NEW DIMENSIONS IN TOOTH IMPLANT AND TRANSPLANTATION — DAVID ANSSARI MOIN

NEW DIMENSIONS IN TOOTH IMPLANT AND TRANSPLANTATION

David Anssari Moin

The printing of this thesis was supported by:
ACTA Research Institute and VU University of Amsterdam

Book design: studio ilse van klei
ISBN:

VRIJE UNIVERSITEIT

NEW DIMENSIONS IN TOOTH IMPLANT AND TRANSPLANTATION

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. V. Subramaniam
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Tandheelkunde
op woensdag 17 januari 2018 om 13.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

David Anssari Moin

geboren te Den Haag

promotoren:	prof.dr. D. Wismeijer prof.dr. J.P.R. van Merkesteyn
copromotoren:	dr. B. A. Hassan dr. A. Tahmaseb Eghbali

CONTENTS

CHAPTER 1

GENERAL INTRODUCTION

A BRIEF HISTORY OF SURGICAL TOOTH REPLACEMENT

Autotransplantation and dental implant placement are currently well established surgical implantation techniques to replace missing teeth. However, their development from anecdotal reports to routine implementation is believed to be a travelogue through time with a span of at least 4 millennia.

From the earliest recorded ancient Chinese inscriptions 4000 BC and archeological samples 600 AD in Honduras to the current procedures of today, there has been an evolution of techniques, materials, and basic science principles (fig. 1). This has resulted in well accepted and successful techniques for the past several decades.

Figure 1. Dating back to 600 AD, the lower mandible of a young Mayan woman, missing incisors replaced by pieces of shell, shaped to resemble teeth. The fragment is currently part of the Osteological Collection of the Peabody Museum of Archaeology and Ethnology at Harvard University.

By the mid 1800's through the first decade of the 1900's the first experimental tooth transplantation and implantations were performed in Europe [1]. Most of the transplantation work appears to revolve around the use of allogenic teeth collected from cadavers and the underprivileged. During this time period, there were likewise experiments going on with innumerable substances that were used as implants, varying from silver and gold cylinders to corrugated porcelain and iridium tubes. Early practitioners had observed that these alloplastic implants would be encapsulated with fibrous material and they had learnt that greater success was achieved for tooth transplantation. Especially if the tooth had a wide open apex chances of revascularisation were higher and if the tooth was immediately transplanted chances of preserving the vitality of the periodontal ligament were improved. However as in other areas of surgery allotransplants have apparent drawbacks and allotransplant teeth have shown to have a survival of only 6 years [2].

Figure 2. 'A fashionable dentist engaged in tooth transplantation' by Thomas Rowlandson, 1787. Collection of the Hunterian Museum, The Royal College of Surgeons of England.

In the 1950's studies proving good success and survival for autotranplantation began to appear [3, 4]. This resulted in increased research and knowledge on autotransplantation with donor teeth surviving up to 41 years post surgery in long-term studies [5, 6]. A recent study by Verweij et al. proved autotransplantation to be very efficacious with an overall 98.2% survival after a median of 13.4 months follow-up [7]. In this study 82% of the transplants were successful and didn't need additional therapy. However, as it has been shown in different studies, autotransplantation is an operator sensitive technique and will be less successful by inexperienced hands [8-10]. The commonly used classical method is challenging and relies mostly on the surgeons' expertise and intuitive flair for adapting the recipient site to be as congruent as possible with the root of the donor tooth in the least achievable amount of tries (with the donor tooth as template) and shortest feasible extra-oral time.

The rise of dental implants came in the late 1970's when a Swedish orthopaedic surgeon named P. Bränemark introduced osseointegrated implants. He had observed in 1952 when removing titanium chambers from rabbit femurs, the bone had actually bonded to the titanium surface. This discovery made a pivotal change in implant dentistry and since then the process has been greatly improved over recent decades. Various long-term studies have shown that tooth replacement with dental implants is considered to be a predictable treatment option with survival and success rates varying between 91 - 93.3% and 85.2 - 88.7%, respectively [11-13].

DIGITAL 3D TECHNOLOGIES CHANGING THE WORLD

With the rise of 3D imaging and 3D printing technology the medical landscape is changing. 3D printing technology has a 'disruptive potential' in revolutionizing current day practice from standard medical devices and standard surgical tooling towards custom 3D printed medical devices and custom 3D printed surgical tooling. This has nourished ideas in the field of dentoalveolar surgery for 3D printing of surgical (guiding) tools for autotransplantation and 3D printing of custom root shaped implants with/or without 3D printing of surgical guiding tools. However, before these applied 3D technologies can be used in the clinic multiple questions in multiple levels need to be assessed.

STUDY OBJECTIVES

The aims of this thesis were to assess the feasibility, accuracy and implication/value of: custom 3D printed surgical tools for (guided) autotransplantation and (guided) custom 3D printed implant placement. The specific research questions dealt with in this work are:

- What is the feasibility and accuracy of 3D printing a custom root analogue implant based on 3D CBCT data? (Chapters 2, 3 and 4)
- What is the biomechanical effect of different root analogue implant designs on alveolar bone? (Chapter 5)
- What is the clinical implication and success of custom root analogue implants? (Chapter 6)
- What is the feasibility and accuracy of computer-assisted template-guided custom designed 3D printed implant placement with custom designed 3D printed surgical

tooling? (Chapters 7)
- What is the clinical implication and success of autotransplantation with 3D printed donor tooth replicas? (Chapters 8, 9 and 10)
- What is the feasibility, accuracy and clinical implication of computer-assisted template-guided autotransplantation of teeth with custom 3D designed/printed surgical tooling? (Chapters 11, 12 and 13)

REFERENCES

1. Hunter J: **A practical treatise on the diseases of the teeth; intended as a supplement to the natural history of those parts.** 1778:111.
2. Schwartz O, Frederiksen K, Klausen B: **Allotransplantation of human teeth. A retrospective study of 73 transplantations over a period of 28 years.** *International journal of oral and maxillofacial surgery* 1987, **16**(3):285-301.
3. Apfel H: **Autoplasty of enucleated prefunctional third molars.** *Journal of oral surgery* 1950, **8**(4):289-296.
4. Serling L: **Surgical repositioning of an impacted mandibular bicuspid.** *Journal of the American Dental Association* 1959, **59**:553-554.
5. Czochrowska EM, Stenvik A, Bjercke B, Zachrisson BU: **Outcome of tooth transplantation: survival and success rates 17-41 years posttreatment.** *American journal of orthodontics and dentofacial orthopedics: official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 2002, **121**(2):110-119; quiz 193.
6. Andreasen JO, Paulsen HU, Yu Z, Bayer T, Schwartz O: **A long-term study of 370 autotransplanted premolars. Part II. Tooth survival and pulp healing subsequent to transplantation.** *European journal of orthodontics* 1990, **12**(1):14-24.
7. **Verweij JP, Toxopeus EE, Fiocco M, Mensink G, van Merkesteyn JP: Success and survival of autotransplanted premolars and molars during short-term clinical follow-up.** *Journal of clinical periodontology* 2016, **43**(2):167-172.
8. **Schwartz O, Bergmann P, Klausen B: Autotransplantation of human teeth. A life-table analysis of prognostic factors.** *International journal of oral surgery* 1985, **14**(3):245-258.
9. Andreasen JO, Paulsen HU, Yu Z, Ahlquist R, Bayer T, Schwartz O: **A long-term study of 370 autotransplanted premolars. Part I. Surgical procedures and standardized techniques for monitoring healing.** *European journal of orthodontics* 1990, **12**(1):3-13.
10. Park JH, Tai K, Hayashi D: **Tooth autotransplantation as a treatment option: a review.** *The Journal of clinical pediatric dentistry* 2010, **35**(2):129-135.
11. Krebs M, Schmenger K, Neumann K, Weigl P, Moser W, Nentwig GH: **Long-term**

evaluation of ANKYLOS(R) dental implants, part i: 20-year life table analysis of a longitudinal study of more than 12,500 implants. *Clinical implant dentistry and related research* 2015, **17 Suppl 1**:e275-286.
12. Lekholm U, Grondahl K, Jemt T: **Outcome of oral implant treatment in partially edentulous jaws followed 20 years in clinical function.** *Clinical implant dentistry and related research* 2006, **8**(4):178-186.
13. Ostman PO, Hellman M, Sennerby L: **Ten years later. Results from a prospective single-centre clinical study on 121 oxidized (TiUnite) Branemark implants in 46 patients.** *Clinical implant dentistry and related research* 2012, **14**(6):852-860.

CHAPTER 2

DESIGNING A NOVEL DENTAL ROOT ANALOGUE IMPLANT USING CONE BEAM COMPUTED TOMOGRAPHY AND CAD/CAM TECHNOLOGY

Published as:

Anssari Moin D, Hassan B, Mercelis P, Wismeijer D

Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology

Clinical oral implants research 2013, 24 Suppl A100:25-27

ABSTRACT

Objectives
The study aim is to introduce a novel preemptively constructed dental root analogue implant (RAI) based on three-dimensional (3D) root surface models obtained from a cone beam computed tomography (CBCT) scan, computer aided designing and computer aided manufacturing technology.

Materials & Methods
One partially edentulous mandibular human cadaver was scanned with the Accuitomo 170 CBCT system. The scan volumes and datasets were used to create 3D surface models of the tooth. A 3D surface mesh of the tooth was stored as a standard triangulation language (STL) file. A high-end selective laser melting technology was used to fabricate the RAI from the STL file. The RAI was produced in a biocompatible titanium alloy (Ti6Al4V). Optical scanning technology was used to measure the RAI, as well as the natural tooth that was extracted. To validate the accuracy of the CBCT 3D root surface and the manufactured Titanium RAI, both surfaces were superimposed on the optical scan of the tooth, which served as the gold "reference" standard.

Results
The differences between the RAI and the optical scan of the original tooth are most noticeable at the level of the apex and the cementenamel junction areas on the buccal and lingual side (divergence of more than 0.15 mm). Surface area measurements show an overall decrease in surface area of 6.33% for the RAI in comparison with the original tooth and an increase of 0.27% when comparing the 3D surface model with optical scan of the original tooth.

Conclusion
With the use of currently available technology it is very well feasible to preemptively create a custom RAI in titanium. However, clinical evidence evaluating the success of this novel dental implant approach is needed.

INTRODUCTION

The application of digital technology in dentistry is becoming more widespread. There is an increasing shift towards utilizing CAD/CAM especially in implant dentistry. This technology has rapidly evolved in the past two decades and was initially applied in restorative dentistry [1]. In implant dentistry, individualized implant abutments and abutment copings as well as other components have been successfully produced using CAD/CAM technology [2]. Currently, there is a burgeoning interest in applying the principles of digital diagnostics, computerized treatment planning and guided implant surgery together with CAD/CAM technology for the fabrication of implant-supported fixed prosthesis. Additionally, CBCT scan technology is combined with CAD/CAM to produce surgical guide templates [3].

One of the new possibilities with these innovative techniques is to produce a customized dental root analogue implant (RAI) as an alternative to the traditional threaded, straight or tapered, implant systems intended to replace a missing tooth. This new implant would have similar dimensions to the original root and should be congruent with the root socket. Anticipated benefits include uncomplicated immediate implant placement, decreased number of surgeries and increasing patient comfort. Moreover, mimicking root features might result in higher esthetic outcome. Few studies describing techniques of creating and placing custom, root analogue implants have been noted in the literature [4, 5]. However, a significant shortcoming with previously reported techniques is that the process entails laser scanning or machine copying of an extracted root with placement of the subsequently created RAI at a second surgery.

It would seem more efficient to obtain a root replica prior to tooth extraction thus allowing for immediate implant insertion negating the need for a subsequent surgery. The aim of this study is to introduce a new method of creating single rooted titanium RAI by combining CBCT 3D data acquisition with CAD/CAM technology.

MATERIALS AND METHODS

Sample preparation and radiographic scan

One partially edentulous human mandibular cadaver not identified by age, sex or ethnic group was obtained from the functional anatomy department. The cadaver was sectioned at the mid-ramus level and fixed in formalin and stored. A declaration was obtained from the functional anatomy department to use this human remains material for research purposes. The lateral lower incisor was selected for this experiment. The tooth was sound with no amalgam fillings or external root resorption and showed no peri-apical laesions. The mandible was scanned with the Accuitomo 170 CBCT system (AccuiTomo 170, 90kVp, 5mA, 30.8Sec, 4x4cm Field of View (FoV), Morita inc., Japan). The scan position was with the occlusal plane parallel to the floor following the manufacturer's recommendations. The isotropic voxel size and slice interval were 0.08mm.

Image analysis

The scan volumes were exported in DICOM 3 format and imported into image analysis software Amira (v5.3, VisageImaging, California, USA). The datasets were used to create 3D surface models of the tooth. The exact procedure for segmenting the tooth was the following: A region of interest limited to the tooth and surrounding periodontium was first selected. Subsequently, a threshold value based on the histogram analysis, the local gray level value and image gradient was selected to separate the root and crown from the surrounding bone. The resulting images were processed using interactive processing tools to remove resulting artefacts. A 3D surface mesh of the tooth was then created and stored as a Standard Triangulation Language (STL) file (Fig. 1a).

CAD/CAM process

A high-end Selective Laser Melting (SLM) technology was used to fabricate the RAI from the STL file. This technology is an additive manufacturing technique, that is capable of building complex shaped three-dimensional objects by successively depositing and melting of thin metal powder layers. Each individual layer is molten by scanning the successive two-dimensional layers using a focused laser beam. The RAI was produced (Fig. 1b) in a biocompatible titanium alloy (Ti6Al4V) on a proprietary technology SLM machine by LayerWise (LayerWise NV, DentWise division, Belgium).

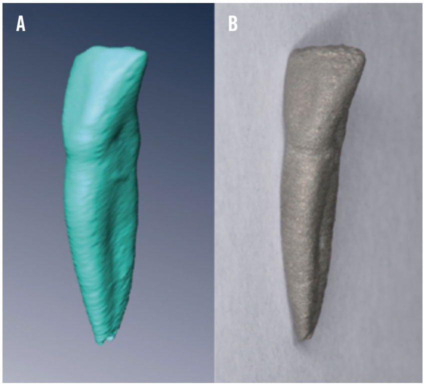


Fig. 1. 3D surface model of the tooth after segmentation (a). CAD/CAM fabricated titanium RAI (b).

Optical scanning

Optical scanning technology was used to measure the RAI, as well as the natural tooth that was extracted. The optical system (Atos II SO, GOM GmbH, Germany) uses a fringe projection system in combination with two high-resolution optical cameras to detect the deflection patterns of the projected fringes on the surfaces to be measured. By utilizing a small measurement volume, a high measurement accuracy and resolution were obtained (typical measurement accuracy of 10 microns is achieved in X, Y and Z direction).

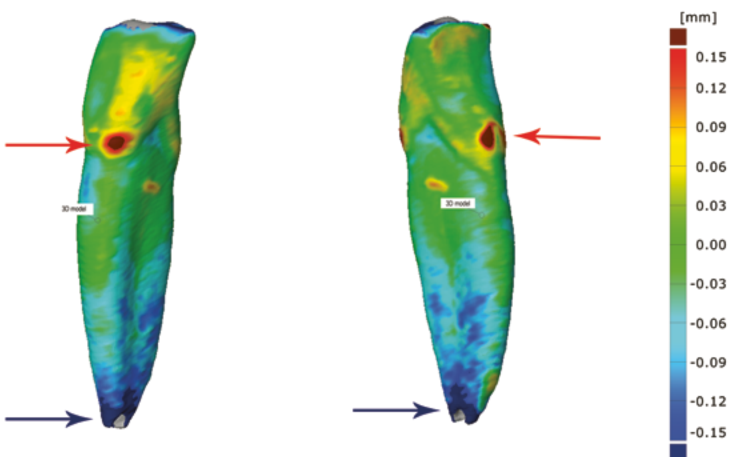
Matching procedure

To validate the accuracy of the CBCT 3D root surface and the manufactured Titanium RAI, both surfaces were superimposed on the optical scan of the tooth, which served as the gold 'reference' standard. The iterative closest point (ICP) registration algorithm was employed to provide maximum alignment. This algorithm brings the two roots to be matched in alignment through minimizing the distance between the two surfaces by calibrating six-degrees (three rotation and three translation) transformation parameters [6]. The aligned surfaces were compared to each other in order to establish the difference among the surfaces. The comparison metric was root mean square difference, which calibrates the mean distance between the two surfaces at anatomically corresponding locations. Additionally, maximum deviation between two surfaces (Hausdorff distance) and the volume was also calculated in order to provide the maximum deviation among the surfaces.

RESULTS

The differences between the RAI and the optical scan of the original tooth are most noticeable at the level of the apex and the cement-enamel junction (CEJ) areas on the buccal and lingual side (Fig. 2). Towards the apical foramen the divergence of the RAI becomes greater than -0.15mm (pointed by the blue arrow's in Fig. 2). The RAI has a greater surface in apical area compared with the original root. The buccal and lingual areas of the CEJ surface (pointed with red arrow's in Fig. 2) of the original tooth is smaller than the RAI. Consequently resulting in a deviation of more than 0.15mm.

Fig. 2. Superimposed surfaces of the RAI and the optical scan of the original tooth. Measurement in millimeters. Notice: optical scan of the tooth served as the reference surface therefore a positive value is a decrease in surface for the RAI and vice versa.



Surface area measurements show an overall decrease in surface area of 6.33% for the RAI in comparison with the original tooth and an increase of 0.27% when comparing the 3D surface model with optical scan of the original tooth (Table 1).

Table 1. Comparison of volume and surface area change between the optical scan of the original tooth, 3D surface model and fabricated RAI.

	3D surface model vs. Optical scan original tooth	Fabricated RAI vs. Optical scan original tooth	Fabricated RAI vs. 3D surface model
Surface area change	0.27%	-6.33%	-6.58%

DISCUSSION

This experiment was performed as a first step towards preoperatively creating an individual root analogue implant. With the combined use of Cone-beam CT 3D data and high-end CAD/CAM technology it was possible to manufacture a RAI with sufficient precision. The 0.27% surface increase of the 3D surface model compared to the original tooth is in concurrence with earlier findings Al-Rawi et. al 2010 [7]. In this particular study by Al-Rawi et al. the accuracy of 3D surface reconstruction of teeth crowns from CBCT scans were reported to be larger than the anatomic truth. During the SLM process of fabricating the RAI a certain amount smoothing and noise reduction occurs, possibly resulting in a decrease of surface area by 6,33%.
Towards the more apical regions of the root the divergence gradually increases up to more than -0,15 mm (Fig. 2), which indicates data loss. This deviation increase might be explained by the fact that bone mass increases in apical direction. Consequently, making a reliable distinction between apex and bone difficult during the segmentation process. A particular finding is the disparity in the CEJ-area of more than 0,15 mm (Fig. 2). One plausible explanation is the damage caused from removal of the tooth by forceps. Resulting in 'indentation like' anomalies. furthermore, CBCT device settings including kVp, mA, scan FOV and voxel size influences the accuracy of the image and the 3D model reconstruction [8].

In this experiment the feasibility of creating an RAI was assessed without attempts to perform any changes on the root surface. However, for functional use of an implant both abutment design and osseointegration are two key factors to a clinically successful treatment. To obtain successful osseointegration primary stability following implant placement is crucial [9, 10]. The currently created RAI will not have sufficient primary stability after placement due to lack of macro retention. Adding macro retention, micro retention (acid etching) and/or combining these with osteoinductive surface modifications (e.g.

Bone Morphogenic Proteins) will possibly result in an abridged and more successful osseointegration when compared to non treated surfaces [11].

Creation of a RAI requires a complete 3D surface model of the tooth derived from the CBCT scan. Specially the root area is important to be intact. Commonly teeth which need to be replaced are damaged. Reconstructing a mirrored 3D surface model based on the contra-lateral tooth might provide a solution in cases with severe damage to the original tooth. Even in situations where teeth have been very recently removed creating a mirrored RAI of the contra-lateral might be an option. Nevertheless differences within teeth and there contra-laterals should be taken in consideration.

New possibilities become available after creating the STL file of the tooth. Through computer 3D designing many alterations can be made to the RAI, adding macro retention fins and preoperatively designing the abutment form. Since the information on abutment design is digital the definitive prosthetic (temporary) crown can be made with CAD/CAM technology. In conclusion, a novel approach to create a custom made RAI using CBCT 3D model and CAD/CAM was proposed. With the use of currently available technology it is very well feasible to preemptively create a custom RAI in titanium with the provisional and definitive prosthetic crown prefabricated. However clinical evidence evaluating the success of this novel dental implant approach is needed.

REFERENCES

1. Duret F, Blouin JL, Duret B: **CAD-CAM in dentistry**. *Journal of the American Dental Association* 1988, **117**(6):715-720.
2. Priest G: **Virtual-designed and computer-milled implant abutments**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2005, **63**(9 Suppl 2):22-32.
3. Tahmaseb A, De Clerck R, Wismeijer D: **Computer-guided implant placement: 3D planning software, fixed intraoral reference points, and CAD/CAM technology. A case report**. *The International journal of oral & maxillofacial implants* 2009, **24**(3):541-546.
4. Kohal RJ, Hurzeler MB, Mota LF, Klaus G, Caffesse RG, Strub JR: **Custom-made root analogue titanium implants placed into extraction sockets. An experimental study in monkeys**. *Clinical oral implants research* 1997, **8**(5):386-392.
5. Pirker W, Kocher A: **Immediate, non-submerged, root-analogue zirconia implants placed into single-rooted extraction sockets: 2-year follow-up of a clinical study**. *International journal of oral and maxillofacial surgery* 2009, **38**(11):1127-1132.

6. Zhang Z: **Iterative point matching for registration of free-form curves and surfaces**. *International Journal of Computer Vision* 1994, **13**:119-158.
7. Al-Rawi B, Hassan B, Vandenberge B, Jacobs R: **Accuracy assessment of three-dimensional surface reconstructions of teeth from cone beam computed tomography scans**. *Journal of oral rehabilitation* 2010, **37**(5):352-358.
8. Hassan B, Couto Souza P, Jacobs R, de Azambuja Berti S, van der Stelt P: **Influence of scanning and reconstruction parameters on quality of three-dimensional surface models of the dental arches from cone beam computed tomography**. *Clinical oral investigations* 2010, **14**(3):303-310.
9. Koh RU, Rudek I, Wang HL: **Immediate implant placement: positives and negatives**. *Implant dentistry* 2010, **19**(2):98-108.
10. Grandi T, Garuti G, Guazzi P, Tarabini L, Forabosco A: **Survival and success rates of immediately and early loaded implants: 12-month results from a multicentric randomized clinical study**. *The Journal of oral implantology* 2012, **38**(3):239-249.
11. Liu Y, Enggist L, Kuffer AF, Buser D, Hunziker EB: **The influence of BMP-2 and its mode of delivery on the osteoconductivity of implant surfaces during the early phase of osseointegration**. *Biomaterials* 2007, **28**(16):2677-2686.

CHAPTER 3

ACCURACY OF PRE-EMPTIVELY CONSTRUCTED, CONE BEAM CT AND CAD/CAM TECHNOLOGY BASED, INDIVIDUAL ROOT ANALOGUE IMPLANT TECHNIQUE: AN IN-VITRO PILOT INVESTIGATION

Published as:

Anssari Moin D, Hassan B, Parsa A, Mercelis P, Wismeijer D

Accuracy of preemptively constructed, Cone Beam CT-, and CAD/CAM technology-based, individual Root Analogue Implant technique: An in vitro pilot investigation

Clinical oral implants research 2014, 25(5):598-602

ABSTRACT

Objectives

The aim of this in-vitro pilot investigation is to assess the accuracy of the preemptive individually fabricated root analogue implant (RAI) based on three-dimensional (3D) root surface models obtained from a cone beam computed tomography (CBCT) scan, computer aided designing (CAD) and computer aided manufacturing (CAM) technology and to measure the discrepancy in congruence with the alveolar socket subsequent to placement of the RAI.

Materials & Methods

Eleven single rooted teeth from nine human cadaver mandibles were scanned with the 3D Accuitomo 170 CBCT system. The 3D surface reconstructions of the teeth acquired from the CBCT scans were used as input for fabrication of the RAIs in titanium using rapid manufacturing technology. The teeth were then carefully extracted. The teeth and RAIs were consequently optically scanned. The mandibles with the empty extraction sockets were scanned with CBCT using identical settings to the first scan. Finally, the preemptively made RAIs were implanted into their respective sockets and the mandibles were again scanned with CBCT using the same scan settings as previous scans.

All 3D surfaces reconstructions (CBCT 3D surface models and optical scan 3D models) were saved for further analysis. 3D models of original teeth and optical scans of the RAIs were superimposed onto each other; differences were quantified as Root Mean Square (RMS) and hausdorff surface distance. In order to obtain an estimate of the fit (congruence) of the RAIs in their respective sockets the volumetric datasets of the sockets were compared with those of the root part of RAIs congruent with the sockets.

Results

Superimposed surfaces of the RAIs and the original tooth reveals discrepancy for RMS, volumetric geometry and surface area varying from 0.08 mm to 0.35 mm, 0.1% to 7.9% and 1.1% to 3.8%, respectively. Comparing volume differences of the alveolus and with the socket corresponding part of the RAI resulted in every case the volume of the socket being greater then the root part of the RAI ranging from 0.6% to 5.9% volume difference.

Conclusion

The preemptive CAD/CAM based RAI technique might offer promising features for immediate implant placement. However, due to the lack of prospective clinical data, further research is needed to fine tune and evaluate this technique.

INTRODUCTION

The use of Cone Beam Computed Tomography (CBCT), Computer Aided Designing (CAD) and Computer Aided Manufacturing (CAM) has become widespread in implant dentistry. Various clinical applications including computerized implant treatment planning, implant-supported fixed prosthesis and guided implant surgery combine the use of CBCT and CAD/CAM technologies (Jung et al. 2009). As technology advances, applications of digitized dental reconstructions will continue to expand. Recently we proposed a novel approach for immediate implant placement designed to replace a (soon to be) missing tooth (Anssari Moin et al. 2011). In contrast to traditional immediate implant approaches using conventional, threaded, cylindrical or tapered implants, this technique provides a preemptively individually made Root Analogue Implant (RAI) based on acquisition of three-dimensional (3D) reconstructions from the CBCT scan and fabrication process through high-end Selective Laser Melting (SLM) technology.

Our pilot study results suggested that the dimensions of the RAI are similar to the original root. However, all steps in the process of fabricating a preemptively made RAI can result in geometrical deviations and structural imperfections. Consequently, these errors can lead to discrepancies in implant fit in the socket, lessened bone to implant contact, decreased mechanical engagement of the implant or highly pressurized implant fit. For successful implementation of the preemptive RAI technique high quality 3D surface models, high accuracy fabrication of the RAI and a congruent fit between the RAI and the extraction socket are required (Anssari Moin et al. 2011; Figliuzzi et al. 2012). The aim of this pilot investigation is to assess the accuracy of the individually fabricated CBCT and CAD/CAM based titanium RAI and to measure the discrepancy in congruence with the alveolar socket subsequent to placement.

MATERIALS AND METHODS

Sample preparation, radiographic scan, optical scan and CAD/CAM process

We built on the method previously described by Anssari Moin et al. 2010. Briefly, eleven single rooted teeth from nine mandibles (not identified by age, gender or ethnic group) were selected. There were 3 central and 1 lateral incisor and 6 canines and 1 premolar tooth. The mandibles were scanned with the 3D Accuitomo 170 CBCT system (AccuiTomo 170, 90kVp, 5mA, 30.8s, 4x4cm Field of View [FoV], voxel 0.08mm3, Morita Inc., Kyoto, Japan) using the recommended scan protocol. Subsequently, eleven RAIs were produced in titanium by rapid manufacturing using SLM technology (LayerWise NV, Dent-Wise Division, Leuven, Belgium). The 3D surface reconstructions of the teeth acquired from the CBCT scans were used as the input for the digital manufacturing process (3D reconstruction details follow below). The files were sliced with a layer thickness of 30μm and produced in a high-end SLM machine equipped with an Ytterbium-fiber laser from Ti6Al4V powder under an argon atmosphere.

The teeth were then carefully extracted to reduce risk of fracturing the bone and roots and to avoid any alterations to the shape of the socket. The teeth and RAIs were consequently optically scanned using an optical system (Atos II SO; GOM GmbH, Braunschweig, Germany). Subsequent to tooth extraction and prior to RAI implantation the mandibles with the empty extraction sockets were scanned with CBCT using identical settings to the first scan. This was conducted in order to obtain the volumes of the sockets after extraction.

Finally, the preemptively made RAIs were implanted into their respective sockets. With finger pressure and the gentle use of a hammer and a mallet good primary stability of the RAI was achieved and checked by palpation and percussion. The nine mandibles with the eleven RAIs in place were again scanned with the 3D Accuitomo 170 CBCT system using the exact same scan settings as with the previous scans.

3D surface reconstructions, surface measurements and volumetric measurements

The CBCT datasets were imported in Amira software for further analysis and image segmentation (v5.3, VisageImaging, Carlsbad, CA, USA). Threshold based segmentation techniques were employed to segment the teeth from their surroundings in the original scan prior to teeth extraction (Fig. 1). The exact procedure for segmenting the tooth was the following: A region of interest limited to the tooth and surrounding periodontium was first selected. Subsequently, a threshold value based on the histogram analysis, the local grey level value and image gradient was selected to separate the root and crown from the surrounding bone. A manual selection, on basis of the sagittal slides, was added for the most apical part of the root if the threshold-based technique did not confine the entire apex area. The resulting images were processed using interactive processing tools to remove resulting artefacts.

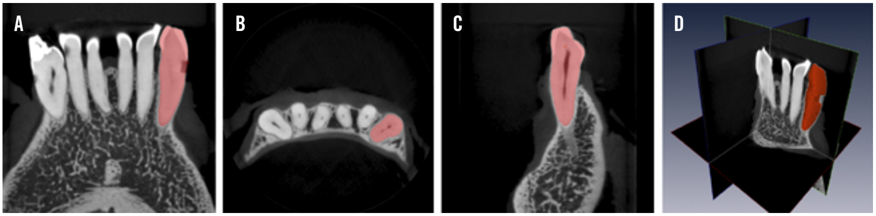


Fig. 1. Example of the segmentation and preparation of RAI no. 2. Coronal (a), axial (b), sagittal (c) and 3D (d) views.

All segmented datasets were converted to 3D surface models using the marching cube algorithm (Lorensen & Cline 1987). The 3D surfaces were saved in the standardized triangulation language (STL) file format. The same format was employed for the optical 3D models of the natural teeth and RAIs (Fig. 2 a,b). Using a 3D iterative closest point registration algorithm (Aloimonos 2004), 3D models of the teeth and the optical scans of the RAIs were superimposed onto each other and differences were quantified as mean (Root Mean Square [RMS]) and maximum (hausdorff) surface distance (Canadian Image Processing and Pattern Recognition Society 2004) (Fig. 2c). The STL of the natural tooth served as the reference standard within alignment of the surfaces.

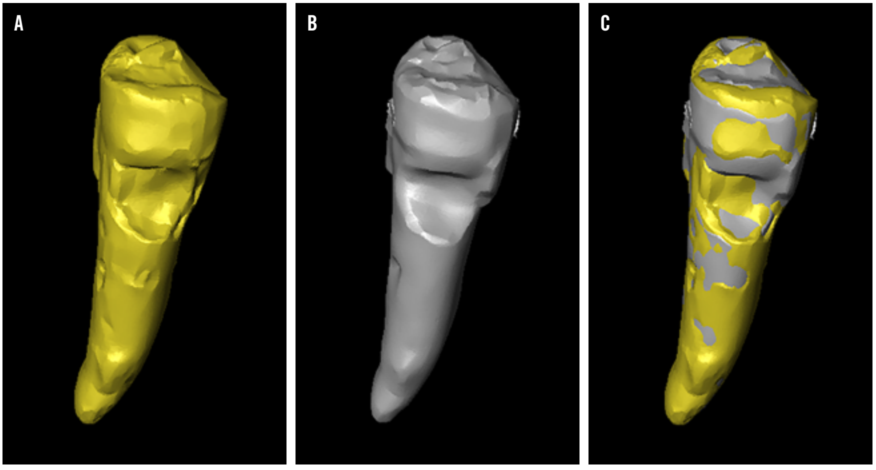


Fig. 2. 3D surface models derived from optical scanning of the natural tooth (a) and from optical scanning of the RAI (b). Surface alignment between natural tooth (yellow) and RAI (grey) in (c). Notice the under-estimation of RAI surface reconstruction in comparison with the natural tooth, especially in the apical area.

In order to obtain an estimate of the fit (congruence) of the RAIs in their respective sockets the volumetric datasets of the sockets were compared with the volumetric datasets of the root part of RAIs congruent with the sockets. The measurement process was as follows: Using tracing tools in Amira, the outline of the socket was followed on each slice starting coronally at the alveolar bone crest and proceeding apically to the apex. On each slice a contour was traced and the confined surface area was automatically selected through the software (Fig. 3).

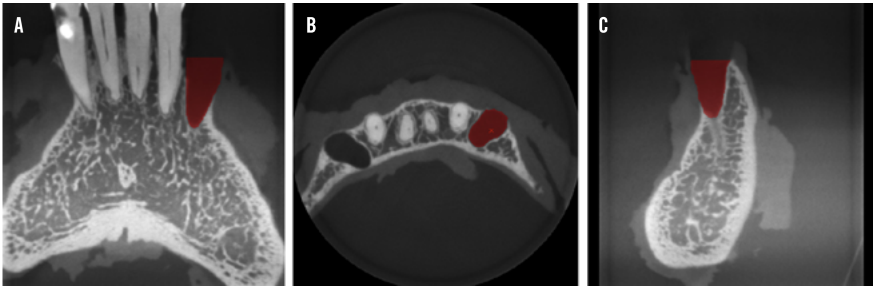


Fig. 3. Example of the volumetric measurement of the socket of RAI no. 2. Coronal (a), axial (b) and sagittal (c) views.

The volumes were obtained through combining the surface areas of the contiguous slices and considering the voxel dimensions. The software then automatically measures the sum total of the volumes of the individual slices producing the total volume of the socket in cubic millimeter. This method has been previously described to follow-up volumetric bone or soft tissue changes with CBCT (Garcia de Paula-Silva et al. 2009). The same volumetric measurement process was applied for to the alveolar socket corresponding part of the implanted RAI.

RESULTS

Comparing the superimposed surfaces of the RAIs and the original tooth reveals in all 11 cases a local disparity at the incisal edge area (Fig. 4, arrow 1). This particular incisal edge area of the RAIs is smaller than the original teeth (maximum 0.15 mm). Towards the more apical area's all RAIs appear to have gradual deviation with their original counterparts (Fig. 4, arrow 3) varying with a minimum of 0.31mm and a maximum of 1.86mm decrease at the most apical part of the RAIs. At the cemento-enamel junction (CEJ) of RAIs no. 2, 4, 5, 6, 7, 8, 9 a local increase in surface area is visible (Fig. 4, arrow 2).

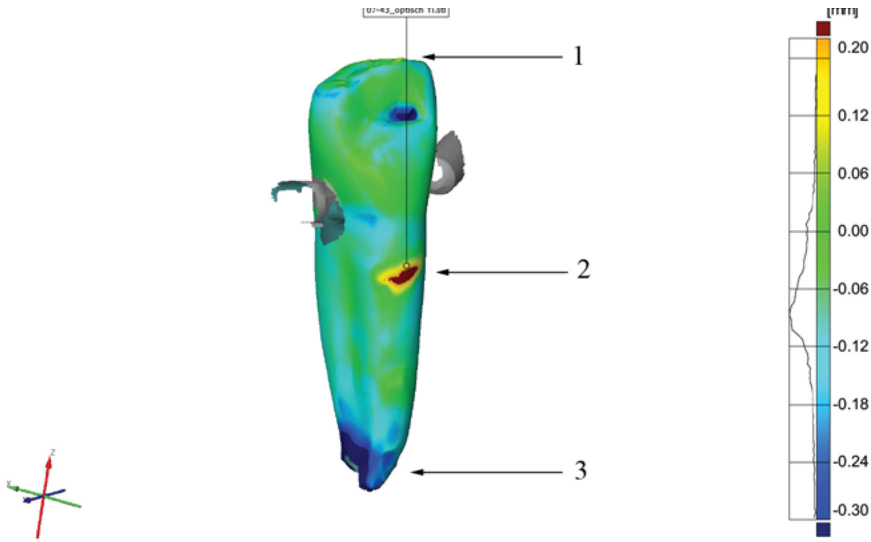


Fig. 4. Superimposed STL files of the optical scan of the original tooth and RAI no. 2. Measurement in millimeters. Notice: optical scan of the tooth served as the reference surface.

The RMS data, volume change and surface area change between the RAI and original tooth was measured for all RAIs (summarized in Table 1, column A, B and C. Note: the natural toot served as reference). The RAIs were smaller then the original teeth in all instances (Fig. 2c). The discrepancy for the RMS, volumetric geometry and surface area varied from 0.08 mm to 0.35 mm, 0.1% to 7.9% and 1.1% to 3.8%, respectively.

To ascertain the extent of congruence of the root part of the RAIs with their equivalent sockets volume differences of the alveolus and with the socket corresponding part of the RAI were calculated (outlined in Table 1, column D. Note: the empty socket served as reference). In every case the volume of the socket was greater then the root part of the RAI ranging from 0.6% to 5.9% volume difference.

	A | RMS±SD (max) natural tooth vs. RAI	B | VOLUME natural tooth vs. RAI	C | SURFACE AREA natural tooth vs. RAI	D | VOLUME Volume socket vs. RAI in socket
RAI 1	0.171±0.122 (1.10)	2.5	1.1	0.6
RAI 2	0.155±0.112 (1.11)	3.4	2.5	5.9
RAI 3	0.098±0.070 (0.77)	3.6	3.8	1.4
RAI 4	0.119±0.086 (1.87)	7.9	3.8	1.7
RAI 5	0.14±0.095 (0.91)	2.2	2.3	2.5
RAI 6	0.14±0.088 (1.01)	3.7	3.6	5.6
RAI 7	0.098±0.067 (0.56)	2.2	1.3	1.7
RAI 8	0.35±0.20 (1.06)	4.4	1.8	2.1
RAI 9	0.13±0.095 (0.86)	0.1	1.4	3.1
RAI 10	0.080±0.043 (0.31)	7.4	3.1	4.1
RAI 11	0.099±0.061 (0.46)	6.0	1.7	1.7

Table 1: Summarized measurements: The natural tooth/socket served as reference standard. Column A: RMS difference and standard deviation (SD) results between the optical scan of the natural tooth and the RAI in millimeters (mm). Maximum errors (hausdorff distance) are reported between brackets. Column B: volume change (%) between the original tooth and fabricated RAI. Column C: surface area change (%) between the original tooth and RAI. Column D: volume difference (%) between the alveolar socket and implanted RAI.

DISCUSSION

Advantages supporting the idea of this approach encompass shortening of the reconstruction treatment time, forbearance of multiple surgical interventions and easy surgical handling, altogether resulting in increased patient comfort. Another proposed advantage of the technique is the minimal marginal alveolar bone resorption as a consequence of the uncomplicated surgical application: atraumatic, flap-less and socket friendly (Pirker et al. 2011; Figliuzzi et al. 2012). Since the RAI is a one-piece and one-stage implant submerged healing is not an option. Hence, after removal of the tooth and insertion of the RAI primary stability is of crucial importance for osseointegration (Lioubavina-Hack et al. 2006). Conventional threaded implants achieve primary stability in immediate implantation situations by means of perforating 3-5 mm apically of the alveolus and screw

retaining the implant into to the lingual/palatal alveolar bone wall (Lang et al. 2012). However with the RAI primary stability is achieved through a good congruence with the alveolar socket, a slight pressurized fit and the macroscopic features of the implant (Pirker et al. 2011). It is of note that a pressurized fit is one of the key factors influencing primary stability. Inaccuracies from the digital planning to the fabrication process of the RAI will lead to decreased fit with the alveolar socket, lessened bone-to-implant contact, and abated primary stability and ultimately resulting in implant failure.
This pilot investigation was conducted to assess the accuracy of the preemptively constructed CBCT and CAD/CAM based RAI technique and measure for discrepancy with the socket after implantation. The results show that the differences between the RAI vs. tooth and socket vs. root-part of the RAI are small. This is in corroboration with previous findings from Anssari Moin et al. 2011 and Figulizz et al 2011.
The particular disparity of the RAIs at the incisal edge can be rationalized by the fact that all the RAIs were supported with pins at the incisal edge during the SLM process. These supports were subsequently removed resulting in inaccuracy at this particular area. The gradual deviation increase in apical direction between the RAI and original tooth has previously been reported to be a cause of increased bone mass in apical direction resulting in lesser accuracy and gradual underestimation of the root during the segmentation process (Anssari Moin et al. 2011). Furthermore, the local incongruity of RAIs no. 2, 4, 5, 6, 7, 8, 9 at the CEJ could be explained as damage to the original tooth caused by extraction by forceps (Anssari Moin et al. 2011).

The study by Figliuzzi et al. 2011 is a clinical case report of the RAI. Since it was unknown what potential distortions or errors of deviation will result when using the preemptively fabricated RAI technique they prepared three different RAIs with sequential percentage dimensional increments of 0%, 5% and 10% of the same object. During surgery the RAI with 0% volume increase was chosen to be implanted. In this current pilot study it has been shown that the volume of the root part of the RAI differs 0.6% up to 5.9% with the socket. Consequently it would be advisable when clinically applying the RAI to have preemptively prepared a RAI with 0% and 5.9% volume increase at the root section. Still, considering the limited amount of incongruence of the RAI with the original tooth and the socket, it is not known if these differences will be of clinical significance. Furthermore, it should be taken into consideration when (digitally) adding macro retention to the RAI volume increase of the RAI might not be of beneficial effect on primary stability (Pirker et al. 2011).

An important drawback of this proof of principle study is the use of cadavers. The voxel size employed in this investigation of 0.08mm might not be achievable in the clinic since real patients' scans suffer from motion artifacts related to slight patient's movement plus artifacts resulting from the presence of anatomical structures outside the center of field of view (Schulze et al. 2011). These artifacts negatively contribute to the quality of the obtained images that effective system resolution would be lower (0.3-0.5mm) than the nominal resolution of 0.08mm reported here (Kalender et al. 2007). Different CBCT systems and scan settings would also influence the quality of the 3D model reconstructions (Loubele et al. 2007; Hassan et al. 2010; Hassan et al. 2010). Additionally, parameters of the SLM technique (Ti6Al4V alloy particle size, wave length, power, scanning rate and laser spot size) will have consequences in the final results of the RAI. However, in this current investigation accuracy of the SLM technique was very high. Mean variation of 0.015 mm to 0.020 mm when comparing the STL with the fabricated RAI.

Restoration of the RAI brings new digital challenges and potentials. Since the information of the RAI is in STL format many alterations can be made to the RAI through computer 3D designing. Preoperatively designing the abutment form of the RAI in combination with 3D surface models of the dentition derived from CBCT might give the prospects of preemptively creating the (temporary) crown with CAD/CAM technology.

In conclusion, within the limitations of this in-vitro investigation, it has been demonstrated that the preemptive CAD/CAM based RAI technique could potentially provide accurate dental implants for immediate implant placement. However, the influence of the different image artefacts on segmentation accuracy could be investigated since the study sample was confined to human cadaver mandibles. Interesting possibilities arise when combining digital prosthetics and RAI technique. However, further clinical research is needed to fine tune and evaluate this technique.

REFERENCES

Aloimonos, J. (2004) IEEE Xplore 3DPVT 2nd International Symposium on 3D Data Processing, Visualization, and Transmission. proceedings: 6-9 September, 2004, Thessaloniki, Greece. *University of Maryland, Institute for Advanced Computer Studies. Institute of Electrical and Electronics Engineers Computer Society, Los Alamitos, California* **18:** 1014.

Anssari Moin, D., Hassan, B., Mercelis, P. & Wismeijer, D. (2011) Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology. *Clinical Oral Implants Research* Epub ahead of print

Canadian Image Processing and Pattern Recognition Society. (2004) IEEE Xplore 1st Canadian Conference on Computer and Robot Vision. proceedings: 17-19 May, 2004, Ontario, Canada. *University of Western Ontario, International Association for Pattern Recognition. Institute of Electrical and Electronics Engineers Computer Society, Los Alamitos, California* **7**: 510.

Figliuzzi, M., Mangano, F. & Mangano, C. (2012) A novel root analogue dental implant using CT scan and CAD/CAM: selective laser melting technology. *International Journal of Oral and Maxillofacial Surgery* **41**: 858-862.

Garcia de Paula-Silva, F.W., Hassan, B., Bezerra da Silva, L.A., Leonardo, M.R. & Wu, M.K. (2009) Outcome of root canal treatment in dogs determined by periapical radiography and cone-beam computed tomography scans. *Journal of Endodontology* **5**:723-726

Hassan, B., Metska, M.E., Ozok, A.R., van der Stelt, P. & Wesselink, P.R. (2010) Comparison of five cone beam computed tomography systems for the detection of vertical root fractures. *Journal of Endodontology* **36**: 126-129.

Hassan, B., Couto Souza, P., Jacobs, R., de Azambuja Berti, S. & van der Stelt, P. (2010) Influence of scanning and reconstruction parameters on quality of three-dimensional surface models of the dental arches from cone beam computed tomography. *Clinical Oral Investigations* **14**: 303-310.

Jung, R.E., Schneider, D., Ganeles, J., Wismeijer, D., Zwahlen, M., Hammerle, C.H. & Tahmaseb, A. (2009) Computer technology applications in surgical implant dentistry: a systematic review. *International Journal of Oral and Maxillofacial Implants* **24** Suppl: 92-109.

Kalender, W.A. & Kyriakou, Y. (2007) Flat-detector computed tomography (FD-CT). *European Radiology* **17**: 2767–2779.

Lang, N.P., Pun, L., Lau, K.Y., Li, K.Y. & Wong, M.C. (2012) A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. *Clinical Oral Implants Research* **23 Suppl 5**: 39-66.

Lioubavina-Hack, N., Lang, N.P. & Karring, T. (2006) Significance of primary stability for osseointegration of dental implants. *Clinical Oral Implants Reseach* **17**: 244-250.

Lorensen, W.E. & Cline, H.E. (1987) Marching cubes: a high resolution 3D surface construction algorithm. *Association for Computing Machinery's Special Interest Group on Computer Graphics and Interactive Techniques* **21**:163–169.

Loubele, M., Guerrero, M.E., Jacobs, R., Suetens, P. & van Steenberghe, D. (2007) A comparison of jaw dimensional and quality assessments of bone characteristics with cone-beam CT, spiral tomography, and multi-slice spiral CT. *International Journal of Oral Maxillofacial Implants* **22**: 446–454.

Pirker, W., Wiedemann, D., Lidauer, A. & Kocher, A.A. (2011) Immediate, single stage, truly anatomic zirconia implant in lower molar replacement: a case report with 2.5 years follow-up. *International Journal of Oral and Maxillofacial Surgery* **40**: 212-216.

Schulze, R., Heil, U., Gross, D., Bruellmann, D.D., Dranischnikow, E., Schwanecke, U. & Schoemer, E. (2011) Artifacts in CBCT: a Review. *Dentomaxillofacial Radiology* **40**: 265–273.

CHAPTER 4

A NOVEL APPROACH FOR CUSTOM THREE-DIMENSIONAL PRINTING OF A ZIRCONIA ROOT ANALOG IMPLANT BY DIGITAL LIGHT PROCESSING

Published as:

Anssari Moin D, Hassan B, Wismeijer D

A novel approach for custom three-dimensional printing of a zirconia root analogue implant by digital light processing

Clinical oral implants research 2017, 28;668–670

ABSTRACT

Objectives

This study aim is to explore the feasibility of fabrication of three-dimensional (3D) printed zirconia root analogue implant (RAI) through digital light processing (DLP) technology.

Materials and Methods

One partially edentulous mandibular human cadaver was scanned with a cone-beam computed tomography (CBCT) system. The scan volumes and datasets were used to create computer-aided design (CAD) model of the RAI.
A high-end DLP 3D printing technology was used to fabricate the RAI from the CAD model. Within this approach solid 3D objects are built by using a DLP projector to translate voxel data so it is reproduced in liquid photopolymer dispersed with a commercial ceramic, thereby light polymerizing the resin to solid. Optical scanning technology was used to measure the tooth and 3D printed RAI. To validate the accuracy of the printed zirconia RAI the optical surface model of the original tooth and CAD model were superimposed.

Results

The differences between the optical scans of the RAI and original tooth are most noticeable towards the apical foramen, showing a disparity for the RAI with a maximum deviation of 0.86 mm. When setting a maximum threshold of 0.5 mm for the 3D printed RAI surface to be deviating from the original tooth model and CAD model, measurements show 1.55 % and 4.86 % of the surface areas are exceeding the threshold distance respectively.

Conclusion

With the use of currently available technology it is well feasible to 3D print in zirconia a custom RAI.

INTRODUCTION

Rapid advancements are being made in the field of three-dimensional (3D) printing processes in the compass of dentistry. Currently distinctive 3D print processes in combination with different materials are being used for fabrication of patient specific 3D parts either for prosthetic or surgical reconstruction of the dental and maxillo-facially compromised patient. One of the new applications of 3D additive manufacturing technologies in the area of implantology is the creation of the pre-emptive titanium custom made Root Analogue Implant (RAI) for immediate implant cases [1, 2]. Proposed benefits of this RAI approach include; uncomplicated immediate implant placement, decreased number of surgeries, less initial bone loss resulting from the absence of the microgap shared with the minimal invasive approach and increasing patient comfort [1-5]. Several studies have proven the feasibility of 3D manufacturing the RAI by powder bed fusion methods, in the manner of Selective Laser Melting (SLM) and Direct Metal Laser Sintering (DMLS) [1-3, 6].

Growing concerns regarding titanium hypersensitivity and corrosion through gradual material degradation encourage further research into biocompatible alternatives [7-9]. Zirconia has been proposed as an alternative implant material to titanium owing to its excellent biomechanical characteristics. Particular advantages of zirconia implants compared to titanium implants include; no metal aura (through time) in cases with deficiency of the buccal bone plate and/or thin biotype mucosa with/without recession of the mucosa, corrosion resistance and hypoallergenicity [10, 11]. Currently the widely applied system for fabrication of 3D zirconia parts is by means of Computer Numerical Control (CNC) milling of an unsintered white monoblock and subsequent firing into a sintered high-strength ceramic. Disadvantages of this method are substantial waste of raw material, limited accuracy and time-consuming process [12].
With recent innovations in rapid prototyping technologies it has become possible to 3D print advanced ceramics. One of such developments is the rise of Digital Light Processing (DLP) technology for 3D printing of ceramics with potential to compete with the current CNC milling techniques of ceramics. The design of this research was based on a previous study by Anssari Moin et al. (2011) in which the possibility of 3D printing a titanium RAI was investigated. The aim of this study was to explore the feasibility of fabrication of 3D printed zirconia RAI through DLP-technology.

MATERIALS AND METHODS

Sample preparation, radiographic scan and RAI 3D model construction

Based on the previously described method by Anssari Moin et al. (2011) we built a 3D

surface model of a RAI. Briefly, human mandibular cadaver with multiple sound teeth, not identified by age, sex or ethnic group was selected. The mandible was scanned with the 3D Accuitomo 170 Cone Beam Computed Tomography (CBCT) system (AccuiTomo 170, 90kVp, 5mA, 30.8Sec, 4x4cm Field of View (FoV), Morita inc., Japan). The scan position was with the occlusal plane parallel to the floor following the manufacturer's recommendations. The isotropic voxel size and slice interval were 0.08mm.
Consequently, the CBCT dataset was imported in Amira software for further analysis and image segmentation (v5.3, VisageImaging, Carlsbad, CA, USA). Threshold based segmentation techniques were employed to segment a sound lateral lower incisor from its surroundings. The exact procedure for segmenting the tooth was the following: A region of interest limited to the tooth and surrounding periodontium was first selected. Subsequently, a threshold value based on the histogram analysis, the local grey level value and image gradient was selected to separate the root and crown from the surrounding bone. A manual selection, on basis of the sagittal slides, was added for the most apical part of the root if the threshold-based technique did not confine the entire apex area. The resulting images were processed using interactive processing tools to remove resulting artefacts. The segmented dataset was converted to 3D surface model using the marching cube algorithm and saved in the standardized triangulation language (STL) file format. Based on the STL model a printable 3D RAI mesh has been reconstructed using Computer Aided Design (CAD) software (SolidWorks 2015 SP3, Dassault Systèmes, Vélizy, France) and stored as a new STL file (fig. 1a).

3D printing process

A high-end DLP 3D printing technology (under current development by ADMATEC Europe BV, Moergestel, Netherlands) was used to fabricate the RAI from the CAD STL file. This technology is an additive manufacturing technique in which solid 3D objects are built by using a DLP projector to translate voxel data so it is reproduced in liquid photopolymer, thereby light polymerizing the resin to solid. By altering the pattern of the projection and incrementing the vertical position of the stage, a specific geometry is built up layer by layer (layerthickness varying from 25 μm to 100 μm). To build a solidified ceramic object, the photopolymer used is a dispersion of a commercial ceramic powder (ZrO_2; Formatec Technical Ceramics BV, Goirle, Netherlands) into a liquid solution of polyacrylate. Subsequently, the residual resin is removed from the solidified object by ethanol and heat treatment and sintered into its final form (fig. 1b). Due to the current patenting process further details cannot be provided.

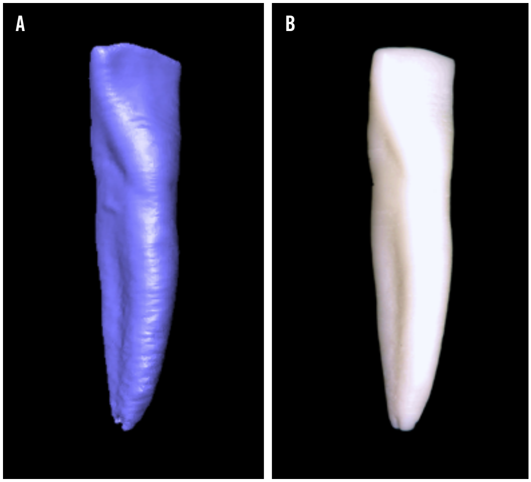


Figure 1. 3D CAD model of a RAI (a). 3D printed by DLP and sintered RAI (b).

Optical scanning and matching procedure

Optical scanning technology was used to measure the differences of the 3D printed RAI, as well as the natural tooth that was extracted. The optical system (Atos II SO, GOM GmbH, Germany) uses a fringe projection system in combination with two high-resolution optical cameras to detect the deflection patterns of the projected fringes on the surfaces to be measured. By utilizing a small measurement volume, a high measurement accuracy and resolution were obtained (typical measurement accuracy of 10 microns is achieved in X, Y and Z direction).

To validate the accuracy of the printed zirconium RAI versus the RAI CAD model versus the optical scan of the natural tooth, all surfaces were superimposed on the optical scan of the tooth, which served as the gold 'reference' standard. The iterative closest point (ICP) registration algorithm was employed to provide maximum alignment. This algorithm brings the two roots to be matched in alignment through minimizing the distance between the two surfaces by calibrating six-degrees (three rotation and three translation) transformation parameters [13]. The aligned surfaces were compared to each other in order to establish the difference among the surfaces. The comparison metric was root mean square difference (RMS), which calibrates the mean distance between the two surfaces at anatomically corresponding locations. Additionally, maximum deviation between two surfaces (Hausdorff distance) and the volume was also calculated in order to provide the maximum deviation among the surfaces.

RESULTS

Comparing the superimposed optical scan surfaces of the original tooth and the CAD model of the RAI to the DLP 3D printed RAI reveals in most areas a surface distance increase for the DLP 3D printed RAI (table 1 and fig. 2). When setting a maximum threshold of 0.1 mm and 0.5 mm for the DLP 3D printed RAI surface to be deviating from the original tooth, measurements reveal 46.38 % and 1.55 % of the surface areas are exceeding the threshold distances respectively (table 1). After repeating this measurement for the DLP 3D printed RAI surface to be deviating from the CAD model, it is shown that 59.33 % and 4.86 % of the surface areas are exceeding the threshold distances of 0.1 mm and 0.5 mm respectively (table 1).

	Optical scan of the tooth vs. Optical scan of the 3D printed RAI	CAD model of the RAI vs. Optical scan of the 3D printed RAI
dSurface area %	6,671932262	7,13760367
RMS (SD) in mm	0.15 (0.099)	0.18 (0.090)
Maximum errors (Hausdorff distance in mm)	0.86	0.66
% exceeding threshold 0.1 mm	46.38	59.33
% exceeding threshold 0.5 mm	1.55	4.86

Table 1. Summarized measurements: The optical scan of the 3D printed RAI served as reference standard.

Towards the apical foramen the greatest disparity for DLP 3D printed RAI compared to the original tooth is noticed with a maximum deviation (Hausdorff distance) of 0.86 mm (table 1, fig. 2). The RMS data and surface area change between the DLP 3D printed RAI versus the original tooth and CAD model are measured and summarized in table 1.

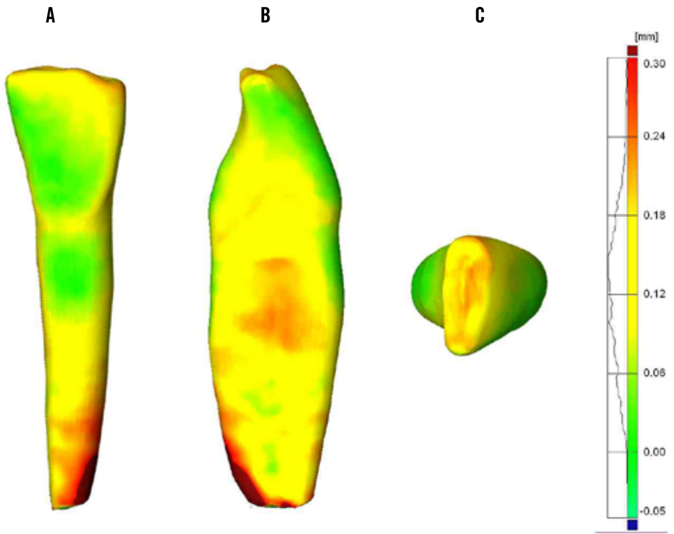


Figure 2. Superimposed surfaces of the optical scans of the RAI and the original tooth. Measurement in millimetres. Frontal (a), sagittal (b) and occlusal (c) views. Notice: optical scan of the tooth served as the reference surface.

DISCUSSION

This experiment was performed as a first step towards preoperatively 3D printing an individual zirconia root analogue implant. With the combined use of Cone beam CT 3D data and high-end DLP 3D printing technology it was possible to fabricate a RAI with a certain amount of precision. However towards the apical area the divergence increases up to 0.86 mm. This increase in deviation can be explained by the fact that the supporting platform from which this object was built during the printing process was situated at the apex of the RAI model resulting in added material. In addition, previous studies by Anssari Moin et. al 2011 & 2012 have shown that during the threshold-based segmentation process from the CBCT data towards the apical area distinction of root and bone becomes more difficult developing in a gradual overestimation nearing the apical area. In general the results show that the printed RAI has a 6.67 % larger surface area and 46.38 % of the printed RAI has a greater distance than 0.1 mm from the original tooth representing a volumetrically larger copy. Nonetheless, when comparing the printed RAI to the CAD model measurements show a larger disparity for surface area change (7.14 %), percentage threshold surpassing for 0.1 mm (59.33 %) and 0.5 mm (4.86 %). This shows that the current stage in which DLP 3D printing technology resides provides less accurate models then the commercially available additive manufacturing techniques for metals such as SLM and DMLS [1, 6]. Numerous factors influence the precision of the DLP 3D printing of ceramics, specially the resolution of the digital mirroring device which a part of the DLP printer and the composition of the ceramic photopolymer. Conversely, fine-tuning of the DLP 3D printing process for ceramics is an engineering challenge and beyond the scope of this study.

With the advancing possibility to 3D print advanced ceramics for implant dentistry new possibilities and questions arise. Potential advantages over CNC milling of unsintered ceramics comprise the precise control over spatially grade composition, microstructure design/distribution and (undercut) shape. How 3D printed zirconia (root analogue) implants with possible (microstructure/porosity) modifications will influence osseointegration and the peri-implant biology needs further research. Nevertheless, we can conclude that with the use of currently available DLP 3D printing technology it is feasible to preemptively fabricate a one-piece zirconia (root analogue) implant.

REFERENCES

1. Anssari Moin D, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2013, **24 Suppl A100**:25-27.
2. Figliuzzi M, Mangano F, Mangano C: **A novel root analogue dental implant using CT scan and CAD/CAM: selective laser melting technology**. *International journal of oral and maxillofacial surgery* 2012, **41**(7):858-862.
3. Mangano FG, De Franco M, Caprioglio A, Macchi A, Piattelli A, Mangano C: **Immediate, non-submerged, root-analogue direct laser metal sintering (DLMS) implants: a 1-year prospective study on 15 patients**. *Lasers in medical science* 2014, **29**(4):1321-1328.
4. Pirker W, Kocher A: **Immediate, non-submerged, root-analogue zirconia implant in single tooth replacement**. *International journal of oral and maxillofacial surgery* 2008, **37**(3):293-295.
5. Pirker W, Kocher A: **Immediate, non-submerged, root-analogue zirconia implants placed into single-rooted extraction sockets: 2-year follow-up of a clinical study**. *International journal of oral and maxillofacial surgery* 2009, **38**(11):1127-1132.
6. Anssari Moin D, Hassan B, Parsa A, Mercelis P, Wismeijer D: **Accuracy of preemptively constructed, Cone Beam CT-, and CAD/CAM technology-based, individual Root Analogue Implant technique: An in vitro pilot investigation**. *Clinical oral implants research* 2014, **25**(5):598-602.

7. Frydman A, Simonian K: **Review of models for titanium as a foreign body**. *Journal of the California Dental Association* 2014, **42**(12):829-833.
8. Wood MM, Warshaw EM: **Hypersensitivity reactions to titanium: diagnosis and management**. *Dermatitis: contact, atopic, occupational, drug* 2015, **26**(1):7-25.
9. Lawson NC, Burgess JO: **Dental ceramics: a current review**. *Compendium of continuing education in dentistry* 2014, **35**(3):161-166; quiz 168.
10. Vohra F, Al-Kheraif AA, Ab Ghani SM, Abu Hassan MI, Alnassar T, Javed F: **Crestal bone loss and periimplant inflammatory parameters around zirconia implants: A systematic review**. *The Journal of prosthetic dentistry* 2015, **114**(3):351-357.
11. Van Dooren E, Calamita M, Calgaro M, Coachman C, Ferencz JL, Pinho C, Silva NR: **Mechanical, biological and clinical aspects of zirconia implants**. *The European journal of esthetic dentistry: official journal of the European Academy of Esthetic Dentistry* 2012, **7**(4):396-417.
12. Klocke E, Gerent O, Schippers C: **Machining of advanced ceramics in the green state**. *Cfi-Ceram Forum Int* 1997, **74**(6):288-290.
13. Zhang Z: **Iterative point matching for registration of free-form curves and surfaces**. *International Journal of Computer Vision* 1994, **13**:119-158.

CHAPTER 5

A PATIENT SPECIFIC BIOMECHANICAL ANALYSIS OF CUSTOM ROOT ANALOGUE IMPLANT DESIGNS ON ALVEOLAR BONE STRESS: A FINITE ELEMENT STUDY

Published as:

Anssari Moin D, Hassan B, Wismeijer D

A Patient Specific Biomechanical Analysis of Custom Root Analogue Implant Designs on Alveolar Bone Stress: A Finite Element Study

International journal of dentistry 2016, 2016:8242535

ABSTRACT

Objectives

Thus the aim of this study is to analyse with the means of FEA the influence of 5 custom RAI designs on stress distribution of peri-implant bone and to evaluate the impact on micro displacement for a specific patient case.

Materials & Methods

A 3D surface model of a RAI for the upper right canine was constructed from the cone beam computed tomography data of one patient. Subsequently, the following (targeted) press-fit design modification FE models were designed: 'Standard', 'Prism', 'Fins', 'Plug' and 'Bulbs', respectively and five congruent bone models were built. Preprocessor software was applied to mesh the models. Two loads were applied; an oblique bucco-apical force (300 N) and a vertical force (150 N). Analysis was performed on the meshed bone-implant models to evaluate stress distributions surrounding bone and deformed contact separation at the peri-implant region was measured.

Results

The Standard design RAI exhibited the highest von Mises stress and highest minimum principal stress values. The lowest von Mises stress levels were numerically observed for the Plug design. The lowest levels of contact separation were measured in the Fins model followed by the Bulbs design under vertical and oblique forces.

Conclusions

Within the limitations of the applied methodology, it has been found that adding targeted press-fit geometry to the RAI standard design, will have a positive effect on stress distribution, lower concentration of bone stress and will provide a better primary stability for this patient specific case.

INTRODUCTION

With technological advances in the field of implant dentistry novel treatment modalities and more efficient options become available. The custom 3D printed root analogue implant (RAI) as defined by Anssari Moin et al. [1, 2] and Figliuzzi et al. [3] is a futuristic treatment option for immediate implantation and immediate loading cases for a soon to be removed tooth. Advantages of the RAI technique when compared to conventional screw shaped multi-piece implants may encompass more cost efficiency, one-piece implant and minimal traumatic surgical intervention [1-6].

An essential factor for realization of all implant-based prosthetic reconstructions is successful osseointegration of the implant. Especially primary stability plays a fundamental role in one stage implant surgery with or without immediate loading [7]. Conventional screw type implants achieve primary stability through mechanical fixation by implant threads in bone [8]. Numerous studies on the factors influencing primary stability (implant shape specifications, surface modifications, bone quality and surgical technique) and the effect on the process of osseointegration have been performed [8-11]. However, primary stability for the RAI technique is based on the (targeted) press-fit phenomenon for achieving successful osseointegration [1-3, 6]. Since the custom RAI is based on Cone Beam Computed Tomography (CBCT), Computer Aided Design (CAD) and 3D printing technology an unlimited array of designs for this custom implant approach are available. Every RAI design option aimed at increasing initial mechanical stability for the root part of the RAI will have a different biomechanical effect on the surrounding bone and influence on the relative micro displacement at bone to implant interface consequently leading to diverse osseointegration results, bone resorption or failures.

Finite Element Analysis (FEA) has become an effective method in investigating bone stress/strain around implants and relative micro displacement between bone to implant interface [12] . However as with all FEA studies the analysis is confined to a limited amount of factors and designs and cannot be generalised, specifically not for individual cases. Thus the aim of this study is to analyse with the means of FEA the influence of 5 custom RAI designs on stress distribution of peri-implant bone and to evaluate the impact on micro displacement for a specific patient case.

MATERIALS AND METHODS

Model design

A patient (male, 64 years of age) presenting a profoundly decayed upper right canine was selected and informed consent was obtained from the patient. Based on the method previously described by Anssari Moin et al. [1, 2] a 3D surface model of a RAI was constructed. In brief the procedure was as follows, the patient was scanned with the 3D Accuitomo 170 CBCT system (AccuiTomo 170, 90kVp, 5mA, 30.8s, 4x4cm Field of View [FoV], voxel 0.08mm3, Morita Inc., Kyoto, Japan) using the recommended scan protocol. Amira software (v4.1, VisageImaging, Carlsbad, CA) was used for image analysis. A region of interest limited to the tooth and its surrounding was initially selected and a threshold segmentation algorithm based on histogram analysis of grey values was used to separate the tooth (root & crown) from surrounding bone and periodontium. Further semi-automated segmentation based on slice-by-slice analysis was implemented to enhance the segmentation by removing any residual artifacts (Fig. 1). The segmented dataset was converted to 3D surface model using the marching cube algorithm and saved in the standardized triangulation language (STL) file format.

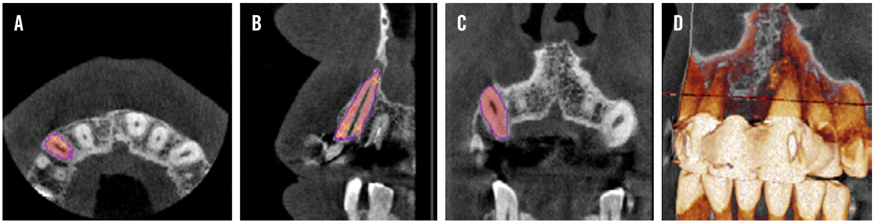


Fig. 1. Segmentation and preparation of the RAI. Coronal (a), axial (b), sagittal (c) and 3D (d) views.

Based on the STL model five different (targeted) press-fit design RAI FE models have been constructed using 3D CAD software (Inventor™, Autodesk GmbH, Munich, Germany). For the five RAI models a standard identical abutment, based on morphological expectation of the original tooth crown and measurements on neighboring teeth, was designed at 2 mm distance coronal from the expected bone level after implantation. Subsequently, the following (targeted) press-fit design modifications were constructed: 1- non-modified Standard, 2- targeted press-fit Prism, 3- targeted press-fit Fins, 4- targeted press-fit Plug, 5- targeted press-fit Bulbs, referred to as 'Standard', 'Prism', 'Fins', 'Plug' and 'Bulbs', respectively. Figure 2 shows the five designs with description of the different geometrical characteristics.

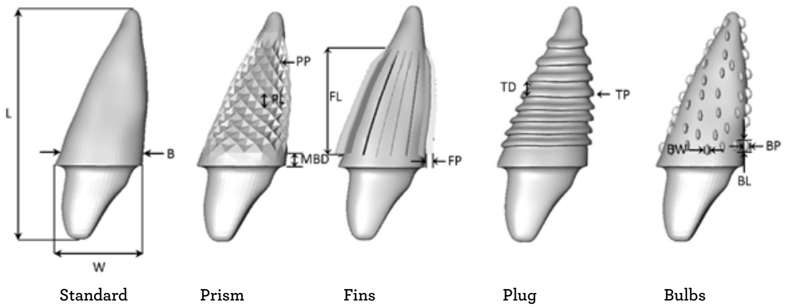


Fig. 2. 3D models of the 5 designs analyzed. Dimensions and notation of geometric properties is as follows: L; total implant length 26.90 mm similar for all designs, W; maximum width of basic implant body 9.55 mm, MBD; shoulder margin to bone (B) distance 2 mm for all models, PI; prism maximum intrusion 0.85 mm, PL; prism maximum length 1.65 mm, FP; fins protrusion 0.80 mm, FL; fins length 12.90 mm, TP; thread protrusion 0.30 mm, TD; thread maximum distance 1.50 mm, BP; bulbs protrusion 0.50 mm, BW; bulbs width 0.55 mm, Bl; bulbs length 1.20 mm.

Five bone models surrounding 3 mm congruent to the respective RAI models were built using Femap software (v 11.0.1, Siemens PLM software, Plano, TX, USA).
Finally, preprocessor software (Femap v 11.0.1, Siemens PLM software, Plano, TX, USA) was applied to mesh the models with quadratic tetrahedral solid elements (Fig. 3). Mesh refinement based on convergence analysis resulted in a mean mesh size of 0.5 mm. Table 1 summarizes the number of elements and nodes for each model.

Model	Elements	Nodes
Standard	235094	336907
Prism	212965	306454
Fins	211820	309433
Plug	389742	567419
Bulbs	371570	550137

Table 1 - Number of elements and nodes used in the 5 FE models.

Material properties, interface, constrains and loading conditions

The following assumptions were made for the RAI FE models: composition of a titanium alloy Ti6Al4V, Young's modulus E = 110 GPa and Poission's ratio ν = 0.35 with the material being homogeneous, isotropic and linearly elastic [13, 14].
The bone models were constructed using a homogenous isotropic linearly elastic mate-

rial of 1 mm inner cortical layer (Young's modulus E = 12.6 GPa, Poission's ratio ν = 0.3 and Shear modulus G = 5.7 GPa) and a 2 mm outer trabecular layer (Young's modulus E = 1.1 GPa, Poission's ratio ν = 0.3 and Shear modulus G = 0.07 GPa) as proposed in the reviewed literature [13, 14].

Bone-to-implant interfaces were assumed to be frictional surfaces to represent a non-osseointegrated contact situation. A Coulomb frictional method (coefficient of friction = 0.3) was adopted to define linear contact behavior [14, 15].
Two loads were applied to simulate an anterior bite force; an oblique bucco-apical force with a magnitude of 300 N set on 135° to the long axis of the implant and a vertical force in apical direction to the long axis of the implant with a magnitude of 150 N, as shown in figure 3 [16, 17].
The nodes in the outer surrounding layer of trabecular bone were constrained in all directions (zero nodal displacement).

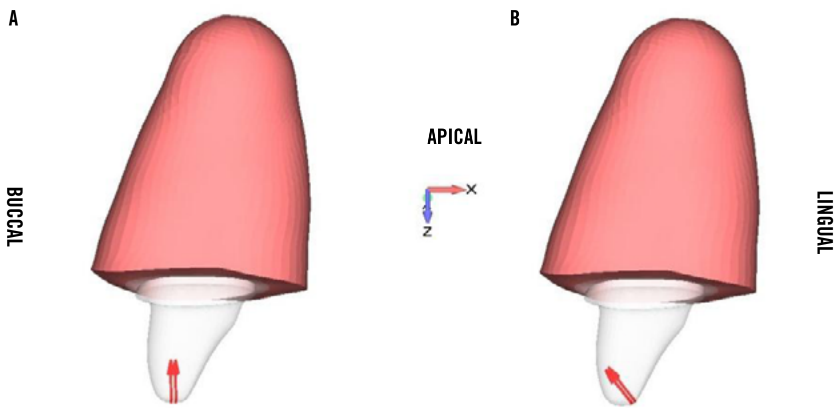


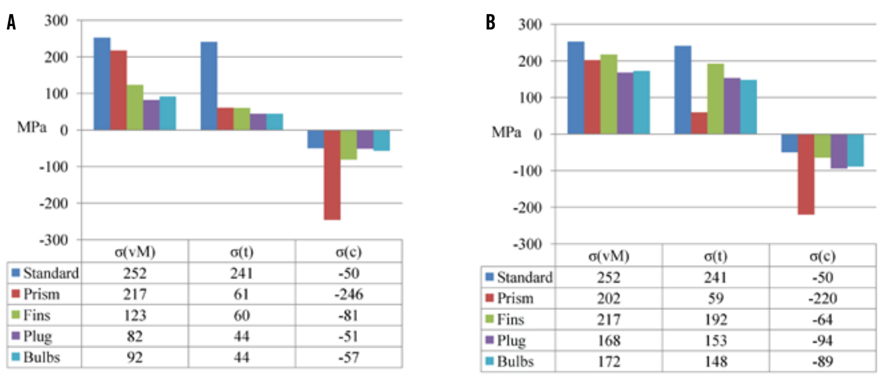
Fig. 3. Overall illustration of a meshed model. The red vectors indicating the direction of the applied vertical (a) and oblique (b) forces.

Analysis

Numerical solving (Nastran v 8.0, Siemens PLM software, Plano, TX) and post-processor analysis (Femap v 11.0.1, Siemens PLM software, Plano, TX, USA) was performed on the meshed bone-implant models to evaluate stress distributions on cortical and trabecular bone and deformed contact separation (micro-motion) at the peri-implant region. Based on previous research the following measurements were recorded; the von Mises equivalent stress (σVM) at the bone peri-implant interface as a quantity of stress level for the load transfer mechanism [12, 18-21], the tensile/maximum (σt) and compressive/ minimum (σc) principal stresses as a criterion to evaluate the bone overloading [19, 20] and finally deformed contact separation (micro-motion in μm) as an indicator for initial implant stability [22, 23].

RESULTS

Figure 4 displays the average measured stress values (in MPa) of the principal and von Mises stresses at the supporting tissues for all groups. Notably, on average the stress levels caused by oblique loading were higher when compared to vertical loading.



A

	σ(vM)	σ(t)	σ(c)
Standard	252	241	-50
Prism	217	61	-246
Fins	123	60	-81
Plug	82	44	-51
Bulbs	92	44	-57

B

	σ(vM)	σ(t)	σ(c)
Standard	252	241	-50
Prism	202	59	-220
Fins	217	192	-64
Plug	168	153	-94
Bulbs	172	148	-89

Fig. 4. Comparison of the maximum von Mises equivalent stress (σ_{VM}), the tensile (σ_t) and compressive (σ_c) principal stresses under vertical (a) and oblique (b) loading components in the 5 designs.

The Standard design RAI exhibited the highest von Mises stress and highest minimum principal stress values (highest compressive stress) under both loading conditions (σVM = 252 and σc = - 50). The lowest von Mises stress levels were numerically observed for the

Plug design under the different loading conditions (Fig. 4a; σVM = 82, Fig. 4b; σVM = 168), indicating a reduction of 67,4% and 33,3%, respectively when compared to the Standard design. Furthermore, the highest measured tensile stress in cancellous bone was 4 MPa for the Standard design (data not shown).

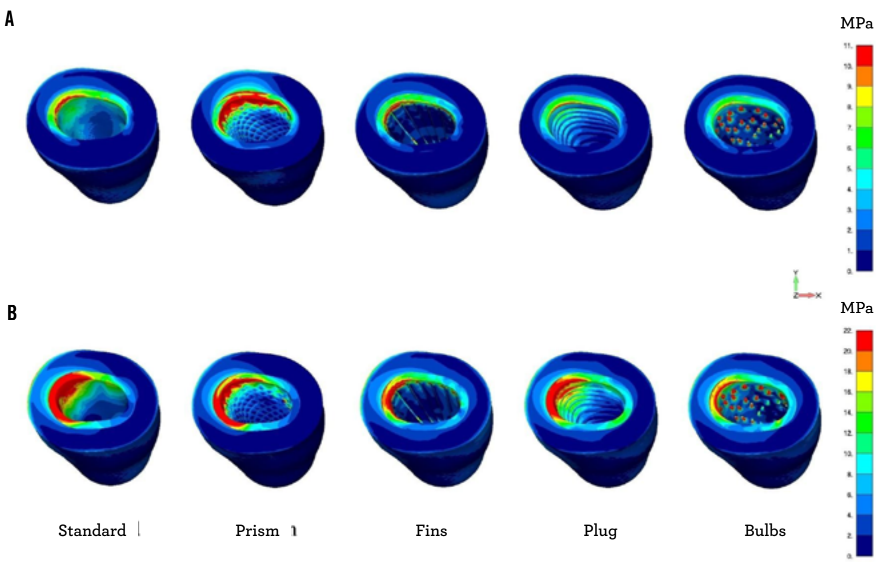


Fig. 5. Distribution patterns of von Mises stress under vertical (a) and oblique (b) loading components.

Comparing behavior of von Mises stress distribution caused by vertical (Fig. 5a) and oblique loading (Fig. 5b), it can be observed that the cortical peri-implant bone exhibited greater stress concentration than trabecular bone. In tension stress, concentrations can be noted at the loaded side for the Standard and Prism under the oblique loading component (Fig. 6).

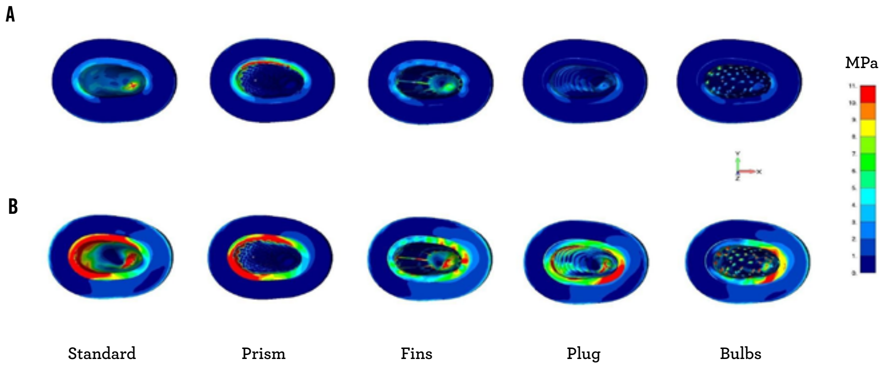


Fig. 6. Distribution patterns of the tensile principal stress under vertical (a) and oblique (b) loading components.

However, under the same conditions the Plug, Fins and Bulb design showed tensile stress intensities on the lingual side and in the buccal area of the protrusive extensions of the design (Fig. 6).

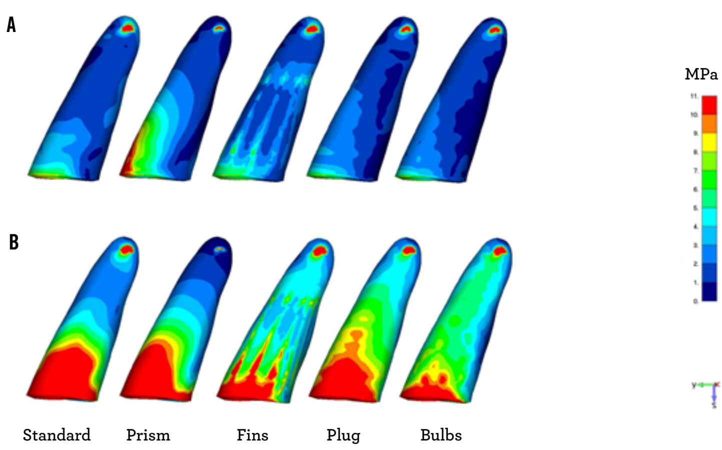


Fig. 7. Distribution patterns of von Mises stress in the cortical outer layer of the surrounding bone under vertical (a) and oblique (b) loading components.

The apical peri-implant area indicated high von Mises stress concentrations in all designs (Fig. 7) and tensile stress peaks under both loading conditions for the Standard, Plug and Fin designs. Comparison of the minimum principal stress illustrated in all models the highest compressive stress concentrations on the lingual side (Fig. 8).

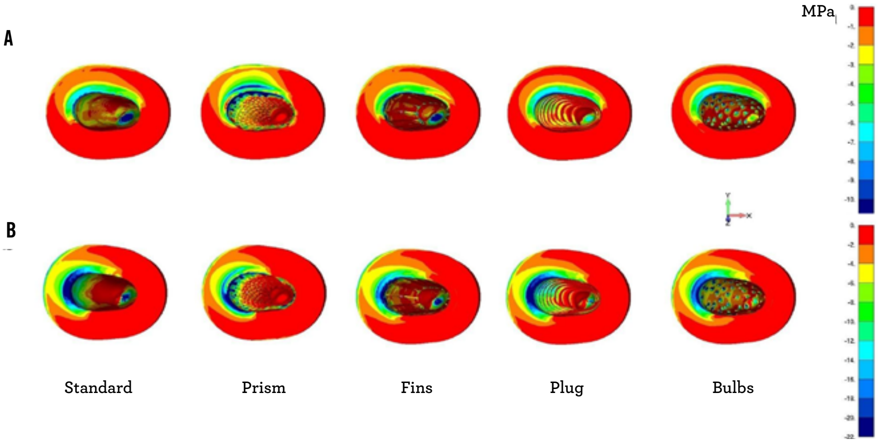


Fig. 8. Distribution patterns of the compressive principal stress under vertical (a) and oblique (b) loading components.

Table 2 shows the micro displacement of the various RAI designs from the peri-implant bone with respect to the loading conditions. The highest magnitude of micro-motion level was measured in the Prism design, 32.10 μm and 32.51 μm under vertical and oblique loading, respectively. Remarkably, the lowest levels of contact separation were measured in the Fins model followed by the Bulbs design under vertical and oblique forces; 5.45 μm, 6.25 μm and 6.35 μm, 6.42 μm, respectively. Micro displacement patterns were located at neck area in direction of the forces and in contra lateral direction in the apical area in all designs (images not shown).

Model	Micro-motion (μm) under vertical loading	Micro-motion (μm) under oblique loading
Standard	10.90	11.72
Prism	32.10	32.51
Fins	5.45	6.25
Plug	9.88	10.69
Bulbs	6.35	6.42

Table 2. Micro-motion measures (μm) on the various models.

DISCUSSION

In this study five different designs of a RAI were analyzed for stress-based biomechanical behavior for a specific patient by means of finite element simulations. In the primary phase of endeosseous healing multiple biomechanical mechanical factors play a role. The von Mises stress was used as an indicator for the load transfer mechanism, principal stresses as indicator to bone overloading and micro-motion as indicator for initial stability. Numerical results from the current study suggest that adding targeted press-fit design characteristics to the standard RAI design will decrease the amount of maximum von Mises stress in the surrounding peri-implant bone, subsequently leading to more favorable load behavior for this patient. Previous studies have assumed maximum bone strength as biological limit to bone failure and activation of bone resorption [15, 19, 21]. Correspondingly, it has been proposed that overloading of cortical bone occurs when the maximum compressive principal stress exceeds -190 MPa and maximum tensile principal stress exceeds 130 MPa [15, 19, 21]. Likewise, trabecular bone overloading will occur when the compressive and tensile principal stresses exceed -5 MPa and 5 MPa, respectively [15, 19, 21]. According to the result of this study it has been found that solitary the prism design exceeded the maximum compressive stress criterion for cortical bone. The standard, fins, plug and bulbs designs exceeded the tensile stress threshold in cortical bone. The threshold for trabecular bone overloading in tension was not reached. However, when observing the compressive stresses under oblique loading in trabecular bone, it can be noted that in the regions of the implant neck all implant designs exceeded the biological limit, inducing a risk to bone loss (Fig. 8). The fins and bulbs designs showed the lowest levels of micro-motion, indicating the most favorable primary stability. Nonetheless, it must be noted that the influence of micro-motion on osseointegration is of scientific debate as some studies have suggested a more positive effect on the tissue differentiation and bone formation around implants under controlled micro-motion up to 50 μm [24].

Additionally, in our study it has been found that the higher oblique loading component causes more stress concentrations on cortical and trabecular bone when compared to vertical loading. Therefore oblique loading in the primary stage after implantation will have a more negative effect on bone healing and should be minimized.
In this current study multiple drawbacks and limitations should be named. The peri-implant surrounding bone was modeled and assumed as a homogeneous, isotropic linearly elastic material. However, it is known that the biomechanical behavior of this living tissue is heterogeneous, anisotropic and non-linear [14, 19, 20]. Moreover a 100% osseous contact between implant and bone was assumed. Contact relationship between implant and bone were defined as linear contact behavior by using a Coulomb frictional model. Although contact behavior should be defined in a non-linear method, several studies are in agreement of adopting a linear frictional model since non-linear contact analysis are highly complex [14, 25]. In clinical situations the actual bone to implant contact directly after insertion of the RAI will be dependent on many factors, i.e.: accuracy of the RAI technique on multiple levels, (peri-apical) bone defects and surgical handling. The quantity of in-situ osseous contact after implantation of the RAI will have profound effect on primary stability and stress behavior. Furthermore, the herein applied loads were static one directional loads of an amplitude of 150 N (vertical) and 300 N (oblique) whereas in clinical situations considerably variable loads can be observed depending on the location of the RAI in the oral cavity and patient characteristics. Despite that simulation methods and FE modeling were beyond the scope of this investigation, the current limitations can be considered as acceptable in a numerical sense and are in agreement with multiple studies [13, 14, 16, 17, 19, 25].
Especially with the rise of custom 3D printed implants questions concerning biomechanical behavior in each specific patient surfaces. Ideally for future implementation of custom 3D designed and printed implants an easy accessible individual patients specific FEA should be performed to get a better understanding of the biomechanical behavior of different implant designs for a specific case.

CONCLUSION

Based on the results of this study and within the limitations of the applied methodology, it has been found that adding targeted press-fit geometry to the RAI standard design, preferably fins or bulbs, will have a positive effect on stress distribution, lower concentration of bone stress and will provide a better primary stability for this patient case.

REFERENCES

1. Anssari Moin D, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2011.
2. Anssari Moin D, Hassan B, Parsa A, Mercelis P, Wismeijer D: **Accuracy of preemptively constructed, Cone Beam CT-, and CAD/CAM technology-based, individual Root Analogue Implant technique: An in vitro pilot investigation**. *Clinical oral implants research* 2012.
3. Figliuzzi M, Mangano F, Mangano C: **A novel root analogue dental implant using CT scan and CAD/CAM: selective laser melting technology**. *International journal of oral and maxillofacial surgery* 2012, **41**(7):858-862.
4. Pirker W, Kocher A: **Immediate, non-submerged, root-analogue zirconia implant in single tooth replacement**. *International journal of oral and maxillofacial surgery* 2008, **37**(3):293-295.
5. Pirker W, Wiedemann D, Lidauer A, Kocher AA: **Immediate, single stage, truly anatomic zirconia implant in lower molar replacement: a case report with 2.5 years follow-up**. *International journal of oral and maxillofacial surgery* 2011, **40**(2):212-216.
6. Mangano FG, De Franco M, Caprioglio A, Macchi A, Piattelli A, Mangano C: **Immediate, non-submerged, root-analogue direct laser metal sintering (DLMS) implants: a 1-year prospective study on 15 patients**. *Lasers in medical science* 2014, **29**(4):1321-1328.
7. Blanco J, Alvarez E, Munoz F, Linares A, Cantalapiedra A: **Influence on early osseointegration of dental implants installed with two different drilling protocols: a histomorphometric study in rabbit**. *Clinical oral implants research* 2011, **22**(1):92-99.
8. Steigenga J, Al-Shammari K, Misch C, Nociti FH, Jr., Wang HL: **Effects of implant thread geometry on percentage of osseointegration and resistance to reverse torque in the tibia of rabbits**. *Journal of periodontology* 2004, **75**(9):1233-1241.
9. Kan JY, Rungcharassaeng K, Kim J, Lozada JL, Goodacre CJ: **Factors affecting the survival of implants placed in grafted maxillary sinuses: a clinical report**. *The Journal of prosthetic dentistry* 2002, **87**(5):485-489.
10. Akkocaoglu M, Uysal S, Tekdemir I, Akca K, Cehreli MC: **Implant design and intraosseous stability of immediately placed implants: a human cadaver study**. *Clinical oral implants research* 2005, **16**(2):202-209.
11. Abuhussein H, Pagni G, Rebaudi A, Wang HL: **The effect of thread pattern upon implant osseointegration**. *Clinical oral implants research* 2010, **21**(2):129-136.
12. Van Staden RC, Guan H, Loo YC: **Application of the finite element method in dental implant research**. *Computer methods in biomechanics and biomedical engineering* 2006, **9**(4):257-270.

13. O'Mahony AM, Williams JL, Spencer P: **Anisotropic elasticity of cortical and cancellous bone in the posterior mandible increases peri-implant stress and strain under oblique loading**. *Clinical oral implants research* 2001, **12**(6):648-657.
14. Huang HL, Hsu JT, Fuh LJ, Tu MG, Ko CC, Shen YW: **Bone stress and interfacial sliding analysis of implant designs on an immediately loaded maxillary implant: a non-linear finite element study**. *Journal of dentistry* 2008, **36**(6):409-417.
15. Lin D, Li Q, Li W, Swain M: **Dental implant induced bone remodeling and associated algorithms**. *Journal of the mechanical behavior of biomedical materials* 2009, **2**(5):410-432.
16. Stanford CM, Brand RA: **Toward an understanding of implant occlusion and strain adaptive bone modeling and remodeling**. *The Journal of prosthetic dentistry* 1999, **81**(5):553-561.
17. Akagawa Y, Sato Y, Teixeira ER, Shindoi N, Wadamoto M: **A mimic osseointegrated implant model for three-dimensional finite element analysis**. *Journal of oral rehabilitation* 2003, **30**(1):41-45.
18. Geng JP, Tan KB, Liu GR: **Application of finite element analysis in implant dentistry: a review of the literature**. *The Journal of prosthetic dentistry* 2001, **85**(6):585-598.
19. Natali AN, Hart RT, Pavan PG, Knets I (eds.): **Mechanics of bone tissue**. London: Taylor & Francis; 2003.
20. An YH, Draughn RA: **Mechanical Testing of Bone and the Bone-Implant Interface**, vol. 1: Taylor & Francis; 2010.
21. Natali AN, Pavan PG: **A comparative analysis based on different strength criteria for evaluation of risk factor for dental implants**. *Computer methods in biomechanics and biomedical engineering* 2002, **5**(2):127-133.
22. Brunski JB: **Avoid pitfalls of overloading and micromotion of intraosseous implants**. *Dental implantology update* 1993, **4**(10):77-81.
23. Brunski JB, Puleo DA, Nanci A: **Biomaterials and biomechanics of oral and maxillofacial implants: current status and future developments**. *The International journal of oral & maxillofacial implants* 2000, **15**(1):15-46.
24. Vandamme K, Naert I, Geris L, Sloten JV, Puers R, Duyck J: **Histodynamics of bone tissue formation around immediately loaded cylindrical implants in the rabbit**. *Clinical oral implants research* 2007, **18**(4):471-480.
25. Lin CL, Lin YH, Chang SH: **Multi-factorial analysis of variables influencing the bone loss of an implant placed in the maxilla: prediction using FEA and SED bone remodeling algorithm**. *Journal of biomechanics* 2010, **43**(4):644-651.

CHAPTER 6

IMMEDIATE NON-SUBMERGED CUSTOM ROOT ANALOGUE IMPLANTS: PROOF OF CONCEPT IN THE FIRST FIVE CASES

Accepted for publication as

Anssari Moin D, Hassan B, Wismeijer D

Immediate non-submerged custom root analogue implants: proof of concept in the first 5 cases

International Journal of Oral and Maxillofacial Implants 2017

ABSTRACT

Objectives
To evaluate the feasibility of a commercially available immediate root analogue implant (RAI) system Replicate® (Natural Dental Implants GmbH, Berlin, Germany).

Materials and Methods
Five consecutive patients in need of an implant in the premolar region were recruited for this pilot study. Following clinical examination, a Cone Beam Computed Tomography scan was made and the dental impressions digitized. On the basis of the superimposition these datasets a 3D envelope was created for the selected tooth. Subsequently, the tooth root at the prospective implant site was segmented to create a 3D surface and the obtained mesh data were used as basis for designing a single piece root analogue implant within the 3D envelope. The designed RAI was fabricated using a 5-axis computer aided manufacturing machine. The RAIs were inserted following flapless minimally invasive root extraction. Following 3 months of uninterrupted healing, definitive restorations were fabricated. Peri-implant clinical and radiographical measurements were obtained up to 12 months follow-up.

Results
All patients functioned well following 12 months of functional loading. Within one patient one of the two RAIs failed early. Peri-implant clinical and radiographical measurements demonstrated a stable situation after 12 months of functional loading.

Conclusions
A novel digital approach for immediately restoring single teeth using root analogue implants was introduced. In the future, long-term evaluation of RAI technique is necessary to evaluate the success and survival of implants that were inserted through this technique.

INTRODUCTION

Combining the technologies of Cone Beam Computed Tomography (CBCT), Computer Aided Design (CAD) and Computer Aided Manufacturing (CAM) allow for new developments in the field of implant dentistry. One application of these advancements is to produce a customized dental root analogue implant (RAI) as an alternative to the traditional threaded, straight or tapered, standard implant systems [1-3]. The RAI is pre-operatively custom designed based on the CBCT and CAD data to fit into the socket of a soon to be extracted tooth. This implant would have similar dimensions to the original root and would be congruent with the root socket. Anticipated benefits include uncomplicated immediate implant placement, decreased number of surgeries and increased patient comfort [1-5]. Moreover, mimicking root features might result in higher esthetic outcome. A few studies describing various techniques of creating and placing custom root analogue implants have been noted in the literature [1-5]. However clinical data regarding the RAI technique remain to date limited. The aim of the present pilot clinical investigation was to evaluate the feasibility of a commercially available RAI system Replicate® (Natural Dental Implants GmbH, Berlin, Germany).

MATERIALS AND METHODS

Study design and participants

The study was designed as a non-randomized, non-controlled prospective pilot cohort. Patients were consecutively recruited from referrals to the specialist outpatient clinic of Implantology department at the Academic Centre for Dentistry Amsterdam (ACTA), VU University of Amsterdam, Amsterdam, The Netherlands. Information concerning the purpose of this study was presented to all patients and an informed consent was obtained from all participants. One patient functioned as a test case, to determine and resolve any procedural difficulties. We subsequently analysed prospectively the next five consecutive RAI implant procedures that were performed with this technique.

The indication for implantation in cases no. 2, and 4 was deep caries lesions. In cases no. 1, 3, and 5 the indications for implantation were vertical root fractures. All indications were confined to replacement of premolar teeth with a minimum of 1.5 mm of bone circumferentially as measured on the CBCT scan. This study was performed in accordance with the guidelines of our institution and followed the Declaration of Helsinki on medical protocol and ethics. The study protocol was reviewed as a pilot study and accordingly approved by the ACTA institutional ethical review board.

Data acquisition and CAD/CAM process

Patients were scanned with the 3D Accuitomo 170 CBCT system (AccuiTomo 170, 90kVp, 5mA, 30.8Sec, 8x8cm Field of View (FoV), Morita inc., Japan). The scan position was with the occlusal plane parallel to the floor following the manufacturer's recommendations. The isotropic voxel size and slice interval were 0.08mm. The CBCT scan volumes were exported in DICOM 3 format.

Two stage putty and wash technique impressions (Panasil, Kettenbach GmbH, Eschenburg, Germany) and bite-registrations (Futar D, Kettenbach GmbH, Eschenburg, Germany) were taken from the patients. The impressions were poured in type IV stone to create master models. High-resolution optical scanning technology was used to scan and digitize the stone casts and bite-registrations and stored as Standardized Triangulation Language (STL) files. The DICOM 3 files and intra-oral surface STL data were imported specialized proprietary analysis software (Replicate, Natural Dental Implants). On the basis of the superimposition these datasets a 3D envelope was created for the selected tooth representing the extension of the root, alveolar bone, marginal bone level, gingival margins, adjacent and antagonist dental structures and anatomical structures (fig. 1).

Subsequently, within this 3D envelope CAD designs of the RAI were made consisting of a root/implant portion and an abutment portion (fig. 1 and 2). CAD designs were additionally made for a RAI try-in and temporary cantilevered bridge (fig. 3).

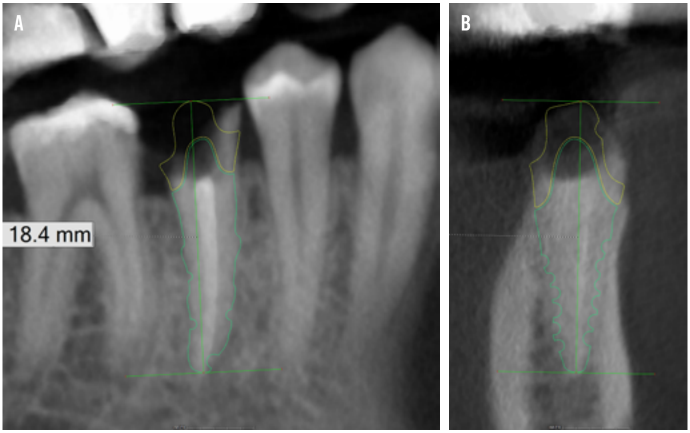


Figure 1. Sagittal (a) and frontal (b) view incorporating possible RAI design for patient no. 4.

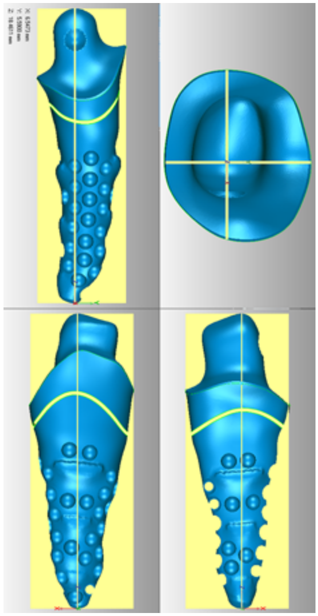


Figure 2. Final RAI CAD design for patient no. 4 consisting of root/implant portion and abutment portion.

CAD data were transferred to 5-axis rapid manufacturing CAM machine to mill the titanium root from a solid medical grade 4 titanium work piece, and to mill the ceramic parts (RAI try-in, abutment portion of the RAI and temporary cantilevered bridge) from pre-sintered white body blanks of tooth coloured Y-TZP zirconia material. Subsequently, the zirconia parts were fired into sintered solid dense objects. The ceramic abutment portion and the titanium root portion were then fused together with a biocompatible glass solder to create a one-piece implant. Finally, the titanium root portion was sandblasted with medical grade zirconia grit and acid etched. The zirconia abutment portion remained a machined smooth surface. The Replicate™ RAIs were then delivered in a sterile packaging.

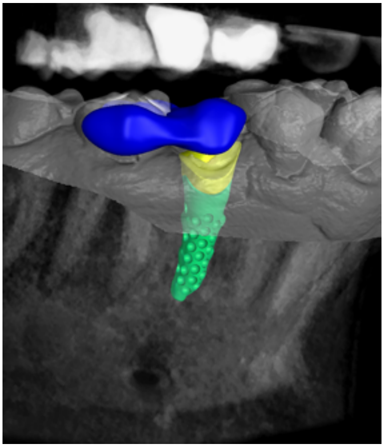


Figure 3. RAI design and temporary cantilevered bridge design within the 3D envelope of patient no. 4

Surgical and prosthetic procedure

All patients were treated according to the same treatment protocol and implants were placed using the same surgical technique by one operator (DAM). Under local anaesthetics (Septanest SP, Septodont Inc., Lancaster, USA) the respective teeth were flapless carefully extracted to reduce risk of fracturing the bone and roots and to avoid any alterations to the shape of the socket. Alveolar surface decontamination and debridement were performed mechanically using curettes and excavators and chemically by meticulous irrigation with sterile saline (2 x 12 ml). Subsequently, the zirconia RAI try-ins were positioned into their respective sockets and visually checked for misfits. In all cases the zirconia try-in seemed well incorporated to the alveolar socket and there was no need for mucosal or osseous corrections. The RAIs were then implanted into their corresponding sockets and with finger pressure and the gentle use of a hammer and a mallet good primary stability of the RAI was achieved and checked by palpation and percussion. In one patient (patient no. 5) it was necessary to suture the ruptured interproximal papilla with non-resorbable monofilament (GORE-TEX, W. L. Gore & Associates Inc, Newark, USA). Finally, one patient (no. 1) received a temporary cantilevered cemented bridge as a protective measure against occlusal loading (fig. 8). The winged extensions of the protective bridge were cemented to neighboring tooth with a resin-based cement (RelyX, 3M ESPE, Seefeld, Germany). Occlusion was checked and necessary adjustments were performed. On the basis of the operator opinion (DAM) the consecutive patients did not receive the temporary cantilevered bridge.

All patients received systemic antibiotics (amoxicillin 500 mg T.I.D.) starting 1 hour prior to surgery and following 7 days after surgery. If necessary, analgesic drugs (acetaminophen 500 mg) were administered during the first post-operative days. Throughout 2 weeks post-operatively patients rinsed with chlorhexidine 0.12% twice a day. One week post-operatively all patients were seen for maintenance care. Oral hygiene methods were reinforced or reinstructed and sutures were removed in one patient (no. 5). After 3 months of uninterrupted healing the protective bridge was removed and impressions (Impregum, 3M ESPE, Seefeld, Germany) were taken for the definitive restoration. The restorations were ceramic built on a zirconia core and were semi-permanently cemented with Durelon (3M ESPE, Seefeld, Germany).

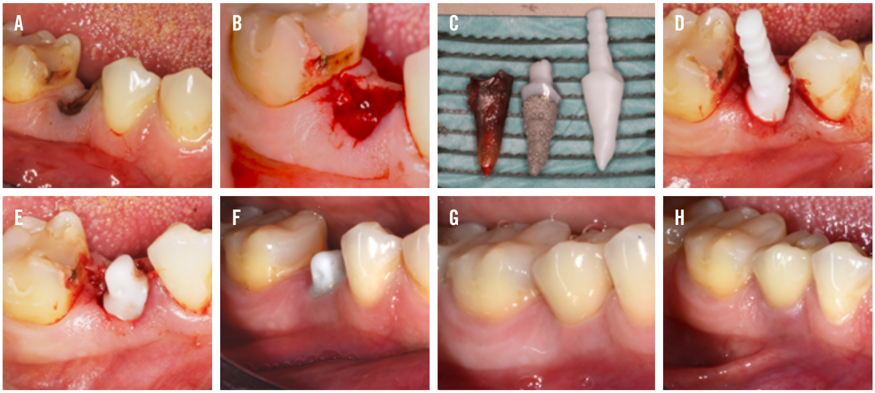


Figure 4. Clinical workflow of patient no. 4. Pre-operative condition (a), alveolus after tooth removal (b), clinical comparison of root and RAI/try-in (c), checking the fitting of the try-in (d), RAI directly after insertion (e), 3-months post-operative view (f), directly after crown placement (g) and 12-months post-restoration (h).

Clinical and radiographic evaluation

Clinical evaluation of the placed implants was performed following definitive restoration placement and 12 months after functional loading. The following parameters were included: probing pocket depths measurement at six sites per implant if the depth was more than 5 mm and bleeding on probing was checked generally, but was not noted when general appearance was healthy.

Radiographical evaluations were performed within the following time points: Directly after implant insertion, after definitive restoration placement and 12 months after functional loading (fig. 5). Digital intra-oral radiographs (Carestream 7200, Carestream Dental LLC, Rochester, USA) of the respected implant sites were obtained using the paralleling long cone technique with an aiming device (film-focus distance 30 cm; Xact X-ray, Fairax, USA). The radiographs were anonymized and organized in random order for analysis. Radiographical bone levels were measured as an average of the mesial and distal aspect from a hypothetical bone position (margin of the glass-fused abutment-titanium joint) to the first bone-to-implant contact. With the known dimensions of the RAI, the radiographical distance was recalculated using ImageJ software (National Institutes of Health, Bethesda, USA) to the physiological extent of the bone level. After 12 months of functional loading another CBCT scan was made to evaluate the peri-implant bone condition. Patients were scanned with the exact same scan settings as with the first CBCT scan. On the basis of this CBCT scan the absence and presence of buccal bone was analyzed.

Descriptive statics were applied to calculate the mean and standard deviation (SD) of the evaluation parameters. No statistical interference testing was performed between the evaluation parameters due to the lack of statistical power.

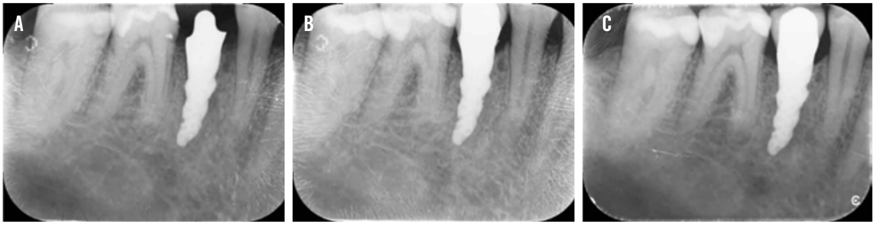


Figure 5. Radiographical evaluation of patient no. 4. Directly after RAI insertion (a), after definitive restauration (b) and 12 months after functional loading (c).

RESULTS

Initially 6 patients were enrolled in this study protocol. However, one patient was lost to follow-up after implant placement due to unknown reasons. The data of this patient are not represented. There were no intra-operative complications noted during the surgeries. In patient no. 5 the RAI for the right second premolar showed mobility and symptoms of peri-implant infection after 4 weeks post-operatively. It was decided to remove the RAI at position of the right second premolar and simultaneously a short implant at the position of the right first molar was inserted (Alpha-Bio 5x6 mm, Alpha Bio, Petach Tikva, Israel). For this patient a 3-unit fixed partial denture was fabricated to fit the RAI (position of the right first premolar) and conventional implant (fig. 6).

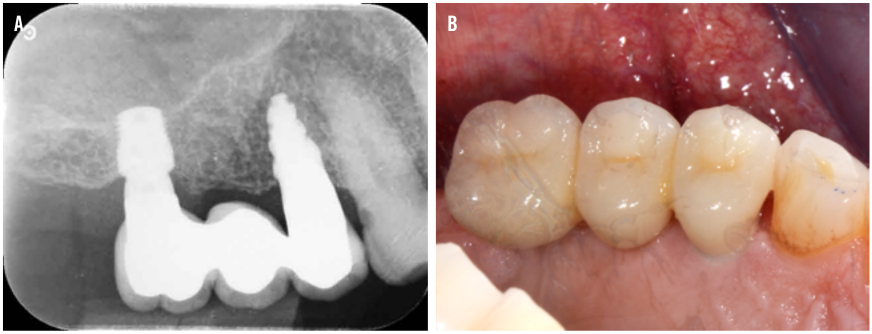


Figure 6. 12-months post-operative x-ray (a) and clinical palatal view (b) of patient no. 5.

At the 12-month post-restoration evaluation, all remaining implants were successful with satisfactory esthetic results. The average in bone levels around the RAIs immediately after implant insertion (0.59 mm (SD 0.52)), directly after restoration (-0.36 mm (SD 1.20)) and 12-months post-function (-0.31 mm (SD 0.90)) appear to be stable with no evident changes in bone level. Analysis of the 12 months post-function CBCT scan showed 2 patients (no. 1 and no. 3) with an absence of buccal bone around the RAIs. In patients no. 2, 4, and 5 the CBCT scans showed presence of circumferential bone around the RAIs after 12 months in function (fig. 7).

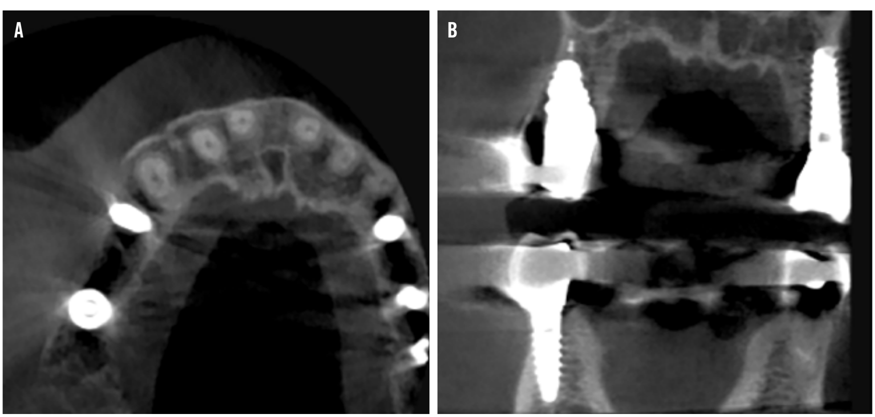


Figure 7. 12-months post-function CBCT scan of patient no. 5 showing the presence of circumferential bone around RAI at position of the upper first premolar in transversal view (a) and frontal view (b).

Probing pocket depth measurements showed no probing depths deeper than 5 mm and a generally healthy mucosal appearance.
In table 1 all case characteristics and measurement of the evaluation parameters are noted.

Patient no.	Gender	Age	Target position	Indication for removal/ implantation	MBL after insertion RAI	MBL after final restoration	MBL after 12 months function	Presence of buccal bone after 12 months function
1	F	66	upper left first premolar	Fracture	0.26	1.22	1.17	No
2	M	57	upper right first premolar	Caries	1.47	0.46	-0.27	Yes
3	F	69	upper right first premolar	Fracture	0.58	-1.84	-1.20	No
4	M	44	lower right second premolar	Caries	0.15	-0.85	-0.82	Yes
5	M	56	upper right first premolar (and upper right second premolar)	Fracture	0.47	-0.79	-0.45	Yes
Mean (SD)					0.59 (0.52)	-0.36 (1.20)	-0.31 (0.90)	

Table 1. Summarized clinical evaluation parameters.

DISCUSSION

This study shows that preoperatively creating a RAI with the Replicate™ system allows for immediate individual implant placement. With the combined use of CBCT 3D data and high-end CAD/CAM technology it was possible to manufacture a RAI with sufficient precision. As has been previously noted in the literature, there are multitude of factors influencing the accuracy of 3D surface model generated from the CBCT data. Clinical factors including bone density and stable patient position during the CBCT scan and technical factors including CBCT device settings (kVp, mA, scan FOV and voxel size) and segmentation accuracy. CAD/CAM process may result in over or under estimation of the RAI and need to be taken into consideration when planning this method of implant surgery. Depending on the amount of under sizing, the RAI could exhibit a loose fitting resulting in a lack of primary stability and subsequent implant failure. When inserting an over-sized RAI into its respective extraction socket this may lead to bone fracture and over pressurized bony walls inducing bone resorption [6]. Therefore, it is crucial to first assess the fit of the RAI in the extraction socket using a mock RAI such as the Replicate™ system included RAI try-in (figure 4c and 4d). In those five study patients the RAI try-ins were well incorporated within their respective sockets and appeared to show a high degree of congruence.

Primary stability is of critical importance for successful osseointegration of the RAI. Especially since the RAIs are one-piece implants with no option for submerged healing. To accomplish a certain amount of primary stability the Replicate™ system designs standard sized protruding bulbs on the mesial and distal aspects of the RAIs. With available technology it is very well feasible to individually design targeted press-fit RAIs with individually designed micro-porosities. However, current knowledge on the effect of bone growth and biomechanics with patient specific designs on RAI size, shape, and press-fit distribution is limited. Also knowledge on the long-term effects on electrochemical corrosion, mechanical stability and of custom shaped implants is nonexistent. It must be emphasized that for custom-medical devices, such as dental implants, the EU-regulations are limited and that safeguards are under the manufacturer's diligence.

As seen in this study 5 of the 6 RAIs were successful after 12 months in function. In one surgical session through an easy minimally invasive approach the RAIs were inserted. None of the cases required any additional adjustments to the alveolar bone or drilling. In patient no. 5 the RAI at position of the right second premolar was lost due to a possible multitude of factors. One plausible explanation is that the root of the right second premolar owing to its history of apical resection surgery resulted in a relatively short RAI with insufficient primary stability (fig. 8). Since the RAI approach relies on a press-fit mechanism to obtain primary stability it is currently uncontrollable to measure the amount of obtained primary stability when inserting the RAI. Therefore, the threshold for sufficient primary stability relies mostly on the surgeon's intuition.

The Replicate™ RAIs are accompanied with a preoperatively fabricated cantilevered bridge (to be attached to a neighboring tooth) as a protective measure against premature loading during the early stages of osseointegration (fig. 9). However, from a clinical point of view we believe this temporary cantilevered bridge will not contribute to a more favorable survival or success of the RAI because of its cantilevered design and the necessity to apply adhesive chemicals (resin bonding, primer and composite cement) near the wound area to attach the bridge. The application of the temporary cantilevered bridge was hence discarded for patients no. 2, 3, 4 and 5. Furthermore, it should be underlined that this study does not have the statistical power to rule out the biological effects of variability in geometry of the RAI with or without the use of the temporary cantilevered bridge.

Figure 8. The RAI try-ins versus their respective original roots of patient no 5. On the left the upper first premolar and on the right the upper second premolar.

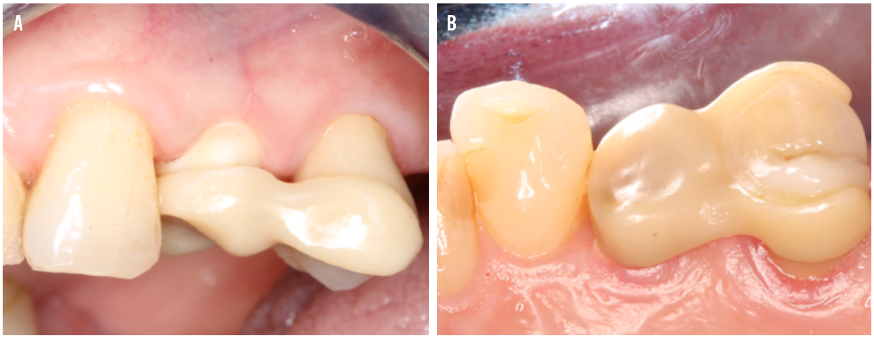


Figure 9. Protective temporary cantilevered bridge for patient no. 1 after 3 months post-operatively. Buccal view (a) and palatal view (b).

A significant finding in this study was the absence of buccal bone on the 12 months post-operative CBCT follow up, suggesting advanced bone loss not corroborated by clinical measurements of peri-implant probing. These contradictory findings could be explained that CBCT image suffer from scatter, beam hardening and beam 'extinction' artefacts in the presence of metal objects such as dental implants caused by the complete absorption of the x-ray beam that no information can reach the detector to reconstruct the images [7, 8]. In a histologically controlled study regarding the accuracy of CBCT in assessing peri-implant buccal bone, the radiographical and histological findings had poor correlation and CBCT was deemed inaccurate for depicting peri-implant bone [9].

To summarize, we believe the future of implant dentistry will include customization of implants and digitalized approaches. Nevertheless, possible disadvantages should also be considered. For the fabrication of a RAI, a pre-operative CBCT-scan is made of the selected tooth. The use of ionizing radiation should be justifiable for each specific patient and should be limited. Therefore, we made a selective CBCT-scans focused on the respective tooth with the smallest field of view possible. Radiation load was kept as minimal as possible. The selective CBCT-scan not only enables the fabrication of the RAI, but also allows the surgeon to carefully plan the extraction of the tooth with consideration of the available surrounding bone and anatomical parameters. It facilitates a shorter and easier surgical procedure, which in turn could minimize the chance of complications. Moreover, in immediate implant cases a pre-operative CBCT scan is standard protocol. We therefore believe this limited amount of additional ionizing radiation is appropriate.

This study aimed to evaluate the RAI technique with the Replicate™ system. Therefore, we reported the technical and clinical characteristics of the procedure. In the future, long-term evaluation of RAI technique is necessary to evaluate the success and survival of implants that were inserted through this technique.

REFERENCES

1. Anssari Moin D, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2013, **24 Suppl A100**:25-27.
2. Anssari Moin D, Hassan B, Parsa A, Mercelis P, Wismeijer D: **Accuracy of preemptively constructed, Cone Beam CT-, and CAD/CAM technology-based, individual Root Analogue Implant technique: An in vitro pilot investigation**. *Clinical oral implants research* 2014, **25**(5):598-602.
3. Anssari Moin D, Hassan B, Wismeijer D: **A novel approach for custom three-dimensional printing of a zirconia root analogue implant by digital light processing**. *Clinical oral implants research* 2016, **Epub ahead of print**.
4. Figliuzzi M, Mangano F, Mangano C: **A novel root analogue dental implant using CT scan and CAD/CAM: selective laser melting technology**. *International journal of oral and maxillofacial surgery* 2012, **41**(7):858-862.
5. Mangano FG, De Franco M, Caprioglio A, Macchi A, Piattelli A, Mangano C: **Immediate, non-submerged, root-analogue direct laser metal sintering (DLMS) implants: a 1-year prospective study on 15 patients**. *Lasers in medical science* 2014, **29**(4):1321-1328.
6. Kohal RJ, Hurzeler MB, Mota LF, Klaus G, Caffesse RG, Strub JR: **Custom-made root analogue titanium implants placed into extraction sockets. An experimental study in monkeys**. *Clinical oral implants research* 1997, **8**(5):386-392.
7. Schulze R, Heil U, Gross D, Bruellmann DD, Dranischnikow E, Schwanecke U, Schoemer E: **Artefacts in CBCT: a review**. *Dento maxillo facial radiology* 2011, **40**(5):265-273.
8. Kovacs M, Fejerdy P, Dobo NC: **[Metal artefact on head and neck cone-beam CT images]**. *Fogorvosi szemle* 2008, **101**(5):171-178.
9. Fienitz T, Schwarz F, Ritter L, Dreiseidler T, Becker J, Rothamel D: **Accuracy of cone beam computed tomography in assessing peri-implant bone defect regeneration: a histologically controlled study in dogs**. *Clinical oral implants research* 2012, **23**(7):882-887.

CHAPTER 7

COMPUTER-ASSISTED TEMPLATE-GUIDED CUSTOM DESIGNED 3D PRINTED IMPLANT PLACEMENT WITH CUSTOM DESIGNED 3D PRINTED SURGICAL TOOLING. AN IN-VITRO PROOF OF A NOVEL CONCEPTY

Published as:

Anssari Moin D, Derksen W, Waars H, Hassan B, Wismeijer D

Computer-assisted template-guided custom-designed 3D-printed implant placement with custom-designed 3D-printed surgical tooling: an in-vitro proof of a novel concept

Clinical oral implants research 2017, 28(5):582-585

ABSTRACT

Objectives
The aim of this study was to introduce a new concept for computer-assisted template-guided placement of a custom 3D designed/3D printed implant with congruent custom 3D designed/3D printed surgical tooling and to test the feasibility and accuracy of this method *in-vitro*.

Materials and Methods
One partially edentulous human mandibular cadaver was scanned with a cone-beam computed tomography (CBCT) system and intra-oral scan system. The 3D data of this cadaver was imported in specialized software and used to analyze the region of a missing tooth. Based on the functional and anatomical parameters an individual implant with congruent surgical tooling and surgical guided template was designed and 3D printed. The guided osteotomy was performed and the custom implant inserted. To evaluate the planned implant position in comparison to the placed implant position the mandible with implant was scanned again with the CBCT system and software matching was applied to measure the accuracy of the procedure.

Results
The angular deflection with the planned implant position was 0.40°. When comparing the 3D positions of the shoulder there is a deviation of 0.72 mm resulting in an apical deviation of 0.72 mm.

Conclusion
With the use of currently available technology it is very well feasible to create in a virtual simulation a custom implant with congruent custom surgical tooling and to transfer this to a clinical setting. However, further research on multiple levels is needed to explore this novel approach.

INTRODUCTION

Today, many different approaches are available in the field of computer-assisted template-guided implant dentistry which can be applied in clinical practice (Tahmaseb et al. 2014; Vercruyssen et al. 2015). With the combination of cone-beam computed tomography (CBCT), intra-oral scan (IOS) and computer-aided design (CAD) technology, in which the acquired files can be combined, it is possible to create a virtual planning environment. This full digital approach allows ideal three-dimensional (3D) virtual simulative execution of dental implant placement based on the combination of anatomical parameters and prosthetic-driven and functional concepts. The information from the digital planning and positioning of the implants can be transferred to the clinical situation by means of a guided surgical template manufactured through stereolithographic rapid prototyping. Certain benefits of computer-assisted template-guided implant placement include uncomplicated predetermined flapless surgical approach with a minimal number of surgeries resulting in decreased patient morbidity and the possibility to immediately (temporary) restore the implant (Tahmaseb et al. 2014; Vercruyssen et al. 2015).

Current research on the topic of computer-assisted template-guided implant surgery has predominantly focused on the analysis of precision and accuracy of different systems (Van Assche et al. 2012). However one great shortcoming of the presently available methods in the virtual simulation is the limitation of freedom where one has to choose from conventional screw shaped implants to meet the anatomical parameters. Consequently, this may result in a planning that in some specific cases, is more driven by the limitation of the implant size/system then the ideal prosthetic concepts. Other options are based on pre implant bone augmentation surgery. Hypothetically, it would seem more ideal to custom design an individual implant to fit the anatomical parameters.

The aim of this study was to introduce a new concept for computer-assisted template-guided placement of a custom designed implant with congruent custom designed surgical tooling and to test the feasibility and accuracy of this method *in-vitro*.

MATERIALS AND METHODS

Sample preparation

One partially edentulous human mandibular cadaver not identified by age, sex or ethnic group was obtained from the functional anatomy department of the University of Amsterdam, The Netherlands. The cadaver was sectioned at the mid-ramus level, fixed in formalin and stored. A declaration was obtained from the functional anatomy department (University of Amsterdam. The Netherlands) to use this human remains material for research purposes.

At the day of the surgery the guided template and custom designed 3D printed surgical tools and implant were prefabricated as described in the hereunder-following subheadings (fig. 1).

Figure 1. The 3D printed surgical tooling and implant, from left to right: guided template, sleeve, 4 drills, osteotome and one piece implant.

The guided template with the sleeve incorporated was positioned and optically checked through designed fenestrations for good fit (fig. 2a). Subsequently, a guided osteotomy was performed by drilling and the shaping finished by gentle tapping with a hammer on the custom printed osteotome (fig. 2b and 2c). Rotational osteotome position was controlled through exact alignment of the '=' sign on the guided template with the guiding groove on the osteotome (fig. 2c and 2d). Finally the implant was inserted into the osteotomy site (fig 2d). With finger pressure and the gentle use of a hammer good primary stability of the implant was achieved and checked by palpation and percussion (fig. 2e and 2f).

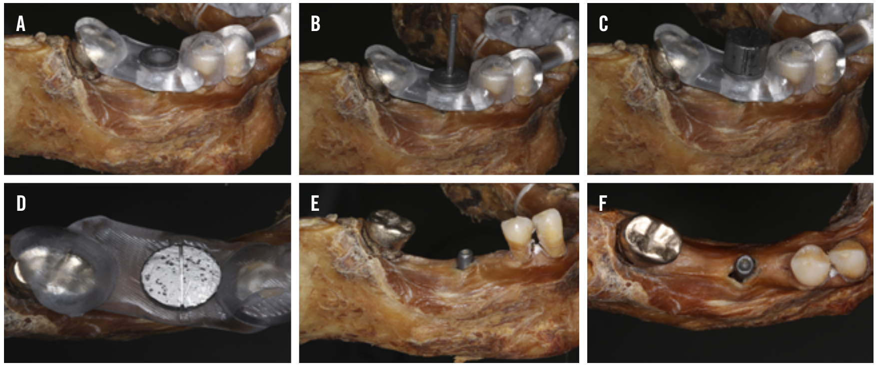


Figure 2. Operative procedure of placing the custom designed 3D printed implant with custom designed 3D printed surgical tooling. Fitting of the guided template (a), guided osteotomy by drilling (b) and osteotome (c), osteotome alignment (d) and placement of the implant (d, e).

3D data acquisition: intra-oral scan and radiographic scan

A full-arch intra-oral scan of this mandible was obtained by using the 3M™ TrueDefinition Scanner (3M ESPE, Seefeld, Germany). The scan files were exported and stored as standardized triangulation language (STL) file format.

The mandible was scanned with the 3D Accuitomo 170 CBCT system (AccuiTomo 170, 90kVp, 5mA, 30.8 Sec, 10x10 cm Field of View (FoV), Morita inc., Japan). The scan position was with the occlusal plane parallel to the floor following the manufacturer's recommendations. The scan volumes were exported in DICOM 3 format.

To measure the accuracy of the implant position after surgery the mandible with the individual implant in place was again scanned with the 3D Accuitomo 170 CBCT system using the exact same scan settings and stored as with the previous scan. The post-operative scan volumes were exported in DICOM 3 format.

Virtual surgical planning and 3D model design of the custom implant and tooling

The DICOM files were imported into the CoDiagnosticX 9 software (Dental Wings GmbH, Ghemnitz, Germany). The CBCT scan was analysed and in the region of missing tooth 45 the anatomical and functional parameters measured. Based on these measurements it was decided the root of tooth 33 could serve as a template for the design of the implant. With the method previously described by Anssari Moin et al. (2011) tooth 33 was segmented. Subsequently, a one piece root shaped implant with abutment was designed in SolidWorks 2015 SP3 software (Dassault Systèmes, Vélizy, France) to meet the predefined anatomical and functional dimensions and stored as a STL file. STL files of the intra-oral scan and implant were imported in CoDiagnosticX 9 software and the implant position determined (fig 3a). Subsequently, the intra-oral surface scan and CBCT scan were superimposed and a tooth supported template based on the implant position was designed (fig 3b, c). Within the template a pre-calculated space was preserved for fitting of a to be custom designed sleeve aimed at guiding the drills and implant during surgery. The guided template design was stored as a STL file.

Accordingly, based on the premeditated positions of the implant and sleeve a set of surgical tools was custom designed with SolidWorks software to create an osteotomy congruent to the implant shape and stored as STL files (fig 3d, 3e, 4). The custom designed tools consisted of a sleeve, 4 drills with increments in diameter and a final (analogue to the) implant shaped osteotome (fig. 4). All osteotomy tools consisted of a cutting/shaping segment and a guiding segment corresponding to the sleeve design (fig. 4).

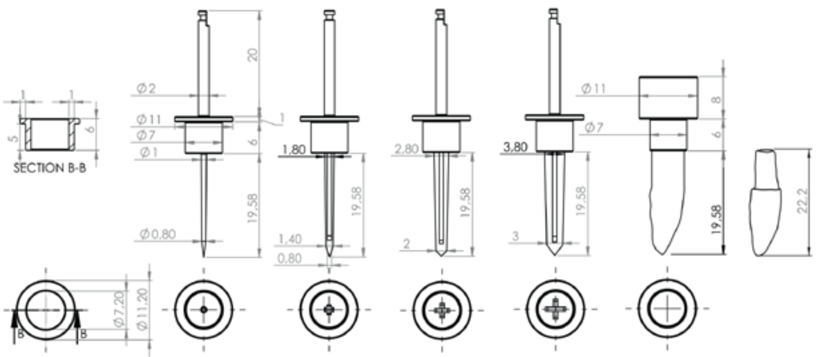


Figure 3. 3D planning of the custom implant and custom tooling.

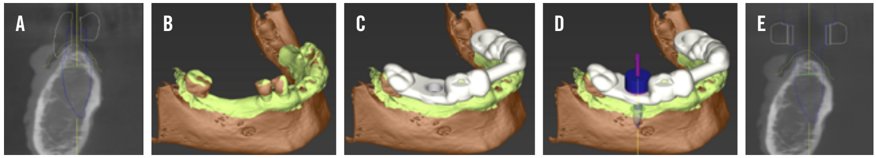


Figure 4. Schematic drawing of the guided osteotomy sequence. The drills and osteotome have identical guiding segments corresponding to the sleeve diameter with predetermined depth and position. Measurements in millimetres.

3D printing of the guided template, surgical tools and implant

Additive manufacturing techniques were used to fabricate the guided template, surgical tools and implant from their respective STL files.

The guided template was 3D printed through a steriolithography procedure in which a vat of liquid photopolymer an ultraviolet laser cures layers of 25 μm thickness to build the requested design (Implantec GmbH, Amstetten, Germany).

The custom designed surgical tools and implant were 3D printed in a titanium-alloy (Ti6Al4V) through a proprietary high-end Selective Laser Melting (SLM) machine equipped with an Ytterbium-fiber laser (30μm thickness) by LayerWise (3Dsystems division, Leuven, Belgium).

Evaluation of the pre-operative planning of implant position and post-operative implant position

The pre- and post-operative DICOM files were imported in CoDiagnostiX 9 software for analysis of accuracy of the custom implant position. The incorporated Evaluation tool in the software was used to match the pre-operatively planned implant position and the post-operative implant position. The following deviations were measured (fig. 5): 3D offset of the shoulder (a), position of the apex of the implant (b) and angulation of the implant (α).

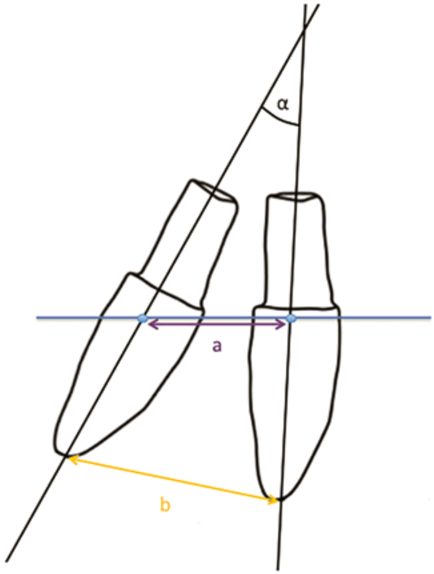


Figure 5. Matching procedure for measuring accuracy of the placed implant position versus the planned implant position. The following parameters were used: a = 3D offset, b = position of the apex of the implant and α = angulation of the implant.

RESULTS

Stabilization and fit of the surgical guide on the cadaver was achieved and checked through the designed fenestrations. The drilling process was uneventful however the final shaping with the guided osteotome was relatively complicated and required constant adjustment since there is rotational freedom in the transversal plane.

The angular deflection (α) with the planned implant position was 0.40° (fig 6). When comparing the bodily 3D positions of the shoulder (a) there is a deviation of 0.72 mm resulting in an apical deviation (b) of 0.72 mm (fig. 6)

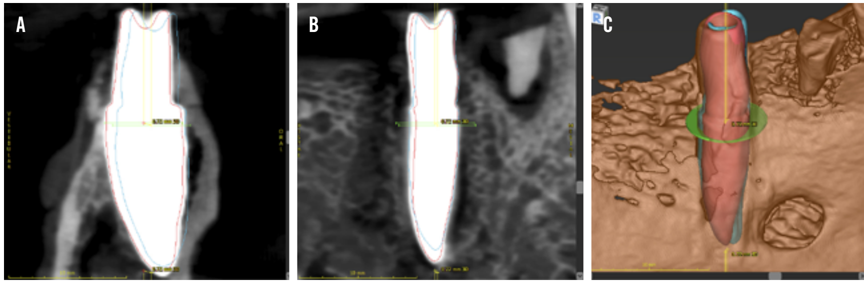


Figure 6. Evaluation of the matching procedure. Frontal (a) and sagittal (b) cross-sections and 3D representation (c).

DISCUSSION

This experiment was performed as a first step towards guided implant placement of a custom designed implant with a congruent custom designed surgical tooling. With the combined use of 3D data acquisition with Cone-beam CT and intra-oral scanning technology, virtual 3D planning software, 3D design software and high-end 3D printing technology it was possible to insert, using guided surgery, with relative accuracy, a custom designed implant.

Comparing accuracy data of this study with the currently available data on accuracy of computer-aided implant placement is incongruous since these are based on conventional screw-type implants inserted by means of conventional surgical tools (Tahmaseb et al. 2014; Van Assche et al. 2012). However, for a general comparison, it is noteworthy to appreciate that the result of this particular experiment lies within the range of positional and angular deviation described in a meta-analysis by Van Assche et al (2012). This meta-analysis revealed mean deviations for entry-point and apex of 0.99 mm (range 0 - 6.5 mm), 1.24 mm (range 0 - 6.9 mm), respectively, and a mean angular deflection of 3.81° (range 0 - 24.9°). Furthermore, methods described in previous computer-aided implant placement studies in increasing accuracy are applicable for this approach as well (Van Assche et al. 2012; Tahmaseb et al. 2014; Vercruyssen et al. 2015).

Novel possibilities arise for template-guided implant surgery, unlimited by the predefined screw-shaped conventional implants. In a virtual 3D environment an ideal implant can be designed to meet the anatomical and functional criteria. Especially in highly atrophied jaws an individual design might be interesting thus making optimised use of the available skeletal housing and resulting in avoidance of (complex) bone augmentation procedures. Correspondingly, since the implant position is pre-calculated also the prosthetic design may be simulated and fabricated for immediate (temporary) restoration. Theoretically,

within the current approach a complete true one-piece 3D individually designed tooth with congruent guided tooling, fabricated in zirconia could be placed.
Besides the freedom of design also material wise new options develop. Some of the possible future ideas of custom printed implants may encompass individualized printing materials and additionally the porosity/microstructure and density of the print material can be individualized to meet specific needs in osseointegration.
Evidence on many levels of this guided custom implant placement approach is needed. Future studies can be focused on evaluating the accuracy, fine tuning the process and assessing success and safety of this guided custom implant.

REFERENCES

Anssari Moin, D., Hassan, B., Mercelis, P. & Wismeijer, D. (2011) Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology. *Clinical Oral Implants Research* doi: 10.1111/j.1600-0501.2011.02359.x.

Tahmaseb, A., Wismeijer, D., Coucke, W. & Derksen, W. (2014) Computer technology applications in surgical implant dentistry: a systematic review. *The International journal of oral & maxillofacial implants*. 29 Suppl:25-42.

Van Assche, N., Vercruyssen, M., Coucke, W., Teughels, W., Jacobs, R. & Quirynen, M. (2012) Accuracy of computer-aided implant placement. *Clinical oral implants research*. 23 Suppl 6:112-123.

Vercruyssen, M., Laleman, I., Jacobs, R. & Quirynen, M. (2015) Computer-supported implant planning and guided surgery: a narrative review. *Clinical oral implants research*. 26 Suppl 11:69-76.

CHAPTER 8

AUTOTRANSPLANTATION OF PREMOLARS WITH A 3D PRINTED TITANIUM REPLICA OF THE DONOR TOOTH FUNCTIONING AS A SURGICAL GUIDE: PROOF OF CONCEPT

Published as:

Verweij JP, Anssari Moin D, Mensink G, Nijkamp P, Wismeijer D, van Merkesteyn JP

Autotransplantation of Premolars With a 3-Dimensional Printed Titanium Replica of the Donor Tooth Functioning as a Surgical Guide: Proof of Concept

Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons 2016, 74(6):1114-1119

ABSTRACT

Autotransplantation of premolars is a good treatment option for young patients with missing teeth. This study evaluates the use of a pre-operatively 3D-printed replica of the donor tooth that functions as a surgical guide during autotransplantation.

Five consecutive procedures were prospectively observed. Transplantations of maxillary premolars with optimal root development were included in this study. A 3D-printed replica of the donor tooth was used to prepare an exactly fitting neo-alveolus at the recipient site before extracting the donor tooth. Procedural time, extra-alveolar time and the number of fitting attempts needed to achieve a good fit of the donor tooth in the neo-alveolus were recorded.

For each transplantation procedure, the surgical time was less than 30 minutes. An immediate good fit of the donor tooth in the neo-alveolus was achieved with an extra-alveolar time of less than one minute for all transplants.

These results show that the extra-alveolar time is very short when the surgical guide is used and therefore the chance of iatrogenic damage to the donor tooth is minimalized. The use of a replica of the donor tooth makes the autotransplantation procedure easier for the surgeon and facilitates optimal placement of the transplant.

INTRODUCTION

Autotransplantation is an old procedure in oral surgery, but is still a very valuable treatment for young patients with missing teeth [1]. Most common is autotransplantation of maxillary premolars to replace missing mandibular premolars [2]. This option is especially useful when orthodontic extraction therapy of maxillary premolars is indicated. Other less frequent indications are transplantation of premolars to replace missing incisors, or transplantation of wisdom teeth to replace heavily damaged molars [3, 4]. Nevertheless, autotransplantation is often not considered in patients with missing teeth or it is dismissed because of the chance of transplant-related complications. This is unfortunate, because autotransplantation could be a very relevant treatment option for single tooth replacement. Particularly because transplanted teeth can function as normal teeth after successful autotransplantation [5].

An update of the surgical technique might help to further improve the already high success and tooth survival rates after autotransplantation and could help to establish autotransplantation as one of the preferred options for single tooth replacement in young patients [6]. This study investigates the use of a computer aided designed (CAD) 3D-printed titanium replica of the donor tooth, which can be used as a surgical guide during the autotransplantation procedure. The surgical guide is used instead of the donor tooth, when preparing an individualised artificial socket (neo-alveolus). This means the donor tooth is extracted after preparation of the neo-alveolus and both extra-alveolar time and the chance of iatrogenic damage are minimized.

The aim of this study is to evaluate the use of this individual pre-operatively 3D-printed donor tooth replica during autotransplantation procedures and assess the advantages of this new technique.

MATERIAL AND METHODS

Study design and participants

This prospective observational study analysed the use of a 3D-printed titanium replica of the donor tooth to facilitate the autotransplantation procedure. The surgical guide was manufactured as previously described by Anssari Moin et al [7].

All patients were referred by their orthodontist and treated at the department of Oral and Maxillofacial Surgery of the Leiden University Medical Center. Autotransplantation with a surgical guide has become the treatment protocol in our center since July 2015. One patient functioned as a test-case, to determine and resolve any procedural difficulties. We subsequently prospectively analysed the first five consecutive transplant procedures that were performed with this technique.

In all cases, the indication for autotransplantation was agenesis of mandibular premolars in patients in whom orthodontic extraction therapy of the maxillary premolars was indicated. Only maxillary second premolars with optimal developmental stage of the donor tooth (50-75% of expected total root development) were included in this study.

3D surface reconstruction

After intake, a selective cone beam computed tomography (CBCT) scan (Planmeca Promax®3D Max, 96kV, 11mA, 130x55mm field of view) of the donor tooth was performed one month prior to autotransplantation. The scan position was with the occlusal plane parallel to the floor following the manufacturer's recommendations.
The scan volumes were exported in DICOM 3 format and imported into image analysis software Amira (v5.3, VisageImaging, California, USA). The datasets were used to create 3D surface models of the donor tooth (Figure 1).

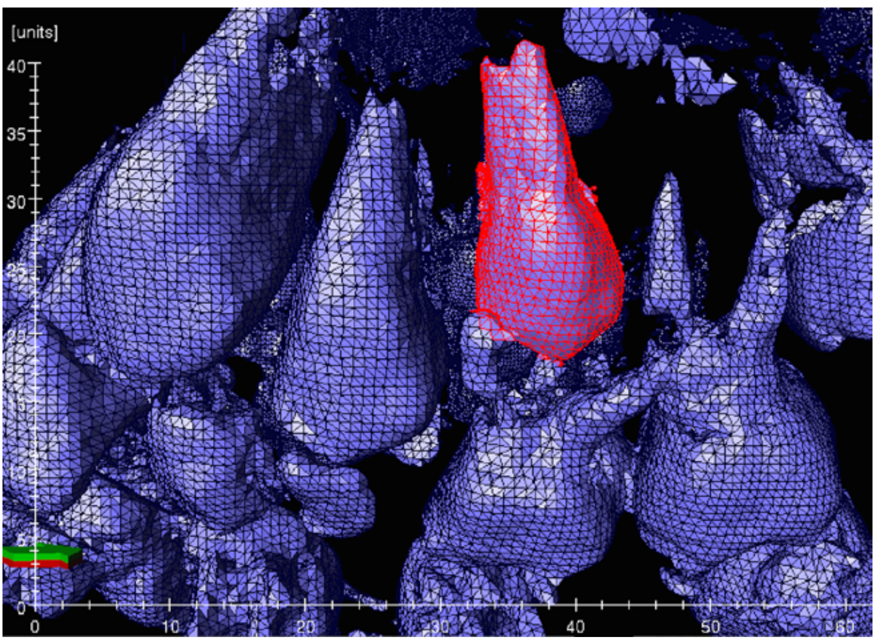


Figure 1. Three-dimensional surface rendering of the donor tooth.

The exact procedure for segmenting the tooth was performed in a standardized manner.

A region of interest limited to the tooth and surrounding periodontium was first selected. Subsequently, a threshold value based on the histogram analysis, the local gray level value and image gradient was selected to separate the root and crown from the surrounding bone (Figure 2). A manual selection, on basis of the sagittal slides, was added for the most apical part of the root if the threshold-based technique did not confine the entire apex area.

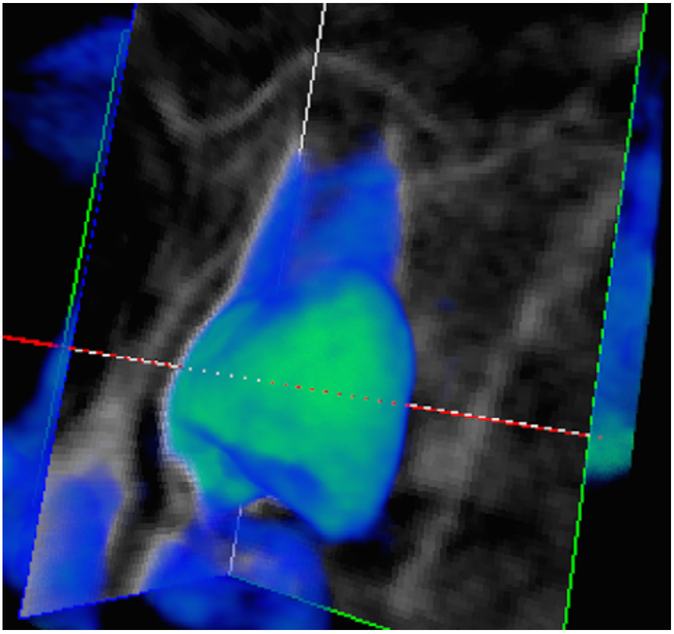


Figure 2. Volumetric segmentation of the donor premolar from the scan.

The resulting images were processed using interactive processing tools to remove resulting artefacts. A 3D surface mesh of the donor tooth was then created and stored as a Standard Triangulation Language (STL) file. The STL files were then reprocessed and retopologized with SolidWorks software 2015 SP3 software (Dassault Systèmes, Vélizy, France) to create a printable mesh.

Printing process

A high-end Selective Laser Melting (SLM) technology was used to fabricate the donor tooth copy from the STL files. This technology is an additive manufacturing technique, that is capable of building complex shaped three-dimensional objects by successively depositing and melting of thin metal powder layers. Each individual layer is molten by scanning the successive two-dimensional layers (30μm thickness) using a focused Ytterbium-fiber laser beam. The donor tooth copy (Figure 3) was produced in a biocompatible grade 23 titanium alloy on a proprietary technology SLM machine by LayerWise (LayerWise NV, 3DSYSTEMS division, Belgium).

Figure 3. Individualized surgical guide.

Surgical procedure

All patients were treated according to the same treatment protocol and the teeth were autotransplanted using the same surgical technique by one experienced surgeon. One procedure was planned under general anaesthesia, because two premolars were transplanted in a young patient that was too anxious to undergo the procedure under local anaesthesia. The other procedures were planned under local anaesthesia (Ultracain D-S, Sanofi-Aventis, Gouda, The Netherlands).

First, the neo-alveolus was prepared at the recipient site with surgical burrs. The 3D-printed replica (surgical guide) was fitted to make sure the donor tooth would fit exactly in the artificial socket (Figure 4).

Figure 4. Fitting the surgical guide.

Subsequently, the donor tooth was extracted by forceps, while care was taken not to damage the cementum, periodontal ligament or apex of the tooth. The surgical guide and donor tooth were optically compared to evaluate possible differences between the 3D-printed replica and the original tooth (Figure 5). The donor tooth was placed into the neo-alveolus in a slight infra-occlusion to prevent occlusal forces postoperatively. A Vicryl Rapide 3-0 suture (Johnson & Johnson International, New Brunswick, NJ, USA) was placed across the occlusal plane to fix to transplanted premolar into place.

Figure 5. Donor tooth and titanium replica (surgical guide).

Data collection

The following preoperative data were collected; the patient's age, gender, donor- and acceptor-sites and root development stage of the donor tooth. Intra-operative data were recorded, including the fitting attempts with the surgical guide, the extra-alveolar time of the donor tooth and the number of fitting attempts needed to place the donor tooth in the newly prepared alveolus (neo-alveolus) at the recipient site.

This study was performed in accordance with the guidelines of our institution and followed the Declaration of Helsinki on medical protocol and ethics. The study protocol was reviewed and approved by the Leiden University Medical centre institutional ethical review board (P15.002).

RESULTS

The first patient was a 12-year old girl. First, the right maxillary premolar was transplanted to the right mandibular premolar position under local anaesthesia. Transplantation of the left maxillary premolar to the left mandibular recipient site was performed two weeks later.

In both procedures the socket was prepared with the titanium replica of the donor tooth until a good fit of the surgical guide was achieved. The donor tooth was subsequently extracted by forceps and care was taken to protect the periodontal ligament of the tooth. The donor tooth was directly placed in the prepared tooth socket at the recipient site and no additional fitting of the donor tooth was necessary. An immediate good fit of the donor tooth in the neo-alveolus was thus achieved in both procedures and the extra-alveolar time was less than one minute for both transplants.
The second patient was a 13-year old boy in whom extraction therapy of the right and left maxillary premolar was planned. After examination of the preoperative CBCT-scan, the left maxillary premolar was found to be the most suitable option for transplantation to the right mandibular recipient site. Autotransplantation was performed under local anaesthesia and the neo-alveolus was prepared by fitting the titanium replica of the left maxillary premolar. The donor tooth was extracted and an immediate good fit in the neo-alveolus was achieved. Extra-alveolar time of the donor tooth was 45 seconds.
The third patient was an 11-year old girl that was treated under general anaesthesia. Transplantation of the right premolar was performed to the right mandibular recipient site. The left premolar was transplanted to the left mandibular recipient site. Each neo-alveolus was again prepared with the replica of the corresponding donor tooth. On both sides an immediate good fit of the donor tooth was achieved with an extra-alveolar time of less than one minute.

Donor tooth (Maxilla)	Recipient site (Mandible)	Fitting attempts	Extra-alveolar time (min:sec)	Procedural time (min)
Right	Right premolar site	1	0:15	20
Left	Left premolar site	1	0:19	20
Left	Right premolar site	1	0:45	30
Left	Left premolar site	1	0:40	20
Right	Right premolar site	1	0:30	25

Table 1: Fitting attempts and extra-alveolar time of donor teeth (maxillary premolars) during autotransplantation procedures with an individualized surgical guide.

DISCUSSION

This study shows that a 3D-printed replica of the donor tooth allows for hands-on pre-operative and intra-operative planning during the autotransplantation procedure. The surgical guide protects the donor tooth from iatrogenic damage by reducing the extra-alveolar time and minimizing the number of fitting attempts during the preparation of a neo-alveolus. This enables a quick and easy autotransplantation procedure.

Successfully transplanted premolars can function as normal teeth with a high long-term survival rate [5]. The procedure is nevertheless still accompanied by the risk of complications, such as root canal obliteration, root resorption, ankylosis, endodontic pathology and periodontitis. Tooth survival and success after autotransplantation mainly depend on the prevention of damage to the periodontal ligament and nerve/apex of the donor tooth [8]. Therefore, several aspects are important in order to maximize the chance of success after autotransplantation. Extraction of the donor tooth should be performed atraumatically without damaging the periodontal ligament and developing apex. Extra-alveolar time should be minimized as much as possible. Iatrogenic damage during implantation at the recipient site should be prevented by minimizing the attempts of fitting the donor tooth in the neo-alveolus. After successful implantation, the donor tooth should be fixed in infra-occlusion to prevent postoperative occlusal forces. A suture splint is advised, as this reduces the chance of ankylosis compared to a more rigid splinting system [9].

The availability of 3D imaging and additive manufacturing technologies has given rise to many improving techniques in dentistry and oral surgery. This includes CAD-CAM manufacturing of crowns and bridges, computer-assisted surgical planning of mandibular reconstruction and orthognathic surgery, and the manufacturing of individualised maxillofacial implants. Rapid prototyping to facilitate autotransplantation of teeth is however new [10].

The use of an individually designed tooth replica to facilitate autotransplantation has several important advantages. It minimalizes the fitting attempts that have to be made to achieve a good fit of the donor tooth in the newly prepared socket. The chances of iatrogenic damage to the periodontal ligament are therefore minimalized and extra-alveolar time is reduced, which can only improve the status of the periodontal ligament of the donor tooth [11, 12]. The chances of iatrogenic damage to the developing apex are also reduced for the same reasons. A replica of the donor tooth furthermore makes the procedure safer for the patient and easier for the surgeon, because exact individualised planning of the autotransplantation is possible with this surgical guide even when intra-operative modifications are necessary. These enhancements will hopefully further improve the success rate and survival rate of transplanted teeth [13].

An alternative for an individualised 3D-printed replica of the donor tooth is the use of predesigned surgical templates of premolars [14, 15].

Such a surgical template (that is not patient-specific) can be sterilised and re-used in subsequent autotransplantation procedures. In this study, we however chose to use an individualised patient-specific 3D-printed replica of the donor tooth. This ensures a good fit of the donor tooth in the neo-alveolus, without the risk of complicating the procedure due to discrepancies between a 'generic' surgical template and the actual donor tooth [16].
To sum up, we believe the future of autotransplantation techniques will include using a surgical guide as an alternative for the donor tooth when preparing the neo-alveolus during autotransplantation of teeth. Nevertheless, possible disadvantages should also be considered. For the manufacture of an individualised replica of the donor tooth, a CBCT-scan is made of the donor tooth. The use of ionizing radiation should be justifiable for each specific patient and should be limited [17]. Therefore, we made a selective CBCT-scan focused on the donor tooth with the smallest field of view possible. Radiation load was kept as minimal as possible. The selective CBCT-scan not only enables the manufacture of the surgical guide, but also allows the surgeon to carefully plan the extraction of the donor tooth. It facilitates a shorter and easier surgical procedure, which in turn could minimize the chance of complications and is beneficial for the patient. We therefore believe this limited amount of additional ionizing radiation is appropriate. Manufacturing of a replica of the donor tooth is furthermore associated with additional costs. We believe this can be compensated by the fact that the surgical guide shortens the surgical time and because higher success and survival rates could prevent expensive treatments in the future [13]. Cost-effectiveness should nevertheless be evaluated.
This study aimed to evaluate our autotransplantation technique using a 3D-printed replica of the donor tooth. Therefore, we reported the technical and intra-operative characteristics of the procedure. In the future, long-term evaluation of the transplanted teeth is necessary to evaluate the success and survival of teeth that were transplanted with the help of this surgical guide.

CONCLUSION

The use of a 3D-printed titanium replica of the donor tooth enables a short and easy autotransplantation procedure. Preparation of the neo-alveolus with optimal placement of the donor tooth is facilitated by this surgical technique and the chance of iatrogenic damage to the donor tooth is minimized. Further research regarding the success rate and survival of transplanted teeth should investigate the clinical advantages of this technique.

REFERENCES

1. Verweij JP, Toxopeus EE, Fiocco M, Mensink G, van Merkesteyn JPR: **Success and survival of autotransplanted premolars and molars during short-term clinical follow-up**. *Journal of clinical periodontology* 2015.
2. Mensink G, van Merkesteyn R: **Autotransplantation of premolars**. *British dental journal* 2010, **208**(3):109-111.
3. Kvint S, Lindsten R, Magnusson A, Nilsson P, Bjerklin K: **Autotransplantation of teeth in 215 patients. A follow-up study**. *The Angle orthodontist* 2010, **80**(3):446-451.
4. Yan Q, Li B, Long X: **Immediate autotransplantation of mandibular third molar in China**. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics* 2010, **110**(4):436-440.
5. Andreasen JO, Paulsen HU, Yu Z, Bayer T, Schwartz O: **A long-term study of 370 autotransplanted premolars. Part II. Tooth survival and pulp healing subsequent to transplantation**. *European journal of orthodontics* 1990, **12**(1):14-24.
6. Nimcenko T, Omerca G, Varinauskas V, Bramanti E, Signorino F, Cicciu M: **Tooth auto-transplantation as an alternative treatment option: A literature review**. *Dental research journal* 2013, **10**(1):1-6.
7. Moin DA, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2013, **24 Suppl A100**:25-27.
8. Tsukiboshi M: **Autotransplantation of teeth: requirements for predictable success**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2002, **18**(4):157-180.
9. Almpani K, Papageorgiou SN, Papadopoulos MA: **Autotransplantation of teeth in humans: a systematic review and meta-analysis**. *Clinical oral investigations* 2015, **19**(6):1157-1179.
10. Cross D, El-Angbawi A, McLaughlin P, Keightley A, Brocklebank L, Whitters J, McKerlie R, Cross L, Welbury R: **Developments in autotransplantation of teeth**. *The surgeon: journal of the Royal Colleges of Surgeons of Edinburgh and Ireland* 2013, **11**(1):49-55.
11. Andreasen JO, Borum MK, Jacobsen HL, Andreasen FM: **Replantation of 400 avulsed permanent incisors. 2. Factors related to pulpal healing**. *Endodontics & dental traumatology* 1995, **11**(2):59-68.
12. Andreasen JO, Borum MK, Jacobsen HL, Andreasen FM: **Replantation of 400 avulsed permanent incisors. 4. Factors related to periodontal ligament healing**. *Endodontics & dental traumatology* 1995, **11**(2):76-89.
13. Shahbazian M, Jacobs R, Wyatt J, Denys D, Lambrichts I, Vinckier F, Willems G: **Validation of the cone beam computed tomography-based stereolithographic**

surgical guide aiding autotransplantation of teeth: clinical case-control study. *Oral surgery, oral medicine, oral pathology and oral radiology* 2013, **115**(5):667-675.

14. Day PF, Lewis BR, Spencer RJ, Barber SK, Duggal M: **The design and development of surgical templates for premolar transplants in adolescents**. *International endodontic journal* 2012, **45**(11):1042-1052.
15. Ashkenazi M, Levin L: **Metal tooth-like surgical templates for tooth autotransplantation in adolescents**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2014, **30**(1):81-84.
16. Shahbazian M, Jacobs R, Wyatt J, Willems G, Pattijn V, Dhoore E, C VANL, Vinckier F: **Accuracy and surgical feasibility of a CBCT-based stereolithographic surgical guide aiding autotransplantation of teeth: in vitro validation**. *Journal of oral rehabilitation* 2010, **37**(11):854-859.
17. Berkhout WE: **[The ALARA-principle. Backgrounds and enforcement in dental practices]**. *Nederlands tijdschrift voor tandheelkunde* 2015, **122**(5):263-270.

CHAPTER 9

REPLACING HEAVILY DAMAGED TEETH BY THIRD MOLAR AUTOTRANSPLANTATION WITH THE USE OF CONE-BEAM COMPUTED TOMOGRAPHY AND RAPID PROTOTYPING

Published as:

Verweij JP, Anssari Moin D, Wismeijer D, van Merkesteyn JPR

Replacing Heavily Damaged Teeth by Third Molar Autotransplantation With the Use of Cone-Beam Computed Tomography and Rapid Prototyping

Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons 2017 (epub ahead of print)

ABSTRACT

This paper describes autotransplantation of third molars to replace heavily damaged premolars and molars. The use of preoperative cone-beam computed tomography planning and 3D-printed replicas of the donor teeth to prepare the artificial tooth socket are specifically described.

In this case, an 18-year old patient received autotransplantation of three third molars to replace one premolar and two molars that were heavily damaged after trauma. Approximately one year after the traumatic incident, autotransplantation with the help of 3D planning and rapid prototyping was performed. The right maxillary wisdom tooth replaced the right maxillary first premolar. Both mandibular wisdom teeth replaced the left mandibular first and second molar.

During the surgical procedure, the artificial tooth sockets were prepared with the help of 3D-printed donor tooth copies in order to prevent iatrogenic damage to the actual donor teeth. These replicas of the donor teeth were designed on the basis of preoperative cone-beam computed tomography and manufactured with the help of 3D-printing techniques. The use of a replica of the donor tooth resulted in a predictable and easy procedure, with extra-alveolar times of less than two minutes for all transplants. The transplanted teeth were placed in infra-occlusion and fixed with a suture splint. Postoperative follow-up showed a physiological integration of the transplanted teeth and successful outcome for all transplants.

In conclusion, this technique facilitates an easy and predictable procedure for autotransplantation of third molars. The use of printed analogues of the to be transplanted teeth reduces the risk of iatrogenic damage and the extra-alveolar time of the donor tooth is minimized. This facilitates a successful outcome.

INTRODUCTION

Autotransplantation of teeth is a valuable form of single tooth replacement therapy in young patients with congenitally missing teeth [1]. The procedure is ideally performed when root development of the donor tooth is 50-75%, because in these cases the transplanted teeth usually function as normal teeth with a good long-term outcome [2]. Autotransplantation of third molars to replace teeth with a bad prognosis is however rarely considered. This is unfortunate, since it can offer a valuable treatment option when trauma or caries has heavily damaged teeth in young patients [3].

Since first molars are the first permanent teeth to erupt, they are sometimes already damaged at a young age. Third molars on the other hand, are the last teeth to develop. Therefore, third molar autotransplantation remains possible until patients are approximately 18 years old. Routine removal of wisdom teeth is common around this age, which makes third molars a useful source of suitable donor teeth.

The introduction of 3D planning has improved modern autotransplantation techniques [4]. Cone-beam computed tomography (CBCT) and rapid prototyping enable preoperative planning and the manufacturing of a replica of the donor tooth. This replica of the donor tooth is subsequently used to prepare the newly formed tooth socket (neo-alveolus) before extracting the donor tooth in order to minimize the extra-alveolar time and facilitate the fit of the donor tooth [5]. These innovations improve the predictability of the autotransplantation technique and could therefore increase the usefulness of autotransplantation as a treatment option to replace heavily damaged teeth even more [6, 7].

This report describes autotransplantation of three third molars to replace one premolar and two molars that were heavily damaged after trauma. The autotransplantation procedure using preoperative CBCT planning and the manufacturing of a 3D printed replica of the donor tooth is specifically described. This information can help surgeons in the consideration of third molar autotransplantation as a treatment option to replace heavily damaged teeth in young patients.

CASE REPORT

An 18-year old girl was brought into the emergency room of our hospital after trauma, due to a vasovagal syncope. She had a fracture in the midline of her mandible and a fracture of the left condylar neck. Dental trauma consisted of fractures of the premolars and first molar on the right side of the mandible and first and second molar on the left side of the mandible. In the upper jaw, the premolars and first molar on the right side and first molar on the left side had also been fractured. Treatment consisted of rigid fixation of the midline fracture with two Champy miniplates and intermaxillary fixation using elastics

for six weeks. After treatment of the mandibular fractures, endodontic treatments of the right mandibular second premolar, left mandibular second molar, both right maxillary premolars, and the left maxillary first molar were necessary (Figure 1).
Six months after the initial trauma, the patient had recovered and functioned well. Removal of the osteosynthesis material concomitant with removal of the four wisdom teeth was first considered. However, in consultation with the patient's dentist, removal of the third molars was deemed undesirable because of the bad prognosis of two left mandibular molars. Autotransplantation to replace these heavily damaged teeth was proposed.

Figure 1. Pre-operative OPT.

Pre-operative planning

A thorough analysis of the prognosis of the damaged teeth was first performed. The first and second left mandibular molars both had a dubious long term prognosis even if extensive necessary treatments would succeed. Furthermore the first maxillary premolar on the right side had a bad prognosis because of a fracture of the root. The remaining teeth either functioned well without pathology, or had been subjected to successful endodontic treatment.
The orthopantomograph (OPT) revealed that root development of the third molars was approximately 70% of expected total root development and autotransplantation was therefore deemed possible. A CBCT-scan was performed for the preoperative planning of the autotransplantation procedure (Figure 2).

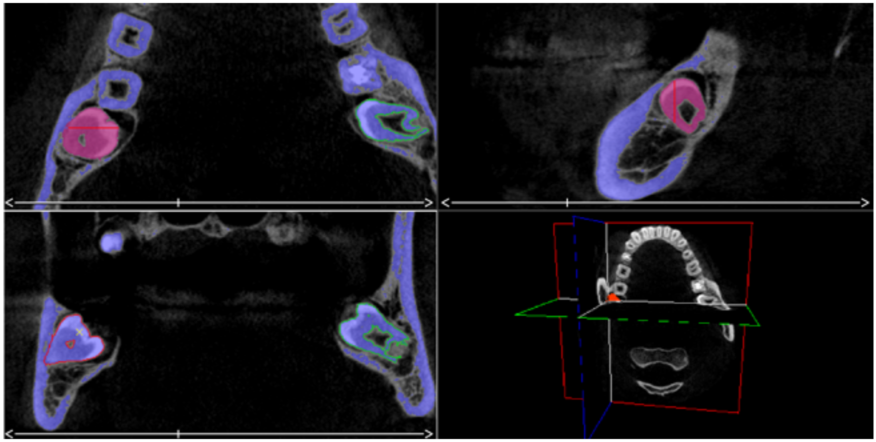


Figure 2. Segmentation procedure

The right maxillary third molar was found to be small enough to replace the damaged right maxillary first premolar. The two mandibular third molars were found to be suitable donor teeth to replace the damaged left mandibular first and second molars. The CBCT-scan confirmed an open apex in all three third molars and autotransplantation of these teeth would therefore be possible without further postoperative treatments.

Manufacturing a 3D-printed replicas of the donor teeth

For each donor tooth, a 3D-printed replica was manufactured as previously described (Figure 3) [5, 8].

Figure 3. 3D printed donor tooth replicas

A CBCT-scan (Planmeca Promax®3D Max) was performed with the occlusal plane parallel to the floor following the manufacturer's recommendation. The scan volumes were exported in DICOM 3 format and imported into image analysis software Amira (version 5.3, VisageImaging, California, USA).
Segmentation of the donor teeth was performed in a standardized manner [8]. First, a region of interest was selected limited to the donor tooth and surrounding periodontium. The root and crown of the donor tooth were separated from the surrounding bone based on a threshold value that was determined from the histogram analysis, local grey level, and image gradient. On the basis of the sagittal slides, a manual selection was subsequently applied for the most apical part of the root to complete the segmentation of the tooth. The images were processed using interactive processing tools to remove any remaining artefacts. A 3D surface mesh of the donor tooth was created and stored as a Standard Triangulation Language (STL) file that was reprocessed (SolidWorks software, Dassault Systèmes, Vélizy, France) to create a printable mesh.
Fabrication of the replicas of the donor teeth was performed using 3D-printing techniques [8]. High-end selective laser melting was used to fabricate the donor teeth copies from the STL files by adding successive two-dimensional layers of 30 μm thickness. Each individual layer is molten using a focused Ytterbium-fibre laser beam. The replicas of the donor teeth were produced in a biocompatible cobalt-chrome alloy by Mundo 3D (Mundo 3D, Kootwijkerbroek, the Netherlands).

The surgical procedure

Approximately one year after the patient had been brought into the emergency room, the first and second mandibular molars on the left side were extracted. One month later, autotransplantation of three third molars to replace the two destructed molars and one heavily damaged premolar was planned, concomitant with removal of the previously inserted Champy plates. Autotransplantation was performed according to our standard surgical technique, with the use of 3D printed replicas of the donor teeth.
Under general anaesthesia, first the Champy plates near the midline of the mandible were removed. The right maxillary first premolar was gently extracted. After visualisation of the right maxillary third molar, the neo-alveolus at the recipient site was prepared with the help of the cobalt-chrome donor tooth copy. The replica showed that minimal shaving of the crown was necessary to adjust the mesiodistal width of the tooth. A good fit of the replica of the donor tooth was subsequently obtained. The right maxillary third molar was then extracted and the mesiodistal width of the crown was adjusted as planned with the donor tooth copy. Visual comparison of the donor tooth and its replica showed no remarkable differences (Figure 4). The donor tooth was placed in a slight infra-occlusion to prevent postoperative forces. An immediate good fit of the donor tooth was achieved with an extra-alveolar time of 1 minute and 56 seconds. A suture was placed across the

occlusal plane to fix the transplanted tooth.

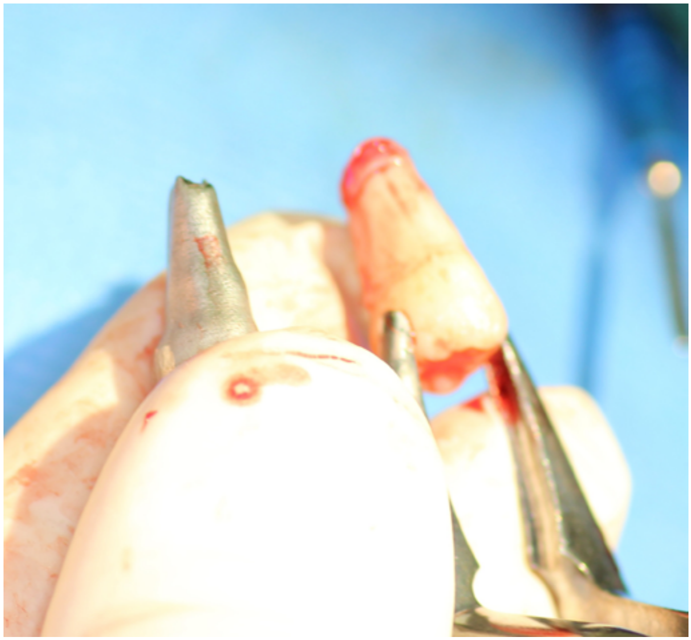


Figure 4. 3D printed replica vs actual tooth (18)

Subsequently, the left and right mandibular third molars were visualized. Two artificial tooth sockets were prepared at the site of the left mandibular first and second molars, with the help of the cobalt-chrome copies of the donor teeth (Figure 5 and 6).

Figure 5. Fitting of donortooth copies 38 and 48.

The replica was fitted to make sure the donor tooth would fit exactly in the artificial tooth socket and the occlusion was checked with the donor tooth copies in the newly prepared tooth sockets. The donor tooth was extracted with an elevator and forceps, while care was taken not to damage the cementum, periodontal ligament, and apex of the tooth. Comparison of the donor tooth copy and the original tooth again showed no differences with regard to the shape of the root and crown in both cases. The left mandibular third molar was placed at the site of the first molar and the right mandibular third molar was placed at the site of the second molar of the left mandible. The donor teeth were again placed in a slight infra-occlusion. For both the left and right third molar, an immediate good fit at the recipient site was achieved with an extra-alveolar time of respectively one minute and nine seconds, and 53 seconds. A suture was placed across the occlusal plane of the donor teeth to fix the transplanted teeth into place and additional sutures were placed to close the incision.

Figure 6. Preparation of the neo-alveoli.

Outcome

Postoperative follow-up showed a good position of the transplants directly after the procedure (Figure 7). Six months after surgery, the transplanted teeth showed physiological integration in the mandible. Normal biological mobility was present without signs of ankylosis of the transplanted teeth. The transplanted teeth showed no pathology and good periodontal health. A small radiolucent zone persisted near the region of the most distal molar (Figure 8). The patient functioned well without any complaints or pathologic symptoms. She was very satisfied with the aesthetic and functional result (Figure 9 and 10).

Figure 7. Two week post-operative OPT.

Figure 8. Six months post-operative OPT.

Figure 9. Clinical view 2-weeks postoperative.

Figure 10. Clinical view 2-weeks postoperative.

DISCUSSION

This report described the use of three-dimensional preoperative planning and the manufacturing of a replica of the donor tooth for autotransplantation of third molars in order to replace heavily damaged premolars and molars.

Autotransplantation has been shown to provide a reliable therapy for missing teeth with high success- and survival-rates [9]. Thus, especially in young patients, autotransplantation should always be considered as a treatment option to replace missing teeth [1]. This can offer biologic and physiologic tooth replacement, after which the transplanted teeth can function as normal teeth with a good long-term prognosis [2, 10]. The procedure is ideally performed when the donor tooth has an open apex [11]. Autotransplantation of teeth with complete root formation is also possible, but does necessitate endodontic treatment before or within two weeks after autotransplantation [12]. In our clinic, the treatment protocol is to perform autotransplantation when root development is 50-75%, as similarly recorded in this case.

Preoperative planning using cone-beam computed tomography (CBCT) could improve this procedure, and possibly even further increase success and survival rates [7]. In this case, a CBCT was performed in order to facilitate preoperative planning and for fabrication of replicas of the donor teeth. The donor teeth, consisting of one maxillary and two mandibular third molars, were first assessed with regard to root development and dimension of the crown. The crown of the upper left third molar was approximately one millimetre wider than the crown of the heavily damaged upper right first premolar. Therefore autotransplantation to replace this destructed tooth was possible after minimal shaving of the crown, in order to correct the mesiodistal width of the crown of the donor tooth. Autotransplantation of both mandibular molars to replace the left mandibular first and second molar was planned, and performed with the help of the replicas of these donor teeth. The use of a replica of the donor tooth to prepare the neo-alveolus has been reported to result in a more controlled and easier autotransplantation procedure, with a minimized extra-alveolar time and procedural time [5, 7]. The donor tooth copy prevents (iatrogenic) damage to the donor tooth during the autotransplantation procedure. These improvements have shown to result in a reduction of complications and increased chances of success [7]. Several cases have been reported on the use of rapid prototyping for the autotransplantation procedure and the fabrication of a 3D-printed replica of the donor tooth [13-17]. However, most reports on autotransplantation focus on premolar transplantation instead of transplantation of third molars. This is noticeable, since third molars are frequently extracted in young patients and therefore often suitable donor teeth. Third molars furthermore develop relatively late and they thus still have an open apex until a patient's age of approximately 18 years. In this case, autotransplantation of incompletely developed third molars was performed and all transplants functioned well during postoperative follow-up.

Although this technique does require the use of CBCT instead of panoramic radiography and is therefore accompanied by more radiation, the use of this very limited amount of additional radiation is in our opinion justified as it enables a predictable procedure with an increased chance of success [7]. The additional costs of manufacturing a replica of the donor tooth are furthermore very limited, especially when printing the donor tooth copy in cobalt-chrome. This technique could even be cost-effective, by preventing complications and increasing the success- and survival-rates after autotransplantation [7].

CONCLUSION

In conclusion, the use of preoperative planning based on cone-beam computed tomography and the preparation of the artificial tooth socket with the help of a 3D-printed replica of the donor tooth facilitates an easy and predictable procedure for autotransplantation of third molars. The risk of iatrogenic damage and the extra-alveolar time of the donor tooth are minimized when using this technique, facilitating a successful outcome.

REFERENCES

1. Verweij JP, Toxopeus EE, Fiocco M, Mensink G, van Merkesteyn JR: **Success and survival of autotransplanted premolars and molars during short-term clinical follow-up**. *Journal of clinical periodontology* 2015.
2. Verweij JP, Toxopeus EE, Fiocco M, Mensink G, Van Merkesteyn JPR: **Long-term prognosis after autotransplantation of premolars and molars**. *International journal of oral and maxillofacial surgery* 2016.
3. Reich PP: **Autogenous transplantation of maxillary and mandibular molars**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2008, **66**(11):2314-2317.
4. Cross D, El-Angbawi A, McLaughlin P, Keightley A, Brocklebank L, Whitters J, McKerlie R, Cross L, Welbury R: **Developments in autotransplantation of teeth**. *The surgeon: journal of the Royal Colleges of Surgeons of Edinburgh and Ireland* 2013, **11**(1):49-55.
5. Verweij JP, Anssari Moin D, Mensink G, Nijkamp P, Wismeijer D, van Merkesteyn JPR: **Autotransplantation of premolars with a 3D printed titanium replica of the donor tooth functioning as a surgical guide: proof of concept in first five transplants.** *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2016.
6. Shahbazian M, Jacobs R, Wyatt J, Willems G, Pattijn V, Dhoore E, C VANL, Vinckier F:

Accuracy and surgical feasibility of a CBCT-based stereolithographic surgical guide aiding autotransplantation of teeth: in vitro validation. *Journal of oral rehabilitation* 2010, **37**(11):854-859.

7. Shahbazian M, Jacobs R, Wyatt J, Denys D, Lambrichts I, Vinckier F, Willems G: **Validation of the cone beam computed tomography-based stereolithographic surgical guide aiding autotransplantation of teeth: clinical case-control study**. *Oral surgery, oral medicine, oral pathology and oral radiology* 2013, **115**(5):667-675.
8. Moin DA, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2013, **24 Suppl A100**:25-27.
9. Almpani K, Papageorgiou SN, Papadopoulos MA: **Autotransplantation of teeth in humans: a systematic review and meta-analysis**. *Clinical oral investigations* 2015, **19**(6):1157-1179.
10. Andreasen JO, Paulsen HU, Yu Z, Bayer T, Schwartz O: **A long-term study of 370 autotransplanted premolars. Part II. Tooth survival and pulp healing subsequent to transplantation**. *European journal of orthodontics* 1990, **12**(1):14-24.
11. Denys D, Shahbazian M, Jacobs R, Laenen A, Wyatt J, Vinckier F, Willems G: **Importance of root development in autotransplantations: a retrospective study of 137 teeth with a follow-up period varying from 1 week to 14 years**. *European journal of orthodontics* 2013, **35**(5):680-688.
12. Chung WC, Tu YK, Lin YH, Lu HK: **Outcomes of autotransplanted teeth with complete root formation: a systematic review and meta-analysis**. *Journal of clinical periodontology* 2014, **41**(4):412-423.
13. Lee SJ, Jung IY, Lee CY, Choi SY, Kum KY: **Clinical application of computer-aided rapid prototyping for tooth transplantation**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2001, **17**(3):114-119.
14. van der Meer WJ, Jansma J, Delli K, Livas C: **Computer-aided planning and surgical guiding system fabrication in premolar autotransplantation: a 12-month follow up**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2015.
15. Keightley AJ, Cross DL, McKerlie RA, Brocklebank L: **Autotransplantation of an immature premolar, with the aid of cone beam CT and computer-aided prototyping: a case report**. *Dental Traumatology* 2010, **26**(2):195-199.
16. Honda M, Uehara H, Uehara T, Honda K, Kawashima S, Honda K, Yonehara Y: **Use of a replica graft tooth for evaluation before autotransplantation of a tooth. A CAD/CAM model produced using dental-cone-beam computed tomography**. *International journal of oral and maxillofacial surgery* 2010, **39**(10):1016-1019.
17. Park JM, Tatad JC, Landayan ME, Heo SJ, Kim SJ: **Optimizing third molar autotransplantation: applications of reverse-engineered surgical templates and rapid**

prototyping of three-dimensional teeth. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2014, 72(9):1653-1659.

CHAPTER 10

AUTOTRANSPLANTATION OF TEETH WITH THE AID OF COMPUTER-AIDED RAPID PROTOTYPING USING A 3D REPLICA OF THE DONOR TOOTH: A SYSTEMATIC LITERATURE REVIEW

Published as:

Verweij JP, Jongkees FA, Anssari Moin D, Wismeijer D, van Merkesteyn JPR

Autotransplantation of teeth using computer-aided rapid prototyping of a three-dimensional replica of the donor tooth: a systematic literature review

International journal of oral and maxillofacial surgery 2017 (epub ahead of print)

ABSTRACT

New autotransplantation techniques have recently been introduced using rapid prototyping to preoperatively fabricate a replica of the donor tooth for preparation of the neo-alveolus. This systematic literature review aims to provide an overview of studies that report about the use of a donor tooth replica during autotransplantation. Reported results of this new procedure are assessed and the different 3D autotransplantation techniques are discussed.

A systematic literature search was conducted in the PubMed, EMBASE, Web of Science and Cochrane databases and 19 articles could be included in this review. These papers described one clinical case-control study, four clinical observational studies, one study with both a clinical observational and an in vitro part, four in vitro studies, and nine case reports.

The in vitro studies showed high surgical accuracy of the printing and planning processes. The case reports all reported successfully transplanted teeth, without signs of pathology. The clinical studies reported a short extra-oral time of the donor tooth, with subsequent success and survival of respectively 80.0% - 91.1% and 95.5% - 100% after 3D autotransplantation. One case-control study showed a significant decrease in extra-oral time and higher success rates when using a replica of the donor tooth.

In conclusion, the use of a preoperatively designed surgical guide for autotransplantation seems to enable accurate positional planning and results in an easy procedure with a short extra-oral time. However, the quality of the existing body of evidence is low and more research is necessary to investigate clinical advantages of this innovative autotransplantation technique.

INTRODUCTION

Autotransplantation of teeth describes the surgical transposition of a donor tooth from a donor site to a surgically prepared artificial socket (recipient site) within the same individual [1].

Primary indications include agenesis of teeth, premature and/or traumatic tooth loss, and replacing heavily damaged teeth [2, 3]. However, many diverse indications can favor physiological tooth replacement with autotransplantation. The most commonly performed procedure is probably the replacement of an absent mandibular premolar by a maxillary premolar in young patients [4]. This treatment option is particularly useful when orthodontic extraction therapy of the maxillary premolars is indicated [5-7].

Ideally, autotransplantation of teeth should take place when root formation is approximately 50-75% of complete expected root development [8-10]. This corresponds with a radiographically open apex of at least 1 mm, which allows revascularization of the pulp chamber and continued root growth [11].

Success and survival rates of transplanted teeth are generally high, with reported rates varying from 79-100% success and 57-100% survival after classic autotransplantation techniques [12, 13]. Success is usually defined as autotransplantation with direct physiologic implantation of the donor tooth, without any signs of pathology and without the need for additional procedures. Survival is defined as the continued presence of the transplanted tooth, even if its function, esthetics or development, are compromised [14].

The most important considerations for a successful tooth transplant are the maintenance of healthy periodontal ligament cells and good tissue adaptation [15]. This is influenced by surgical factors, among which the number of fitting attempts with the donor tooth; the distance between the new alveolus and the root of the donor tooth; the extra-alveolar time; skill of the surgeon; and level of trauma during extraction of the donor tooth [11, 16].

In classic autotransplantation techniques, the extracted donor tooth serves as a template to prepare the new tooth socket at the recipient site. This involves manipulation of the vulnerable donor tooth, since multiple fitting attempts are usually required to achieve optimal adaptability between the recipient bone and the root surface of the transplanted tooth [15]. Every fitting attempt further increases the risk of trauma of the periodontal ligament and extends the extra-oral time [16]. In modern autotransplantation techniques, the risk of damage to the donor tooth is minimized by using a preoperatively designed surgical template instead of the donor tooth [1]. This replica of the donor tooth is usually produced based on a preoperative cone-beam computed tomography (CBCT) scan and functions as a surgical guide enabling a quick and straightforward autotransplantation procedure [7].

The aim of this systematic review was to provide an overview of studies that report about autotransplantation with the use of a surgical guide to prepare the neo-alveolus at the recipient site before extracting the donor tooth. The outcome of this new procedure is assessed and the different autotransplantation techniques are discussed.

MATERIAL AND METHODS

This literature review was conducted in accordance with the PRISMA guidelines [17].

Study identification
An electronic database search was conducted from inception until 24 March 2016, without any restrictions concerning publication year or publication language. The following databases were searched: PubMed, EMBASE, Web of Science and COCHRANE (Appendix 1). The reference lists and citation lists of relevant articles were subsequently manually scanned to identify any additional studies. Duplicates were removed and all articles were gathered in an electronic Endnote database.

Specific inclusion and exclusion criteria were set to include in vitro studies, case reports and clinical retrospective/prospective studies. The inclusion criteria for in vitro studies were studies that reported about autotransplantation with the use rapid prototyping techniques in humans (i.e. an individually designed replica of the donor tooth). All studies regarding the fabrication process, planning process, and surgical autotransplantation procedures were included in this review. Exclusion criteria were all studies that did not report on individual templates. Studies that reported on non-individualized templates or archetype templates were therefore also excluded.

Case reports and clinical studies were included only if the paper described autotransplantation with the use of rapid prototyping techniques in humans (i.e. an individually designed replica of the donor tooth). Both prospective and retrospective randomized controlled trials, case-control studies, observational studies, case series and case reports were included in this review. There were no restrictions on the outcome parameters. The neo-alveolus at the recipient site had to be prepared with the help of an individual three-dimensional model of the donor tooth. Studies that used classic autotransplantation techniques (i.e. preparing the neo-alveolus with the donor tooth itself) were excluded.

Data extraction
The titles and abstracts of all identified reports were screened by two independent investigators (JV & FJ). If eligibility could not be decided by title of abstract, the full text of the article was retrieved. If eligibility of a paper could not be decided in consensus between the two review authors, a third investigator (RM) was consulted.

Data collection was conducted using predefined data extraction forms including information on study design, participant characteristics, intervention, comparisons, and outcomes. The primary outcome of interest in this literature review was success after autotransplantation with a replica of the donor tooth. The specific advantages and disadvantages of 3D-techniques for the autotransplantation procedure were analyzed. Outcome of the in vitro studies furthermore included both the fabrication accuracy of the replica, and the accuracy of the planning/placement of the donor tooth. Outcomes of the case reports and clinical studies included success and survival rates, ankylosis, root resorption, clinical and/or radiographic abnormalities, healing stage, fitting attempts, and extra-alveolar time of the donor tooth.

Quality evaluation & risk of bias
For in vitro studies, the *Checklist for Reporting in vitro Studies* (CRIS guideline) was used to assess the quality of the studies [18]. The checklist registered if the in vitro studies reported on: sample size calculation, meaningful difference between groups, sample preparation and handling, allocation sequence, randomization, and blinding and statistical analysis.

For case reports, the CARE guideline was used to assess if the case report was written according to the guideline [19]. The criteria of the CARE CHECKLIST included: the words *case report* in the title, 2-5 key words, abstract, introduction, patient information, clinical findings, timeline, diagnostic assessment, therapeutic intervention, follow-up and outcomes, discussion, patient perspective and informed consent.

Non-randomized clinical studies were assessed using the *methodological index for non-randomized studies (MINORS)* [20]. This MINORS checklist registered if the clinical studies reported the aim of the study, method for inclusion and follow-up of patients, the protocol used for data collection, the method used for evaluation of the endpoints, and the study size including loss to follow-up. For comparative studies the equivalence of the compared groups and statistical analyses were also evaluated. To further assess the potential risk of bias of the clinical studies, the tool of the *Cochrane Handbook for Systematic Reviews of Interventions* was used [21]. This tool assesses risk of bias in the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias. Studies meeting all of these criteria were classified as having a low risk of bias; those that did not meet one of the criteria were classified as having a moderate risk of bias and those that did not meet two or more criteria were classified as presenting a high risk of bias.

Outcome measures and data analysis / data synthesis

The findings were reported and three 'summary of findings' tables were constructed based on the study type (in vitro studies, case reports, clinical studies). For in vitro studies the results were subdivided into the accuracy of the printing versus the planning technique. For case reports the results were pooled in terms of success and survival. For clinical studies the results were also pooled in terms of success and survival, as well as for extra-oral time of the donor tooth.

Statistical analysis

No statistical meta-analysis was performed in this review.

RESULTS

Literature search and included studies

We identified 370 titles using the search strategies outlined above. After removal of duplicates, 247 titles were left. After screening by title and abstract, we identified 34 eligible articles. Of these papers the full texts were examined. Fourteen did not meet the inclusion criteria, and one article was a clinical update of a study published earlier [22]. Thus, 19 studies were included in this review. One paper described both in vitro and clinical results; therefore five in vitro studies, nine case reports, and six clinical studies were assessed. No randomized controlled trials or systematic reviews were identified in our search. A flowchart of the selection and inclusion process is presented in Figure 1.

Figure 1: Flowchart of the study selection process.

Quality evaluation and risk of bias

The quality of the evidence of the five in vitro studies was low, when assessed according to the CRIS guideline. All of the studies had a detailed explanation about sample preparation and sample handling. None of the included studies had a sample size calculation and allocation sequence.

The quality of evidence of the case reports was low, since all case reports did not meet all the criteria of the *CARE checklist* [19]. The nature of case reports (n=1) furthermore evidently results in a low quality of evidence.

The clinical studies were all descriptive studies, except for one case-control study. The five descriptive studies scored between 9 and 14 points out of 16 points (MINORS score). The case-control study scored 19 out of 24 points (MINORS score). The risk of bias was high according to the Cochrane tool in all six clinical studies.

Appendix 2 represents the checklist scores of all the individual studies. Appendix 3 represents the risk of bias according to the Cochrane tool in the clinical studies.

In vitro studies

The characteristics and outcomes of the five included in vitro studies are shown in Table 1. The sample size ranged from 1 to 50 transplants. Three studies investigated the fabrication accuracy of the replica of the donor tooth (i.e. the agreement between the replica and the donor tooth). One study investigated the accuracy of 3D planning (i.e. the agreement between the planning and the placement of the transplant). One study assessed the accuracy of both the fabrication process of the replica, and the planning process of the autotransplantation procedure.

Shahbazian et al. [23], Lee et al. [24], Lee et al. [22] and Khalil et al. [25] assessed the accuracy of the fabrication of the replica tooth compared to the donor tooth. Shahbazian et al. [23] found that the accuracy level of the replica was within 0.25 mm and concluded that this enabled the use of stereolithographic models for in vivo planning of CBCT-based autotransplantation. Lee et al. [24] found that the 3D CT image is on average 0.149mm smaller than the real anatomic teeth and the replica of the donor tooth is on average 0.067mm smaller than the CT-image. Lee et al. [22] assessed the accuracy of two types of printing technologies: fused deposition modeling (FDM) and PolyJet. The FDM technique models turned out to be slightly smaller, where the PolyJet models were slightly bigger than the original donor tooth. Although these differences were statistically significant, they were regarded as clinically insignificant. Khalil et al. [25] assessed the accuracy of three different printing technologies: stereolithography apparatus (SLA), FDM, and PolyJet.

They concluded that the dimensional differences for the 3D printing technologies were well below the clinically required surgical accuracy level of 0.25 mm and therefore a reliable replica can be produced with these three techniques.

Anssari Moin et al. [16], and Shahbazian et al. [23] assessed the accuracy of the planning technique using a surgical drilling guide and replica of the donor tooth. Anssari et al. [16] assessed autotransplantation using computer guided templates and custom-designed surgical tools. They reported and cervical deviation of 1.25 mm and apical deviation of 0.89 mm. The angular deflection of the transplanted tooth in relation to the planned donor tooth position was 3.1°. Shahbazian et al. [23] concluded that stereolithographic surgical guidance enables a more efficient and predictable treatment method for autotransplantation.

Case reports

The characteristics and outcomes of the included case reports are reported in Table 2. Eight studies reported on a single tooth transplant and one study reported on two transplanted teeth within on patient.

Four case reports described donor teeth with an open apex, varying from 50% to 90% root formation. [26-29] The other five case reports, described six transplanted teeth with complete root formation in which endodontic therapy was performed according to the standard autotransplantation protocol. Vanderkar et al. [30] described transplantation of a central incisor. Lee et al. [31] reported about transplantation of a mesiodens. The follow-up time varied between 6 to 48 months.

The extra-oral time of the donor tooth varied between immediate transplantation to 3 minutes. [32] At the end of follow up, all transplanted teeth survived and met the success criteria. There was no need for additional (surgical) procedures. All ten transplants were thus present as clinically normal teeth without any signs of pathology.

Clinical studies

The characteristics and outcome of the included clinical studies are reported in Table 3. Five observational studies described a sample size ranging from 5 to 182 transplanted teeth. One case-control study described 24 teeth that were transplanted using a guided technique with a 3D replica of the donor tooth and 24 matched control using a classic autotransplantation technique. The clinical studies reported success rates after 3D autotransplantation that varied between 80.0% and 91.1% [33, 34]. The survival rates varied between 95.5% and 100 % [15, 34].

Lee et al. [35] reported that the extra-oral time and the risk of injury to the donor tooth were minimized as a result of computer-aided rapid prototyping. In their study, the survival rate after one year was 100% in 22 transplants, although several occasions of narrowed periodontal spaces were observed. In a case-control study by Shahbazian et al. [34] a significant decrease of extra-oral time was found when comparing the traditional method with 3D autotransplantation. In this study, the average extra-alveolar time was less than 1 minute for the 3D group and 3-10 minutes in the control group [34]. This is in concordance with findings by Verweij et al. [7] who also found an extra-alveolar time of less than one minute after five 3D autotransplantation procedures. They furthermore described an immediate good fit of the donor tooth in all cases (i.e. no additional fitting attempts with the donor tooth itself). Jang et al. [33] reported about five autotransplantations, of which 4 out of 5 had an immediate good fit, and in one case the extra-oral time was 2 minutes. Lee et al. [35] described 22 cases and found a remarkable longer mean extra-oral time of 7 minutes. These results correspond with the findings by Lee et al. [24] Kim et al. [15] reported a mean extra-oral time of 7.6 minutes, ranging from immediate implantation to 25 minutes. In their study, the increased extra-alveolar time was caused by transplantation of teeth with complete root development in which an extra-oral endodontic treatment was performed intra-operatively [15].

Shahbazian et al. [34] reported that the procedural time was significantly reduced when using a replica of the donor tooth, compared to traditional techniques. They reported a procedural time of respectively 40-90 minutes for traditional autotransplantation and 30-45 minutes for 3D autotransplantation. Verweij et al. [7] reported procedural times of 20-30 minutes for 3D autotransplantation.

Unsuccessful outcomes after 3D autotransplantation included root resorption, ankylosis, and clinical/radiographic abnormalities. Shahbazian et al. [34] observed four cases of replacement resorption and two cases of progressive infection-related resorption out of 24 transplants with the traditional autotransplantation technique, compared to one case of resorption out of 24 transplants with a replica of the donor tooth. Jang et al. [33] and Lee et al. [35] found no radiographic signs of root resorption in respectively 5 and 22 teeth that were transplanted with the help of a replica. Kim et al. [15] described 168 patient that were treated with 3D autotransplantation, of which 4 cases showed root resorption (2.4%) and ankylosis was observed in 18 cases (10.7%). Lee et al. [24] observed root resorption in 4 of 251 cases (1.6%).

TABLES

Table 1: Characteristics and outcomes of the in vitro studies.

Study	Year	Study sample	Results
			Fabrication accuracy
Shabazian et al.	2010	1 completely formed premolar	Linear measurements: agreement between -0.25 mm and +0.25 mm in 79%, overestimation in 3%, underestimation in 18%.
Lee et al.	2012	12 random teeth	The computer-aided rapid prototyping model was on average 0.067mm smaller than the 3D CT image. The 3D CT image was on average 0.149mm smaller than real anatomic teeth.
Lee et al.	2015	50 completely formed molars	Volumetric measurements: FDM -1.48%, PolyJet + 0.71%. Statistically significant, but both clinically acceptable replicas.
Khalil et al.	2016	6 completely formed random teeth	All 3D printing technologies provided high accuracy of CBCT-based tooth replica fabrication compared to the natural tooth. Dimensional differences between the real anatomic teeth and the printed models were well below the clinically required accuracy level of 250 μm and therefore clinically insignificant.
			Placement accuracy
Shabazian et al.	2010	1 completely formed premolar	No reshaping of the neo-alveolus after preparation with the use of a stereolithographic surgical guide. Immediate good fit without manipulation of the donor tooth reducing periodontal ligament injury.
Anssari Moin et al.	2016	1 completely formed canine	The angular deflection with the planned donor tooth position was 3.1°. When comparing the bodily 3D positions, there was a deviation of 0.89 mm.

Table 2: Characteristics and outcomes of the case reports.

Study	Year	Study sample	Success	Survival	Extra-oral time	Follow up time (months)
Harzer et al.	2009	Incompletely formed premolar	No signs of pathology (resorption/ ankylosis). Successful regeneration of the PDL		Immediate	20
Honda et al.	2010	Completely formed mandibular third molar	Postoperative endodontic treatment as planned. No signs of pathology.	Transplant is functional and present at the end of follow-up.	NR	48
Keightley et al.	2010	Incompletely formed premolar	No signs of pathology. Transplant is responsive to electric pulp testing and ethyl chloride after six months. Continued root formation. The tooth is clinically normal.		<1 min	6
Lee et al.	2014	Completely formed mesiodens	Normal postoperative appearance without signs of pathology. No external root resorption/replacement resorption.	Transplant is functional and present at the end of follow-up.	NR	36
Pang et al.	2011	Incompletely formed premolar.	No abnormality in mobility, percussion and periodontal disease. No root resorption. Recipient bony site had insufficient bone volume, therefore also sinus lift and allogenic bone graft was performed.	Transplant is functional and present at the end of follow-up.	30 sec	24

Park et al.	2014	Completely formed molars	Mobility and probing depth normal. Visual lamina dura. Absence of root resorption and inflammation. Function normal.	Transplant is functional and present at the end of follow-up.	NR	10
Park et al.	2013	Completely formed premolar	Radiographic, periodontal probing and visual inspection met the success criteria. Clinically good occlusion.	Transplant is functional and present at the end of follow-up.	3 min	36
Van der Meer et al.	2015	Incompletely formed premolar	The transplanted tooth showed signs of vitality during pulp testing and continuous root development. Pulp obliteration was observed.		“a minimum”	12
Vanderkar et al.	2015	Completely formed impacted central incisor	Postoperative endodontic treatment as planned. Esthetics and functions good, also after orthodontic treatment.	Transplant is functional and present at the end of follow-up.	NR	16

Table 3: Characteristics and outcomes of the clinical studies.

Study	Year	Study sample	Success	Survival	Extra-oral time	Follow up time (months)
Jang et al.	2013	5 incompletely formed molars	No complaints. Normal probing depth. No ankylosis or root resorption. Continued root development.	All transplants were present at the end of follow-up. 100% survival.	Immediate – 2 minutes.	24-90
Kim et al.	2005	163 third molars, 5 second molars, 12 premolars, 1 canine, and 1 impacted incisor.	81.9% classified as complete healing.	Nine transplants were extracted.	Immediate – 25 min.	2-60
Lee et al.	2001	22 undefined teeth	No direct conclusions on success.	No direct conclusions on survival.	3-17.5 minutes	NR
Lee et al.	2012	182 third molars (open – completely formed)	Root resorption in 1.6% of cases. Other complications not mentioned.	No direct conclusions on survival.	Immediate-25 min. Mean 7 minutes.	NR
Shabazian et al.	2013	Cases: 24 premolars	One case replacement resorption, One case apical infection	No teeth were extracted. 100% survival.	<1 min	12
		Controls: 24 premolars	Four cases ankylosis, Two cases progressive infection related resorption	Two teeth were extracted.91.7% survival.	3-10 min	12
Verweij et al.	2016	5 incompletely formed premolars	No direct conclusions on success.	No direct conclusions on survival.	15-45 seconds	NR

DISCUSSION

Autotransplantation is considered a valuable treatment option for tooth replacement [7, 16, 25]. The aim of this study was to provide an overview of papers reporting on '3D autotransplantation' with a replica of the donor tooth and assess the outcomes of these studies. All types of human studies (case reports, in vitro, clinical studies) were included. Information that was extracted from the studies included the accuracy of the fabrication of a replica of a donor tooth, accuracy of the planning of 3D autotransplantation, the extra-alveolar time of the donor tooth, the number of fitting attempts, and the success and survival rates of 3D autotransplantation.

The regarded clinically acceptable accuracy of a model tooth is a measurement difference of less than 0.25 mm [22, 25]. Several printing techniques were assessed in the studies that were included in this review, namely solid-based FDM, PolyJet modeling, SLA, and Simplant Pro 12.1. All assessed printing techniques were found to produce models well within the clinically acceptable accuracy level. This shows the advanced level of accuracy that the current 3D printing techniques offer and show that different printing techniques can produce in a replica that is practically identical to the donor tooth.

The accuracy of the replica and accuracy of the planning of the autotransplantation procedure were within the clinically required surgical accuracy. Nevertheless, the planned position versus the actual position of the transplant differed more than 1 millimeter in several cases. Because autotransplantation is often part of orthodontic treatment, usually an optimal position and angulation of the transplant can however easily be obtained by the orthodontist. If orthodontics is not part of the treatment plan after autotransplantation, an acceptable position of the transplant is usually achieved either directly after autotransplantation, or after small corrections through natural migration of the teeth.

It has been hypothesized that the use of a replica of the donor tooth results in an easier autotransplantation procedure with a higher chance of success [7]. One important factor that induced this hypothesis is the fact that a replica of the donor tooth enables preparation of the neo-alveolus before extraction of the donor tooth and thereby reduces the risk of iatrogenic damage to the donor tooth by reducing the extra-alveolar time and manipulation of the donor tooth (including the number of fitting attempts). Andreasen et al. [9] observed normal periodontal healing when the extra-oral time did not exceed 18 minutes. The clinical studies reported a mean extra-oral time ranging from 0 to 7 minutes, if no extra-oral endodontic treatment was performed. The case reports all reported an extra-oral time of less than three minutes, so well below 18 minutes.

The reported success and survival rates for autotransplantation with an individualized surgical guide range from 80.0% to 91.1% and 95.5% to 100%, respectively [15, 33-35]. Published success and survival rates for classic autotransplantation range from 79% to 100% and 57% to 100% respectively [12, 13]. Although all studies that were included in this review supported the hypothesis that 3D autotransplantation could increase the chance of successful autotransplantation, no conclusive high-level evidence was present in the current literature. No randomized controlled trails were available. One case-control study that was included in this review showed higher success and survival rates in the 3D autotransplantation group compared to classic techniques. The study nevertheless also had a high risk of bias, especially since it obtained the results for the classic autotransplantation technique using historical controls [34].

Several advantages of the 3D autotransplantation procedure are generally mentioned. Preparing the neo-alveolus with a 3D-printed replica of the donor tooth means that the extra-alveolar time of the donor tooth is generally very short. Multiple fitting attempts during the placement of the donor tooth can be avoided because the size and shape of the neo-alveolus are sufficiently prepared with the replica. A surgical template for the preparation of the neo-alveolus can therefore help better maintain the periodontal ligament cells of the donor tooth. Furthermore, the use of a replica results in an easy procedure because the placement, location, and angulation of the transplant can be determined with the replica without the risk of damaging the transplant. This results in a more controlled, easier autotransplantation procedure.

Instead of using an individualized replica of the donor tooth, it is also possible to use prefabricated archetype templates. Two studies by Ashkenazi et al. [1] and Day et al. [11] reported on the production of these archetype series of metal templates, based on the most prevalent sizes of teeth, after analyzing respectively 84 and 125 extracted teeth. In their procedure, the surgeon estimates the size of the donor tooth after extraction and picks a corresponding metal template to prepare the neo-alveolus. These templates evidently offer some of the same benefits that a replica provides. Advantages of a template versus a replica furthermore include the lack of CBCT-analysis and thus reduction of ionizing radiation. Standard archetype templates will furthermore probably involve lower costs, because the metal templates can be re-used after sterilization as opposed to an individually designed replica of the donor tooth. Templates however lack the precision that a replica of the donor tooth offers. The exact size and shape of the neo-alveolus is compromised, and therefore an increase of extra-alveolar time and fitting attempts can be expected. This could subsequently compromise the success rate of the procedure. We therefore prefer the use of an individually designed replica of the donor tooth.

Quality assessment of the included studies showed that the level of evidence was low and risk of bias was high in all available studies. Because there are no uniform reporting forms or quality assessment tools available for case reports and in vitro studies, respectively the CARE guidelines and CRIS guidelines were used to assess the quality of these studies. The level of evidence with regard to the clinical situation is evidently low for these types of studies. The MINORS checklist and Cochrane tool for assessing bias furthermore showed that also in the clinical studies the risk of bias was high. Therefore, no high level of evidence was available on this subject. This indicates the need for well-designed studies, preferably randomized controlled trials, to assess the advantages of 3D autotransplantation and compare this novel technique with classic autotransplantation.

CONCLUSION

The classic autotransplantation procedure has proven to be a good treatment option for tooth replacement in carefully selected patients. By producing an individualized tooth model using CBCT and rapid prototyping, the risk of iatrogenic injury of the periodontal ligament of the donor tooth could be reduced. This can contribute to higher success and survival rates. In the current studies, however, the level of evidence was generally low and the risk of bias was high. Therefore, more research is necessary to conclusively determine the advantages and outcomes of '3D autotransplantation' with a replica of the donor tooth.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge J.W. Schoones, information specialist of the Waleus Liberary of the Leiden University Medical Center, for his help in the construction of the search strategy and subsequent database with eligible papers.

REFERENCES

1. Ashkenazi M, Levin L: **Metal tooth-like surgical templates for tooth autotransplantation in adolescents**. *Dental traumatology : official publication of International Association for Dental Traumatology* 2014, **30**(1):81-84.
2. Czochrowska EM, Stenvik A, Bjercke B, Zachrisson BU: **Outcome of tooth transplantation: survival and success rates 17-41 years posttreatment**. *Am J Orthod Dentofacial Orthop* 2002, **121**(2):110-119; quiz 193.
3. Almpani K, Papageorgiou SN, Papadopoulos MA: **Autotransplantation of teeth in**

humans: a systematic review and meta-analysis. *Clin Oral Investig* 2015, **19**(6):1157-1179.

4. Mensink G, van Merkesteyn R: **Autotransplantation of premolars**. *British dental journal* 2010, **208**(3):109-111.
5. Kvint S, Lindsten R, Magnusson A, Nilsson P, Bjerklin K: **Autotransplantation of teeth in 215 patients. A follow-up study**. *The Angle orthodontist* 2010, **80**(3):446-451.
6. Yan Q, Li B, Long X: **Immediate autotransplantation of mandibular third molar in China**. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics* 2010, **110**(4):436-440.
7. Verweij JP, Moin DA, Mensink G, Nijkamp P, Wismeijer D, van Merkesteyn JP: **Autotransplantation of Premolars With a 3-Dimensional Printed Titanium Replica of the Donor Tooth Functioning as a Surgical Guide: Proof of Concept**. *J Oral Maxillofac Surg* 2016.
8. Kristerson L: **Autotransplantation of human premolars. A clinical and radiographic study of 100 teeth**. *International journal of oral surgery* 1985, **14**(2):200-213.
9. Andreasen JO, Paulsen HU, Yu Z, Bayer T, Schwartz O: **A long-term study of 370 autotransplanted premolars. Part II. Tooth survival and pulp healing subsequent to transplantation**. *European journal of orthodontics* 1990, **12**(1):14-24.
10. Paulsen HU, Andreasen JO, Schwartz O: **Pulp and periodontal healing, root development and root resorption subsequent to transplantation and orthodontic rotation: a long-term study of autotransplanted premolars**. *Am J Orthod Dentofacial Orthop* 1995, **108**(6):630-640.
11. Day PF, Lewis BR, Spencer RJ, Barber SK, Duggal M: **The design and development of surgical templates for premolar transplants in adolescents**. *International endodontic journal* 2012, **45**(11):1042-1052.
12. Cross D, El-Angbawi A, McLaughlin P, Keightley A, Brocklebank L, Whitters J, McKerlie R, Cross L, Welbury R: **Developments in autotransplantation of teeth**. *The surgeon : journal of the Royal Colleges of Surgeons of Edinburgh and Ireland* 2013, **11**(1):49-55.
13. Tsukiboshi M: **Autotransplantation of teeth: requirements for predictable success**. *Dental traumatology : official publication of International Association for Dental Traumatology* 2002, **18**(4):157-180.
14. Aslan BI, Ucuncu N, Dogan A: **Long-term follow-up of a patient with multiple congenitally missing teeth treated with autotransplantation and orthodontics**. *Angle Orthod* 2010, **80**(2):396-404.
15. Kim E, Jung JY, Cha IH, Kum KY, Lee SJ: **Evaluation of the prognosis and causes of failure in 182 cases of autogenous tooth transplantation**. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005, **100**(1):112-119.
16. Anssari MD, Derksen W, Verweij J, van MR, Wismeijer D: **A Novel Approach for Computer-Assisted Template-Guided Autotransplantation of Teeth With Custom 3D**

Designed/Printed Surgical Tooling. An Ex Vivo Proof of Concept. *J Oral Maxillofac Surg* 2016.

17. Moher D, Liberati A, Tetzlaff J, Altman DG: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement**. *Int J Surg* 2010, **8**(5):336-341.
18. Krithikadatta J, Gopikrishna V, Datta M: **CRIS Guidelines (Checklist for Reporting In-vitro Studies): A concept note on the need for standardized guidelines for improving quality and transparency in reporting in-vitro studies in experimental dental research**. *J Conserv Dent* 2014, **17**(4):301-304.
19. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D: **The CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development**. *Glob Adv Health Med* 2013, **2**(5):38-43.
20. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J: **Methodological index for non-randomized studies (minors): development and validation of a new instrument.** *ANZ J Surg* 2003, **73**(9):712-716.
21. Higgins JPT GS: **Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from** http://www.handbook.cochrane.org.; 2011.
22. Lee KY, Cho JW, Chang NY, Chae JM, Kang KH, Kim SC, Cho JH: **Accuracy of three-dimensional printing for manufacturing replica teeth**. *Korean J Orthod* 2015, **45**(5):217-225.
23. Shahbazian M, Jacobs R, Wyatt J, Willems G, Pattijn V, Dhoore E, VAN LC, Vinckier F: **Accuracy and surgical feasibility of a CBCT-based stereolithographic surgical guide aiding autotransplantation of teeth: in vitro validation**. *J Oral Rehabil* 2010, **37**(11):854-859.
24. Lee SJ, Kim E: **Minimizing the extra-oral time in autogeneous tooth transplantation: use of computer-aided rapid prototyping (CARP) as a duplicate model tooth**. *RestorDent Endod* 2012, **37**(3):136-141.
25. Khalil W, EzEldeen M, Van De Casteele E, Shaheen E, Sun Y, Shahbazian M, Olszewski R, Politis C, Jacobs R: **Validation of cone beam computed tomography-based tooth printing using different three-dimensional printing technologies**. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2016, **121**(3):307-315.
26. Harzer W, Ruger D, Tausche E: **Autotransplantation of first premolar to replace a maxillary incisor - 3D-volume tomography for evaluation of the periodontal space**. *Dent Traumatol* 2009, **25**(2):233-237.
27. Keightley AJ, Cross DL, McKerlie RA, Brocklebank L: **Autotransplantation of an immature premolar, with the aid of cone beam CT and computer-aided prototyping: a case report**. *Dent Traumatol* 2010, **26**(2):195-199.
28. Pang NS, Choi YK, Kim KD, Park W: **Autotransplantation of an ectopic impacted premolar with sinus lift and allogenic bone graft**. *Int EndodJ* 2011, **44**(10):967-975.

29. van der Meer WJ, Jansma J, Delli K, Livas C: **Computer-aided planning and surgical guiding system fabrication in premolar autotransplantation: a 12-month follow up**. *Dent Traumatol* 2015.
30. Vandekar M, Fadia D, Vaid NR, Doshi V: **Rapid Prototyping as an Adjunct for Autotransplantation of Impacted Teeth in the Esthetic Zone**. *J Clin Orthod* 2015, **49**(11):711-715.
31. Lee Y, Chang SW, Perinpanayagam H, Yoo YJ, Lim SM, Oh SR, Gu Y, Ahn SJ, Kum KY: **Autotransplantation of mesiodens for missing maxillary lateral incisor with cone-beam CT-fabricated model and orthodontics**. *Int EndodJ* 2014, **47**(9):896-904.
32. Park YS, Jung MH, Shon WJ: **Autotransplantion of a displaced mandibular second premolar to its normal position**. *Am J OrthodDentofacial Orthop* 2013, **143**(2):274-280.
33. Jang JH, Lee SJ, Kim E: **Autotransplantation of immature third molars using a computer-aided rapid prototyping model: a report of 4 cases**. *J Endod* 2013, **39**(11):1461-1466.
34. Shahbazian M, Jacobs R, Wyatt J, Denys D, Lambrichts I, Vinckier F, Willems G: **Validation of the cone beam computed tomography-based stereolithographic surgical guide aiding autotransplantation of teeth: clinical case-control study**. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2013, **115**(5):667-675.
35. Lee SJ, Jung IY, Lee CY, Choi SY, Kum KY: **Clinical application of computer-aided rapid prototyping for tooth transplantation**. *Dent Traumatol* 2001, **17**(3):114-119.

APPENDICES

Appendix 1: Search strategy

((“Tooth”[mesh] OR “Tooth”[tw] OR “teeth”[tw] OR Bicuspid*[tw] OR Cuspid*[tw] OR Incisor*[tw] OR Molar*[tw] OR premolar*[tw]) AND (“Transplantation, Autologous”[Mesh] OR Auto-transplant*[tw] OR auto-graft*[tw] OR Autotransplant*[tw] OR autograft*[tw] OR Autologous Transplant*[tw] OR “Autografts”[mesh] OR (autogen*[tw] AND transplant*[tw])) AND (Surgical guid*[tw] OR “Guide”[tw] OR “Guides”[tw] OR “Guiding”[tw] OR “Surgical template”[tw] OR “Surgical templates”[tw] OR “Template”[tw] OR “Templates”[tw] OR “Replica”[tw] OR “Replica Techniques”[Mesh] OR replica*[tw] OR “Rapid prototyping”[tw] OR “Prototyping”[tw] OR prototyp*[tw] OR “Reverse-engineered”[tw] OR Reverse-engineer*[tw] OR “Stereolithographic”[tw] OR Stereolithograph*[tw] OR Stereo-lithograph*[tw] OR Cone beam compute*[tw] OR “Cone beam”[tw] OR “Cone-beam”[tw] OR CBCT*[tw] OR “3-dimensional”[tw] OR “Three-dimensional”[tw] OR (“3D”[tw] NOT 3d molar*[ti]) OR “3 D”[tw] OR “three D”[tw] OR “Computer-aided rapid prototyping”[tw]

OR "Computer-aided"[tw] OR "CARP"[tw] OR "duplicate"[tw] OR duplicate model*[tw] OR duplicate model*[tw] OR model tooth*[tw] OR model teeth*[tw] OR replica graft*[tw] OR "cad cam"[tw] OR "cad/cam"[tw] OR cad model*[tw] OR cam model*[tw] OR computer aided plan*[tw] OR "tooth-like"[tw] OR tooth like*[tw] OR immature teeth*[tw] OR immature tooth*[tw] OR "Cone-Beam Computed Tomography"[mesh] OR "Computer-Aided Design"[mesh] OR "Imaging, Three-Dimensional"[mesh] OR "Computer Simulation"[mesh] OR systematic[sb] OR "Surgery, Computer-Assisted"[mesh] OR "Dimensional Measurement Accuracy"[mesh]))

Appendix 2: Quality assessment according to guidelines for in vitro studies, case reports, and clinical studies.

CRIS guidelines for in vitro studies

Study and reference	Sample size calculation	Meaningful difference between groups	Sample preparation and handling	Allocation sequence	Randomization and blinding	Statistical analysis
Anssari Moin et al. (2016)	N	N	Y	N	N	N
Ashkenazi et al. (2014)	N	N	Y	N	N	N
Day et al. (2012)	N	N	Y	N	N	Y
Khalil et al. (2016)	N	N	Y	N	N	Y
Lee et al. (2015)	N	N	Y	N	Y	Y
Lee et al. (2012)	N	N	Y	N	Y	Y
Shabaian et al. (2010)	N	N	Y	N	N	Y

Y = yes, N = no

CARE guidelines for case reports

Study and reference	1	2	3	4	5	6	7	8	9	10	11	12	13
Harzer et al. (2009)	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N
Honda et al. (2010)	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N
Keightley et al. (2010)	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N
Lee et al. (2014)	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N
Pang et al. (2011)	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N
Park et al. (2014)	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N
Park et al. (2013)	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Vander Meer et al. (2015)	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N
Verderkar et al (2015)	N	N	N	Y	Y	Y	N	Y	Y	Y	Y	N	N

Y = yes, N = no

MINORS criteria for clinical studies

Study	1	2	3	4	5	6	7	8	9	10	11	12	Total
Jang et al. (2013)	2	0	0	2	1	2	2	0	/	/	/	/	9
Kim et al. (2005)	2	2	2	2	1	2	1	2	/	/	/	/	14
Lee et al. (2001)	2	1	2	2	1	2	2	0	/	/	/	/	12
Lee et al. (2012)	2	2	1	2	1	0	2	0	/	/	/	/	10
Shahbazian et al. (2013)	2	2	2	2	0	2	2	0	2	2	2	1	19
Verweij et al. (2016)	2	2	2	2	0	0	2	0	/	/	/	/	10

0=not reported, 1=reported but inadequate, 2=reported and adequate. Maximum scores for observational and clinical studies are respectively 16 and 24 points.

Appendix 3: Risk of bias of clinical studies according to the Cochrane tool.

Author	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Estimatated potential risk of bias
Jang et al. (2013)	No	No	No	No	No	Unclear	Unclear	High
Kim et al. (2005)	No	No	No	No	No	Unclear	Unclear	High
Lee et al. (2001)	No	No	No	No	No	Unclear	Unclear	High
Lee et al. (2012)	No	No	No	No	No	Unclear	Unclear	High
Shabazian et al. (2013)	No	Yes	No	Yes	No	No	Unclear	High
Verweij et al. (2016)	No	No	No	No	No	Unclear	Unclear	High

CHAPTER 11

A NOVEL APPROACH FOR COMPUTER-ASSISTED TEMPLATE-GUIDED AUTOTRANSPLANTATION OF TEETH WITH CUSTOM 3D DESIGNED/PRINTED SURGICAL TOOLING. AN EX VIVO PROOF OF CONCEPT

Published as:

Anssari Moin D, Derksen W, Verweij JP, van Merkesteyn R, Wismeijer D

A Novel Approach for Computer-Assisted Template-Guided Autotransplantation of Teeth With Custom 3D Designed/Printed Surgical Tooling. An Ex Vivo Proof of Concept

Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons 2016, 74(5):895-902

ABSTRACT

Purpose
The aim of this study was to introduce a novel method in performing an accurate autotransplantation with computer-assisted guided templates and congregating custom designed surgical tooling and to test the feasibility and accuracy of this method *ex vivo*.

Methods
A partially edentulous human mandibular cadaver was scanned with a cone-beam computed tomography (CBCT) system and intra-oral scan system. The 3D data of this cadaver was imported in specialized software and used to analyze the region of the recipient site and the donor tooth was selected. Subsequently, congruent to the donor tooth, custom surgical tooling and surgical guided template was designed and 3D printed. The guided osteotomy was performed and the donor tooth transplanted. To evaluate the planned donor tooth position in comparison to the transplanted donor tooth position the mandible with implant was scanned again with the CBCT system and software matching was applied to measure the accuracy of the procedure.

Results
The angular deflection of the transplanted donor tooth with the planned donor tooth position was 3.1°. When comparing the 3D positions of the shoulder there is a deviation of 1.25 mm and an apical deviation of 0.89 mm.

Conclusion
With the use of currently available technology it is very well feasible to accurately plan and create in a virtual simulation a donor tooth position with congruent custom surgical tooling and to transfer this to a clinical setting with 3D

INTRODUCTION

Autotransplantation is a relatively longstanding technique with a well-recognized application for replacing congenitally missing teeth or teeth lost due to trauma. Considering the alveolar and maxillo-facial bone growth of paediatric or adolescent patients autotransplantation can be a preferred treatment option rather than an implant [1, 2]. Autotransplantation has numerous advantages since it is an autogenic biological approach for tooth replacement [1-3].

Research has shown variable long-term results dependent on various factors [4, 5]. Three most critical factors negatively influencing survival of the donor tooth can be stated [6-10]; 1. Damage to the periodontal ligament (PDL) of the donor tooth by trying to fit in the donor tooth at the recipient sites' neo-alveolus. 2. Extended extra-alveolar time traumatizing viable PDL cells on the donor tooth. 3. Distance between the neo-alveolus and the root of the donor tooth. The commonly used classical method for minimizing the negative influences of the previously mentioned aspects is challenging and relies mostly on the surgeons' expertise and intuitive flair for adapting the recipient site to be as congruent as possible with the root of the donor tooth in the least achievable amount of tries and time [10].

Within recent developments in the field of Cone-Beam Computed Tomography (CBCT) and additive manufacturing technology different approaches have been suggested to plan, create custom donor tooth templates and surgical guides to assist and increase survival of the autotransplant by minimising the extra-alveolar time, amount of try-ins and reduce neo-alveolus-to-donor tooth distance [11-13].

Hypothetically, it would seem more ideal to precisely virtually plan, execute and transfer the planning to the clinical situation in order to have a neo-alveolus accurately congruent to the donor tooth at the desired pre-defined recipient location.

The aim of this study was to introduce a novel method in performing an accurate autotransplantation with computer-assisted guided templates and congregating custom designed surgical tooling and to test the feasibility and accuracy of this method *ex vivo*.

MATERIALS AND METHODS

3D data acquisition: optical scan and radiographic scan

One partially edentulous human mandibular cadaver not identified by age, sex or ethnic group was obtained from the functional anatomy department. The cadaver was sectioned at the mid-ramus level and fixed in formalin and stored. A declaration was obtained from the functional anatomy department to use this human remains material for research purposes. Full-arch intra-oral scan of this mandible was made using the 3M™ TrueDefinition Scanner

(3M ESPE, Seefeld, Germany). The scan files were exported and stored as standardized triangulation language (STL) file format.
The mandible was scanned with the 3D Accuitomo 170 CBCT system (AccuiTomo 170, 90kVp, 5mA, 30.8Sec, 10x10cm Field of View (FoV), Morita inc., Japan). The scan position was with the occlusal plane parallel to the floor following the manufacturer's recommendations. The scan volumes were exported in DICOM 3 format.
For measurement of accuracy and precision of the donor tooth position after insertion into the neo-alveolus, the mandible with the donor tooth transplanted was again scanned with the 3D Accuitomo 170 CBCT system using the exact same scan settings and stored as with the previous scan.

Virtual Surgical planning and 3D model design of the custom implant and tooling
The DICOM files were imported into the CoDiagnostiX 9 software (Dental Wings GmbH, Ghemnitz, Germany). The CBCT scan was analysed, donor tooth selected and for the recipients' region of a missing tooth the anatomical and functional parameters measured (fig. 1a). Based on this analysis it was decided that tooth 33 would serve as the donor tooth. With the method previously described by Anssari Moin et. al tooth 33 was segmented and stored a STL file [14]. STL files of the intra-oral scan and donor tooth were imported in CoDiagnostiX 9 software and the donor tooth position at the recipient site determined (fig. 1b an 1c). Subsequently, the intra-oral surface scan and CBCT scan were superimposed and a tooth-supported template based on the donor tooth position was designed (fig 1c and 1d). Within the template a precalculated space was preserved for fitting of a to be custom designed sleeve aimed at guiding the drills and osteotome during neo-alveotomy. The guided template design was stored as a STL file.

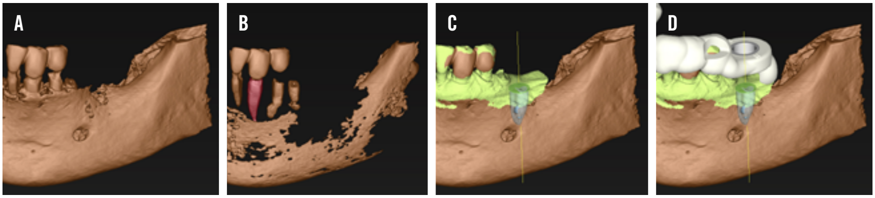


Figure 1. Virtual 3D planning of the donor tooth position.

Accordingly, based on the premeditated positions of the donor tooth and sleeve a set of surgical tools was custom designed with SolidWorks 2015 SP3 software (Dassault Systèmes, Vélizy, France) to create a neo-alveolus congruent to the root shape of the donor tooth and stored as STL files (fig. 2). The custom designed tools consisted of a sleeve, 4 drills with increments in diameter and a final (analogous to the) root of the donor tooth shaped osteotome (fig. 2). All osteotomy tools consisted of a cutting/shaping segment and a guiding segment corresponding to the sleeve design.

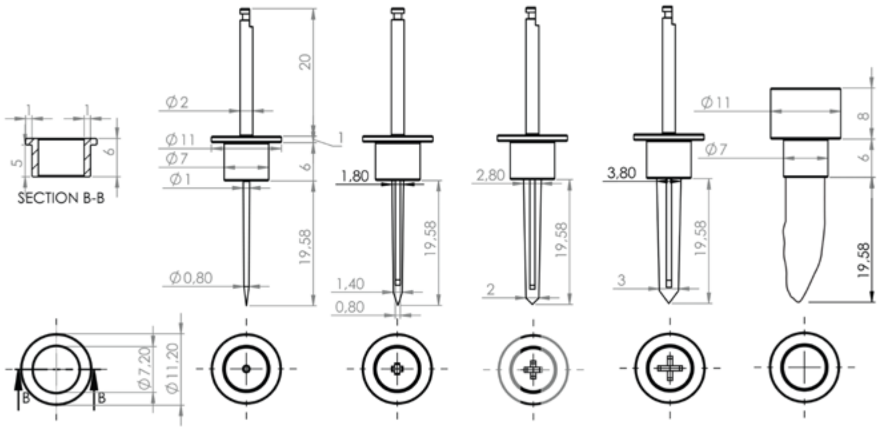


Figure 2. Schematic drawing of the guided neo-alveotomy sequence. The drills and osteotome have identical guiding segments corresponding to the sleeve diameter with predetermined depth and position. Measurements in millimetres.

3D printing of the guided template, surgical tools and implant

Additive manufacturing techniques were used to fabricate the guided template, surgical tools and implant from their respective STL files (fig. 3).

The guided template was 3D printed through a steriolithography procedure in which a vat of liquid photopolymer an ultraviolet laser cures layers of 25 μm thickness to build the requested design (Implantec GmbH, Amstetten, Germany).

The custom designed surgical instruments were 3D printed through a proprietary high-end Selective Laser Melting (SLM) machine equipped with an Ytterbium-fiber laser (30μm thickness) in a biocompatible titanium-alloy grade 5 by LayerWise (3Dsystems, Leuven, Belgium).

Figure 3. The 3D printed surgical tooling from left to right: guided template, sleeve, 4 drills and osteotome.

Sugical procedure

The guided template with the sleeve incorporated was positioned and optically checked through designed fenestrations for good fit (fig. 4a). Subsequently, guided osteotomy was performed at the recipient site by drilling and the shaping finished by gentle tapping with a hammer on the custom printed osteotome (fig. 4b and 4c). Rotational osteotome position was controlled through exact alignment of the '=' sign on the guided template with the guiding groove on the osteotome (fig. 4c). Thereafter, the donor tooth was carefully removed and transplanted into the neo-alveolus at the recipient site (fig. 4d and 4e). Stability of the donor tooth was achieved and checked by palpation.

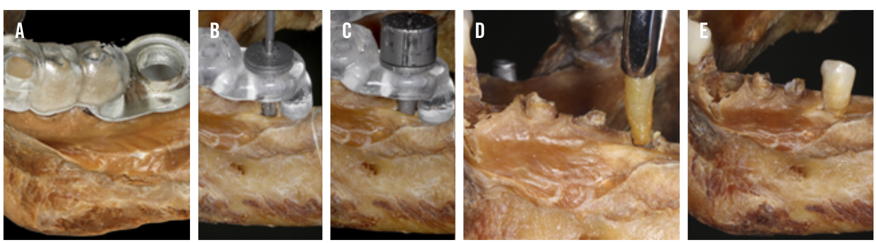


Figure 4. Clinical process of the template guided autotransplantation. Fitting of the guided template (a), guided alveotomy by drilling (b), guided shaping of the neo-alveolus by osteotome (c) and transplantation of the donor tooth in the neo-alveolus (d, e).

Evaluation of the pre-operative planning of donor tooth position and post-operative donor tooth position

The pre- and post-operative DICOM files were imported in CoDiagnostiX 9 software for analysis of accuracy of the donor tooth position. The incorporated Evaluation tool in the software was used to match the pre-operatively planned donor tooth position and the post-operative donor tooth position. The following deviations were measured (fig. 5): 3D offset (a), position of the apex of the tooth (b) and angulation of the tooth (α).

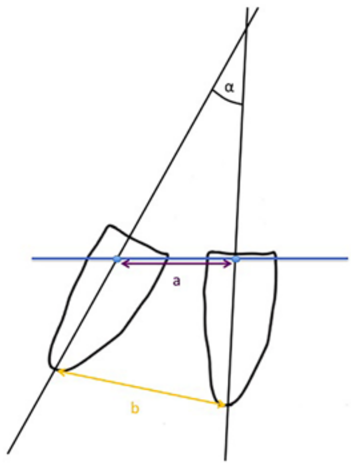


Figure 5. Matching procedure for measuring accuracy of the transplanted donor tooth position versus the planned donor tooth position. The following parameters were used: a = 3D offset, b = position of the apex of the tooth and α = angulation of the tooth.

RESULTS

Good stabilization and fitting of the surgical guide was achieved and checked through the designed fenestrations (fig 4a). The drilling process was uneventful however the final shaping with the guided osteotome was relatively complicated and required constant adjustment since there is rotational freedom in the transversal plane (fig 4c). During removal of the donor tooth the crown of tooth fractured due to brittleness of formaldehyde stored state of the mandible. The crown was temporarily glued for visual purposes only (fig. 4d and 4e). The angular deflection (α) with the planned donor tooth position was 3.1° (fig 6). When comparing the bodily 3D positions (a) there is a deviation of 1.25 mm resulting in an apical deviation (b) of 0.89 mm (fig. 6)

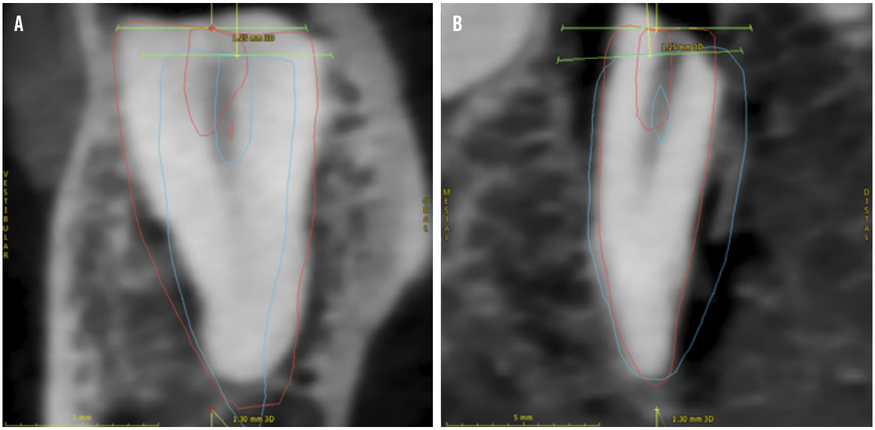


Figure 6. Evaluation of the matching procedure. Frontal (a) and sagittal (b) cross-sections.

DISCUSSION

This experiment was performed as a first step towards guided autotransplantation with a computer-assisted guided template and congregating custom designed surgical tooling. With the combined use of 3D data acquisition with Cone-beam CT and intra-oral scanning technology, virtual 3D planning software, 3D design software and high-end 3D printing technology it was possible to transplant through guided surgery, with relative accuracy, a donor tooth into the neo-alveolus.

Pre-operatively fabricated tooth replicas and stereolithographic guides as a means for simplification and increase of success rate for autotransplantation have been proposed in the literature [13, 15, 16]. A study by Shahbazian *et al.* suggested benefits in the CBCT planned surgical guide by reducing the surgical time and being a less invasive technique, causing fewer failures than a conventional approach [13]. In this study the CBCT based surgical template served as a guide for the drilling procedure and subsequently the final shaping of the neo-alveolus was performed by free-hand preparation. However the question surfaces to what extent accurately aligning the bony wall of the neo-alveolus, as proposed in this research, will influence the clinical outcome.

Within the field of implant dentistry computer-assisted template guided insertion of implants has been extensively researched. Methods described in these studies for increasing accuracy of the guided implant placement are to a certain extent applicable for this approach as well. Comparing accuracy data of this study with the currently available data on accuracy of computer-aided implant placement is incongruous since these are based on conventional screw-type implants inserted by means of conventional surgical tools. Nonetheless, for a general comparison, it is noteworthy to appreciate that the result of this particular experiment lies within the range of positional and angular deviations for guided implant placement described in a meta-analysis by Van Assche et. al [17]. This meta-analysis revealed mean deviations for entry-point and apex of 0.99 mm (range 0 - 6.5 mm), 1.24 mm (range 0 - 6.9 mm), respectively, and a mean angular deflection of 3.81° (range 0 - 24.9°).

Final shaping of the neo-alveolus is performed by a custom printed osteotome in the shape of the donor tooth's root and is of critical importance in accurate fit of the donor tooth. The shape of this specific osteotome is designed through a combination process of segmentation of the root of the donor tooth and CAD reprocessing/designing the osteotome. Previous research has shown that 3D surface reconstructions based on CBCT segmentations can vary from the actual shape resulting in an over- or underestimation of the actual root shape depending on selected threshold values and CBCT scan settings [15, 18, 19]. Especially towards the more apical areas segmentation of the root becomes increasingly difficult due to the increase in bone-mass [18].

This novel approach has hypothesized benefits on the prognosis of the transplanted tooth. Reduction of the extra-oral time and amount of try-ins of the transplanted tooth have well-known positive effects on the vitality of the periodontal ligament [5-7, 10]. Furthermore, as a general rule it has been stated that a smaller distance between neo-alveolus and donor tooth will provide a more favorable revascularization of the periodontal ligament and apex. However with this approach a near exact donor root shaped alveolus can be created instead of a closely contoured recipient site, subsequently raising questions concerning optimal bone-to-root distances for autotransplantation as stated previously. Nonetheless, more evidence on many levels of this guided autotransplantation approach is needed. Future studies can be focused on evaluating the accuracy, fine tuning the process and assessing success of this guided autotransplantation with custom 3D designed/printed surgical tooling.

REFERENCES

1. Sharma AB, Vargervik K: **Using implants for the growing child**. *Journal of the California Dental Association* 2006, **34**(9):719-724.
2. Zachrisson BU, Stenvik A, Haanaes HR: **Management of missing maxillary anterior teeth with emphasis on autotransplantation**. *American journal of orthodontics and dentofacial orthopedics: official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 2004, **126**(3):284-288.

3. Park JH, Tai K, Hayashi D: **Tooth autotransplantation as a treatment option: a review**. *The Journal of clinical pediatric dentistry* 2010, **35**(2):129-135.
4. Czochrowska EM, Stenvik A, Bjercke B, Zachrisson BU: **Outcome of tooth transplantation: survival and success rates 17-41 years posttreatment**. *American journal of orthodontics and dentofacial orthopedics: official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 2002, **121**(2):110-119; quiz 193.
5. Mensink G, van Merkesteyn R: **Autotransplantation of premolars**. *British dental journal* 2010, **208**(3):109-111.
6. Tsukiboshi M: **Autotransplantation of teeth: requirements for predictable success**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2002, **18**(4):157-180.
7. Hupp JG, Mesaros SV, Aukhil I, Trope M: **Periodontal ligament vitality and histologic healing of teeth stored for extended periods before transplantation**. *Endodontics & dental traumatology* 1998, **14**(2):79-83.
8. Andreasen JO: **Interrelation between alveolar bone and periodontal ligament repair after replantation of mature permanent incisors in monkeys**. *Journal of periodontal research* 1981, **16**(2):228-235.
9. Nethander G: **Oral restoration with fixed partial dentures on transplanted abutment teeth**. *The International journal of prosthodontics* 1995, **8**(6):517-526.
10. Schwartz O, Bergmann P, Klausen B: **Autotransplantation of human teeth. A life-table analysis of prognostic factors**. *International journal of oral surgery* 1985, **14**(3):245-258.
11. Keightley AJ, Cross DL, McKerlie RA, Brocklebank L: **Autotransplantation of an immature premolar, with the aid of cone beam CT and computer-aided prototyping: a case report**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2010, **26**(2):195-199.
12. Lee SJ, Jung IY, Lee CY, Choi SY, Kum KY: **Clinical application of computer-aided rapid prototyping for tooth transplantation**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2001, **17**(3):114-119.
13. Shahbazian M, Jacobs R, Wyatt J, Denys D, Lambrichts I, Vinckier F, Willems G: **Validation of the cone beam computed tomography-based stereolithographic surgical guide aiding autotransplantation of teeth: clinical case-control study**. *Oral surgery, oral medicine, oral pathology and oral radiology* 2013, **115**(5):667-675.
14. Anssari Moin D, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2011.
15. Shahbazian M, Jacobs R, Wyatt J, Willems G, Pattijn V, Dhoore E, C VANL, Vinckier F: **Accuracy and surgical feasibility of a CBCT-based stereolithographic surgical**

guide aiding autotransplantation of teeth: in vitro validation. *Journal of oral rehabilitation* 2010, **37**(11):854-859.

16. Park JM, Tatad JC, Landayan ME, Heo SJ, Kim SJ: **Optimizing third molar autotransplantation: applications of reverse-engineered surgical templates and rapid prototyping of three-dimensional teeth**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2014, **72**(9):1653-1659.
17. Van Assche N, Vercruyssen M, Coucke W, Teughels W, Jacobs R, Quirynen M: **Accuracy of computer-aided implant placement**. *Clinical oral implants research* 2012, **23 Suppl 6**:112-123.
18. Anssari Moin D, Hassan B, Parsa A, Mercelis P, Wismeijer D: **Accuracy of preemptively constructed, Cone Beam CT-, and CAD/CAM technology-based, individual Root Analogue Implant technique: An in vitro pilot investigation**. *Clinical oral implants research* 2012.
19. Al-Rawi B, Hassan B, Vandenberge B, Jacobs R: **Accuracy assessment of three-dimensional surface reconstructions of teeth from cone beam computed tomography scans**. *Journal of oral rehabilitation* 2010, **37**(5):352-358.

CHAPTER 12

ACCURACY OF COMPUTER-ASSISTED TEMPLATE-GUIDED AUTOTRANSPLANTATION OF TEETH WITH CUSTOM 3D DESIGNED/PRINTED SURGICAL TOOLING. A CADAVERIC STUDY

Published as:

Anssari Moin D, Verweij JP, Waars H, van Merkesteyn R, Wismeijer D

Accuracy of Computer-Assisted Template-Guided Autotransplantation of Teeth With Custom Three-Dimensional Designed/Printed Surgical Tooling: A Cadaveric Study

Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons 2017, 75(5):925 e921-925 e927

ABSTRACT

Purpose
The aim of this cadaveric study was to assess the accuracy of the computer-assisted template-guided autotransplantation of teeth with custom 3D designed/printed surgical tooling.

Methods
Ten partially edentulous human mandibular cadavers were scanned with a cone-beam computed tomography (CBCT) system and intra-oral scan system. The 3D data of these cadavers were imported in specialized software and used to analyze the region of the recipient sites and the donor teeth were selected. Subsequently, congruent to the donor teeth, custom surgical tooling and surgical guided templates were designed and 3D printed. The guided osteotomies were performed and the donor teeth transplanted. To evaluate the planned donor teeth positions in comparison to the transplanted donor teeth positions the mandibles were scanned again with the CBCT system and software matching was applied to measure the accuracy of the procedure.

Results
The mean angular deflection of the transplanted donor teeth with the planned donor teeth positions was 5.6° (5.4 SD). When comparing the 3D positions of the shoulders there is a mean deviation of 3.15 mm (1.16 SD) and a mean apical deviation of 2.61 mm (0.78 SD).

Conclusion
The described method of computer-assisted template-guided autotransplantation of teeth with custom 3D designed/printed surgical tooling could potentially provide a relatively accurate alternative for the currently available treatment approaches. Further research should focus on improving the accuracy of this technique and evaluating clinical success and advantages of this method.

INTRODUCTION

The use of Cone-Beam Computed Tomography (CBCT) and additive manufacturing technology is becoming more widespread in the field of autotransplantation of teeth [1]. As technology advances more digitalized approaches can be introduced to aid and simplify the autotransplantation techniques [1-3]. Recently we proposed a novel approach for computer-assisted template-guided autotransplantation of teeth with custom 3D designed/printed surgical tooling [4]. The currently proposed technique further develops the 3D planning of autotransplantation, providing a full digital workflow, virtual planning of the autotransplantation and full template guided preparation of the neo-alveolus. Our pilot study suggested that it was feasible to precisely execute and translate the digital autotransplantation planning to the clinical situation in order to have a neo-alveolus congruent to the donor tooth at the desired pre-defined recipient location prior to extraction of the donor tooth. Reported benefits of this method include a reduced extra-oral time of the transplant, reduced amount of fitting procedures, and adequate bone-to-root distance resulting in a more favourable prognosis of the donor tooth. However, all the steps in the process of digitalizing clinical information, transferring the digital planning, and executing the autotransplantation can lead to cumulative geometrical errors. This can consequently result in a discrepancy of the planned donor tooth position and the actual donor tooth position.
Our proposed method is recommended for flapless procedures and the donor tooth position (neo-alveolus) is planned with consideration of critical anatomical structures. Therefore, it is of great importance to identify the possible deviations of planned donor tooth position versus the realized donor tooth position. The aim of this cadaveric study was therefore to assess the accuracy of the computer-assisted template-guided autotransplantation of teeth with custom 3D designed/printed surgical tooling.

MATERIALS AND METHODS

The 3D data acquisition, virtual surgical planning, and 3D printing of the surgical tooling were previously described by Anssari Moin et al [4]. The 3D autotransplantation surgical procedure was previously described by Verweij et al [1]. We built on these methods.

3D data acquisition: optical scan and radiographic scan

Ten partially edentulous human mandibular cadavers, not identified by age, sex or ethnic group, were obtained from the functional anatomy department of the University of Amsterdam, The Netherlands. The cadavers were sectioned at the mid-ramus level, fixed in formalin and stored. A declaration was obtained from the functional anatomy

department (University of Amsterdam, The Netherlands) to use the human remains for research purposes.
Full-arch intra-oral scans of the mandibles were made using the 3M™ TrueDefinition Scanner (3M ESPE, Seefeld, Germany). The scan files were exported and stored as standardized triangulation language (STL) file format.
The mandibles were scanned with the 3D Accuitomo 170 CBCT system. They were positioned in the scanner with the occlusal plane parallel to the floor following the manufacturer's recommendations. The scan volumes were exported in DICOM 3 format.
For measurement of the accuracy and precision of the donor tooth position after insertion into the neo-alveolus, the mandibles with the transplanted donor teeth were again scanned with the 3D Accuitomo 170 CBCT system using the exact same scan settings and stored as the previous scan.

Virtual surgical planning and 3D model design of the custom tooling

The DICOM files were imported into the CoDiagnostiX 9 software (Dental Wings GmbH, Ghemnitz, Germany). The CBCT scans were analysed for the recipients' region of a missing tooth and the anatomical and functional parameters were measured (fig. 1a). Based on this analysis, donor teeth were selected for autotransplantation.
Donor teeth were scanned, segmented and stored as STL files using the method that was previously described by Anssari Moin et. al [5]. STL files of the intra-oral scan and donor teeth were imported in CoDiagnostiX 9 software and the donor teeth positions at the recipient sites determined (fig. 1b an 1c). Subsequently, the intra-oral surface scans and CBCT scans were superimposed and tooth-supported templates based on the donor teeth positions were designed (fig 1c and 1d). Within the templates a precalculated space was preserved for fitting of to be custom designed sleeves aimed at guiding the drills and osteotomes during the preparation of neo-alveolus. The guided template designs were stored as STL files.

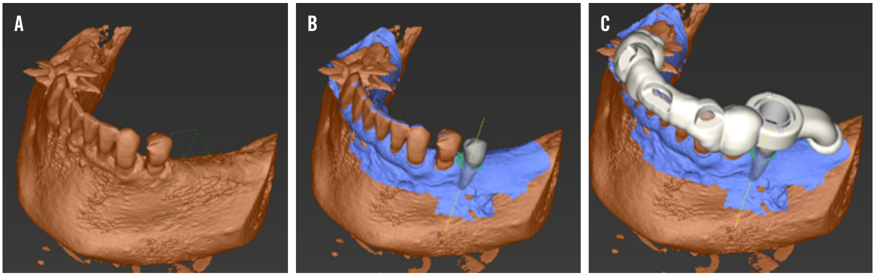


Figure 1. Virtual 3D planning of the donor tooth position for cadaver No. 1. Anatomical and functional parameters analysis of the recipient site (a). Planning of the donor tooth position (b). Design of the tooth-supported template (c).

Based on the planned positions of the donor teeth and sleeves, sets of surgical tools were custom designed with SolidWorks 2015 SP3 software (Dassault Systèmes, Vélizy, France). These individually designed surgical tools were designed according to the exact size and shape of the neo-alveolus, congruent to the root shapes of the donor teeth. Designs were stored as STL files (fig. 2). For each procedure, the custom designed tools consisted of a sleeve, 5 drills with increments in diameter and a final (analogous to the) root of the donor tooth shaped osteotome (fig. 2). All osteotomy tools consisted of a cutting/shaping segment and a guiding segment corresponding to the sleeve design. Within the guiding segments of the osteotomes and sleeves corresponding patrix-matrix grooves were designed to prevent rotational freedom of the osteotome (fig. 2). Subsequently, the guided templates were redesigned with a specific indentation to ensure correct positioning of the sleeves (fig .2).

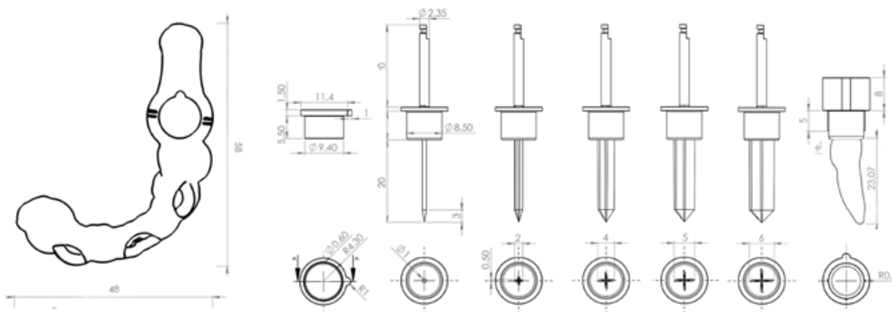


Figure 2. Schematic drawing of the guided neo-alveotomy sequence for cadaver No. 1. The drills and osteotome have identical guiding segments corresponding to the sleeve diameter with predetermined depth and position. Measurements in millimetres.

3D printing of the guided template and surgical tools

Additive manufacturing techniques were used to fabricate the guided templates, surgical tools from their respective STL files (fig. 3). The guided templates were 3D printed through a stereolithography procedure in which an ultraviolet laser cures layers of 25 μm thickness in a vat of liquid photopolymer to build the requested design (Dental Printing Services B.V., Doetinchem, Netherlands).

The custom designed surgical instruments were 3D printed through a proprietary Selective Laser Melting (SLM) machine equipped with an Ytterbium-fiber laser (30 μm thickness) in a Cobalt-Chrome alloy (Mundo 3D Printing, Kootwijkerbroek, Netherlands).

Figure 3. The 3D printed surgical tooling for cadaver No. 1. From left to right: guided template, sleeve, 5 drills and osteotome.

Surgical procedure

The guided templates with the sleeves were positioned and optically checked through designed fenestrations for good fit (fig. 4b). Subsequently, guided osteotomies were performed at the recipient sites by drilling and the shaping finished by gentle tapping with a hammer on the custom printed osteotomes (fig. 4c). Subsequently, the donor tooth was carefully removed and transplanted into the neo-alveolus at the recipient site (fig. 4d and 4e). Stability of the donor tooth was achieved and checked by palpation (fig. 4e).

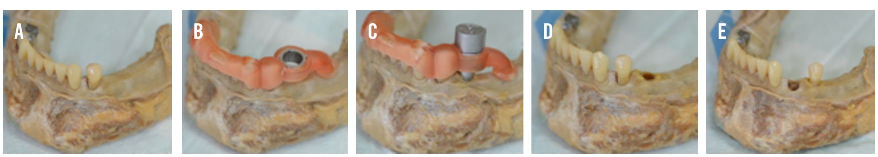


Figure 4. Clinical process of the template guided autotransplantation of cadaver No. 1. Pre-operative situation (a), fitting of the guided template (b), guided shaping of the neo-alveolus by osteotome (c) and transplantation of the donor tooth in the neo-alveolus (d, e).

Evaluation of the pre-operative planning of donor tooth position and post-operative actual donor tooth position

The pre- and post-operative DICOM files were imported in CoDiagnostiX 9 software for analysis of accuracy of the donor tooth position. The incorporated 'Evaluation tool' in the software was used to match the pre-operatively planned donor tooth position and the post-operative donor tooth position. The following evaluative parameters were measured (fig. 5): 3D offset (a), position of the apex of the tooth (b) and angulation of the tooth (α). Descriptive statistical analysis was used to calculate the mean and standard deviation (SD) of the evaluation parameters.

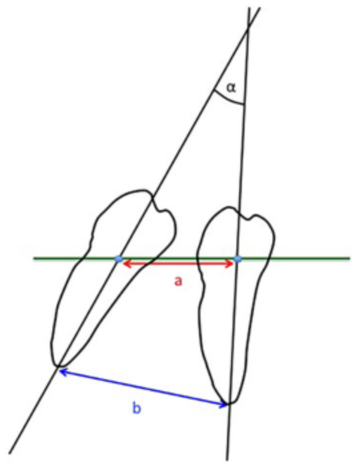


Figure 5. Matching procedure for measuring accuracy of the transplanted donor tooth position versus the planned donor tooth position. The following parameters were used: a = 3D offset, b = position of the apex of the tooth and α = angulation of the tooth.

RESULTS

In ten human cadaveric mandibles 3D autotransplantation with custom designed surgical tooling was performed. Within these mandibles, 4 incisors, 2 canines, and 4 premolars were transplanted to another location within the same mandible.
Good stabilization and fitting of the surgical guides was achieved and checked through the designed fenestrations for all cadavers (fig 4b). The drilling process was uneventful, however after the final shaping with the guided osteotome the surgical guides for cadavers No. 1, 2 and 9 showed fractures (fig 4c). Most probably the pressure produced by tapping on the osteotome caused these fractures. The donor teeth were successfully transplanted into their respective neo-alveoli. In one try the donor teeth were fitted and there was no need for additional fitting attempts or adjustments to the neo-alveoli.
Comparing the superimposed images of the pre-operatively planned donor teeth positions and the post-operative donor teeth positions reveals a mean angular deflection (α) of 5.6° (5.4 SD). When comparing the bodily 3D positions (a) there is a mean deviation of 3.15 mm (1.16 SD) resulting in a mean apical deviation (b) of 2.61 mm (0.78 SD). The data are summarized in Table 1.

	Transplant/tooth number	3D offset (mm)	Position of the apex (mm)	Angulation (°)
Cadaver 1	34	1.26	2.20	3.4
Cadaver 2	32	3.93	3.19	1.6
Cadaver 3	44	4.74	4.08	0.7
Cadaver 4	44	2.61	1.33	1.1
Cadaver 5	31	4.31	2.66	10.7
Cadaver 6	33	4.53	3.27	15.7
Cadaver 7	32	2.92	2.72	11.1
Cadaver 8	31	2.50	2.30	2.8
Cadaver 9	44	2.08	1.83	0.8
Cadaver 10	33	2.62	2.53	7.7
Mean (SD)		3.15 (1.16)	2.61 (0.78)	5.6 (5.4)

Table 1. Measurements of accuracy parameters of the transplanted donor tooth position versus the planned donor tooth position. The following parameters were measured: 3D offset (mm), position of the apex of the tooth (mm) and angulation of the tooth (°).

DISCUSSION

Autotransplantation is an established technique for the replacement of missing teeth. It has numerous advantages over titanium implant placement, since autotransplantation provides an autogenic biological method for tooth replacement [6-8]. Nonetheless, autotransplantation as a treatment option is often dismissed because the commonly used classical method is challenging and relies mostly on the surgeons' skill and expertise [9-11]. Several important factors in the success of autotransplantation include the cautious extraction of the donor tooth, the extra-oral time, the number of fittings with the donor tooth during preparation of the neo-alveolus, and the adaptation of the neo-alveolus to the root of the donor tooth. Different methods, incorporating 3D imaging and 3D printing technologies, have been proposed to update and facilitate the surgical technique in order to achieve higher success rates after autotransplantation [1-3]. However, these methods still require free-hand preparation of the donor site. This paper introduces a guided technique for autotransplantation. Advantages supporting the idea of this approach encompass minimally invasive flapless surgery, accurately pre-defined donor tooth position and easy surgical handling [4]. As seen in the results the guided preparation of the neo-alveolus went uneventful and in one try the donor teeth fitted into their neo-alveoli. Measurement of accuracy of guided implant systems is a complicated process, partially influenced by the applied software and by the correct threshold-based superimposition of the pre- and post-operative 3D images. As it has been shown in the research by van Ascche et al., angular deviation parameter is the most accurate parameter since this measurement is not dependent on the length of the implant [12, 13]. Especially, the horizontal deviation parameter (b) needs to be interpreted with caution in this research because the apex of the tooth is not necessarily in line with the axis of the tooth as it is with dental implants. After autotransplantation with individually designed and printed surgical guides, the current study found a mean apical deviation of 2.61 mm (0.78 SD) and mean angular deviation of 5.6 degrees (5.4 SD) when comparing the planned position and actual position of the transplanted teeth. These values are within the generally accepted ranges that are reported for surgical guides in implant treatment [14, 15]. Nevertheless, these deviations can be clinically relevant in autotransplantation. The current technique should therefore be improved to enable more accurate planning of autotransplantation.

As mentioned hitherto, the accuracy of any methodology is the result of cumulative errors from translating clinical information to digital data and vice versa. Multiple aspects influence the accuracy of this method, ranging from 3D data acquisition quality (CBCT and 3D intra-oral optical scan) to the amount of pre-calculated tolerance of the surgical tools and 3D printing accuracy. In our approach, we printed the surgical templates in an acrylic resin and used a metal guiding sleeve to ensure stable alignment of the guiding segments. However, the potential of 2 errors can be eliminated when the surgical guide would be designed as a sleeveless construct and printed in a metal alloy [12, 13]. Therefore, the pre-calculated tolerance of sleeve fitting in the surgical guide and potential of surgical guide fracture/bending could be marginalized and accuracy might be improved further. Moreover, in the current study all the teeth were transplanted into an edentulous part of the mandible without distal dental support of the guided templates. This could cause bending or tilting of the guide, subsequently causing an angular deviation (and apical deviation) of the transplant. Using the surgical guide with stable (dentulous) support on both sides of a diastema would probably result in a more accurate outcome [15]. This suggests that the current findings are an underestimation of the accuracy of the technique in the clinical setting.

In conclusion, within the limits of this cadaveric study, it has been demonstrated that the described method of computer-assisted template-guided autotransplantation of teeth with custom 3D designed/printed surgical tooling could potentially provide a relatively accurate alternative for the currently available treatment approaches. Further research should focus on further improving the accuracy of this technique and evaluating clinical success and advantages of this method.

REFERENCES

1. Verweij JP, Moin DA, Mensink G, Nijkamp P, Wismeijer D, van Merkesteyn JP: **Autotransplantation of Premolars With a 3-Dimensional Printed Titanium Replica of the Donor Tooth Functioning as a Surgical Guide: Proof of Concept**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2016, **74**(6):1114-1119.
2. Shahbazian M, Jacobs R, Wyatt J, Denys D, Lambrichts I, Vinckier F, Willems G: **Validation of the cone beam computed tomography-based stereolithographic surgical guide aiding autotransplantation of teeth: clinical case-control study**. *Oral surgery, oral medicine, oral pathology and oral radiology* 2013, **115**(5):667-675.
3. Lee SJ, Jung IY, Lee CY, Choi SY, Kum KY: **Clinical application of computer-aided rapid prototyping for tooth transplantation**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2001, **17**(3):114-119.
4. Anssari Moin D, Derksen W, Verweij JP, van Merkesteyn R, Wismeijer D: **A Novel Approach for Computer-Assisted Template-Guided Autotransplantation of Teeth With Custom 3D Designed/Printed Surgical Tooling. An Ex Vivo Proof of Concept**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2016, **74**(5):895-902.
5. Anssari Moin D, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2011.
6. Sharma AB, Vargervik K: **Using implants for the growing child**. *Journal of the California Dental Association* 2006, **34**(9):719-724.
7. Zachrisson BU, Stenvik A, Haanaes HR: **Management of missing maxillary anterior teeth with emphasis on autotransplantation**. *American journal of orthodontics and dentofacial orthopedics: official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 2004, **126**(3):284-288.
8. Park JH, Tai K, Hayashi D: **Tooth autotransplantation as a treatment option: a review**. *The Journal of clinical pediatric dentistry* 2010, **35**(2):129-135.
9. Tsukiboshi M: **Autotransplantation of teeth: requirements for predictable success**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2002, **18**(4):157-180.

10. Hupp JG, Mesaros SV, Aukhil I, Trope M: **Periodontal ligament vitality and histologic healing of teeth stored for extended periods before transplantation**. *Endodontics & dental traumatology* 1998, **14**(2):79-83.
11. Schwartz O, Bergmann P, Klausen B: **Autotransplantation of human teeth. A life-table analysis of prognostic factors**. *International journal of oral surgery* 1985, **14**(3):245-258.
12. Van Assche N, Quirynen M: **Tolerance within a surgical guide**. *Clinical oral implants research* 2010, **21**(4):455-458.
13. Koop R, Vercruyssen M, Vermeulen K, Quirynen M: **Tolerance within the sleeve inserts of different surgical guides for guided implant surgery**. *Clinical oral implants research* 2013, **24**(6):630-634.
14. Tahmaseb A, Wismeijer D, Coucke W, Derksen W: **Computer technology applications in surgical implant dentistry: a systematic review**. *The International journal of oral & maxillofacial implants* 2014, **29 Suppl**:25-42.
15. Van Assche N, Vercruyssen M, Coucke W, Teughels W, Jacobs R, Quirynen M: **Accuracy of computer-aided implant placement**. *Clinical oral implants research* 2012, **23 Suppl 6**:112-123.

CHAPTER 13

A CASE REPORT OF A COMPUTER-ASSISTED TEMPLATE-GUIDED AUTOTRANSPLANTATION OF A THIRD MOLAR WITH CUSTOM 3D DESIGNED/ PRINTED SURGICAL TOOLING

Accepted for publication as:

Anssari Moin D, Verweij JP, Wismeijer D,
van Merkesteyn JPR

Computer-assisted template-guided autotransplantation of a third molar with custom 3D designed/printed surgical tooling: A case report

Journal of Oral and Maxillofacial Surgery 2017

ABSTRACT

This report describes a case of a 20-year old male receiving autotransplantation of the left maxillary third molar to replace a congenitally missing left mandibular second premolar with the use of a computer-assisted template-guide and custom 3D designed/printed surgical tooling.

The autotransplantation method was based on a virtual 3D planning through a digital workflow. Subsequently, the 3D planning of the autotransplantation with congregating custom designed surgical tools is translated via 3D printing.

During the surgical procedure, the template-guided osteotomy of the neo-alveolus was prepared with the use of the 3D printed surgical tools. In one try and with an extra-alveolar time of 20 seconds the donor tooth was transplanted. The use of this method resulted in a predictable and easy procedure, with the following measured deviations: 3D offset (2.59 mm), position of the apex of the tooth (3.88 mm) and angulation of the tooth (6.0°). Postoperative follow-up showed a physiological integration of the transplanted tooth and successful outcome.

In conclusion, the use of a computer-assisted template-guide and custom 3D designed/printed surgical tooling facilitates an easy and predictable procedure for guided preparation of the neo-alveolus for autotransplantation. Reducing the extra-alveolar time and preparing a neo-alveolus prior to donor tooth removal when using this technique minimize the risk of damage to the periodontal ligament cells of the donor tooth facilitating a successful outcome.

INTRODUCTION

Autotransplantation is a relatively longstanding technique with a well-recognized application for replacing congenitally missing teeth or teeth lost due to trauma [1, 2]. Considering the alveolar and maxillo-facial bone growth of paediatric or adolescent patients autotransplantation can be a preferred treatment option rather than an implant [3, 4]. Autotransplantation has numerous advantages since it is an autogenic biological approach for tooth replacement [1-4].

Within recent developments in the field of Cone-Beam Computed Tomography (CBCT) and additive manufacturing technology different approaches have been suggested to plan, create custom donor tooth templates and surgical guides to assist and increase survival of the autotransplant by minimising the extra-alveolar time, amount of try-ins and reduce neo-alveolus-to-donor tooth distance [5-8]. Our studies suggested a feasible method to precisely execute and translate the digital autotransplantation planning to the clinical situation in order to have a neo-alveolus congruent to the donor tooth at the desired pre-defined recipient location prior to extraction of the donor tooth [5, 9].

This report describes the autotransplantation of the left maxillary third molar to replace the left mandibular first molar with the use of a computer-assisted template-guide and custom 3D designed/printed surgical tooling. The autotransplantation procedure based on a virtual 3D planning thru a digital workflow is specifically described.

REPORT OF A CASE

A 20-year old male was referred for orthognathic surgery and surgical tooth replacement at the hiatus of the region of the left mandibular second premolar to the department of oral and maxillofacial surgery at the Leiden University Medical Center. The patient was diagnosed with class II mandibular retrognathia and disruptive development of lower left mandible causing an asymmetrical malocclusion (inversed Spee curve), angulated impaction of the left second and third mandibular molars and a congenitally missing left second premolar causing a hiatus at the location of the left second mandibular premolar (fig. 1 and 2). A thorough analysis of the treatment options and prognosis in concurrence with a multi-disciplinary team was implemented. The proposed treatment consisted of removal of the impacted left second and third mandibular molars and right maxillary third molar, repositioning and advancement of the mandible via bilateral sagittal split osteotomy (BSSO), autotransplantation of the upper left third molar into the hiatus at the second mandibular premolar and, pre- and post-operative orthodontic regulation. The autotransplantation was planned to be performed with the aid of computer-assisted template-guided neo-alveolus preparation with custom 3D designed/printed surgical tooling.

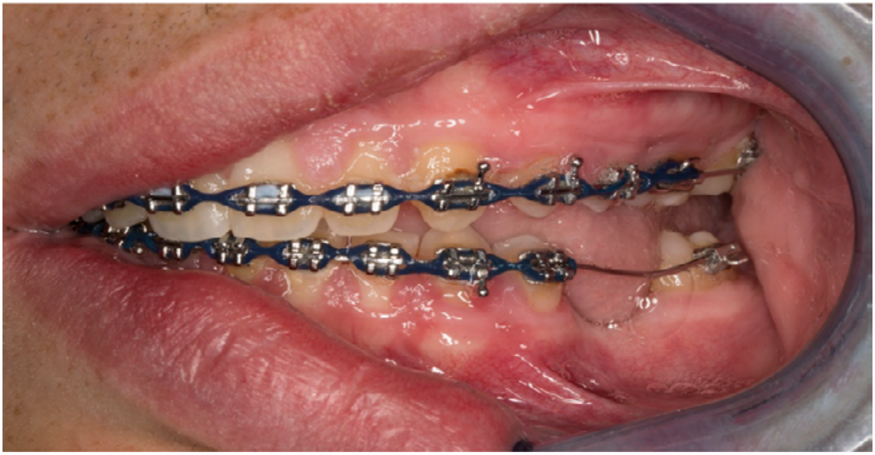


Figure 1. Pre-operative clinical oblique view on the intra-oral condition.

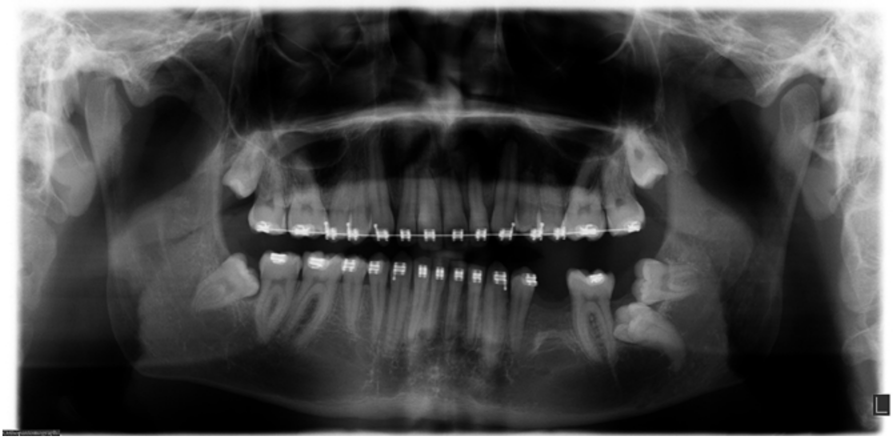


Figure 2. Pre-operative panoramic radiograph of the condition.

Pre-operative 3D planning and 3D printing of the surgical tools

The 3D data acquisition, virtual surgical planning, and 3D printing of the surgical tooling were previously described by Anssari Moin et al [5]. The 3D autotransplantation surgical procedure was previously described by Verweij et al [8]. We built on these methods. A CBCT-scan (Promax®3D Max, Planmeca, Helsinki, Finland) was performed for the preoperative planning of the BSSO and autotransplantation procedure. The DICOM files of this CBCT scan were imported into the CoDiagnostiX 9 software (Dental Wings GmbH, Ghemnitz, Germany). The CBCT scans was analysed for the recipients' region of the hiatus and the anatomical and functional parameters were measured. Based on this analysis, the left maxillary third molar was found to be an ideal donor tooth selected for autotransplantation. Subsequently, the donor tooth was segmented and stored as a standardized triangulation language (STL) file using the method that was previously described by Anssari Moin et. al [10].

Optical 3D scans from the stonecast of this patient were made using the 3M™ TrueDefinition Scanner (3M ESPE, Seefeld, Germany). The scan files were exported and stored as STL file format.

STL files of the optical 3D scan and donor tooth were imported in CoDiagnostiX 9 software and the donor tooth position at the recipient site determined (fig. 3a and b). Then, the optical 3D surface scan and CBCT scan were superimposed and a tooth-supported template based on the donor tooth position was designed (fig .3c). Within the template a precalculated space was preserved for fitting of to be custom designed guiding segments of the drills and osteotomes. The guided-template design was stored as a STL file.

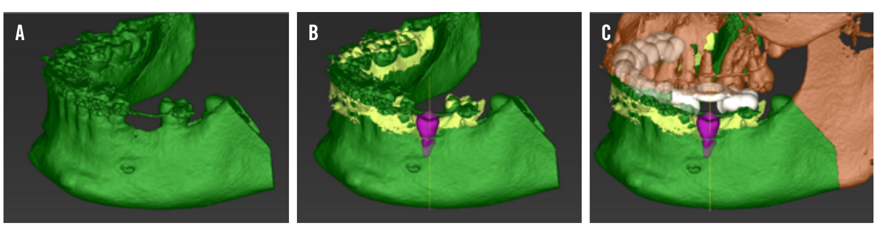


Figure 3. 3D surface reconstruction of the recipient site (a), virtually planned donor tooth position (b) and tooth-supported guided-template (c).

Based on the planned position of the donor tooth and guiding segment of the template, a set of surgical tools was custom designed with SolidWorks 2015 SP3 software (Dassault Systèmes, Vélizy, France). These individually designed surgical tools were designed according to the exact size and shape of the planned neo-alveolus, congruent to the root shape of the donor tooth. Designs were stored as STL files. For this procedure, the custom

designed tools consisted of a guided-template, 9 drills with increments of 1 mm in diameter, a root shaped osteotome and a replica of the selected tooth. Within the guiding segments of the osteotome and guided-template a corresponding patrix-matrix groove was designed to prevent rotational freedom of the osteotome.
Additive manufacturing technology was used to 3D print from the STL files the guided-template and the custom designed surgical instruments through a proprietary Selective Laser Melting (SLM) machine equipped with an Ytterbium-fiber laser (30 μm thickness) in a Cobalt-Chrome alloy (fig. 4) (Mundo 3D Printing, Kootwijkerbroek, Netherlands).

Figure 4. 3D printed surgical tools and guided-template for guided osteotomy at the recipient site.

The surgical procedure

Under general nasotracheal intubation anaesthesia, the mandibular third molars, the left second mandibular molar and the right maxillary third molar were extracted. Subsequently, through the BSSO the mandible was repositioned and the mandibular segments fixated with three bi-cortical screws on either side. Satisfactory occlusion was achieved.
For the autotransplantation the 3D printed guided-template was positioned and good stabilization and fit of the surgical guide was realized (fig. 5a). Then, the neo-alveolus was prepared using the custom 3D printed guided osteotomy tools (fig. 5b). Since the 3D printed donor tooth replica showed root divergence, minor free-hand final shaping of the neo-alveolus was performed and good fit of the replica was obtained. Subsequently, the donor tooth was extracted, while care was taken not to damage the cementum, periodontal ligament, and apex of the tooth. Comparison of the donor tooth copy and the

original tooth showed no differences with regard to the shape of the root and crown. The left maxillary third molar was placed in the prepared neo-alveolus at the hiatus of the left mandibular second premolar (fig. 5c). In one go an immediate good fit at the recipient site was achieved with an extra-alveolar time of 20 seconds. A suture was placed across the occlusal plane of the donor tooth to fix the transplanted tooth into place. Two weeks post-operatively an endodontic treatment was performed (fig. 6).

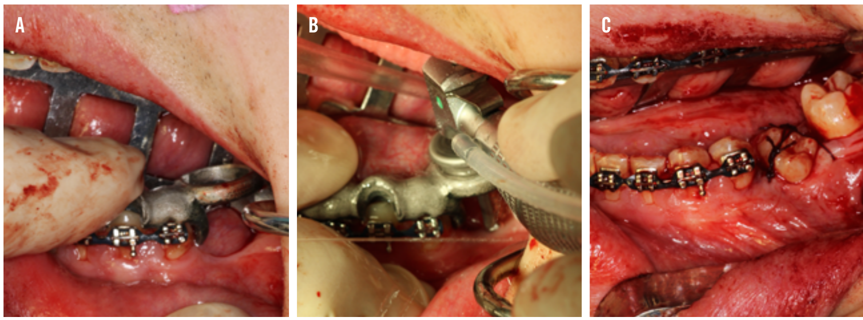


Figure 5. Clinical process of the template guided autotransplantation. Fitting of the guided template (a), guided alveotomy by drilling (b), and transplantation of the donor tooth in the neo-alveolus (c).

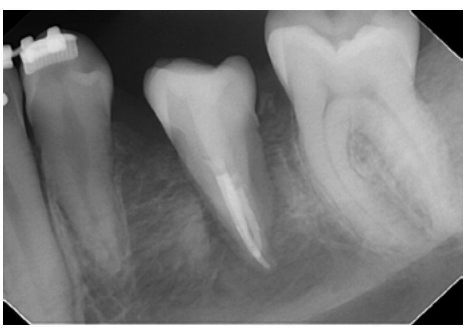


Figure 6. Endodontic treatment performed 2-weeks post-operatively.

Outcome

For postoperative evaluation directly after surgery a CBCT scan with exact same scan settings as the first CBCT scan was made. The pre- and post-operative DICOM files were subsequently imported in CoDiagnostiX 9 software for analysis of accuracy of the donor tooth position. The incorporated Evaluation tool in the software was used to match the pre-operatively planned donor tooth position and the post-operative donor tooth position (fig. 7). The following deviations were measured; a 3D offset of 2.59 mm, position of the apex of the tooth of 3.88 mm and angulation of the tooth of 6.0°.

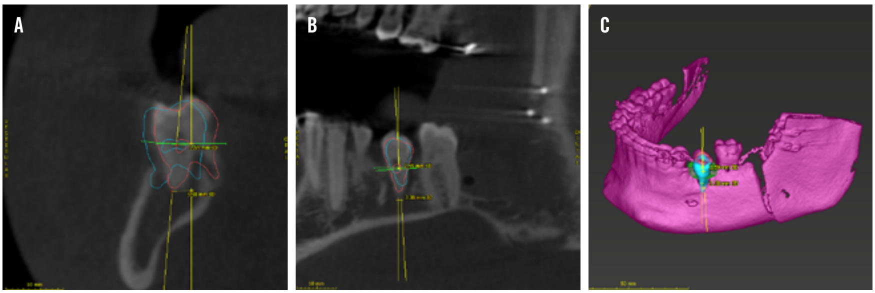


Figure 7. Evaluation of the matching procedure. Frontal (a), sagittal (b) cross-sections and 3D representation (c).

Clinical postoperative follow-up after 6 months showed a good physiological integration of the transplant (fig. 8). Normal physiological mobility was present without signs of ankylosis of the transplanted tooth. The transplanted tooth showed no pathology and good periodontal health. Final orthodontic regulation will be undertaken.

Figure 8. 6 months postoperative radiograph showing a good physiological integration of the transplant.

DISCUSSION

This report described an autotransplantation with the use of a computer-assisted guided-template and congregating custom designed surgical tooling. With the combined use of 3D data acquisition with Cone-beam CT and intra-oral scanning technology, virtual 3D planning software, 3D design software and high-end 3D printing technology it was possible to transplant through guided surgery, with relative accuracy, a donor tooth into the neo-alveolus.

The traditional autotransplantation techniques rely mostly on the surgeon's expertise to adapt the recipient site to be congruent with the donor tooth [11]. In the traditional approach the donor tooth is used as a template to prepare the neo-alveolus, resulting in multiple fitting attempts and an extended extra-alveolar time. This may have negative influences on the survival and success of the autotransplantation [11, 12]. Therefore, various techniques have been described as a means to simplify the autotransplantation procedure [5-8]. In several studies the use of CBCT-based prefabricated replica of the donor tooth to prepare the neo-alveolus was evaluated [6, 8]. In these studies it was reported that a more controlled and easier autotransplantation procedure, with a minimized extra-alveolar time and procedural time with use of 3D printed donor tooth replicas was possible [6, 8]. However, the use of 3D printed replicas still requires full-thickness flap elevation and free hand preparation of the neo-alveolus.

The applied method for autotransplantation in this report was built on 3D planning through a full digital workflow translated with 3D printing into a full template guided preparation of the neo-alveolus. Since this method is recommended for flapless procedures and the donor tooth position (neo-alveolus) is planned with consideration of critical anatomical structures, accuracy of this method is of critical importance. As realized in this study the deviations of pre-operatively planned donor tooth position and the post-operative donor tooth position were 2.59 mm for 3D offset, 3.88 mm for position of the apex of the tooth and 6.0° of angulation. These measurements seem to be within the range of a recent report on the accuracy of template-guided autotransplantation [9]. Multiple factors influence the process of digitalizing clinical information, transfer of digital planning, and execution of the autotransplantation resulting in a discrepancy of the planned donor tooth position. In this report the guiding segments of the osteotomy tools were only 3 mm in height. Subsequently, this minimal amount of friction from the guiding segments within the guided-template allowed for a certain amount of freedom in the horizontal plane. As seen on the evaluation figures (7a and b) this amount of freedom in the horizontal plane resulted in a donor tooth position mostly deviating in the horizontal plane and not in the vertical direction. Moreover, the selected tooth for transplantation was a left maxillary third molar with a complex root shape. Since the roots of this tooth were divergent minor freehand adjustments to the neo-alveolus were necessary after

guided preparation. This freehand preparation will also have had an influence on the realized donor tooth position versus the planned donor tooth position.
Whereas this technique requires 3D data acquisition via CBCT scanning instead of panoramic radiography and is therefore accompanied by more ionizing radiation, the use of this limited amount of additional radiation is in our opinion not superfluous and justified as it enables a predictable procedure with an increased chance of success. Especially in this case where the use of CBCT scanning was a necessity for the planning of the BSSO.

CONCLUSION

In conclusion, the use of a computer-assisted template-guide and custom 3D designed/printed surgical tooling facilitates an easy and predictable procedure for guided preparation of the neo-alveolus for autotransplantation. Reducing the extra-alveolar time and preparing a neo-alveolus prior to donor tooth removal when using this technique minimize the risk of damage to the periodontal ligament cells of the donor tooth facilitating a successful outcome.

REFERENCES

1. Andreasen JO, Paulsen HU, Yu Z, Ahlquist R, Bayer T, Schwartz O: **A long-term study of 370 autotransplanted premolars. Part I. Surgical procedures and standardized techniques for monitoring healing**. *European journal of orthodontics* 1990, **12**(1):3-13.
2. Park JH, Tai K, Hayashi D: **Tooth autotransplantation as a treatment option: a review**. *The Journal of clinical pediatric dentistry* 2010, **35**(2):129-135.
3. Zachrisson BU, Stenvik A, Haanaes HR: **Management of missing maxillary anterior teeth with emphasis on autotransplantation**. *American journal of orthodontics and dentofacial orthopedics: official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 2004, **126**(3):284-288.
4. Sharma AB, Vargervik K: **Using implants for the growing child**. *Journal of the California Dental Association* 2006, **34**(9):719-724.
5. Anssari Moin D, Derksen W, Verweij JP, van Merkesteyn R, Wismeijer D: **A Novel Approach for Computer-Assisted Template-Guided Autotransplantation of Teeth With Custom 3D Designed/Printed Surgical Tooling. An Ex Vivo Proof of Concept**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2016, **74**(5):895-902.
6. Lee SJ, Jung IY, Lee CY, Choi SY, Kum KY: **Clinical application of computer-aided**

rapid prototyping for tooth transplantation. *Dental traumatology: official publication of International Association for Dental Traumatology* 2001, **17**(3):114-119.
7. Shahbazian M, Jacobs R, Wyatt J, Denys D, Lambrichts I, Vinckier F, Willems G: **Validation of the cone beam computed tomography-based stereolithographic surgical guide aiding autotransplantation of teeth: clinical case-control study**. *Oral surgery, oral medicine, oral pathology and oral radiology* 2013, **115**(5):667-675.
8. Verweij JP, Moin DA, Mensink G, Nijkamp P, Wismeijer D, van Merkesteyn JP: **Autotransplantation of Premolars With a 3-Dimensional Printed Titanium Replica of the Donor Tooth Functioning as a Surgical Guide: Proof of Concept**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2016, **74**(6):1114-1119.
9. Anssari Moin D, Verweij JP, Waars H, van Merkesteyn R, Wismeijer D: **Accuracy of Computer-Assisted Template-Guided Autotransplantation of Teeth With Custom Three-Dimensional Designed/Printed Surgical Tooling: A Cadaveric Study**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2017.
10. Anssari Moin D, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2013, **24 Suppl A100**:25-27.
11. Schwartz O, Bergmann P, Klausen B: **Autotransplantation of human teeth. A life-table analysis of prognostic factors**. *International journal of oral surgery* 1985, **14**(3):245-258.
12. Tsukiboshi M: **Autotransplantation of teeth: requirements for predictable success**. *Dental traumatology: official publication of International Association for Dental Traumatology* 2002, **18**(4):157-180.

CHAPTER 14

SUMMARY AND CLOSING REMARK

The aim of this work was to explore the potential of innovative 3D printing applications in dentoalveolar surgery. The emphasis was principally on custom 3D printed surgical tools and implants for (guided) surgical tooth replacement. Thru the various studies the posed research aims were investigated.

In **chapters 2, 3, and 4** the feasibility and accuracy of 3D printing a custom root analogous implant or tooth replica based on 3D surface models obtained from volumetric CBCT data was assessed. The results showed it to be well feasible to reconstruct 3D surface models from CBCT data as relatively accurate 3D models for custom RAIs or tooth replicas. The question subsequently arose what the biomechanical effects of custom implant designs would be on alveolar bone stress. In **chapter 5** this research question was analyzed and within the limitations of the applied methodology, it was concluded that adding targeted press-fit geometry to the standard root analogue implant design, will most probably have a positive effect on stress distribution, lower concentration of bone stress and will provide a better primary stability. After gaining principal knowledge on the root analogue implant technique it was decided to perform a pilot study to evaluate the clinical implications of this approach. **Chapter 6** describes and evaluates the technical and clinical implications of the custom RAI technique with a commercially available system in the first pilot cases. The RAI approach allowed for uncomplicated immediate implant placement with potential esthetical and patient comfort benefits.

On the basis of the 3D technologies for custom RAI fabrication 3D replication of teeth for autotransplantation was established. **Chapters 8, 9 and 10** aimed to evaluate the use of this individual pre-operatively 3D-printed donor tooth replica during autotransplantation procedures and assess the advantages of this technique. It was concluded that the use of 3D printed analogues of the to be transplanted teeth reduces the risk of iatrogenic damage and the extra-alveolar time of the donor tooth is minimized facilitating a successful outcome.

With advancing 3D technologies and founded on the previously mentioned approaches, a method for computer-assisted template-guided custom (root) shaped osteotomy/neo-alveoletomy with custom 3D designed/printed surgical tooling was developed. In **chapters 7** this method was investigated for its feasibility and accuracy for custom 3D printed implants with good results. For autotransplantation the feasibility, accuracy and clinical application was studied in **chapters 11, 12 and 13**. The results show that translating the full-digital planning with 3D printing to the clinical setting to be an accurate method with easy surgical handling.

CLOSING REMARK

The applied 3D technologies in this manuscript through which a pre-operatively fully digitally planned tooth replacement can be realized with 3D printing show disruptive potential to transform current day practice towards a fulsomely patient-custom approach.

CHAPTER 15

LIST OF PUBLICATIONS

1. Irshad M, Scheres N, Anssari Moin D, Crielaard W, Loos BG, Wismeijer D, Laine ML: **Cytokine and matrix metalloproteinase expression in fibroblasts from peri-implantitis lesions in response to viable Porphyromonas gingivalis**. *Journal of periodontal research* 2013, **48**(5):647-656.
2. Galassi F, Kaman WE, Anssari Moin D, van der Horst J, Wismeijer D, Crielaard W, Laine ML, Veerman EC, Bikker FJ, Loos BG: **Comparing culture, real-time PCR and fluorescence resonance energy transfer technology for detection of Porphyromonas gingivalis in patients with or without peri-implant infections**. *Journal of periodontal research* 2012, **47**(5):616-625.
3. Jepsen K, Jepsen S, Laine ML, Anssari Moin D, Pilloni A, Zeza B, Sanz M, Ortiz-Vigon A, Roos-Jansaker AM, Renvert S: **Reconstruction of Peri-implant Osseous Defects: A Multicenter Randomized Trial**. *Journal of dental research* 2016, **95**(1):58-66.
4. Anssari Moin D, Derksen W, Verweij JP, van Merkesteyn R, Wismeijer D: **A Novel Approach for Computer-Assisted Template-Guided Autotransplantation of Teeth With Custom 3D Designed/Printed Surgical Tooling. An Ex Vivo Proof of Concept**. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2016, **74**(5):895-902.
5. Anssari Moin D, Derksen W, Waars H, Hassan B, Wismeijer D: **Computer-assisted template-guided custom-designed 3D-printed implant placement with custom-designed 3D-printed surgical tooling: an in-vitro proof of a novel concept**. *Clinical oral implants research* 2016.
6. Anssari Moin D, Hassan B, Parsa A, Mercelis P, Wismeijer D: **Accuracy of preemptively constructed, Cone Beam CT-, and CAD/CAM technology-based, individual Root Analogue Implant technique: An in vitro pilot investigation**. *Clinical oral implants research* 2012.
7. Anssari Moin D, Hassan B, Wismeijer D: **A Patient Specific Biomechanical Analysis of Custom Root Analogue Implant Designs on Alveolar Bone Stress: A Finite Element Study**. *International journal of dentistry* 2016, **2016**:8242535.
8. Anssari Moin D, Hassan B, Wismeijer D: **A novel approach for custom three-dimensional printing of a zirconia root analogue implant by digital light processing**. *Clinical oral implants research* 2016.
9. Anssari Moin D, Hassan B, Mercelis P, Wismeijer D: **Designing a novel dental root analogue implant using cone beam computed tomography and CAD/CAM technology**. *Clinical oral implants research* 2013, **24 Suppl A100**:25-27.
10. Verweij JP, Anssari Moin D, Mensink G, Wismeijer D, van Merkesteyn JP: **[Autotransplantation 2.0. Considerations, results and the latest techniques]**. *Nederlands tijdschrift voor tandheelkunde* 2016, **123**(7-8):348-353.
11. Verweij JP, Anssari Moin D, Mensink G, Nijkamp P, Wismeijer D, van Merkesteyn JP: **Autotransplantation of Premolars With a 3-Dimensional Printed Titanium Replica**

of the Donor Tooth Functioning as a Surgical Guide: Proof of Concept. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons* 2016, **74**(6):1114-1119.

12. Anssari Moin D, Hassan B, Wismeijer D; **Immediate non-submerged custom root analogue implants: proof of concept in the first 5 cases.** Accepted for publication in the *International Journal of Oral and Maxillofacial Implants* 2017
13. Anssari Moin D, Verweij JP, Wismeijer D, van Merkesteyn JPR; **Computer-assisted template-guided autotransplantation of a third molar with custom 3D designed/printed surgical tooling: A case report.** Submitted to the *Journal of Oral and Maxillofacical Surgery* 2017.
14. Anssari Moin D, Waars H, Wismeijer D; **Accuracy of computer-assisted template-guided custom designed 3D printed implants placement with custom designed 3D printed surgical tools. A cadaveric study.** Submitted to *Clinical Oral Implants Research* 2017
15. Verweij JP, Anssari Moin D, Wismeijer D, van Merkesteyn JPR; **Replacing heavily damaged teeth by third molar autotransplantation with the use of cone-beam computed tomography and rapid prototyping**. Accepted for publication in the *Journal of Oral and Maxillofacical Surgery* 2017.
16. Verweij JP, Jonkees F, Anssari Moin D, Wismeijer D, van Merkesteyn JPR; **Autotransplantation of teeth with the aid of computer-aided rapid prototyping using a 3D replica of the donor tooth: a systematic literature review.** Accepted for publication in the *International Journal of Oral and Maxillofacical Surgery* 2017.
17. Anssari Moin D, Verweij JP, Waars H, van Merkesteyn JPR, Wismeijer D; **Accuracy of computer-assisted template-guided autotransplantation of teeth with custom 3D designed/printed surgical tooling. A cadaveric study.** Epub ahead of print *Journal of Oral and Maxillofacical Surgery* 2017.

CHAPTER 16

ACKNOWLEDGEMENTS

Spending precious days, weekends and nights in dark obscure operating rooms on experiments with cadavers, dogs and humans, it is tempting for me to claim the sole credit of this work. However, as much as I am inclined to do so, I cannot ignore that the people around me whom gave me many heated discussions, disturbances of my solitary confinement, exchange of ideas and offerings of advice and have helped crafting this PhD dissertation. Therefore, this dissertation would not be complete without emphasizing my gratitude to the people who made its completion possible.

Promotor prof. dr. Wismeijer who gave me the opportunity to work on my crazy ideas and gave confidence, support and trust in this project.

Co-promotor dr. Hassan who taught me many dark secrets of the academic world and beyond.

Promotor prof. dr. van Merkesteyn who gave me the opportunity and trust to collaborate on the researches.

Prof. dr. Loos who gave me the opportunity and trust to work on the peri-impantitis research.

Dr. Laine who taught me a lot on scientific research. It is a great pleasure working with you; you are truly a wonderful human being.

Dr. Verweij, it is a great pleasure working with you. You are a great scientist.

The complete teams of the departments of Periodontology and Implantology for their support in everything.

I would like to thank all my friends who gave me the necessary distractions from my research.

Finally, my deep and sincere gratitude to my family for their continuous and unparalleled love, help and support.

Thank you all!

Doordat dit boek is gedrukt op CyclusOffset in plaats van een niet-recycled papier, is de milieu-impact verminderd met:

105 kg
afval

25 kg
CO²

252 km
afgelegd met een gemiddelde EU-wagen

2466 liter
water

328 kWh
energie

171 kg
hout