures. Type 2: Implant fully embedded in bone but bone regeneration procedures are indicated to improve bone contour. Type 3: Implant with dehiscence or fenestration that needs bone regeneration procedures. Predictions are depicted in rows and intraoperative outcomes in columns. The highlighted diagonal cells represent the cases where the prediction coincided with the real outcome. The absolute values as well as the categorization of the strength of agreement Kappa evaluation (<0.2: Poor, 0.21-0.4: Fair, 0.41-0.6: Moderate, 0.61-.8: Good, 0.81-1: Very Good)(23) are presented in the last two columns.

Bone topography			Intraoperative			Kappa	
			1	2	3		
Control	Prediction	1	7	3	1	0.15	Poor
		2	4	1	3		
		3	1	1	3		
Test 1		1	9	0	1	0.53	Moderate
		2	1	3	1		
		3	0	4	4		
Test 2		1	4	1	1	0.67	Good
		2	0	3	1		
		3	1	0	9		

Table 3. Need for GBR prediction. Predictions are depicted in rows and intraoperative outcomes in columns. The highlighted diagonal cells represent the cases where the prediction coincided with the real outcome. The absolute values as well as the categorization of the strength of agreement Kappa evaluation (<0.2: Poor, 0.21-0.4: Fair, 0.41-0.6: Moderate, 0.61-.8: Good, 0.81-1: Very Good)(23) are presented in the last two columns.

GBR topography			Intraoperative situation		Kappa	
			No	Yes		
Control	Prediction	No	6	4	0.35	Fair
		Yes	3	9		
Test 1		No	8	1	0.64	Good
		Yes	3	10		
Test 2		No	4	2	0.53	Moderate
		Yes	2	13		

Table 4. Barrier membrane prediction. Type 1: Collagen membrane (BioGide, Geistlich Pharma AG, Switzerland). Type 2: ePTFE membrane (Gore-tex, W.L. Gore and associates, USA). Type 3: PEG membrane (MembraGel, Institut Straumann AG, Switzerland). Predictions are depicted in rows and intraoperative outcomes in columns. The highlighted diagonal cells represent the cases where the prediction coincided with the real outcome. The absolute values as well as the categorization of the strength of agreement Kappa evaluation (<0.2: Poor, 0.21-0.4: Fair, 0.41-0.6: Moderate, 0.61-.8: Good, 0.81-1: Very Good)(23) are presented in the last two columns.

Membrane topography			Intraoperative situation				Kappa	
			None	Type 1	Type 2	Type 3		
Control	Prediction	None	6	4	0	0	0.12	Poor
		Type 1	4	5	1	2		
Test 1		None	8	1	0	0	0.57	Moderate
		Type 1	3	9	1	0		
Test 2		None	4	2	0	0	0.41	Moderate
		Type 1	2	9	1	2		
		Type 2	0	0	1	0		

Table 5. Implant type prediction. Type 1: Astra S (Dentsply Implants, Sweden). Type 2: Straumann Standard Plus (Institut Straumann AG, Switzerland). Type 3: Straumann Bone Level (Institut Straumann AG, Switzerland). Type 4: Astra TX (Dentsply Implants, Sweden). Predictions are depicted in rows and intraoperative outcomes in columns. The highlighted diagonal cells represent the cases where the prediction coincided with the real outcome. The absolute values as well as the categorization of the strength of agreement Kappa evaluation (<0.2: Poor, 0.21-0.4: Fair, 0.41-0.6: Moderate, 0.61-.8: Good, 0.81-1: Very Good)(23) are presented in the last two columns.

Implant type			Intraoperative situation				Kappa	
			Type 1	Type 2	Type 3	Type 4		
Control	Prediction	Type 1	3	0	0	0	0.76	Good
		Type 2	0	9	2	0		
		Type 3	0	1	6	0		
Test 1		Type 1	14	0	1	2	0.74	Good
		Type 2	0	4	0	0		
		Type 3	0	0	2	0		
Test 2		Type 1	5	1	0	1	0.72	Good
		Type 2	0	6	1	0		
		Type 3	0	1	6	0		

Table 6. Implant diameter prediction. Predictions are depicted in rows and intraoperative outcomes in columns. The highlighted diagonal cells represent the cases where the prediction coincided with the real outcome. The absolute values as well as the categorization of the strength of agreement Kappa evaluation (<0.2: Poor, 0.21-0.4: Fair, 0.41-0.6: Moderate, 0.61-.8: Good, 0.81-1: Very Good)(23) are presented in the last two columns.

Implant diameter (mm)			Intraoperative situation						Kappa	
			3.3	3.5	4	4.1	4.8	5		
Control	Prediction	3.3	1	0	0	0	0	0	0.67	Good
		3.5	0	1	1	0	0	0		
		4	0	0	1	2	0	0		
		4.1	0	0	0	11	0	0		
		4.8	0	0	1	0	2	0		
Test 1		3.5	0	1	2	0	0	0	0.78	Good
		4	1	0	12	0	0	0		
		4.1	0	0	0	5	0	0		
		5	0	0	0	0	0	1		
Test 2		3.3	1	0	0	0	0	0	0.8	Very Good
		3.5	0	1	0	0	0	0		
		4	0	0	4	1	0	0		
		4.1	0	0	1	12	0	0		

Table 7. Implant length prediction. Predictions are depicted in rows and intraoperative outcomes in columns. The highlighted diagonal cells represent the cases where the prediction coincided with the real outcome. The absolute values as well as the categorization of the strength of agreement Kappa evaluation (<0.2: Poor, 0.21-0.4: Fair, 0.41-0.6: Moderate, 0.61-.8: Good, 0.81-1: Very Good)(23) are presented in the last two columns.

Implant length (mm)			Intraoperative situation								Kappa	
			6	8	9	10	11	12	13	15		
Control	Prediction	6	2	0	0	0	0	0	0	0	0.33	Fair
		8	0	6	0	1	0	1	0	0		
		9	0	0	1	0	0	0	0	0		
		10	0	2	0	3	0	1	0	0		
		12	0	0	0	3	1	0	0	0		
Test 1		6	2	0	0	0	0	0	0	0	0.48	Moderate
		8	0	5	1	0	0	0	0	0		
		9	0	1	2	0	0	0	0	0		
		10	0	2	1	1	0	0	0	0		
		11	0	1	3	0	3	0	0	0		
Test 2		6	2	0	0	0	0	0	0	0	0.75	Good
		8	0	5	0	1	0	0	0	0		
		9	0	0	1	1	0	0	0	0		
		10	0	1	0	4	0	0	0	0		
		11	0	0	0	0	1	0	0	0		
		12	0	0	0	1	0	1	0	0		
		13	0	0	0	0	0	0	1	0		
		15	0	0	0	0	0	0	0	1		

Table 8. Surgical appointment time prediction. The time predicted by the clinician is contrasted with the real surgical appointment time, which was recorded from the moment the patient entered the operating room until the patient received the postoperative instructions and was dismissed. These time recordings include standardized photographic documentation of different surgical steps as a routine procedure performed in every implant surgery at the Department for Fixed and Removable Prosthodontics and Material Science of the University of Zürich.

	Surgical appointment time prediction (minutes)		Real surgical appointment time (minutes)		*p*
	Mean	SD	Mean	SD	
Control	**98.43**	32.85	**92,88**	39.8	*0.61*
Test 1	**101.53**	28.82	**113,77**	43.77	*1*
Test 2	**107.31**	45.76	**142,77**	47.25	*0.58*

6.2.2. Complications and unexpected events:

The distribution and nature of deviations from the planned surgical protocol are presented in Table 9. The different treatment groups presented similar rates of deviations, but the nature of the incidences varied. These were categorized in technical problems and intraoperative surgical plan modifications.

Among the technical problems, the splint-related complications were predominant. Some splints required modification before or during the surgery in order to allow their use. The rate of splint modifications and the time required to do so are summarized in Table 10. Conventional splints required less time to be amended than computer-assisted splints. Time differences reached statistical significance between Control and Test 1 groups ($p=0.006$) (Control – Test 2: $p=0.02$, Test 1 – Test 2: $p=0.44$).

The rate of cases where the bed preparation and implant insertion could not be fully completed by using the surgical splint was 3.8% in the conventional group (1/26), 45.8% for the Test 1 group (11/24), and 47.8% in the Test 2 group (11/23) (Table 11). The reasons were technical problems (splint-related or unavailability of specific guiding instruments for specific implant types or positions), lack of implant primary stability, positional changes to optimize implant location (in the vertical and/or horizontal planes) or logistic matters (late arrival of splint).

Table 9. Distribution and nature of deviations from the planned surgical protocol.

Treatment group	Problem classification	Cases where events occurred / cases studied	Explanation
Control	Technical problems	8 / 26	Mouth opener interfered with occlusal splint (n=1) Inadequate position and dimensions of splint's access canal (n=2) Misleading splint: anatomy of reference tooth not adequate (n=1) Not specified (n=5)
	Intraoperative surgical plan modifications	7 / 26	Shorter implant combined with a free-hand deeper implant placement to avoid bony dehiscence (n=2) Longer implant combined with a transalveolar sinus lift (n=1) Wider implant due to sufficient mesio-distal dimension (n=1) One-piece implant instead of a two-piece implant due to clinician´s preference (n=1) Unexpected GBR (n=2)
Test 1	Technical problems	6 / 24	Splint did not sit correctly on abutment teeth (n=3) No available implant transfers with the adequate length (n=1) Excessive torque during implant osteotomy preparation (n=1) Late arrival of the splint (n=1) Not specified (n=2)
	Intraoperative surgical plan modifications	11 / 24	Longer and tapered implant to improve primary stability (n=1) Shorter implant combined with a free-hand deeper implant placement to avoid bony dehiscence (n=2) Free-hand deeper implant placement to avoid dehiscence (n=2), to prevent marginal bone remodeling in cases of thin mucosa (n=1)

			Free-hand horizontal implant position modification due to prosthetic reasons (n=3), to avoid bony dehiscence (n=1), to improve primary stability (n=1)
Test 2	Technical problems	10 / 23	Splint did not sit correctly on abutment teeth (n=4) Excessive friction of instruments with splint holes (n=4) Not specified (n=2)
	Intraoperative surgical plan modifications	9 / 23	Wider implant to improve primary stability (n=1) Shorter implant combined with a free-hand deeper implant placement without specifying reason (n=1) Free-hand deeper implant placement to prevent marginal bone remodeling in cases of thin mucosa (n=1), to embed final mm of rough surface in bone (n=1), not specified (n=2) Free-hand horizontal implant position modification due to prosthetic reasons (n=2), to avoid bony dehiscence (n=1)

Table 10. Splint modification rate and the time invested (minutes). Statistically significant differences between groups are identified by different letters, such as A and B, printed under the column "p". Groups with the same letter are considered to be not statistically significantly different from each other.

	Cases where events occurred / cases evaluated	Time invested to modify splint			p
		Mean	SD	Range	
Control	8/26	1.63	0.45	0.92 – 2.08	A
Test 1	5/24	6.91	5.32	2 – 13.7	B
Test 2	9/23	4.56	3.02	0.98 – 10.23	A, B

Table 11. Partial or complete impossibility to use surgical splint.

Treatment group	Cases where events occurred / cases evaluated	Explanation
Control	1 / 26	Implant placed without guide due to detection of misleading surgical splint (n=1)
Test 1	11 / 24	Free-hand deeper implant placement to avoid dehiscence (n=3), to embed final millimeter of rough surface in bone (n=1), to prevent marginal bone remodeling in cases of thin mucosa (n=1), to sink last 3 mm of rough surface in bone since available guided transfers were too short (n=1) Free-hand horizontal implant position modification due to prosthetic reasons (n=3), to avoid bony dehiscence (n=1) Free-hand implant placement in a different position to obtain primary stability (n=1) Conventional splint used due to late arrival of computer-assisted surgical splint (n=1) Free-hand implant placement due to excessive insertion torque when placing implant through guide (n=1)
Test 2	11 / 23	Free-hand implant insertion due to unavailability of guided transfers for a specific implant type (n=1), due to splint tension that bent splint (n=1) Free-hand deeper implant placement to avoid dehiscence (n=1), not specified (n=3), to prevent marginal bone remodeling in cases of thin mucosa (n=1) Free-hand horizontal implant position modification due to prosthetic reasons (n=3) Free-hand placement of a wider implant to obtain primary stability (n=1)

6.2.3. Implant and prosthetic outcome:

The survival rate of implants at prosthetic delivery and 2-week follow-up examination was 100% for every group. No biological or technical complication was observed for any implant or reconstruction. All prosthetic reconstructions fulfilled esthetic, hygienic and functional standards. In one implant, the planned screw-retained reconstruction had to be substituted by a cement-retained reconstruction due to the buccal-distal emergence of its screw access hole. The implant belonged to Test group 1, but the planned surgical protocol was modified as follows: the implant had to be replaced manually by a longer and tapered implant since guided implant placement resulted in a lack of primary stability (Figures 1, 2 and 3).

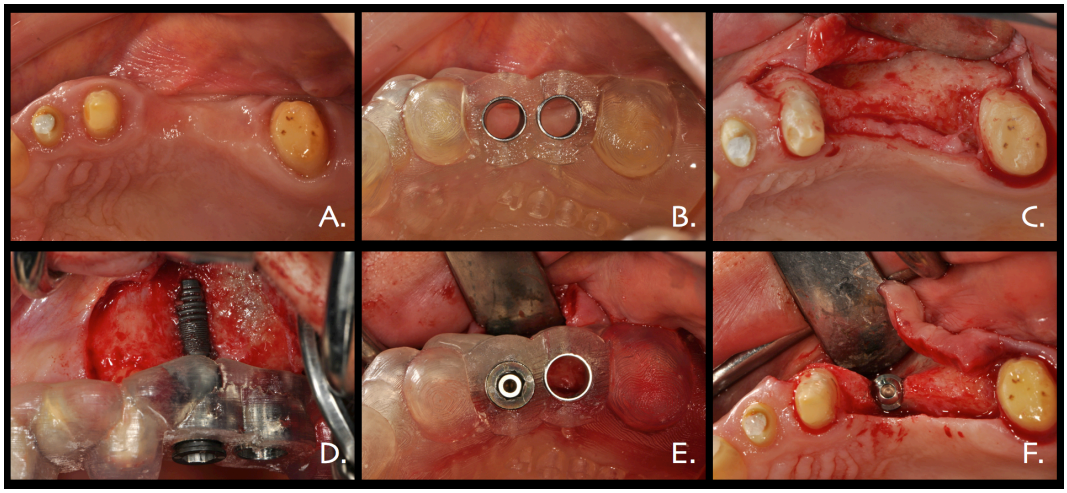

Figure 1. Test group 1 implant placement where surgical protocol modification was necessary. Following the planned protocol the implant had no primary stability. A. Surgical site of study implant 24. B. Surgical splint. C. Surgical site after flap elevation. D. Cylindrical implant placed according to planned surgical protocol with lack of primary stability. E. Occlusal view of implant driver inserted in implant guiding cylinder. F. Occlusal view of implant position after planned implant placement protocol.

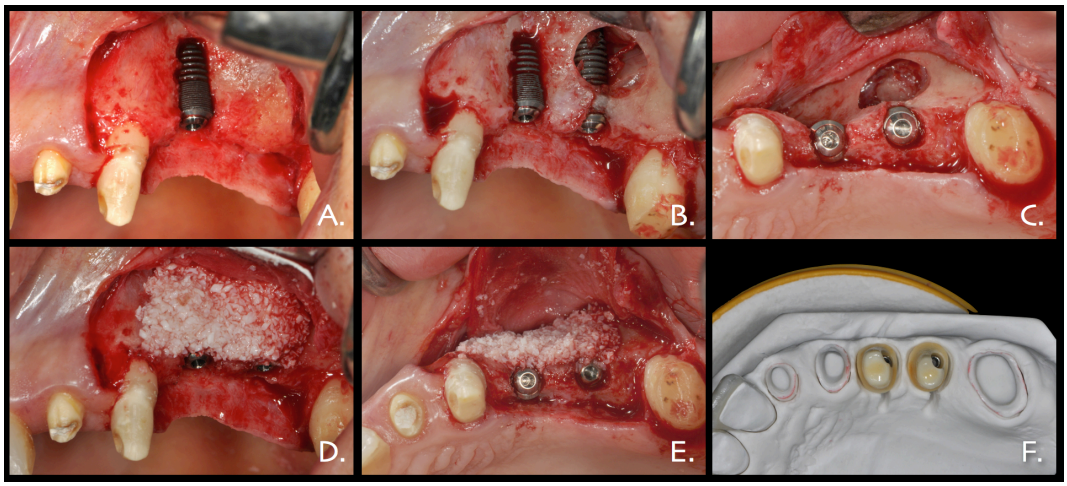

Figure 2. A. Intrasurgical protocol modification. A longer tapered implant was placed after free-hand additional implant site instrumentation to obtain better primary stability. B, C: Simultaneous sinus lift and implant placement of implant 25. D, E: Guided bone regeneration of buccal aspect of both implants. F. Implant prosthetic abutments with buccal-distal emergence of screw access hole.

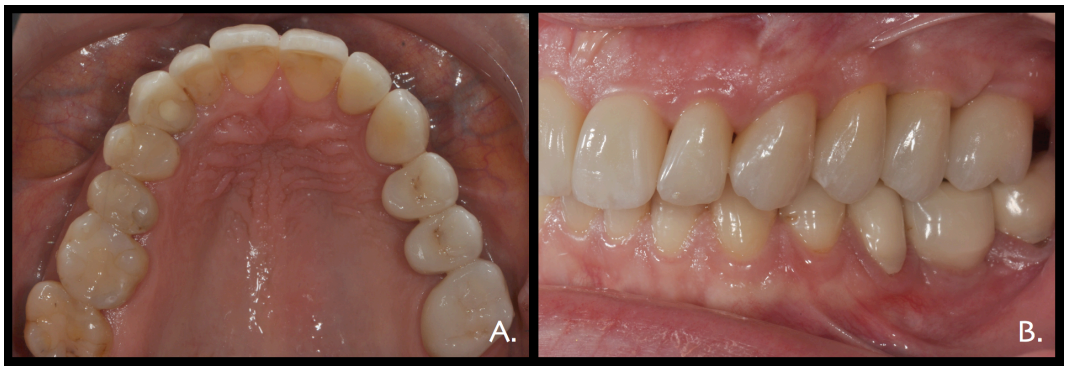

Figure 3. Cement-retained prosthetic reconstruction over implants 24 and 25. A. Occlusal view. B. Buccal view.

6.3. Patient-related outcomes:

6.3.1. Treatment perception

Table 12 presents patients' treatment perception before and after the treatment.

Before treatment, 53% of the patients allocated to the conventional protocol were satisfied with this allocation; the remaining would have preferred to be treated with the CAIP protocol. The percentage of patients allocated to the computer-assisted protocol that were satisfied with this treatment allocation was 83%. These percentages remained stable after implant surgery: The percentage of patients in the conventional group that would still prefer conventional was 53%, while the percentage in computer-assisted amounted to 86%.

Comparatively, the percentage of patients that would have desired a different treatment randomization before treatment was higher for the conventional (37%) than for the computer (6%) group.

After treatment, the percentage desiring to have been treated in another group decreased by 9% in the conventional group (26%), while it decreased by 3% in the computer-assisted protocols (3%).

The percentage of undecided participants before treatment was 11% for both protocols. It increased by 26% in the conventional group (37%) and decreased by 2% for the computer-assisted (9%).

Table 12. Patients' treatment perception before and after treatment.

Before treatment	Control		Test 1		Test 2		Global CAIPP	
	N	%	N	%	N	%	N	%
Convention	10	**53%**	0	**0%**	2	**11%**	2	**6%**
Computer	7	**37%**	15	**88%**	14	**78%**	29	**83%**
Equal	2	**11%**	2	**12%**	2	**11%**	4	**11%**
Total	*19*	*100%*	*17*	*100%*	*18*	*100%*	*35*	*100%*
After treatment	Control		Test 1		Test 2		Global CAIPP	
	N	%	N	%	N	%	N	%
Convention	12	**63%**	1	**6%**	0	**0%**	1	**3%**
Computer	5	**26%**	13	**76%**	17	**94%**	30	**86%**
Equal	7	**37%**	2	**12%**	1	**6%**	3	**9%**
Total	*19*	*100%*	*17*	*100%*	*18*	*100%*	*35*	*100%*

6.3.2. Intraoperative comfort:

Patients' intraoperative comfort values are shown in Tables 13 and 14. No statistically significant differences between treatment groups were observed for any of the intraoperative variables studied. No differences were observed between perceived and real surgery duration.

Table 13. VAS evaluation of patients' intraoperative symptomatology and surgical duration.

Perceived Symptomatology	Control						Test 1						Test 2					
	n	**Median**	**Min**	**Max**	**IQR**	**p**	***n***	**Median**	**Min**	**Max**	**IQR**	**p**	***n***	**Media**	**Min**	**Max**	**IQR**	**p**
Intraoperative comfort	*21*	22	0	72	42	A	*19*	17	0	55	32	A	*19*	38	3	65	26	A
Intraoperative pain	*21*	4	0	72	10,5	A	*19*	3	0	50	8	A	*19*	6	0	83	32	A
Immediate postoperative pain	*21*	0	0	45	3,5	A	*19*	0	0	71	10	A	*19*	4	0	54	15	A
Perceived Duration	Control						Test 1						Test 2					
	n	**Median**	**Min.**	**Max.**	**IQR**	**p**	***n***	**Median**	**Min.**	**Max.**	**IQR**	**p**	***n***	**Media**	**Min.**	**Max.**	**IQR**	**p**
Expected duration	*21*	50	0	65	24,5	A	19	50	4	73	1	A	19	50	0	69	12	A

Table 14. Perceived surgery length.

Perceived Duration	Control				Test 1				Test 2			
	n	**Mean**	**SD**	**p**	***n***	**Mean**	**SD**	**p**	***n***	**Mean**	**SD**	**p**
Time estimate (min)	*21*	92,86	54,71	A	*19*	107,1	47	A	*19*	102,37	41,48	A
Real time (min)	*20*	92,95	41,42	A	*16*	109,63	48,02	A	*18*	130,17	54	A

In order to contemplate other variables that could potentially influence patients' intraoperative and immediate postoperative periods, the study sample was split according to surgery duration (less than 100 min: n=26, more than 100 min: n=28), number of surgical sites (one: n=58, two: n=10), number of implants (one: n=43, more than one: n=24), need for GBR (yes: n=40, no: n=29), surgery location (maxilla: n=42, mandible: n=31 / incisors and canine region: n=12, premolar and molar region: n=61) and patient gender (female: n=43, male: n=30).

Longer surgeries were associated to more intraoperative discomfort (p=0.017), more intraoperative pain (p=0.000), and a longer surgery duration perception (p=0.002).

Surgeries involving 2 surgical sites yielded higher levels of immediate postoperative pain than single site surgeries (p=0.035).

Surgeries including GBR and those where more than one implant was placed were associated to a longer surgery duration perception (p=0.027 and p=0.033, respectively).

Surgery location and gender showed no statistically significant influence on the intraoperative and immediate postoperative period.

6.3.3. Postoperative morbidity:

The three treatment protocols triggered similar postoperative periods according to the evolution of the studied patient-related outcomes (Figures 4 to 19). A gradual reduction of signs and symptoms was observed from day 1 to day 7 ($p>0.000$).

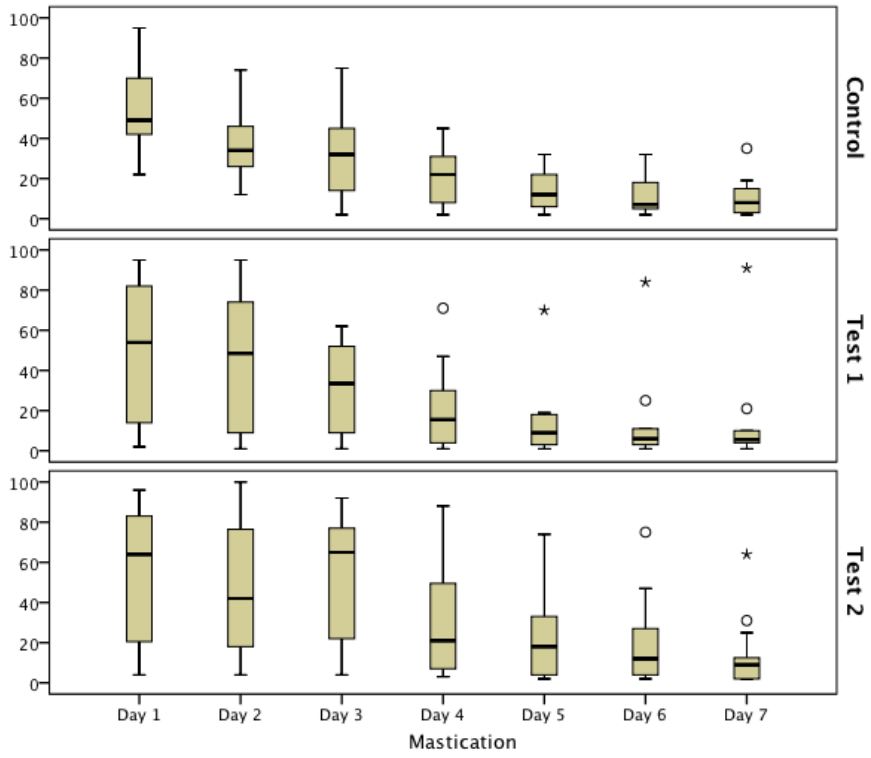

Figure 4. Implant surgery influence (quantified by a 100-mm VAS) on patients' mastication during the first postoperative week.

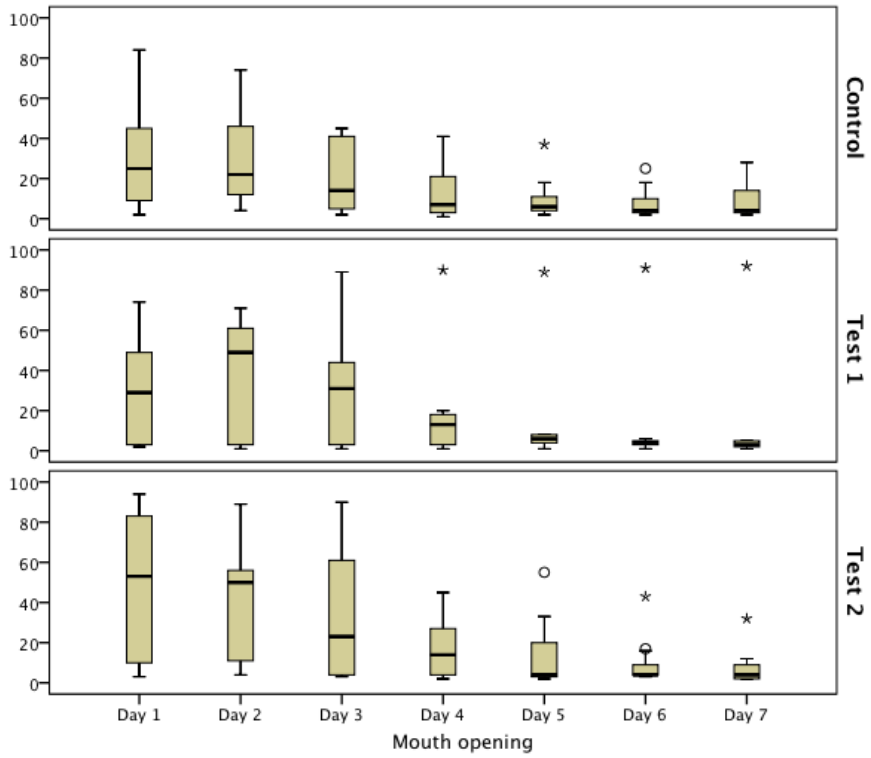

Figure 5. Implant surgery influence (quantified by a 100-mm VAS) on patients' mouth opening during the first postoperative week.

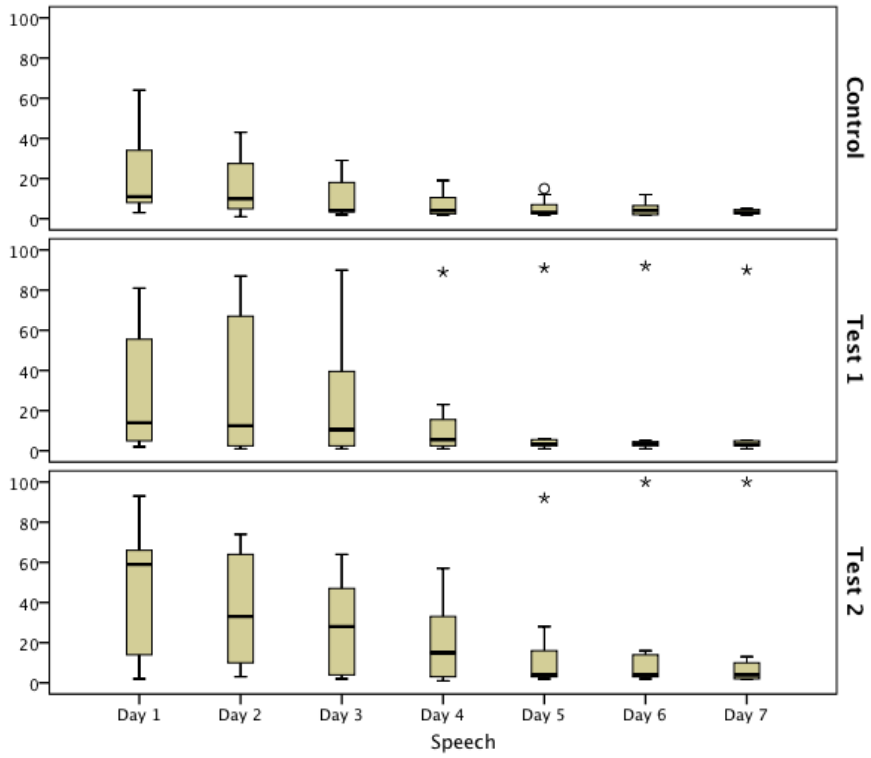

Figure 6. Implant surgery influence (quantified by a 100-mm VAS) on patients' speech during the first postoperative week.

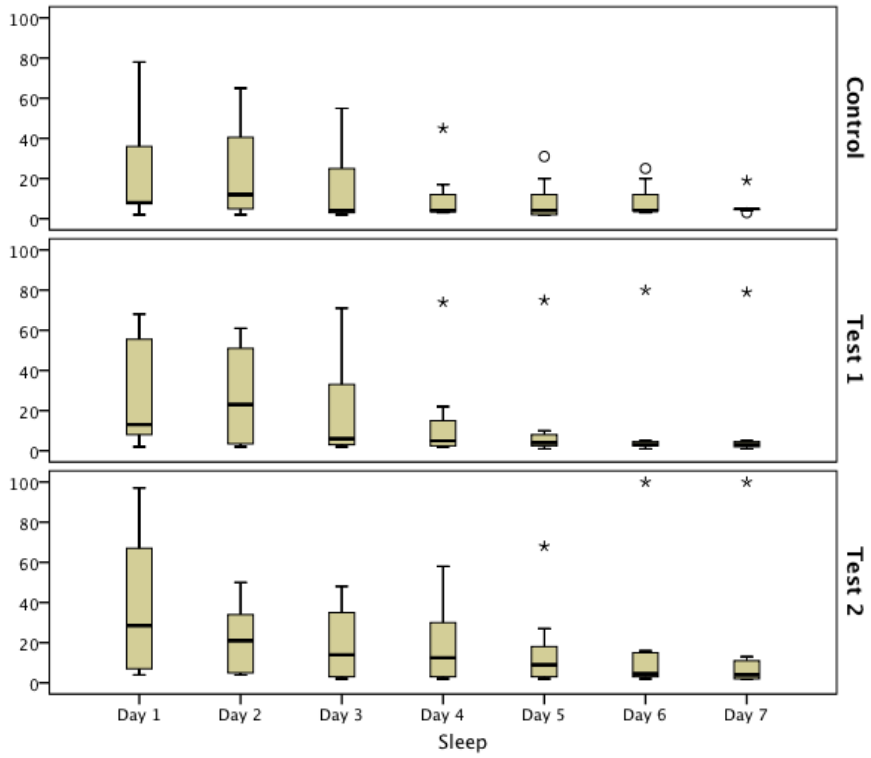

Figure 7. Implant surgery influence (quantified by a 100-mm VAS) on patients' sleep during the first postoperative week.

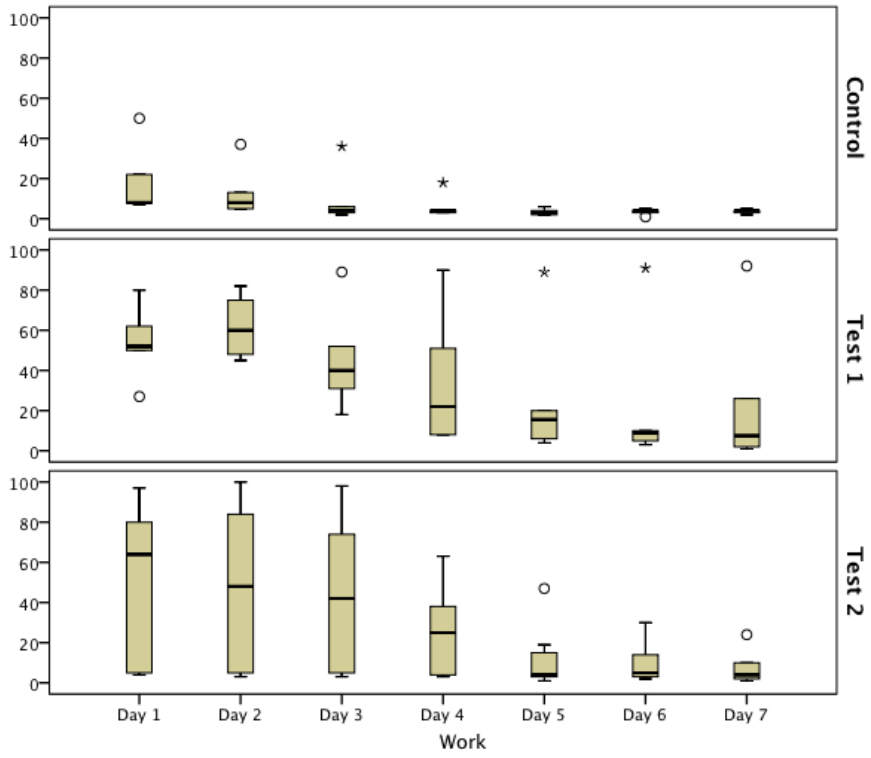

Figure 8. Implant surgery influence (quantified by a 100-mm VAS) on patients' working capability during the first postoperative week.

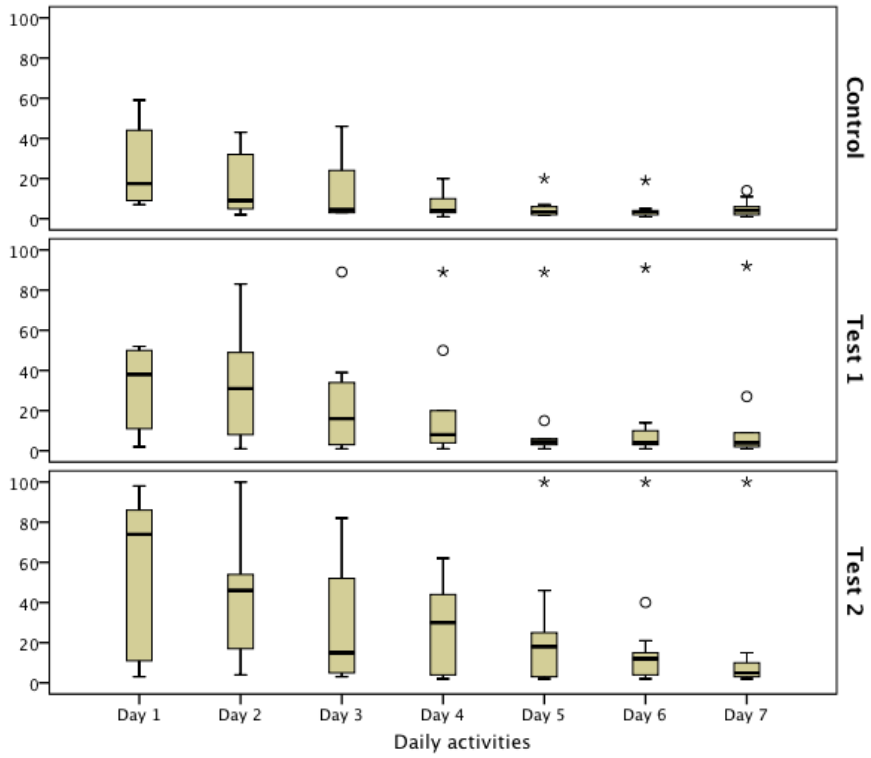

Figure 9. Implant surgery influence (quantified by a 100-mm VAS) on patients' daily activities during the first postoperative week.

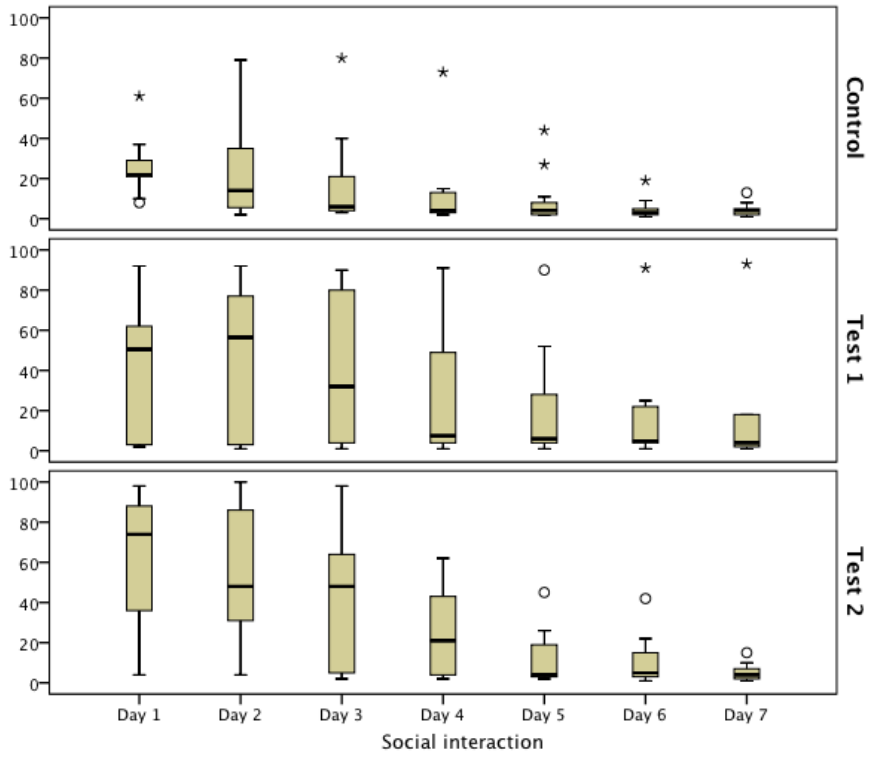

Figure 10. Implant surgery influence (quantified by a 100-mm VAS) on patients' social interaction during the first postoperative week.

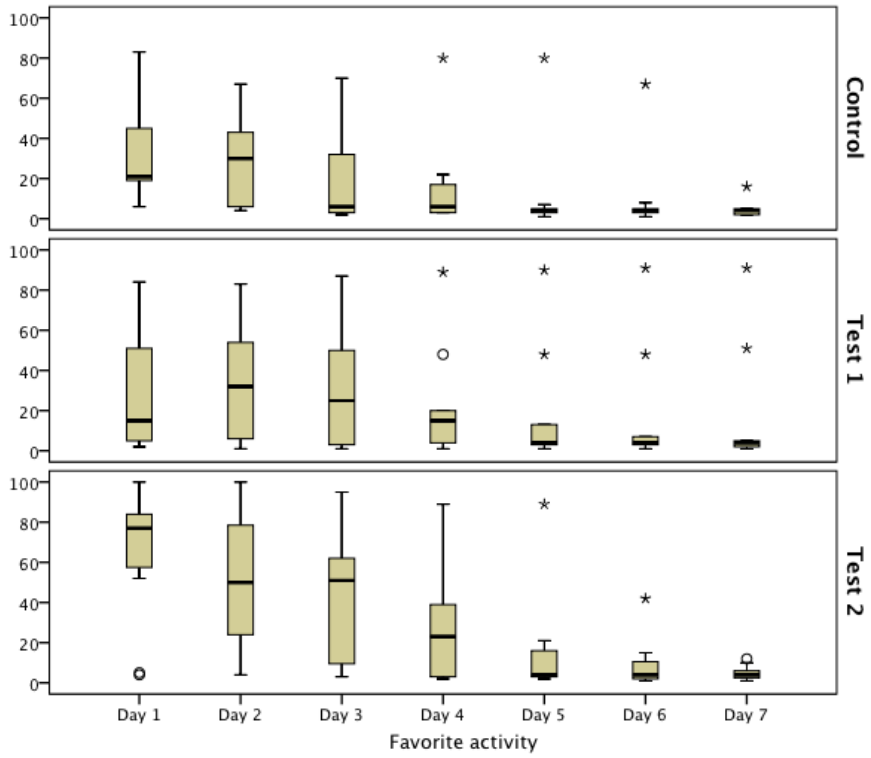

Figure 11. Implant surgery influence (quantified by a 100-mm VAS) on patients' favorite activity during the first postoperative week.

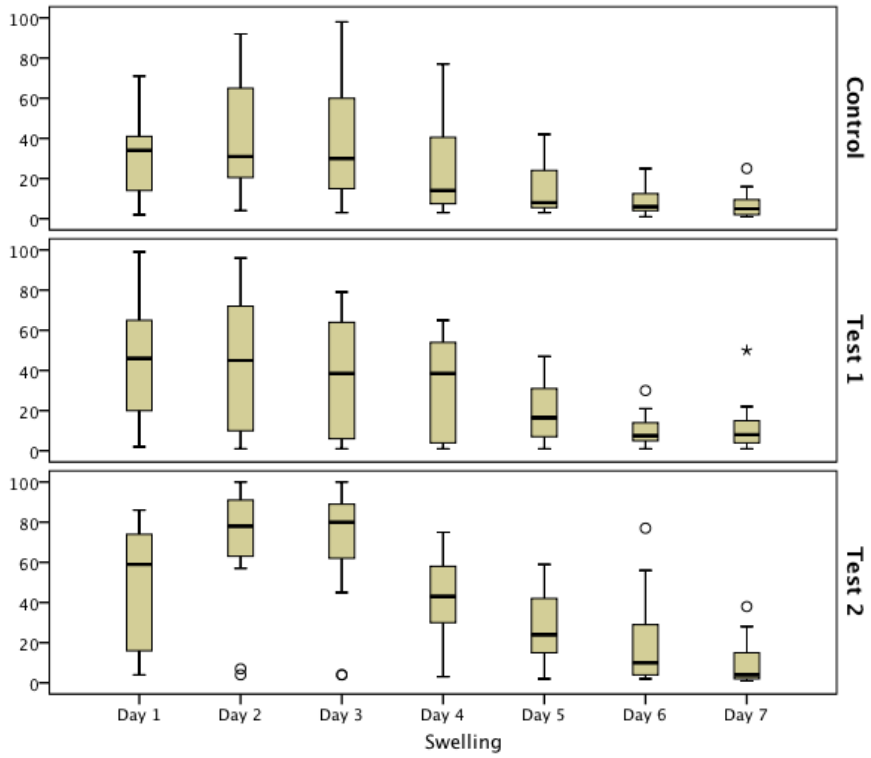

Figure 12. Swelling (quantified by a 100-mm VAS) experienced by the patient during the first postoperative week.

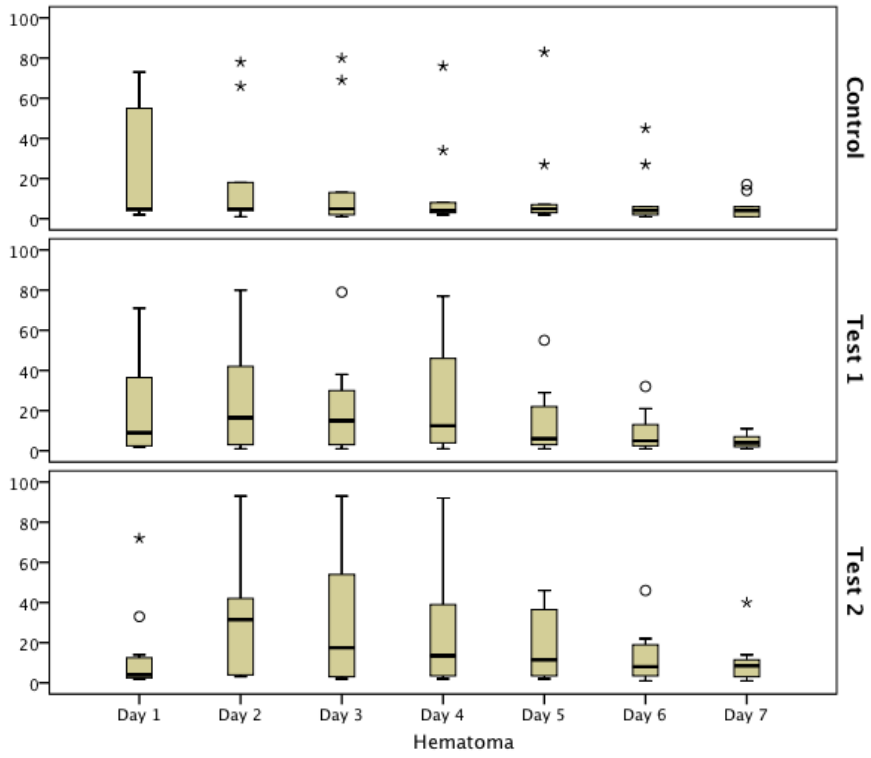

Figure 13. Bruising (quantified by a 100-mm VAS) experienced by the patient during the first postoperative week.

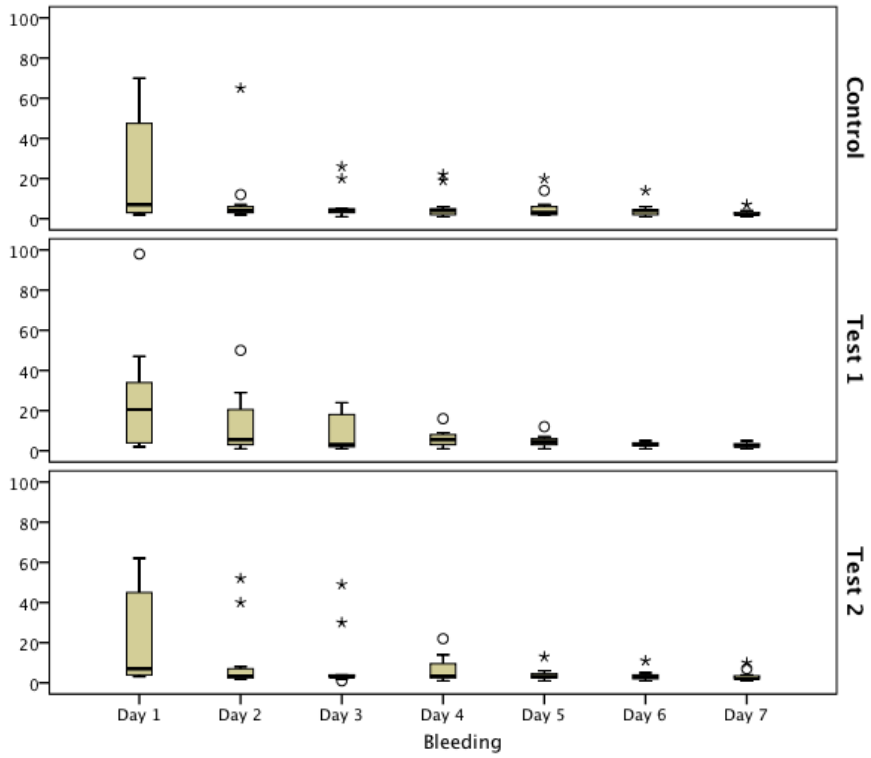

Figure 14. Bleeding (quantified by a 100-mm VAS) experienced by the patient during the first postoperative week.

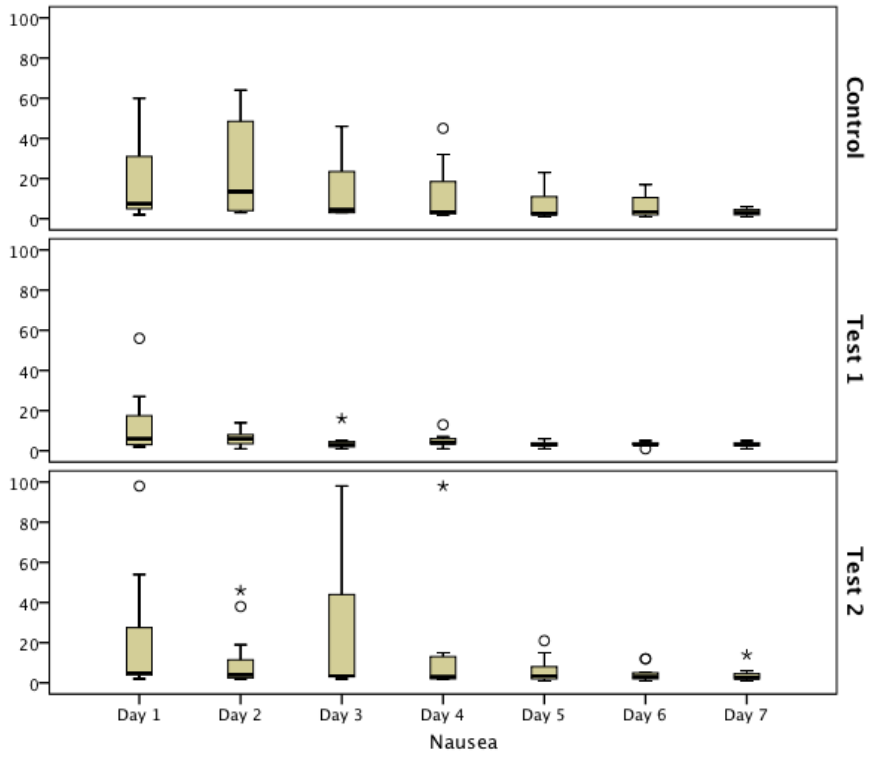

Figure 15. Nausea (quantified by a 100-mm VAS) experienced by the patient during the first postoperative week.

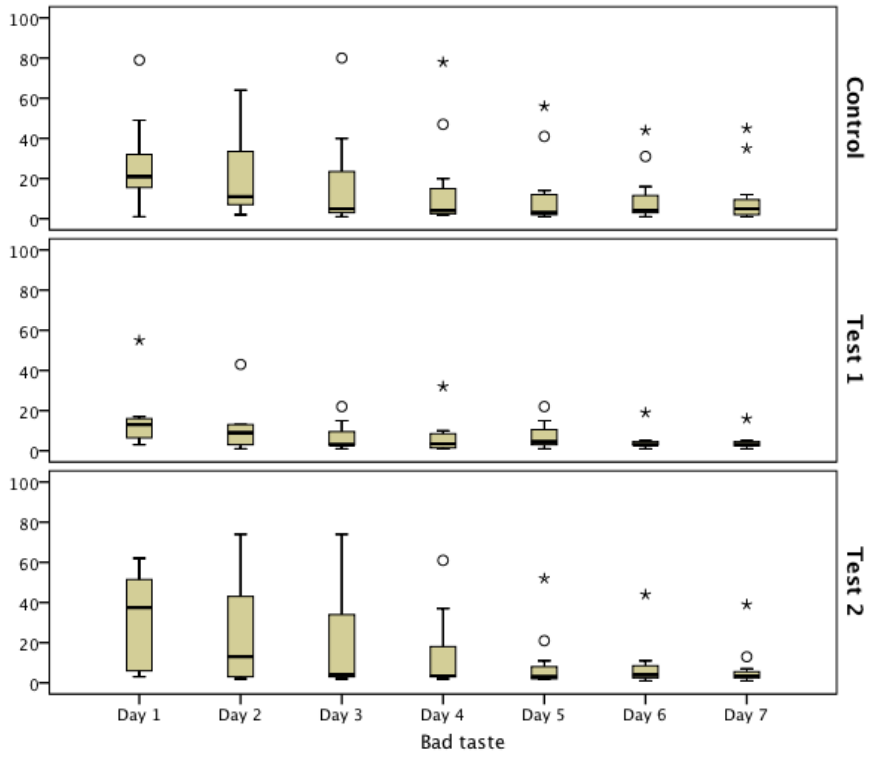

Figure 16. Bad taste (quantified by a 100-mm VAS) experienced by the patient during the first postoperative week.

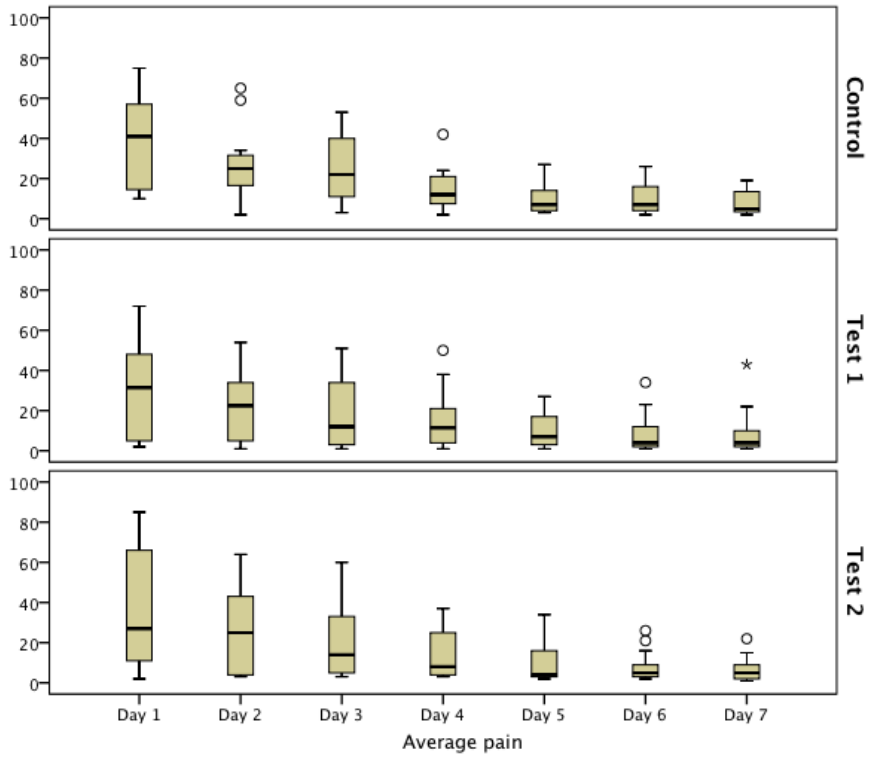

Figure 17. Average pain (quantified by a 100-mm VAS) experienced by the patient during the first postoperative week.

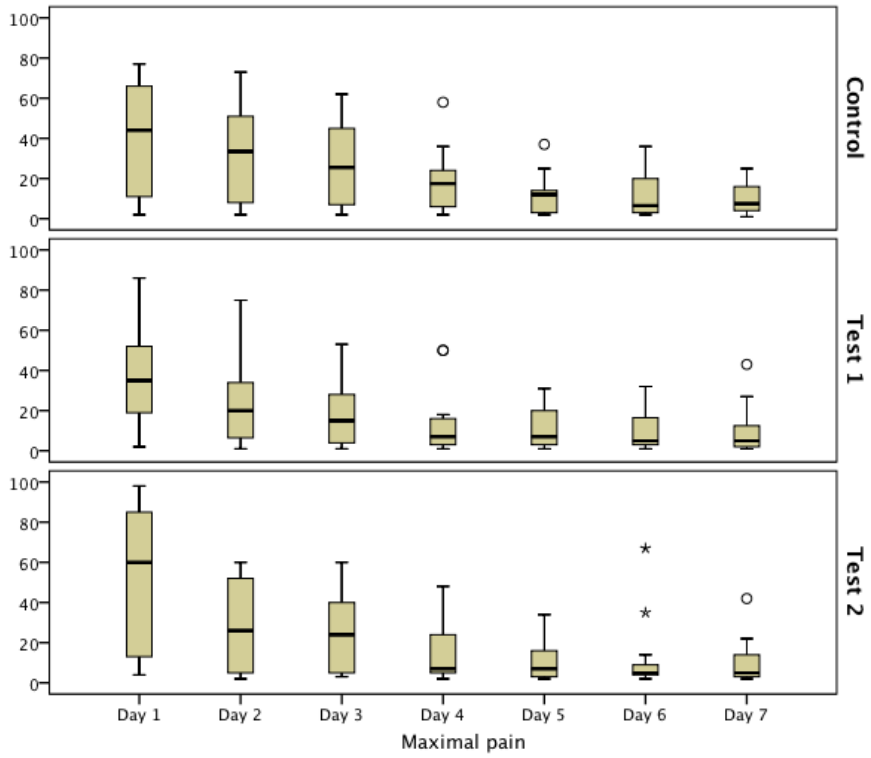

Figure 18. Maximal pain (quantified by a 100-mm VAS) experienced by the patient during the first postoperative week.

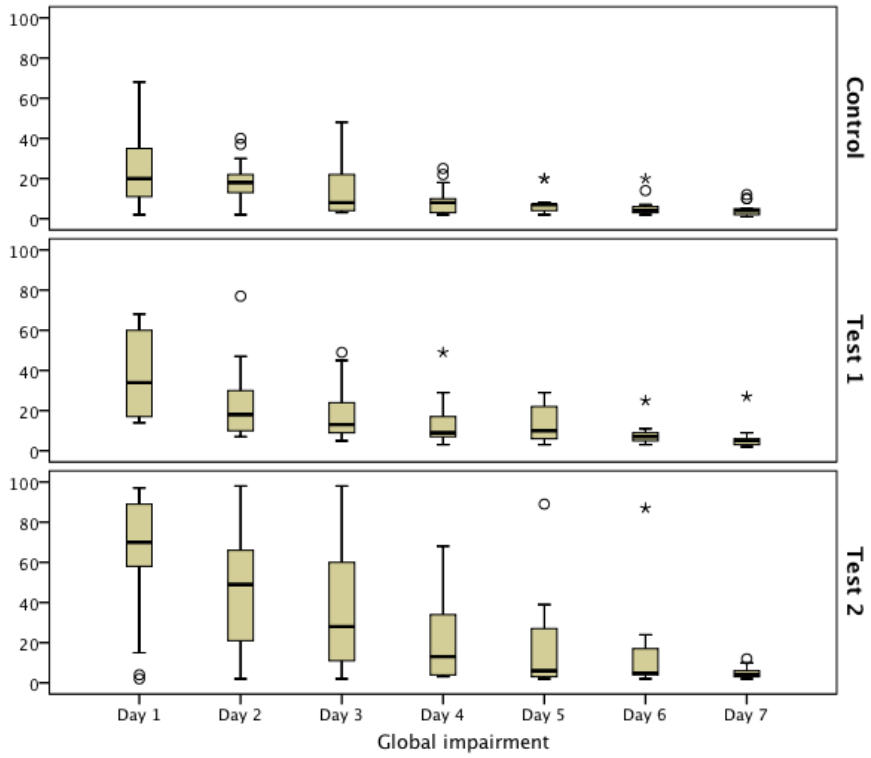

Figure 19. Overall influence (quantified by a 100-mm VAS) on patients' quality of life during the first postoperative week.

When the three treatment group data was pooled together, the level with which patients reported a range of symptoms is displayed in tables 15 - 18. A gradual reduction of the signs and symptoms was observed from day 1 to day 7 (p>o.ooo). Swelling was the only parameter studied that had its peak on day 2 and then decreased gradually until day 7. The values for bruising, bleeding and nausea were low during the observation period. Pain, both average and maximal, was higher during the first day and decreased gradually until day 4, where it stabilized in a value close to zero. This coincided with the analgesic intake, which dropped at day 4.

Table 15. Number of patients reporting limitation of various daily activities.

Activity	Amount of limitation (categorization of VAS)	Postoperative day						
		1	2	3	4	5	6	7
Chewing	>8 - 10	10	5	3	2	0	1	2
	>6 - 8	11	10	9	2	4	2	1
	>4 - 6	11	6	9	5	2	3	0
	>2 - 4	11	20	13	13	9	7	5
	>0 - 2	16	16	19	28	34	33	35
	0	1	6	9	12	14	17	21
Mouth opening	>8 - 10	6	2	2	2	2	3	2
	>6 - 8	6	7	4	0	1	0	0
	>4 - 6	11	10	9	5	1	1	0
	>2 - 4	7	11	8	7	4	1	2
	>0 - 2	25	24	30	27	40	40	38
	0	7	10	11	13	16	19	22
Speech	>8 - 10	3	2	1	1	2	3	2
	>6 - 8	8	6	2	1	1	0	0
	>4 - 6	8	6	6	1	0	0	0
	>2 - 4	5	6	6	7	1	0	1
	>0 - 2	28	32	35	37	40	37	35
	0	9	11	13	16	19	23	25
Sleep	>8 - 10	3	1	1	1	1	2	1
	>6 - 8	7	4	1	1	2	1	1
	>4 - 6	5	7	5	2	0	0	0
	>2 - 4	5	6	7	6	2	1	0
	>0 - 2	24	31	36	38	37	37	35
	0	7	11	13	15	21	22	26
Work	>8 - 10	5	4	3	1	2	3	2
	>6 - 8	8	2	1	2	0	0	0
	>4 - 6	6	10	5	2	1	0	0
	>2 - 4	4	3	5	4	0	1	2
	>0 - 2	14	20	25	26	28	29	25
	0	7	10	12	15	19	19	23
Daily activities	>8 - 10	7	5	3	2	2	3	2
	>6 - 8	6	1	2	1	1	0	0
	>4 - 6	13	10	4	4	1	0	0
	>2 - 4	6	9	7	3	4	2	1
	>0 - 2	23	28	36	40	36	37	34
	0	5	9	11	13	19	21	26

Social interaction	>8 - 10	8	6	4	1	2	2	2
	>6 - 8	8	7	4	2	0	0	0
	>4 - 6	4	5	7	7	3	2	0
	>2 - 4	11	9	5	4	5	3	0
	>0 - 2	21	25	31	35	33	35	36
	0	9	11	12	14	20	21	25
Favorite activities	>8 - 10	10	4	4	2	3	2	2
	>6 - 8	9	8	4	1	3	2	0
	>4 - 6	8	9	6	4	1	3	1
	>2 - 4	6	7	6	6	2	0	0
	>0 - 2	17	22	28	33	33	35	34
	0	8	11	12	14	19	20	24

Table 16. Number of patients reporting postoperative signs and symptoms.

Symptom	Amount of limitation (categorization of VAS)	Postoperative day						
		1	2	3	4	5	6	7
Swelling	>8 - 10	4	10	9	0	0	0	0
	>6 - 8	9	13	10	8	0	1	0
	>4 - 6	13	9	7	9	6	2	1
	>2 - 4	10	12	11	14	13	6	4
	>0 - 2	233	15	21	23	30	39	38
	0	4	5	6	10	14	15	21
Hematoma	>8 - 10	0	2	2	1	1	0	0
	>6 - 8	6	5	5	3	0	0	0
	>4 - 6	3	4	2	5	2	2	0
	>2 - 4	1	5	5	3	7	5	1
	>0 - 2	37	30	34	36	32	30	36
	0	16	17	15	15	20	25	26
Bleeding	>8 - 10	1	0	0	0	0	0	0
	>6 - 8	3	2	1	1	0	0	0
	>4 - 6	7	3	1	0	0	0	0
	>2 - 4	5	3	3	2	1	0	0
	>0 - 2	32	37	41	42	40	34	35
	0	14	18	17	19	22	29	29
Nausea	>8 - 10	1	1	1	1	0	0	0
	>6 - 8	0	2	1	0	0	0	0
	>4 - 6	4	3	5	2	0	0	0
	>2 - 4	4	3	1	2	3	0	0
	>0 - 2	34	37	37	30	37	35	33
	0	20	18	19	20	23	28	30
Bad taste	>8 - 10	1	2	1	0	0	0	0
	>6 - 8	2	3	4	4	0	1	0
	>4 - 6	8	7	3	1	4	2	1
	>2 - 4	13	6	6	3	2	1	2
	>0 - 2	20	35	34	39	37	35	32
	0	10	10	15	17	21	25	29

Table 17. Number of patients reporting average pain, maximal pain and global impairment.

	Amount of limitation (categorization of VAS)	Postoperative day						
		1	2	3	4	5	6	7
Average pain	>8 - 10	1	1	0	0	0	0	0
	>6 - 8	8	3	1	0	0	0	0
	>4 - 6	12	7	6	2	0	0	1
	>2 - 4	14	16	9	9	5	6	2
	>0 - 2	26	29	36	40	41	36	35
	0	3	8	11	13	18	22	25
Maximal pain	>8 - 10	6	1	0	0	0	0	0
	>6 - 8	10	2	2	0	0	1	0
	>4 - 6	13	12	8	4	0	0	2
	>2 - 4	12	10	12	9	6	6	3
	>0 - 2	19	30	33	38	40	36	34
	0	3	8	9	13	17	21	24
Global impairment	>8 - 10	8	2	2	0	2	2	0
	>6 - 8	7	3	1	1	0	0	0
	>4 - 6	9	8	7	3	0	0	0
	>2 - 4	10	14	11	7	7	2	1
	>0 - 2	25	29	29	38	35	37	37
	0	4	7	13	14	19	22	24

Table 18. Number of patients reporting on analgesic intake.

	Number of analgesics / day	Postoperative day						
		1	2	3	4	5	6	7
Analgesic intake	3	17	27	19	13	5	3	0
	2	20	14	13	7	5	3	2
	1	15	6	9	12	13	10	7
	0	12	17	23	32	41	48	54

The necessity to perform a simultaneous GBR procedure during the implant surgery had a significant impact on the patients' quality of life. These patients suffered more interference than those not needing bone regeneration techniques on the following variables: mouth opening: day 3 and 4, speech: day 3 and 4, daily activities: day 3, 4, and 5, social interaction: day 2, 3 and 4, favorite activities: day 3, swelling: day 2, 3, 4, 5, 6, hematoma: day 2, nausea: day 3, average pain: day 3 and 4, maximal pain: day

2, overall influence on daily activities: day 2, 3, 4 and 5, analgesic intake: day 2, 3, 4, 5 and 6.

The quantity of surgical sites involved in the surgical procedure had a more limited influence on the postoperative period. Cases with two surgical sites showed statistically significant differences on hematoma occurrence at day 1 and working interference during day 2.

Surgery length had again a great influence on the postoperative period. Longer surgeries had a greater adverse impact on the patient's chewing ability during day 2, 3, 4, 5 and 6, mouth opening during day 1, 2, 3, 4, 5 and 6, speech during day 1, sleep during day 1, interference with daily activities during day 2 and 3, swelling during day 2, 3, 4 and 5, bruising at day 5, average pain suffered during day 2 and 4, maximal pain experienced at day 2 and 3, analgesic intake during day 2, 3 and 4.

Implant surgery location had no influence on the patients' quality of life.

Gender seemed to influence certain aspects of the postoperative period. Women had a greater impairment in the following parameters: mouth opening during day 5 and 6, sleep impairment at day 6, and global impairment on daily activities at day 5.

6.4. Time and costs:

6.4.1. Time analysis:

Time derived from each working step for the three treatment groups is represented in Table 19. Time compilations based on treatment phases are presented in Table 20. Statistically significant differences between groups are identified by different letters, such as A and B, printed under the column "p" in the table. Groups with the same letter are considered to be not statistically significantly different from each other.

Table 19. Time derived from each working step. Alginate = preliminary registrations, Cast = study cast fabrication and cast mounting on articulator, Wax-up = diagnostic wax-up production, Cast optical = cast optical scan, Rx template = radiographic template production, Rx exam = radiographic exam, Start HW = start hardware, Start SW = start software, Import DICOM = Import DICOM data, Prepare data = prepare radiographic data, Implant plan = plan implant position and dimensions, Export = export data, Qx template = Surgical template production, Flap = Flap elevation, Study implant = study implant placement, GBR = guided bone regeneration procedure, Suture = wound closure. Statistically significant differences between groups are identified by different letters, such as A and B, printed under the column "p". Groups with the same letter are considered to be not statistically significantly different from each other.

		Control						Test 1						Test 2					
		n	**Media**	**Min**	**Max**	**IQR**	**p**	***n***	**Media**	**Min**	**Max**	**IQR**	**p**	***n***	**Media**	**Min**	**Max**	**IQR**	**p**
Diagnostic	Alginate	22	5.83	3.30	20.38	2.75	A	21	5.9	2.27	8.03	2.38	A	17	5.93	2.17	13	3.36	A
	Cast	26	40	29	45	5.25	A	24	37	22	45	10.25	A	23	25	12	50	11	A
	Wax-up	26	14	9	45	11.25	A	24	17	9	45	17.5	A	23	17	10	45	18	A
	Cast optical	26	0	0	0	0	A	13	9.91	6.35	18	1.67	B	22	19.5	12.1	30	3,67	C
	Rx templat	26	70	50	150	13	A	24	62	35	75	10	A	23	0	0	0	0	B
Radiology	Rx exam	23	8.23	1.37	14.17	1.65	A	22	9	4	20	7	A ,B	21	13	4.05	23	4	B
Planning	Start HW	26	0	0	0	0	A	23	1.72	1.05	2.68	0.45	B	22	1.02	0.95	2.03	0.22	B
	Start SW	26	0	0	0	0	A	23	0.58	0.32	1.37	0.15	B	22	0.55	0.50	0.85	0.13	B
	Import DICOM	26	0	0	0	0	A	23	1.73	0.72	4.45	2.12	B	22	1.07	0.70	2.83	0.55	B
	Prepare Data	26	0	0	0	0	A	23	2.40	1.47	7.45	1.27	B	22	5.85	5.03	10.95	0.84	B
	Implant plan	26	5.5	1.23	16	7.09	A	23	3.48	1.58	8.65	3.55	A ,B	22	2.02	1.65	2.80	0.63	B
	Export	26	0	0	0	0	A	23	2.93	1.37	13.28	4.23	B	22	2.07	0.85	4.95	0.93	B
Template	Qx templat	23	4.38	2	11	3.53	A	23	151 20	576 0	288 00	100 80	B	22	432 0	216 0	144 00	600 0	C
Surgery	Flap	24	6.07	1.85	17	4.83	A	23	6.51	2.45	23	6.82	A	21	6.45	3.63	27	5.64	A
	Study implant	24	20.92	9.02	54	12.8	A	22	23.17	9	43.85	21.8	A	23	18.48	6.33	45	18.12	A
	GBR	13	14.8	5.22	37.97	16.3	A	9	20	5.5	21.27	8.97	A	14	15.22	6.57	75	12.80	A
	Suture	24	9.09	3.02	34	7.7	A	19	13.4	4.08	39.98	9.62	A	20	15.41	1.37	36.72	9.75	A

Table 20. Global time summaries. Global prosthetic phase = Alginate + Cast + Wax-up + Rx template + Optical scan, Global Surgical Plan = Start HW + Start SW + Import DICOM + Prepare data + Plan + Sleeve + Export, Global Surgery Single Implant = Flap elevation + Study implant placement + GBR + Suture + Time to modify surgical template, Global Time Excluding Template Production = Global prosthetic phase, Rx exam, + Global surgical plan + Global Surgery single Implant, Global Dental Office Time = Alginate + Rx exam + Global surgical plan + Global surgery single implant. Statistically significant differences between groups are identified by different letters, such as A and B, printed under the column "p". Groups with the same letter are considered to be not statistically significantly different from each other.

	Control						Test 1						Test 2					
	n	**Median**	**Min**	**Max**	**IQR**	**p**	***n***	**Median**	**Min**	**Max**	**IQR**	**p**	***n***	**Median**	**Min**	**Max**	**IQR**	***n***
Global Prosthetic Phase	26	129.06	111.3	236.5	18.16	A	24	136.99	79,65	154.02	21.88	A	23	73.5	46.7	100	23.02	B
Global Surgical plan	22	5.5	1.23	16	7.09	A	23	13.31	9.67	27.27	10.48	B	23	13.7	11.45	20.50	2.75	B
Global Surgery single implant	24	44.9	20.85	108.57	41.82	A	20	51.2	24.3	92.48	30.99	A	20	55.9	16.05	142.65	36.94	A
Global time excluding template production	22	194.37	155.82	321.03	56.73	A	22	215.01	183.25	277,32	35.98	A	22	153.55	115.5	240.15	36.18	B
Global dental office time	22	70.37	40,25	133.25	40.66	A	22	79.12	57.25	128.88	38.26	A	22	82.14	42.5	182.68	37.78	A

A graphic representation of times derived from the different working steps of the three treatment protocols studied are presented in Figures 20 to 24.

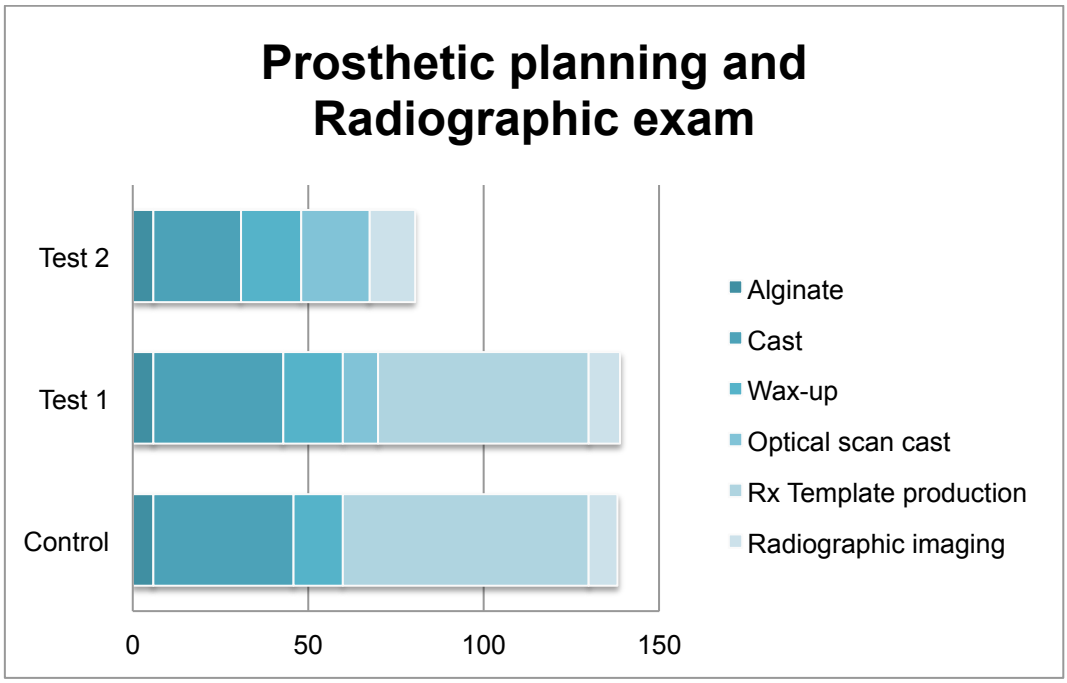

Figure 20. Bar graph representation of the time invested (median of minutes) to fulfill the prosthetic planning phase and radiographic exam.

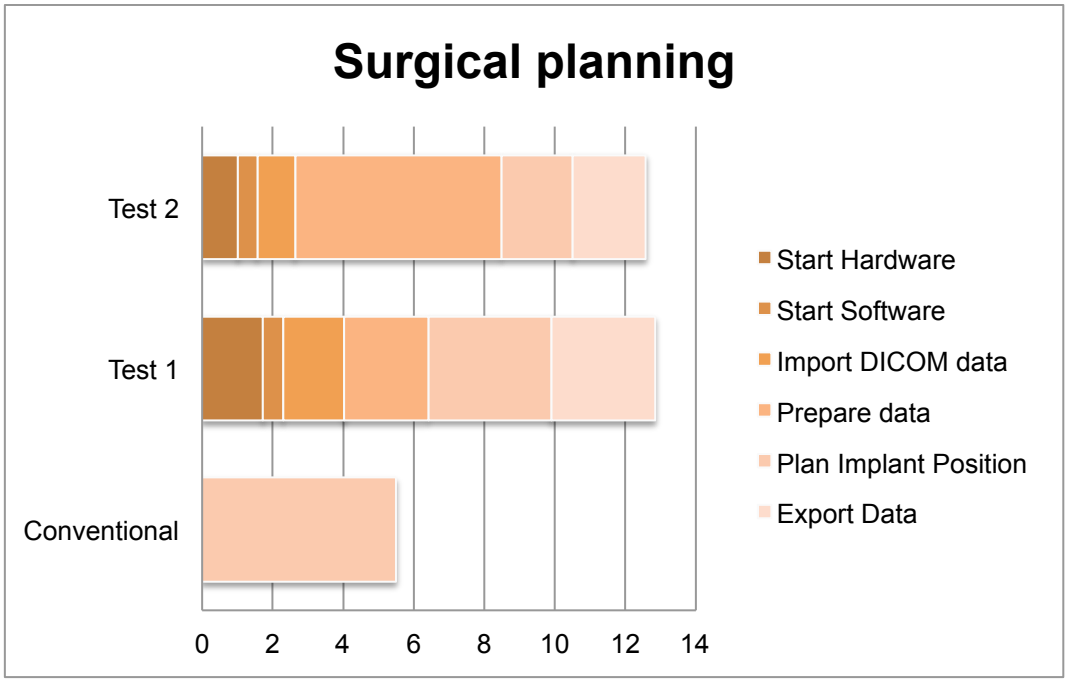

Figure 21. Bar graph representation of the time invested (median of minutes) to fulfill the surgical planning.

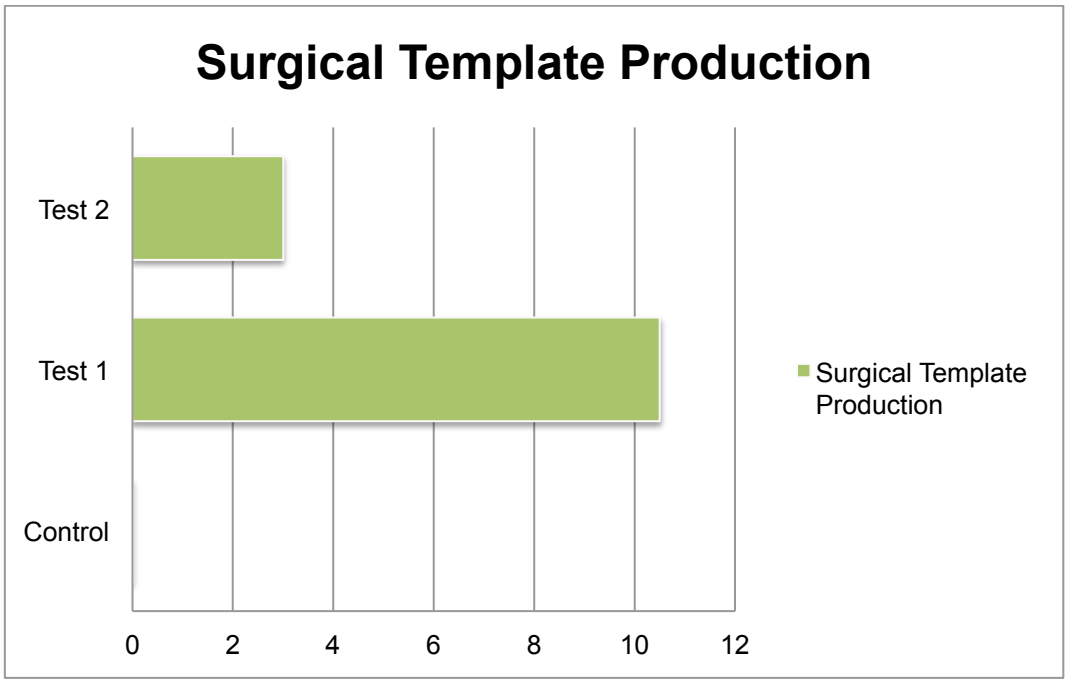

Figure 22. Bar graph representation of the waiting time (median of days) required to receive the surgical template.

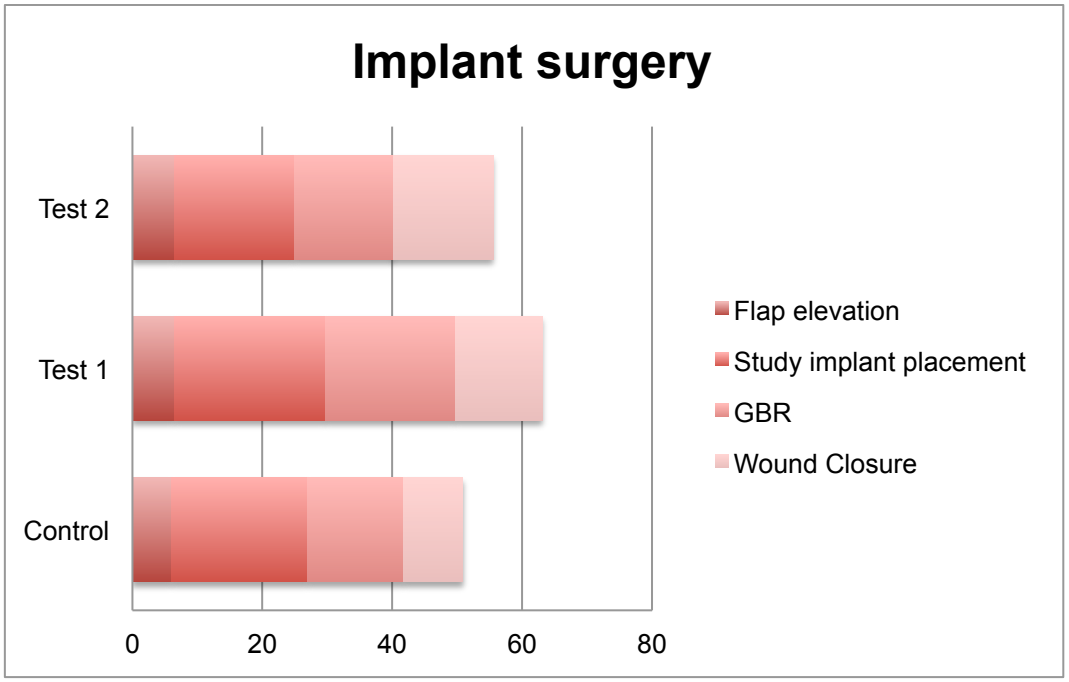

Figure 23. Bar graph representation of the time invested (median of minutes) during the different surgical steps.

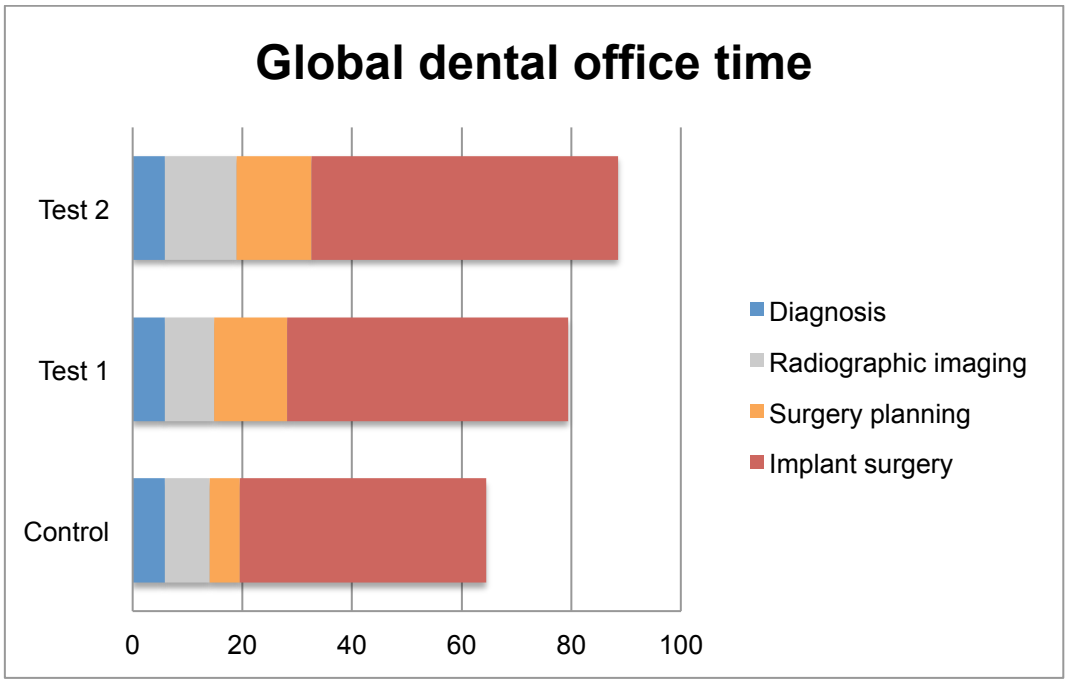

Figure 24. Bar graph representation of the time invested (median of minutes) by the dentist in the different steps of the implant planning and placement protocols. Diagnosis = Preliminary registrations, Radiographic imaging = Radiographic exam, Surgery planning = Global surgical plan, Implant surgery = Global surgery single implant.

6.4.2. Economical analysis:

Cost calculations for every clinical procedure are detailed in Table 21.

Table 21. Cost analysis for the different steps of the implant planning and placement protocols. Surgical template costs were represented as the mean cost of all templates ordered.

				Control		Test 1		Test 2	
		SSO / *VZLS* position	Tax points	n	CHF	n	CHF	n	CHF
Prosthetic phase	Patient information	4250	68	1	210.8	1	210.8	1	210.8
	Alginate impressions	4090	12	2	74.4	2	74.4	2	74.4
	Intermaxillary registration	4075	11	1	34.1	1	34.1	1	34.1
	Cast production	*012*	*4*	4	88.8	4	88.8	4	88.8
	Cast articulation	*032*	*5*	1	27.75	1	27.75	1	27.75
	Antagonist cast articulation	*036*	*4,8*	1	26,64	1	26,64	1	26,64
	Wax-up per unit	*048*	*7,1*	1	39,41	1	39,41	1	39,41
	Radiographic template production	*513*	*53,8*	1	322,48	1	322,48	0	0
	Cast optical scan	*Not applicable*	*5*	0	0	1	27.75	2	55.5
Radiographic imaging	Radiographic exam	OPG: 4054 CBCT: 4059	OPG: 45 CBCT: 113	1	139.5	1	350.3	1	350.3
Surgical splint	*Surgical splint production*	*Not applicable*	*Not applicable*	1	0	1	350	1	409.33
Implant surgery	Anesthesia	4065	11	1	68.2	1	68.2	1	68.2
	Implant placement	4253	192	1	595.2	1	595.2	1	595.2
TOTAL					**1728,53**		**2389,53**		**2117,05**

6.5. Accuracy:

The global deviation values between the baseline reference position and the final implant position for the different planes evaluated are depicted in Table 22. Sixteen cases (Control: 10, Test 1: 3, Test 2: 3) could not be analyzed due to technical limitations (final casts didn´t allow reliable file overlapping).

No differences were observed between groups for global deviation at occlusal point or depth. Statistically significant differences were observed between Conventional and the other two CAIPP groups for global deviation at implant shoulder ($p<0.000$), apex ($p<0.000$) and implant angulation ($p<0.000$).

However, the basis for these inconsistencies seems to be methodological rather than clinical. The absence of a volumetric radiograph in the Conventional group made the determination of the precise baseline reference position difficult. The implant position was fully determined by prosthetic guidelines inside a virtual surface reconstruction of the study model with the diagnostic wax-up (Figure 25). The absence of bone references allowed a range of implant positions that fulfilled the prosthetic criteria, fact that disabled the validity of the baseline reference position and, therefore of any comparison between groups (Figure 26).

In 23 cases (Control: 1, Test 1: 11, Test 2: 11) intraoperative changes of the treatment protocol occurred, which prevented totally or partially the fully guided implant placement. An analysis excluding theses cases was also performed and is depicted in Table 22.

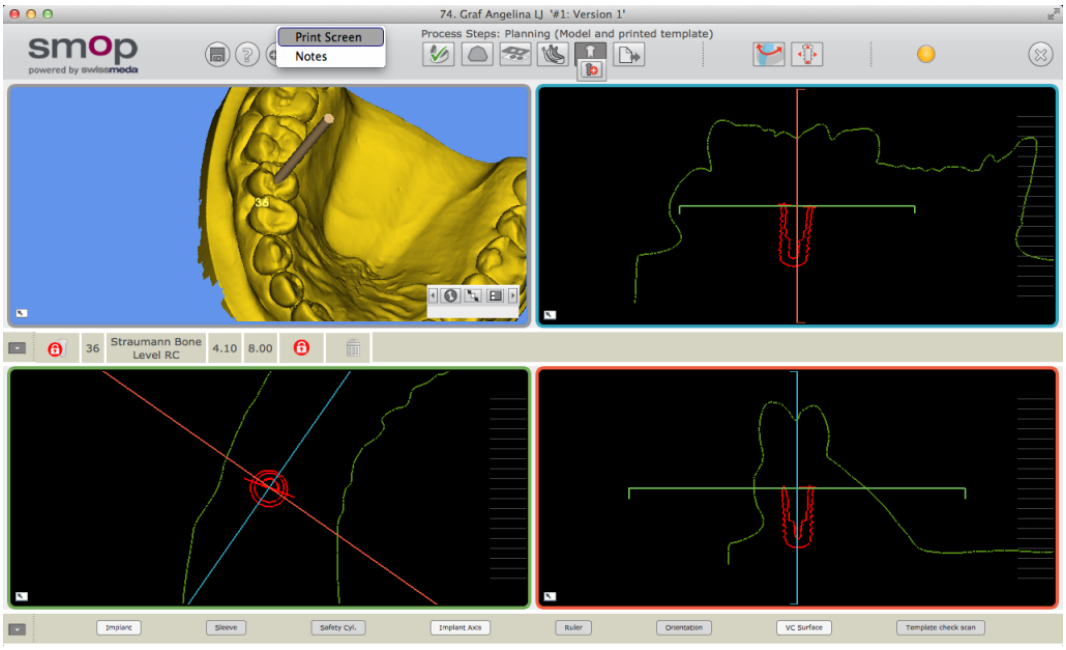

Figure 25. Baseline implant position determination in the Control group. The implant position (red silhouette) is fully determined by prosthetic guidelines inside a surface geometry reconstruction of the study model with the diagnostic wax-up (green silhouette).

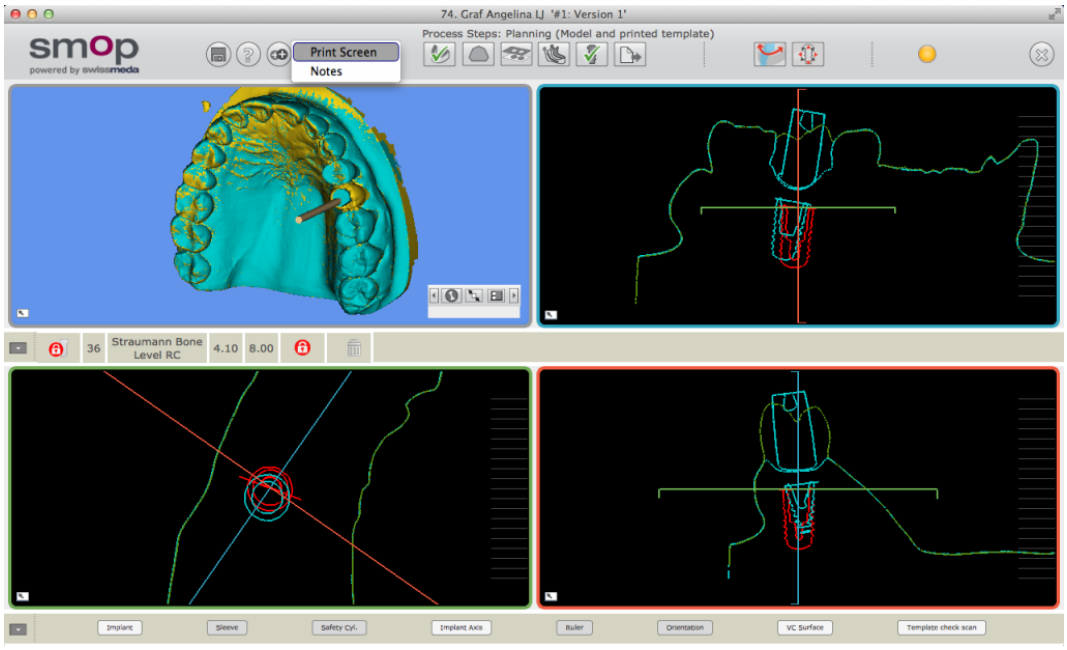

Figure 26. Superposition of the surface geometry of the final model with the scanning post (turquoise silhouette) and the surface geometry of the study model with the diagnostic wax-up (green silhouette). A significant discrepancy is visible between the planned implant position (red implant) and the final implant position (turquoise implant).

Table 22. Global deviation values between the baseline reference position and the final implant position. The parameters mean, standard deviation (SD), maximum (Max) and minimum (Min) have been used to describe the sample distribution. The table presents results after analyzing every case evaluated (Overall Data) and after excluding the cases where a fully guided implant placement was not possible (Data after exclusion of surgical splint deviation cases). Statistically significant differences between groups are identified by different letters, such as A and B, printed under the column "p". Groups with the same letter are considered to be not statistically significantly different from each other.

	Control				Test 1				Test 2			
Overall data (n)	16				21				20			
	Mean	SD	Max – Min	p	Mean	SD	Max – Min	p	Mean	SD	Max – Min	p
Occlusal	0.65	0.26	0.23 – 1.2	A	0.59	0.44	0.09 – 1.76	A	0.76	0.5	0.17 – 1.78	A
Shoulder	1.25	0.62	0.57 – 2.55	A	0.53	0.36	0.05 – 1.33	B	0.72	0.31	0.16 – 1.22	B
Apex	2.32	1.24	0.77 – 5.29	A	0.97	0.57	0.25 – 2.49	B	1.08	0.57	0.36 – 2.54	B
Depth at shoulder	0.28	1.01	-1.17 – 2.18	A	0.2	0.65	-1.14 – 1.19	A	-0.1	1	-2.33 – 1.47	A
Angle	7.36	3.36	1.5 – 13.6	A	4.23	2.68	0.8 – 10.7	B	3.13	2.12	0.6 – 8.2	B
Data after exclusion of surgical splint deviation cases (n)	16				11				11			
	Mean	SD	Max – Min	p	Mean	SD	Max – Min	p	Mean	SD	Max – Min	p
Occlusal	0.65	0.26	0.23 – 1.2	A	0.43	0.23	0.09 – 1.08	A	0.53	0.3	0.17 – 1.11	A
Shoulder	1.25	0.62	0.57 – 2.55	A	0.54	0.33	0.05 – 1.33	B	0.61	0.27	0.27 – 1.05	B
Apex	2.32	1.24	0.77 – 5.29	A	0.9	0.43	0.34 – 2.49	B	1.02	0.64	0.36 – 2.54	B
Depth at shoulder	0.28	1.01	-1.17 – 2.18	A	0.11	0.62	-0.61 – 1.19	A	-0.32	0.9	-2.33 – 0.66	A
Angle	7.36	3.36	1.5 – 13.6	A	2.41	1.4	0.8 – 7.10	B	2.69	1.78	0.6 – 6.5	B

Confounding factors such as splint support nature (Embedded: n=28 or Free-end: n=6), anatomical location of the implant (Maxilla: n=23, Mandible: n=12), region of the implant site (Anterior teeth: n=6, Posterior teeth: n=29 / Right side: n=19, Left side:

n=16), implant length (>9mm: n=29 or ≦9mm: n=38) did not prove to have an influence on the differences between groups.

A graphic representation of the discrepancy direction for occlusal, implant shoulder and implant apex planes is presented in Figures 27, 29, and 31 for the overall data analysis and in Figures 28, 30, and 32 after excluding the cases where a fully guided implant placement was not possible.

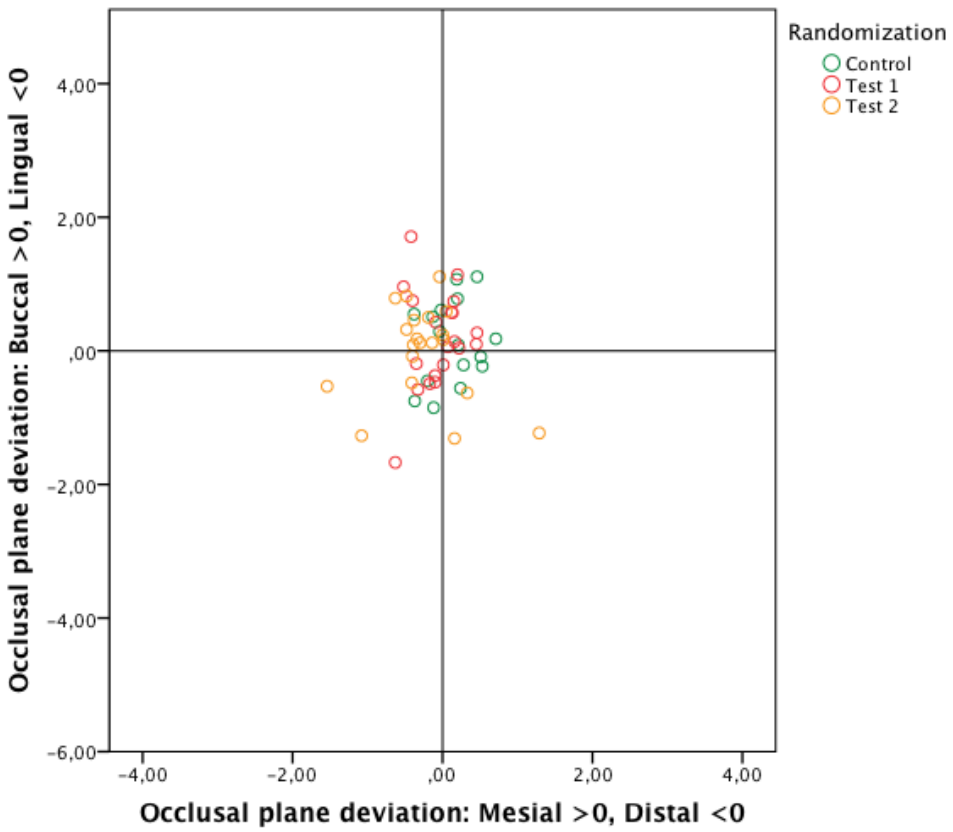

Figure 27. Graphic representation of the inaccuracy directions at the occlusal plane when overall data was analyzed.

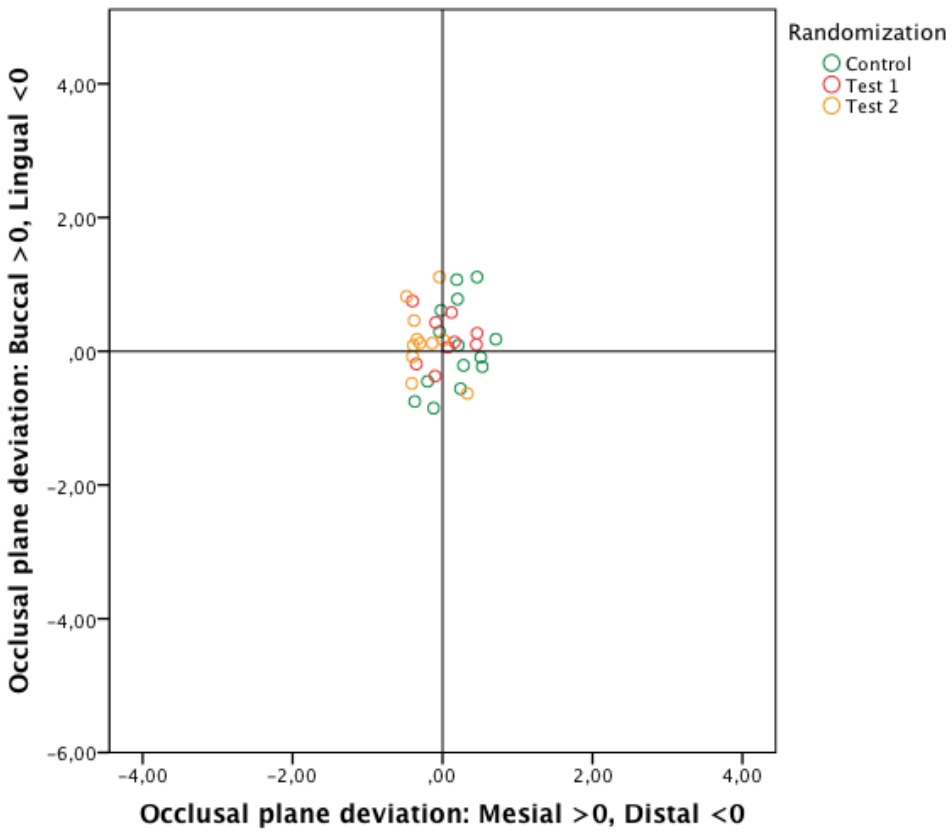

Figure 28. Graphic representation of the inaccuracy directions at the occlusal plane after excluding the cases where a fully guided implant placement was not possible.

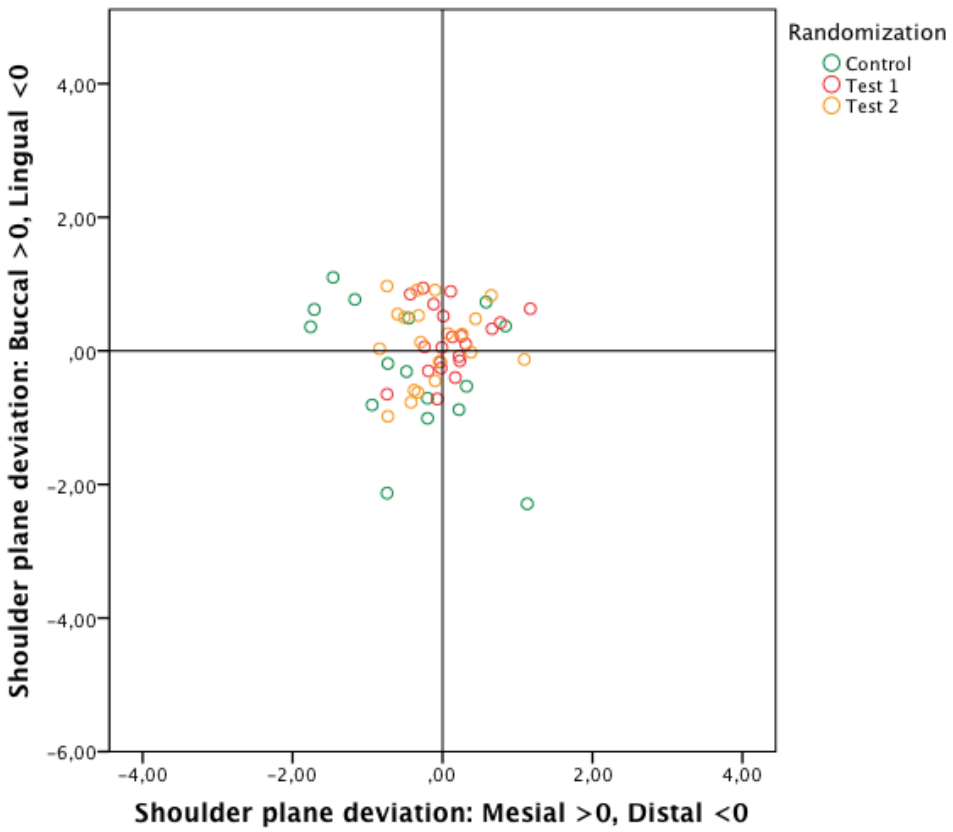

Figure 29. Graphic representation of the inaccuracy directions at the implant shoulder plane when overall data was analyzed.

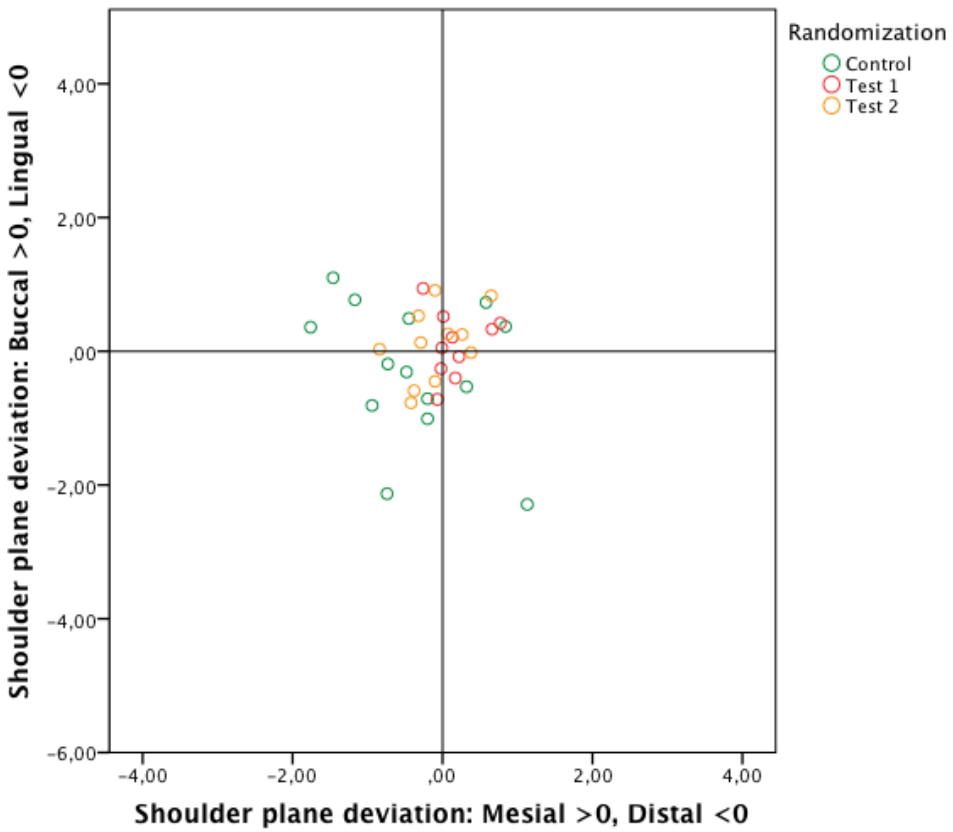

Figure 30. Graphic representation of the inaccuracy directions at the implant shoulder plane after excluding the cases where a fully guided implant placement was not possible.

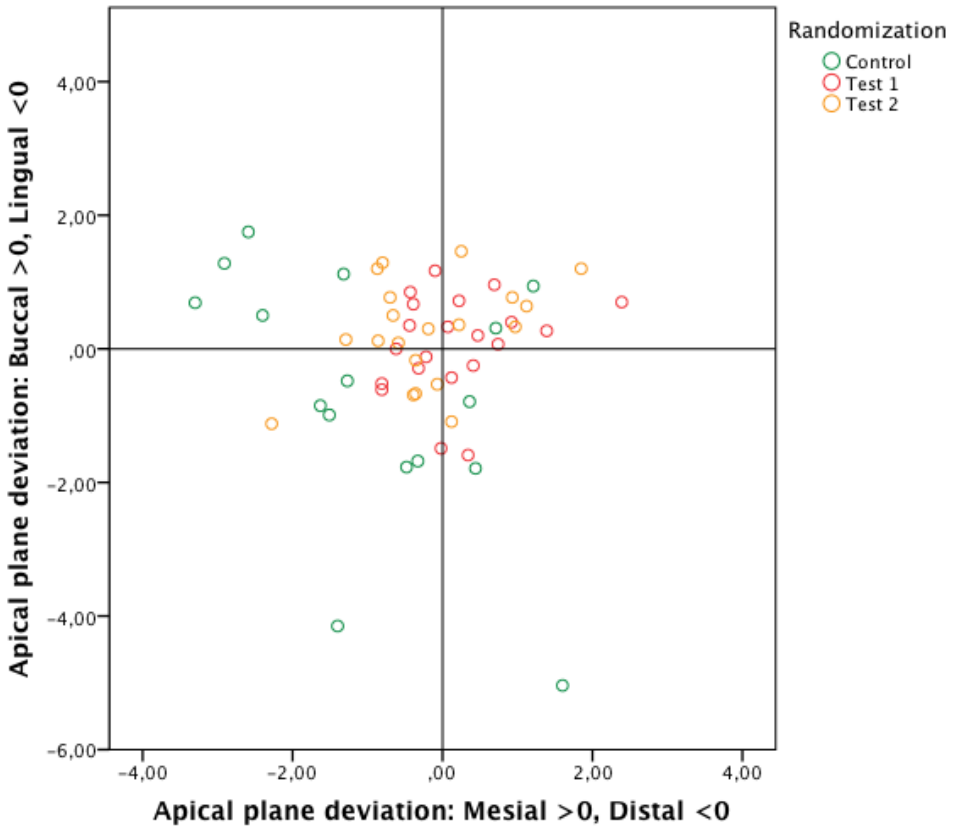

Figure 31. Graphic representation of the inaccuracy directions at the implant apex plane when overall data was analyzed.

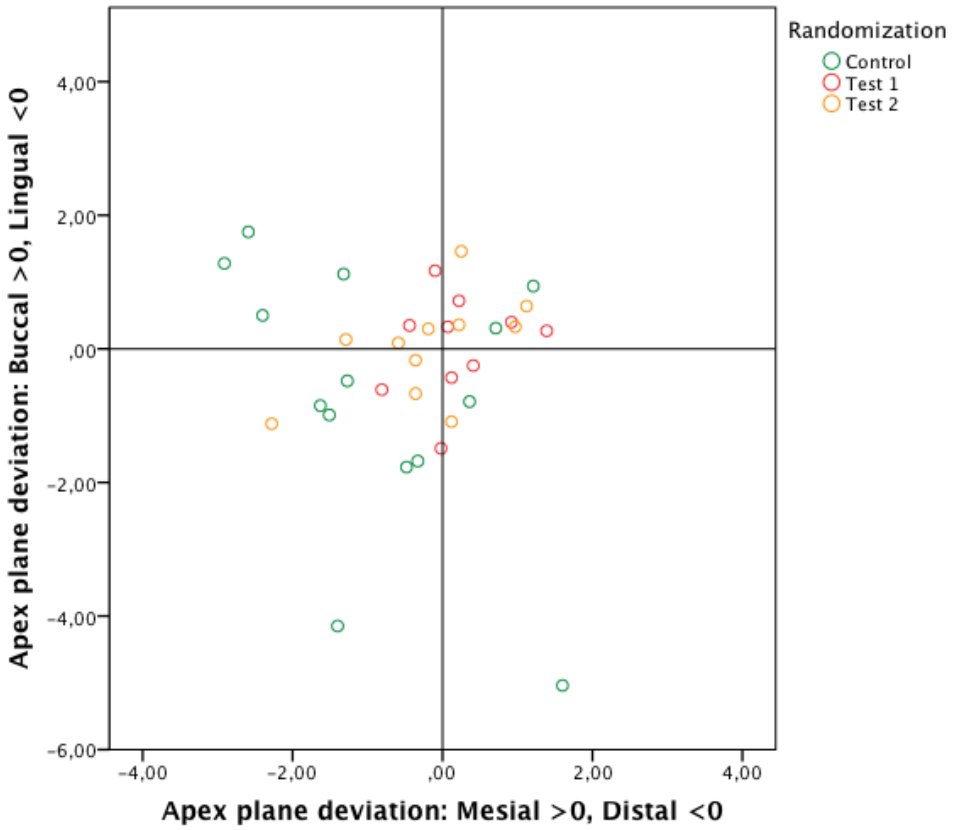

Figure 32. Graphic representation of the inaccuracy directions at the implant apex plane after excluding the cases where a fully guided implant placement was not possible.

Table 23 categorizes discrepancies between groups according to mesial-distal and buccal-oral directions. No differences were detected on the mesio-distal and bucco-oral distribution of discrepancies between groups.

Table 23. Categorization of the accuracy discrepancies into mesio-distal and bucco-oral directions. The table presents results after analyzing every case evaluated (Overall Data) and after excluding the cases where a fully guided implant placement was not possible (Data after exclusion of surgical splint deviation cases).

	Control		Test 1		Test 2	
Overall Data (n)	16		21		20	
	Mesial	Distal	Mesial	Distal	Mesial	Distal
Occlusal	9	7	12	9	5	15
Shoulder	5	11	12	9	5	15
Apex	5	11	12	9	7	13
	Buccal	Lingual	Buccal	Lingual	Buccal	Lingual
Occlusal	9	7	15	6	13	7
Shoulder	7	9	13	8	12	8
Apex	7	9	12	9	14	6
	Control		Test 1		Test 2	
Data after exclusion of surgical splint deviation cases (n)	16		11		11	
	Mesial	Distal	Mesial	Distal	Mesial	Distal
Occlusal	9	7	8	3	2	9
Shoulder	5	11	8	3	3	8
Apex	5	11	8	3	5	6
	Buccal	Lingual	Buccal	Lingual	Buccal	Lingual
Occlusal	9	7	8	3	8	3
Shoulder	7	9	7	4	7	4
Apex	7	9	7	4	7	4

7. Discussion

7.1. Preliminary remarks:

In the present investigation, implant-prosthetic rehabilitation of all patients was achieved irrespective of the protocol used. All implants were placed successfully and exhibited osseointegration at the time of delivery of the prostheses. The prosthetic rehabilitation could be accomplished in all patients without any significant complications.

Nevertheless, certain differences between treatment groups were detected. The following discussion will focus on these.

7.2. Clinician-related outcomes:

7.2.1. Predictability of surgical planning:

The diagnostic potential of two treatment concepts has been evaluated by studying the clinicians' capacity to predict intrasurgical findings during the planning phase. The main difference between both treatment concepts was the nature of the radiographic examination employed and the visualization tools used. While 2D x-rays visualized in a light table were employed in the Control group, 3D radiographs inspected in a dedicated implant planning software were used in the CAIPP groups.

The results have shown that a 3D radiographic evaluation combined with a dedicated implant planning software allows the clinician to foresee the nature of the bony defect and therefore predict the necessity and materials needed to perform GBR procedures. The implant length could be also predicted more precisely, which suggests a better visualization of the available bone volume with the 3D evaluation.

This superior diagnostic and subsequent therapeutic potential of 3D imaging over conventional 2D radiographic exams has been documented for specific anatomical regions (3, 7, 24). Fortin et al. (7) showed that 3D imaging combined with a specific implant planning software could allow a better visualization of the bone volume complexity in severely resorbed posterior maxillae and therefore permit the clinician to perform less invasive treatment alternatives to those indicated after implant planning with conventional 2D x-rays. Two thirds of the sinus floor augmentation procedures indicated after conventional planning could be avoided by alternative implant placement strategies when the cases where analyzed three-dimensionally with a dedicated planning software. They concluded that panoramic x-rays systematically underestimate available remaining bone for implant placement in the severely resorbed maxilla. These findings were corroborated by Temmerman et al. (24), who observed a constant underestimation in the upper premolar region mesio-distal dimensions of OPGs compared to CBCT measurements.

Nevertheless, even though a 3D volume understanding of the residual bone

combined with a virtual implant planning software can improve the preoperative surgical predictability, 3D radiology still exposes the patient to greater ionizing radiation than conventional X rays (3, 25). The radiographic technique should be chosen weighing the benefits and risks for the patient. Intraoral and panoramic radiology provide enough information to predictably plan most implant surgeries, as proven by the successful and complication-less implant placement in every case of the Control Group in this study. Therefore the routine indication of 3D radiology for every implant case should be considered an unacceptable practice (3). Three-dimensional radiology should be reserved for cases where conventional radiology fails to adequately provide information on relevant anatomical boundaries or pathologies, in cases where these techniques provide additional information that can help minimize the risk of damage to critical anatomical structures or improve implant planning or positioning, or as part of ethically approved clinical research, as occurred in the present investigation (3).

7.2.2. Complications and unexpected events:

Despite CAIPP protocols are commonly marketed as easy and predictable, complications and unexpected events have been regularly reported (15). The results of the present study highlight the occurrence of a relevant amount of surgical protocol deviations caused by unanticipated technical difficulties or peroperatively-detected suboptimal treatment outcomes that required some kind of plan adjustment. The nature of the unexpected events that lead to protocol deviations could be categorized into splint-related problems and implant positioning problems.

Most of the splint-related problems concerned the misfit between the splint and the residual dentition. The most probable reasons for these imprecisions are distortion of impression material after impression taking, inaccuracies derived from cast model fabrication and digitization, or fabrication errors of the acrylic guides either manually or by means of CAD/CAM. The distribution of splint-related incidences was similar between groups, however the time required to solve the problem varied. Misfit was fixed by locating the resin interference either visually or with silicone interference-locating materials (Fit Checker, GC Corporation, Japan) and by eliminating it with burs

until the splint sat firmly in position without buckling. The fastest adjustments were made in the conventional group, followed by the Test 2 group, and finally by the Test 1 group. The fact that conventional splints only covered the first mm of the occlusal table and incisal edges may account for the simplicity to locate and eliminate interferences. On the other hand, splints in Test group 1 were made up of an opaque resin that covered the entire surface of teeth and mucosa, which delayed the interference localization. Splints in Test group 2 had a tubular design that allowed punctual contacts between the splint and residual dentition. The clinician had the opportunity to specify where and how many contacts should the splint have. This fact, added to the open splint design and reduced volume which allowed a better visibility, could explain the speed to locate and adapt the Test 2 splints.

Another splint-related problem, which was associated mostly to splints in Test group 2, was the excessive friction between the drill keys and the splint. In this group the splint was produced by 3D printing and the traditional metallic sleeves were replaced by resin printed sleeves with a slightly reduced sleeve diameter. This method intends to reduce the tolerance between the drill key and the splint sleeve in order to minimize sleeve-connected positioning errors. A recent investigation has proven a reduction of drill lateral movements when 3D printed sleeves are compared to metallic sleeves (21). However, this tight fit between components is likely to have caused these reported incidences, which simply require a tougher insertion of the drill keys in the splint for their resolution.

Other reported technical problems related to the splints imply the incompatibility of certain implant types with guided implant placement protocols at the time of the study performance, or late arrival of splints. Both problems could have been avoided with a superior understanding of the CAIPP system used and a better case planning. On the other hand, the planning software should ideally incorporate an up-to-date, company-independent library of available implants and prosthetic components to allow a comprehensive implant treatment planning without marketing-based limitations given by certain manufacturers.

The other category of protocol deviation sources was that related to implant malpositions. Numerous clinical inconsistencies in the vertical or axial position were noticed and corrected intrasurgically. The exact reason for these discrepancies is difficult to elucidate since they could be the result of punctual or accumulative limitations or errors in any of the CAIPP workflow steps (26) or be caused by surgical plan modifications undertaken intraoperatively to compensate a suboptimal preoperative planning. The false preoperative planning could be caused by discrepancies between the perceived computer image-based anatomical environment and the real intra-surgical situation. And these could be partially explained by image resolution limitations, radiographic artifacts and the difficulty to precisely define the alveolar bone cortical boundaries (27, 28). No matter what the origin was, these results confirm the necessity to systematically perform a strict intraoperative implant position control in every case even when performing CAIPP protocols. A blind belief in the computer-assisted surgical guide determined implant positions could lead to implant misplacement problems (29, 30). The fact that every prosthetic reconstruction in the study, except one, could be restored as planned, with a screw-retained prosthesis that fulfilled hygienic, functional and esthetic criteria, confirm the appropriateness of the final implant positions obtained. Different treatment outcomes would have been probably obtained if the implant positioning would not have been strictly monitored and no intrasurgical adaptation made.

When the incidence and nature of the complications detected in the present study is compared with those reported in the last systematic review on CAIPP protocols (15), some discrepancies are noticeable. According to the literature review, fracture of the surgical splint was the most commonly reported unexpected event (9, 12, 31-33). Conversely, this complication was never reported in our study. The most common complications were splint misfit and suboptimal implant position that was corrected intrasurgically by the clinician. Other reported complications, such as uncontrolled gingival removal (31, 34), alterations in the implant prosthetic connection (31), implant misplacement (29, 30), unexpected lack of bone for implant placement (35), limited oral aperture that hinder instrumentation (29, 35-37) or infections (14, 32), were also not reported in the present study. This is most likely due to the different nature of treatment

protocols assessed. While in the present study a precise population segment and treatment protocol (partial edentulous patients receiving tooth-supported splints) was evaluated, the systematic review included the entire array of treatment protocols enclosed under the term "Guided Surgery". This data collection hinders the understanding of the particular complications or unexpected events derived from specific treatment protocols. According to the authors, a categorization of the different CAIPP protocols is always mandatory, since different CAIPP protocols lead to significant outcome differences (18). On the other hand, the review results confirm the prevalence of intraoperative unexpected events when CAIPP protocols are performed. Events such as lack of implant primary stability (9, 31, 34, 36-38), or the occurrence of unexpected bone dehiscences or fenestrations (37) have been reported. These lead to intrasurgical adjustments that sometimes imply changes in the planned implant position, length or diameter (35, 37). These CAIPP complications and subsequent protocol modifications are consistent with those described in the present investigation and must be contemplated when performing computer-assisted implant placement techniques.

Comparing the rate and nature of complications and unexpected events to those of conventional protocols is a difficult task (12, 13). This statement can be explained by several factors: First, to our knowledge, no prospective clinical evaluation of the complication risk of a defined conventional protocol exists. Indeed, "conventional" is a very broad term comprising a vast array of clinical methodologies that are often less systematized than CAIPP protocols. Consequently, compared to the strictness of CAIPP schemes, conventional protocols are more clinically adaptable and allow intraoperative modifications that are hence not registered as complications or unforeseen events. Second, some incidences associated to CAIPP protocols, such as tensional forces in the splint caused by the intimate contact between instruments and the splint, are not relevant to the conventional scenario. Since conventional splints do not imply full guidance of the surgical instruments, tension generation and subsequent splint fracture or implant misplacement are less probable. These facts hinder a quantitative comparison between both protocols. The fact that in the present investigation the rate of complications was similar between groups is less relevant than the nature of the

complications themselves. Understanding the possible unexpected events will help the clinician prepare himself to confront the probable incidences.

The nature of complications registered in the conventional protocol was less splint-related and more related to intraoperative observations that lead to intrasurgical decisions to modify the foreseen protocol (need to implement a GBR or changes in implant diameter or length). This could reflect the scarcer amount of information available in the conventional protocol compared to the CAIPP protocols since bi-dimensional x-rays were available. Still this protocol didn´t escape from the need to adjust misfitting splints and from a critical evaluation of the splint quality since in one case the splint design was misleading and could not be used for implant placement.

Nevertheless problems with conventional splints are more forgiving than those in CAIPP splints. According to the study results, only one splint in the conventional group could not be used for implant placement, in contrast with the 22 cases in the CAIPP groups where the guided osteotomy and implant insertion couldn´t be fully executed. After adjustment, conventional splints could be further used to provide usefull anatomical information during implant placement. On the other hand, due to the absence of prosthetic anatomical references incorporated in the CAIPP splints, their surgical value once a splint-related complication is detected is minimal. The surgeon fully relies on the preoperative 3D radiograph-based planning, and fit and design of the surgical guide for a successful implant procedure. If, for some reason, the guide presents a serious misfit, fracture or an obvious planning error the surgeon is left without any prosthetic reference aid and can either abort the procedure or perform a free-hand implantation, which in certain clinical scenarios can result challenging and less compatible with a successful implant position.

The results of the present study confirm the statement that CAIPP techniques cannot be regarded as easier then conventional techniques (15). Even more, in a high percentage of cases the CAIPP protocol had to be complemented with conventional implant positioning means, therefore guided surgery techniques should only be recommended to clinicians with experience in conventional techniques.

7.2.3. Implant and prosthetic outcome:

In the present investigation all implants could be placed in a position compatible with osseointegration and allowed a functional, hygienic and esthetic prosthetic reconstruction independently of the treatment protocol used. Both implants and reconstructions are being followed-up for longer time periods and the results will be reported in future publications. Nevertheless, the fact that no implant was lost at the time of prosthetic delivery and that their position permitted a satisfactory prosthetic reconstruction represents a valuable finding since intraoperative complications leading to the implantation failure or misplacement have been often reported for CAIPP protocols (15, 17, 39). According to a recently published systematic review, survival rates of implants placed with CAIPP protocols are similar to those of implants placed conventionally (19). However, this information should to be interpreted with care, since CAIPP protocols are very heterogeneous and their categorization may lead to important differences between procedures. Significant accuracy differences have been acknowledged between different CAIPP protocols (18), therefore it seems logical to believe that survival and success rates will be also influenced by the different degree of inaccuracies. Moreover, placement errors or intrasurgical complications that lead to the impossibility to place the implant in the planned position are not reflected as failures in the survival analysis (34, 40), therefore masking the survival interpretation.

The present investigation has concentrated in partial edentulous patients with a single-splint open-flap approach. This CAIPP protocol seems to render the highest accuracy values(18) and therefore could explain the generalized successful implant placement. Nevertheless, a strict monitoring of the implant osteotomies is mandatory since implant malpositions can occur if relying fully on the surgical guide as recognized by the high number of surgical protocol modifications needed in both CAIPP protocols studied. A blind osteotomy preparation relying fully on the surgical guide may lead to imprecision values as high as 6.5 mm at the implant shoulder level or 24.9º angular deviations (41). These numbers are obviously outliers but values much smaller than these will cause unacceptable results in modern implant dentistry.

It must be noted than one patient needed to receive a cement-retained crown instead of the initial screw-retained reconstruction planned. This occurred in a case of Test group 1 where the guided implant placement lead to a lack of implant stability and the decision to place another longer and tapered implant was taken intraoperatively. The implant was placed freehand since the CAM guide was unusable. This action lead to a slightly buccal-distal orientation of the implant axis that precluded the intended screw-retained reconstruction. The implant osseointegrated correctly and the cement-retained reconstruction fulfilled every prosthetic success parameter. This incident highlights the difficulty to solve unexpected intrasurgical incidences with CAIPP protocols and the importance to be experienced with conventional implant surgery before implementing CAIPP protocols.

7.3. Patient-related outcomes:

7.3.1. Treatment perception:

Often new technologies are perceived as being better than standard ones. The industry is responsible for marketing these innovations as improvements of the standard method, even without any scientific evaluation in the background. CAIPP protocols have been sold to the clinician as better techniques than the conventional ones due to the 3D preoperative planning and computer-generated guided stents that allowed a more precise implant placement. However, this statement is vague since information regarding comparison with conventional protocols is scarce. Nevertheless, this enthusiasm is often transmitted from the clinician to the patient, making him perceive the CAIPP protocol as more innovative and better. Patients may identify clinicians that perform these techniques as better professionals. Our study pretended to evaluate patient´s treatment perception towards the conventional and computer implant planning and placement protocols before and after the treatment.

Before treatment, the percentage of participants satisfied with their allocation was greater in the computer-assisted groups (83%) than in the conventional group (53%). This fact could be interpreted as a positive contemplation of the computer-assisted protocols by inexperienced patients. No information has been found in the literature regarding preoperative patient perception toward CAIPP protocols. However, outside the dental field, research suggests that, for certain customers, innovativeness has a positive influence on their product perception. New technologies are not only evaluated from their functional side but also from a symbolic side and are usually rated as better than the old technologies(42). Patients received a standard information sheet to avoid any operator subjectivity during protocol information. However, the information the patients had before seeking treatment (media, colleagues) cannot be standardized and may have influenced the treatment election.

After treatment, the percentage of participants satisfied with their allocation in the conventional group changed very slightly with respect to the pretreatment

evaluation (before: 53%, after: 50%). The percentage willing to have undergone a different protocol decreased in 16%, while the undecided percentage increased in 18%. This could be interpreted as a positive influence of the treatment protocol on the patients' perception since less patients would have liked another protocol and more patients moved to the undecided choice. These participants that moved to the undecided may be satisfied with the conventional treatment but still consider the computer-assisted a positive alternative. Not deniable is the fact that still 21% of patients would have preferred to be treated by computer-assisted protocols, which reinforces the idea that CAIPP protocols are perceived positively by the patients.

When the same consideration was made on the computer-assisted patients, the percentage of patients satisfied with the allocation increased in 5% after the treatment (88%), while the percentage willing to have undergone a conventional procedure was very low (3%) and the undecided percentage reduced in 3% (9%).

Nkenke et al. (13) also evaluated the patient´s postoperative treatment perception towards conventional and CAIPP protocols with a questionnaire completed at day 1 post-surgery. The conventional group received an open flap approach while the CAIPP group consisted in a flapless mucosa-supported guided surgery. Patients in the CAIPP group would be more willing to repeat the surgical procedure and would recommend it more intensely to a friend than those in the conventional group. This perception is surely linked to the fact that patients in the CAIPP group had less postoperative pain and swelling due to the flapless surgical procedure. In the present investigations, conventional or computer-assisted allocation had no influence on the postoperative period so the evolution of the patient's perception would be linked to other factors, among which the symbolic aspect of technological innovativeness could play a role.

7.3.2. Intraoperative and postoperative period evaluation:

Patient centered outcomes have been evaluated during the intraoperative and postoperative periods of partial edentulous patients treated with three implant placement protocols. Overall no statistically significant differences have been observed between groups. Patients reported low pain levels and discomfort during the surgery and it´s length matched their perception. The surgery influenced the patients' quality of life mostly during the first 4 postoperative days. Signs and symptoms peaked on day one for most of the variables studied and decreased gradually thereafter. When the global data was analyzed to differentiate factors that could have an influence on the peroperative and postoperative period, factors such as surgery duration, number of surgical sites and performance of GBR procedures revealed significant.

Intraoperative pain and comfort may be influenced by patient's anxiety level, anesthetic efficacy, operator skills and surgery invasiveness and duration (43-47). Our results confirm the fact that longer surgeries resulted in higher intrasurgical pain and discomfort. The longest surgeries were recorded for Test 2 group, which could have influenced the absolute lower intraoperative comfort levels reported. Our results also showed that surgeries involving 2 surgical sites yielded higher levels of immediate postoperative pain. The highest levels of immediate postoperative pain were reported for both CAIPP protocols, which had the greatest number of multiple implant site surgeries. Other indicators of surgical invasiveness, such as number of implants placed or the performance of GBR, did not prove to influence the intrasurgical symptomatology but motivated a longer surgical length perception.

Regarding the postoperative signs and symptoms registered during the first postoperative week, treatment duration and surgical invasiveness influenced significantly the patients' quality of life. Longer surgeries and those needing a GBR caused greater swelling and pain levels during the first 3 to 4 postoperative days and hindered significantly the chewing and mouth opening ability of patients until day 7. These symptoms could be responsible for the daily activity impairment reported during

the first 5 postoperative days. Arisan et al. (12) compared implant placement protocols that led to differences in surgery duration and invasiveness. They compared two computer assisted implant placement protocols with a conventional protocol in completely edentulous patients. The guided implant placement procedures evaluated involved a flapless mucosa-supported single-splint approach and an open-flap bone-supported multiple-splint approach. The flapless single-splint guided protocol allowed quicker and less invasive surgeries, which resulted in gentler postoperative periods compared to the other two groups. The study results point out that faster and less invasive surgeries could have a positive impact on patients' postoperative period.

It is interesting to mention that another study (48) comparing the flapless or flapped execution of a CAIPP protocol found no postoperative differences, or even less postoperative discomfort, when the open flap procedure was performed. These results stand against most investigations that report lower swelling and pain levels for flapless procedures over flapped techniques (11-13). A differential trait between this investigation and the others is that both flapless and flapped approaches took the same time to be executed. This fact may highlight the relevance of the intrasurgical duration over the flap technique itself on the postoperative morbidity.

According to the results of the present study, the use of computer-assisted implant placement techniques in partially edentulous patients did not influence patient´s intraoperative or postoperative period. It seems that the nature of the CAIPP protocol employed and its ability to reduce the surgical duration or avoid the surgical flap elevation could have an impact on patients' morbidity. However, the similar surgical invasiveness and duration resulting from the conventional and computer-assisted implantation techniques employed in the study precluded this extrapolation.

7.4. Time and Costs:

The general aim of this investigation was to comprehensively study the cost-benefit ratio of conventional and computer-assisted implant planning and placement protocols in partially edentulous patients. Time and economical costs are objective variables that can be easily derived from both treatment techniques. Even though two particular CAIPP protocols have been investigated, the overall comparison between conventional and computer-assisted procedures for this study population yields the inference that both protocols require similar diagnostic, radiographic imaging, and intraoperative treatment times, while computer-assisted protocols entail longer surgical planning times and longer surgical splint production waiting times. Economical costs are also higher for the CAIPP protocols mainly due to surgical splint production expenses, plus initial setup costs derived from the planning software license and dedicated guided-surgery drilling kits required. Nevertheless, costs have to always be contrasted against the technique's benefits, which have been highlighted throughout the investigation results (higher preoperative diagnostic potential and better patient perception for CAIPP protocols).

Certain particularities between CAIPP protocols generated some differences that are also worth discussing. While every treatment required similar initial diagnostic steps (preliminary alginate impressions and intermaxillary registrations, plaster cast production and articulation, diagnostic wax-up fabrication), the Test 2 protocol eliminated the requirement for a radiographic template production. This implies a substantial time and expense reduction (Median: 60 min and 322 CHF) and grants the clinician the freedom to use CBCT exams lacking prosthetic references. In this protocol, the optical scan of the diagnostic wax-up was superimposed to a CBCT DICOM file to allow for virtual prosthetically guided implant planning. The ability to fuse surface scans with 3D radiographic images makes the classic "prosthetic referencing before radiographic imaging" sequence transposable and could prevent patients with CBCTs without prosthetic references from undergoing further radiographic exams.

However, scanning casts required an investment that is also reflected in the

study's treatment results. Most guided surgical splint companies using CAD-CAM technologies require the patient´s plaster model optical scan to superimpose it with the DICOM radiologic data before designing the surgical splint. This is required because STL files allow for more accurate surface determinations, and therefore more accurate surgical splint sitting, than DICOM data. Surface STL files stand as a stable basis for precise surgical splint virtual design, while DICOM files offer imprecise surface estimates due to technical limitations (49). In the present investigation, both computer-assisted protocols required an optical scan of the study model to aid in the splint production. Optical scans were performed using a laboratory scanner that needed around 10 minutes to produce a model´s STL file. Additionally as mentioned before, the Test 2 protocol required a second optical scan of the model with the diagnostic wax-up in order to incorporate a prosthetic reference into the virtual implant planning. The need to scan two models reflects the scanning time and cost differences between Test group 1 and 2.

Concerning the radiographic exam expenses, small time and economical differences were observed between groups. However, more relevant biologic expenses have to be taken into account when considering radiology. Indeed, ionizing radiation has well-known cumulative adverse effects on living cells (50). Therefore, every radiographic exam should show a net benefit to the patient and the resulting radiation dose should be kept as low as reasonably achievable (ALARA principle) (51). Even though broad ranges of radiation doses have been reported for each available imaging modality, which makes their ionization potential comparison challenging, it is accepted that 3D radiology produces doses that are an order of magnitude greater than those of intraoral or panoramic techniques (3, 25). Consequently, cross-sectional imaging should be reserved for cases where the clinical examination and conventional radiography offer insufficient information for a predictable, risk-free implantation (3). Exceptionally, patients in the present study were randomized to conventional or cross-sectional radiology before any clinical examination could be performed as part of an ethically approved clinical research.

The imaging modality chosen will also influence the nature of the implant

planning going to be performed and correspondingly the related expenses. While conventional x-rays only allow for a bi-dimensional implant planning using transparent foil and a light table, numerous virtual planning software have been developed to analyze and position implants in the cross-sectional exam. Even though benefits have been described for the 3D implant planning (thorough anatomical understanding, and therefore a more predictable surgical protocol)(4, 37), certain additional expenses are derived, such as longer planning times (Median: Conventional: 5.5 min, Computer: 13.3 min (Test 1) and 13.7 min (Test 2)) and higher economical expenses due to the software license acquisition. Until today, there is no agreement on the expenses resulting from this additional time required for planning in the CAIPP protocol and whether or not the patient should be charged for the longer preparation time of the surgeon.

Nevertheless the greatest time differences between groups in the present investigation appear when analyzing the surgical template production time. In the Control group, the surgical splint was directly derived from a modification of the radiologic template. The radiopaque markers were eliminated by drilling access canals in the palatal aspect of the crowns to be implanted. Obviously, this procedure required less time and costs than the industrial production and delivery of computer-assisted guided splints (Median: 4.38 min). Both CAIPP protocols included in the study had a diverse splint production method that resulted in cost and time differences. The 3D printing employed by Test 2 resulted in cheaper and faster reception splints than the stereolithographically-produced splints of Test 1 group. The reason for this was methodological, since the Test 2 company delivered an open STL file of the splint design that subsequently was printed in an in-house 3D printer. Since a 3D printer was available at the University of Zürich the production time could be narrowed down to a median of 3 days and the costs reduced. On the other hand, in the Test 1 group the final splint was produced and delivered by post mail in a median of 10.5 days with higher expenses. This price difference was influenced also by delivery services and customs duties derived from this protocol.

A reduction in the intraoperative time could be a desirable advantage of guided implant placement as compared with conventional protocols. Several studies

have evaluated guided surgery duration but always in totally edentulous patients. Arisan and coworkers compared conventional open flap surgery with two guided surgical protocols: an open flap bone-supported multiple-splint system and a flapless mucosa-supported single-guide approach (12). The flapless approach showed significantly less intraoperative time (25.53 ± 5.48 min) compared with the other two open flap approaches (Conventional: 68.71 ± 11.4 min, Guided: 60.94 ± 13.07 min). No differences were found between the conventional open-flap versus the guided open-flap multiple-splint approach. These findings could imply that the time reduction would be more related to the flapless approach than to the guided nature of the surgery. Nevertheless, other researchers compared flapless versus open flap guided surgery and found no time differences between groups (Guided flapless: 59.38 min, Guided open flap: 57.5 min)(48). This highlights the multifactorial nature of the treatment's duration origin.

The present study concentrated in partial edentate cases and time was recorded only for a single implant placement. All surgeries were performed by postgraduate students or senior faculty under the supervision of an experienced surgeon in a University training environment. Both, the operator and the assistant were familiar with the surgical instruments and protocols for every study group. No difference was found between groups for implant placement time (around 25 minutes). The fact that the burs and implant insertion were fully guided for the computer-assisted protocols did not increase the placement speed of single implants. Among the possible explanations for these findings are the fact that even though using fully guided bur and implant protocols every drill was thoroughly controlled for perfect orientation by checking the osteotomy direction using indicators after each working step to prevent "blind" drilling and possible implant malposition. Operator skills and meticulousness will certainly influence treatment time. Moreover, the greater number and complexity of surgical instruments needed to perform the computer assisted implant placement could also have increased the treatment time.

The appreciation that guided protocols are faster than conventional was not proven for single implant placement in partially edentulous patients. Nevertheless it

could be true when more implants would be prepared and placed simultaneously. However, this supposition is out of this study's scope and would need further research.

7.5. Accuracy:

The accuracy of three different treatment protocols to transfer the planned implant position into the clinical scenario has been evaluated. No differences have been observed between CAIPP treatment protocols on any of the accuracy parameters evaluated. When compared with the Conventional protocol, discrepancies have been detected at the implant shoulder, implant apex planes, and implant angulation measurements. Nevertheless, the basis for these inconsistencies seems to be methodological rather than clinical. An uncertain baseline implant position in the Conventional group generated accuracy numeric values that are vague and not representative of the real treatment's precision. In fact, the final implant position in every case of the Conventional group allowed a screw-retained restoration, which fulfilled completely functional, hygienic and esthetic standards, without harming adjacent anatomic structures. The incongruity between clinical parameters and investigation numeric values evidences the imprecision of the accuracy discrepancies obtained for this group and highlights the importance of collecting clinical variables that are more clinically relevant and less likely corrupted by methodological limitations.

When focusing only on the accuracy values obtained for the CAIPP groups, their results entail positioning errors that are below those generally reported for guided surgery. In the last decade a significant amount of data has been published on the accuracy of these protocols, which has led to the publication of several systematic reviews and meta analyses (17, 18, 39, 52, 53). According to the last review (17), the overall mean deviation of these protocols is of 1,04 mm at the entry point, 1.45 mm at the apex and a 3.81° overall mean angulation error. The fact that the accuracy values obtained in the present study are around 0.5 mm more precise than those extracted from the pooled data of a systematic review is an expected finding since a narrow particular treatment protocol and population were studied: tooth-supported single-splint CAIPP protocols.

Guided surgery is a term that unites diverse therapeutic protocols under the same name. This heterogeneity of treatment modalities generates a broad array of treatment outcomes that hinders the legitimacy of a global accuracy value for guided surgery as a hole. A clear distinction between treatment protocols should be made when assessing guided surgery outcomes. Van Asche et al. (18) showed that certain factors had a significant influence on the accuracy of guided surgery and that they could be used to subcategorize the term. In their systematic review, the global accuracy data was sorted and analyzed according to possible influencing parameters, such as splint support (tooth, mucosa, bone), number of templates (single splint vs. multiple splint systems), use of fixation pins, implantation jaw, template production method and guided implant insertion. Statistically significant favorable results were found for tooth- and mucosa-supported splints over bone-supported ones, for single splint protocols over multiple splint, for splints fixated with pins over those not fixated, and for implants placed guided through the surgical splint over those placed without splint control. Further reviews have confirmed similar results (17).

When the accuracy of tooth-supported splints was individualized, average values of 0.73 mm at the entry point, 0.98 mm at the apex and 3.08º angular deviation were obtained (18). These numbers match precisely those obtained in the present study, where only tooth-supported single-splint protocols were evaluated. Tooth-supported splints provide the highest implant placement accuracy, which highlights the relevance of splint stability during radiographic imaging and implant placement (54, 55). Therefore, a clear specification of the CAIPP protocol used is mandatory to critically evaluate and compare treatment outcomes. Moreover, this subcategorization could allow to customize safety margins and narrow treatment indications.

Moreover, splint guidance, not only during the osteotomy preparation but also during the implant insertion seems to significantly influence the accuracy of CAIPP protocols (18). In the present study the precision values suffered a slight improvement when the cases where implants inserted non-guided were excluded. This could be interpreted as an acknowledgement of the intrinsic precision potential of the CAIPP protocols when strictly followed.

As previously discussed, a great amount of information concerning accuracy of CAIPP protocols has been published, however information on precision of conventional implant placement is very scarce. A comparison of CAIPP accuracy values with those obtained from conventional protocols would be desirable in order to understand their relative accuracy and clinical value. Unfortunately, due to methodological reasons, data on accuracy of conventional implant placement is limited. In contrast to the CAIPP protocols, establishing a three-dimensional baseline measurement for the conventional protocol is difficult since routinely no 3D diagnosis or planning is performed.

In vitro studies have partially bypassed this problem by radiologically scanning the study phantom preoperatively and setting a baseline reference implant position using 3D implant planning software. Nevertheless, the experimental conditions of these investigations are far from clinical reality and divergent results have been published (Table 20), which limit their clinical extrapolation.

Table 24. In vitro articles published reporting on accuracy of conventional implant placement protocols (Entry and Apex deviation measurements presented in mm, Angle measurements presented in degrees). *Values estimated from graph present in the publication.

Author (year)	Guide-support	**Entry**	**Apex**	**Angle**
		Mean ± SD *Max - Min*	**Mean** ± SD *Max - Min*	**Mean** ± SD *Max - Min*
Sarment et al. (2003)(56)	Total edentulism	**1.5** ± 0.7 *1.8 - 1*	**2.1** ± 0.97 *2 - 3.7*	**8º** ± 4.5 *6.8 - 8.7*
Brief et al. (2005)(57)	Partial edentulism	**1.35** ± 0.56 *? - 2.16*	**1.62** ± 0.68 *? - 2.68*	**4.59º** ± 2.84º *? - 10.66º*
Nickening et al. (2010)(58)	Unilateral posterior edentulism	Group 1**: 3.2** Group 2: **2.92** Group 1: *0 - 7.7* Group 2: *0 - 8.6*	Group 1: **4.24** Group 2: **4.28** Group 1: *4 - 7* Group 2: *0 - 8.4*	Group 1: **9.8º** ± 4.25 Group 2: **10.9º** ± 4.5 Group 1: *3.7º - 17º* Group 2: *2º - 20º*
Nokar et al. (2011)(59)	Partial edentulism	**2.5 ***	-	**5.9 ***
		-	-	-

Recently, a clinical study has managed to obtain a numeric representation of the accuracy of conventional implant placement in partially edentulous patients (60). The investigation used a split-mouth design on 10 patients with bilateral single-gap edentulous spaces. Participants underwent a preoperative CBCT scan with a radiographic template that allowed the virtual planning of an implant in each edentulous gap. Thereafter, two surgical splints were produced: a computer-generated splint based on the virtually planned position of one implant and a conventional splint to aid the placement of the second implant. Each implant was placed either according to the computer or the conventional implant placement protocols and afterwards a second postoperative CBCT was performed. The CAIPP protocol obtained more precise values than the conventional protocol in every category examined. Besides the study outcomes, the relevance of this investigation lays on the fact of being the first study to

obtain a numeric accuracy value for conventional implant placement in single-gap edentulous cases: Entry: 1.99 mm (SD 1), Apex: 2.54 mm (SD 1.23), Angle: 6.13º (SD 3.68º). When these discrepancies are compared with those obtained by the CAIPP treatment groups in our study, the assumption that guided surgery allows a more accurate implant placement than conventional implantation is confirmed.

However, these absolute accuracy measurements should be interpreted with care since a numeric discrepancy between a virtually planned implant position and the real final position does not consistently imply an implant malposition. Cross-sectional radiographic images associated with an implant planning software provide accurate measurements and predictable implant planning competences, however due to technical limitations the information available during the virtual planning can differ from that present intrasurgically and create differences between the planned position and the ideal intrasurgical position. For instance, several studies acknowledge the potential underestimation of bone volumes when CBCT evaluations are compared with histological measurements (28, 61, 62). Moreover, other factors that modulate implant planning such as mucosa thickness (63) or esthetic parameters (soft tissue scalloping or neighboring crown anatomy) (64) are difficult to visualize and integrate during the virtual planning and will influence the implant placement. In the present study, 23 computer-assisted cases needed modifications of the planned guided implant placement protocol to adapt the implant position to the ideal clinically determined position. This changes generated a negative influence on the study's absolute accuracy values but possibly a positive impact on the real clinical outcome. On the other hand, it must be acknowledged that there is not a distinct valid implant position, but rather a range of ideal positions that are compatible with a restoration that fulfills every esthetic, functional and hygienic standard. Therefore, numerical accuracy values have a relative validity and should be interpreted with care. They should be matched with clinically oriented parameters in order to better understand their clinical relevance.

In the present study no CBCT was performed on patients randomized to the conventional group since an implant planning and placement protocol with conventional radiographs wanted to be evaluated. The absence of radiographic

references allowed for a relatively large range of locations compatible with an ideal prosthetically-guided implant position during the planning. Consequently, most discrepancy measures stood imprecise and therefore not valid for comparison with the other CAIPP groups. Indeed, the only valid parameter extractable from the conventional group was the prolongation of the axial implant position at the occlusal table, which is a fully prosthetically-determined parameter and therefore reliable in the three groups. No differences were observed between protocols for this parameter. The absolute vales were small and as proven by the successful screw-retained prosthetic outcome of all except one restoration, clinically irrelevant (Control: 0.65 mm, Test 1: 0.44 mm, Test 2: 0.53 mm). The occlusal plane accuracy values have a direct clinical link since the possibility to screw-retain the restoration is directly related to the occlusal emergence of the implant axis, which determines the screw access hole position. In our study all, except one implant, could be screw retained as planned. The only case that needed to be restored with a cement-retained restoration corresponded to a case in the Test group 1 that obtained no primary stability after the guided placement and had to be replaced by another longer implant drilled and inserted free-hand. The new implant position resulted in a buccal-distal orientation of the implant axis (numeric angular discrepancy between planned and final position: 10.7º) that would have caused an access hole emerging through the distal marginal ridge, condition that could weaken the ceramic integrity and hamper the esthetics of the reconstruction (65).

Few references exist in the scientific literature evaluating accuracy of implant placement protocols studying clinical-oriented parameters. Arisan et al.(66) compared the accuracy of free-hand and computer-aided placement methods in fully edentate patients without focusing on absolute discrepancy distances. Instead clinical parameters were studied. Their investigation concluded that CAIPP protocols resulted in less implant positioning errors (interproximal emergence, insufficient interimplant distance and improper implant parallelism) than free-hand methods. This statement may be valid for edentulous jaws, where few anatomic reference points exist and where splint stabilization is challenging. In our study population, partially edentulous patients, where the splint can be better stabilized, results differ. All implants placed allowed for the production of a prosthetic restoration that fulfilled the esthetic, functional and

hygienic standards. Therefore, once again it should be emphasized that a subcategorization of the CAIPP concept is mandatory in order to extract clinically meaningful conclusions.

Another important point is the fact that hardly any study informs on the direction of the deviation in a transversal plane (67). Matching the absolute discrepancy values with the mesio-distal and bucco-oral direction of the deviation improves the treatment's inconsistency understanding and permits clinically relevant interpretations. Deviations in the buccal direction are more dangerous from an esthetic point of view than those to the oral direction (68). A deviation of 1 mm at the entry point with a buccal vector could be detrimental when planning a screw-retained implant-supported single crown to replace a maxillary central incisor. Conversely, the same deviation with a palatal vector would be less problematic. No statistically significant direction trend was observed at any of the three horizontal planes studied for any of the treatment groups. The inconsistency values were small and compatible with an uneventful surgery and prosthetic reconstruction.

8. Conclusions

8.1. General conclusion:

The comprehensive evaluation of the benefits and costs derived from conventional and CAIPP protocols, comprising tooth-supported, single-splint, guided implant insertion, open-flap procedures, has uncovered differences which grant higher preoperative diagnostic potential and improved patient treatment perception to the CAIPP protocols, while requesting higher economical expenses and time investment than conventional treatments.

8.2. Specific conclusions:

1. CAIPP protocols proved a higher diagnostic potential than conventional protocols since the nature of the bony defect expected, the necessity and type of materials needed to perform GBR procedures, and the implant length could be preoperatively better predicted.
2. The rate of complications and unexpected events was high for the three groups. These incidences could be divided into splint-related incidences and voluntary surgical protocol deviations to adjust suboptimal implant positions. Conventional protocols had less splint-related incidences than CAIPP protocols. Splint-related incidences in the CAIPP protocols were mostly related to splint misfit. Based on the high incidence of intraoperative surgical protocol modifications to adjust suboptimal implant placements, a strict intraoperative implant position monitoring is mandatory for both conventional and CAIPP protocols.
3. All implants could be placed in a position compatible with osseointegration and allowed a functional, hygienic and esthetic reconstruction independently of the treatment protocol used.

4. Patients manifested an improved treatment perception of CAIPP protocols over conventional protocols before and after treatment.
5. Overall, no statistically significant differences have been observed between groups for intraoperative and postoperative quality of life parameters. Patients reported low pain levels and discomfort during the surgery and it´s length matched their perception. The surgery influenced the patients' quality of life mostly during the first 4 postoperative days. Signs and symptoms peaked on day one for most of the variables studied and decreased gradually thereafter.
6. CAIPP and conventional protocols required similar diagnostic, radiographic imaging, and intraoperative treatment times, while computer-assisted protocols entailed longer surgical planning times and longer surgical splint production waiting times. Economical costs were also higher for the CAIPP protocols due to surgical splint production expenses, and initial setup costs derived from the planning software license and dedicated guided-surgery drilling kits required.
7. Both CAIPP protocols have proven similar precision capacity to transfer the planned implant position to the final clinical position. Conventional protocols revealed higher inaccuracy values at the implant shoulder, implant apex and implant angulation assessments. Nevertheless, these discrepancies have most likely a methodological origin and must be interpreted with care.

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Appendix I: Patient Study Information Document

1. Conventional protocols

The standard implant planning and placement protocol used for decades implies a preliminary clinical evaluation and a two-dimensional X-ray exam. This radiograph is then viewed on a light viewer where bone measurements can be performed. This allows the dentist to determine the position of the implants taking into account anatomical structures, such as bone height availability, nerves, etc.

In a second step, a tunnel is drilled into the bone and an implant is inserted fee-hand. The drilling instruments and implant are directed by the operator's hand. The surgeon transfers the planned position into the patient's mouth with the help of preoperative x-rays and a surgical stent that is prepared by the laboratory technician.

The advantages of this procedure are good long-term success rates, relative simplicity, cost efficiency and reduced x-ray exposure.

Among the disadvantages are the two-dimensional X-ray examinations, which don´t allow the assessment of bone width at the implantation area, and the fact that the position of the implant is heavily dependent on manual skill of the surgeon, since there is no guidance of the drilling instruments.

2. Computer-assisted technology

With the development of the computer implant planning and placement protocols it is possible to plan preoperatively the optimal implant position using 3-D x-rays (digital volume tomogram, DVT) and computer software programs. The bone morphology can be studied three-dimensionally, allowing to measure bone height and width. The implant surgery is

simulated before the actual intervention, which allows detecting possible difficulties such as bone insufficiency.

Based on the virtual planning, a drilling template is produced industrially to fully guide the drilling instruments and implant into the patient's mouth.

The advantages from this protocol are the three-dimensional bone evaluation, preoperative virtual implant planning and the instrument guidance given by the surgical splint.

The disadvantages comprise higher costs and the higher x-ray exposure levels.

Further advantages and disadvantages of these two methods are currently investigated in our clinic. Your contribution will help us to better evaluate the value of these two methods.

Please select which of the two methods would you prefer?

Appendix II: Ethical Committee approval

Universitat Internacional de Catalunya

Barcelona, 13 de febrero de 2013

Sr. Manuel Sancho Puchades
manuel19.82@telefonica.net
manuel.sancho@zzm.uzh.ch

Estimado Sr.

Por la presente, le comunico que la Comisión Académica del Doctorado en Ciencias de la Salud, en la su sesión del 8 de febrero de 2013, y una vez estudiada su solicitud ha acordado:

Se acuerda admitir al Sr. Manuel Sancho Puchades al Periodo de Investigación del Doctorado en Odontología.

Se acuerda aprobar el Proyecto de Tesis titulado "Efficiency of conventional and computer assisted, template guided implant planning and placement - a randomized controlled clinical trial", y nombrar al Dr. Federico Hernández Alfaro y al Dr. David Schneider como Directores 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.

Aprovecho la oportunidad para saludarlo cordialmente,

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

Universitat Internacional de Catalunya

REGISTRE GENERAL

Sortida 1/0282

Data 14 02 13

Kantonale Ethik-Kommission Zürich (KEK)

Kantonale Ethikkommission (KEK)
Präsident Abteilung 5
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Zentrum für Zahnmedizin
der Universität Zürich
Klinik für Kronen- und Brückenprothetik
Herr Dr. med. et med. dent. David Schneider
Plattenstrasse 11
8032 Zürich

Datum: 15. März 2011

Beschlussmitteilung der Ethikkommission

Die Abteilung 5 hat das folgende Forschungsprojekt per Präsidialentscheid begutachtet.

Titel des Forschungsprojektes Studiencode: Ref. KEK-Zh-Nr. 2011-0020/5

Efficiency of conventional and computer-assisted, template guided implant planning and placement: a randomized controlled clinical trial

Zusammensetzung der Ethikkommission

Die Ethikkommission tagte in der nachfolgend erwähnten Zusammensetzung und war damit beschlussfähig (Art. 32 und Art. 10 Abs. 3 der Verordnung über klinische Versuche mit Heilmitteln vom 17.10.2001 in Verbindung mit § 9 des Reglements der Kantonalen Ethikkommission).

					am Beschluss beteiligt		
					ja	nein	
	Name, Vorname	Berufliche Stellung / Titel	m	f		abwesend	In Ausstand
Vorsitz	Fischer, Jan A.	Prof. Dr. med.	☒	☐	☒	☐	☐

Hauptprüfer/in (verantwortliche/r Studienleiter/in am Versuchsstandort)

Name, Vorname, Titel: Schneider David, Dr. med. dent.

Funktion: Oberassistent

Adresse: Universität Zürich, Klinik für Kronen- und Brückenprothetik, Teilprothetik und zahnärztliche Materialkunde, Zentrum für Zahnmedizin, Plattenstrasse 11, 8032 Zürich

Die Ethikkommission stützt ihre Beurteilung auf die Unterlagen, wie sie aufgeführt sind:

- ☒ im beiliegenden „Basisformular zur Einreichung eines biomedizinischen Forschungsprojektes" vom 03.03.2011
- ☒ im beiliegenden Begleitbrief vom 03.03.2011
- ☒ in der Rubrik „begutachtete Unterlagen" (siehe weiter unten) sowie auf die Beschlussmitteilung C mit Auflagen vom 1. März 2011

Art des Verfahrens:

- ☐ normales Verfahren
- ☒ vereinfachtes Verfahren
- ☐ Nachbegutachtung

Die Ethikkommission kommt zu folgendem **Beschluss**:

- ☒ **A positiv**
- ☐ **B positiv mit Empfehlungen**
- ☐ **C Auflagen**
  - ☐ Nachbegutachtung durch Ethikkommission notwendig
  - ☐ Schriftliche Mitteilung an Ethikkommission ausreichend
- ☐ **D negativ (mit Begründung und Erläuterung für die Neubeurteilung)**
- ☐ **E Nicht-Eintreten (mit Begründung)**

Der Beschluss gilt auch für die namentlich aufgeführten weiteren PrüferInnen im Zuständigkeitsbereich der Ethikkommission (gemäss separater detaillierter Liste)

Begutachtete Unterlagen
- Patienteninformation und Einverständniserklärung vom 03.03.2011

(erweiterbar)

Empfehlungen

(erweiterbar)

Auflagen

(erweiterbar)

Begründung für negativen Beschluss und Erläuterung für Neubeurteilung

(erweiterbar)

Begründung für Nicht-Eintreten

(erweiterbar)

Pro Memoria: **Pflichten des/der Hauptprüfers/in**

- Meldepflicht bei:
  - a) schwerwiegenden unerwünschten Ereignissen unverzüglich (Arzneimittel: nur bei schwerwiegenden unerwarteten Nebenwirkungen)
  - b) neuen Erkenntnissen, die während des Versuchs verfügbar werden und die Sicherheit der Versuchspersonen und/oder die Weiterführung des Versuchs beeinflussen können.
  - c) Änderung des Protokolls (Versuchsplans)
  - d) Ende oder Abbruch der Studie
- Zwischenbericht: einmal pro Jahr
- Meldungs- oder Bewilligungspflicht von Studien bei Swissmedic bzw. anderen Bundes- oder kantonalen Behörden (bei gesponserten Studien ist dies die Pflicht des Sponsors)
- Schlussbericht

Die Ethikkommission bestätigt, dass sie nach ICH-GCP arbeitet.

Gegen diesen Beschluss kann innert dreißig Tagen, von der Mitteilung an gerechnet, beim Regierungsrat des Kantons Zürich schriftlich Beschwerde eingereicht werden. Die Beschwerdeschrift muss einen Antrag und dessen Begründung enthalten. Der angefochtene Entscheid ist beizulegen oder genau zu bezeichnen. Die angerufenen Beweismittel sind genau zu bezeichnen und soweit möglich beizulegen.

Für die Ethikkommission:

Ort, Datum: Zürich, 15. März 2011 Name(n):

Unterschrift(en):

Prof. Dr. med. Jan A. Fischer
Präsident Abteilung 5

lic. iur. et theol. Niklaus Herzog
Juristischer Sekretär KE

Beilage(n)
Basisformular vom 03.03.2011

CER Comitè d'Ètica de Recerca | Universitat Internacional de Catalunya

CARTA DE CONFORMITAT DEL CER PER A PROJECTES AVALUATS I APROVATS PER UN CEIC

Codi de l'estudi:CIR-ECL-2013-03
Versió del protocol:1.0
Data de la versió:20/03/13
Títol:"Efficiency of conventional and computer-assisted, template guided implant planning and placement-a randomized controlled clinical trial"

Sant Cugat del Vallès, 07 de maig de 2013

Investigador: Manuel Sancho Puchades

Títol de l'estudi: :"Efficiency of conventional and computer-assisted, template guided implant planning and placement-a randomized controlled clinical trial"

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, ratifica l'aprovació dels CEICs aportada, d'acord amb el reglament vigent.

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.

Quedo a disposició per a qualsevol dubte o aclaració al respecte.

Atentament,

Dr. Josep Argemí
President CER-UIC

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