Investigational pilot clinical trial of a prototype optoelectronic computer-aided navigation device for dental implant surgery

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Abstract

Purpose: New digital technologies enable real-time 3-D guidance of dental implant surgery. The aim of this investigational clinical trial was to demonstrate safety and effectiveness of a prototype optoelectronic navigation device in comparison with the conventional method of planning and conducting dental implant surgery.

Materials and methods: Study participants with loss of up to four teeth were recruited from the pool of patients referred to the University of Toronto Graduate Prosthodontics clinic. The first 10 participants were allocated to either a conventional or CA-navigation implant surgery study arm in a small pilot randomized trial. The subsequent 10 participants received implants using the prototype CA-navigation device. All study participants were restored with crowns or fixed dental prostheses after 3 months healing, and monitored over the following 12 months. The primary outcome was to assess safety of the prototype CA-navigation device by documenting all surgical, biological and prosthetic adverse events and device-related complications. Secondary outcomes were to establish whether the dental implants were placed in positions suitable for prosthetic restoration by having 4 blinded investigators independently assessing deidentified clinical photographs and radiographs. Further secondary outcomes were to assess the surgeons' perception of ease of use of the prototype CA-navigation device by use of a questionnaire and to measure implant performance clinically and radiographically after one year.

Results: No surgical, biological or prosthetic adverse events were experienced while using the prototype CA-navigation device. All implants (n=21) were positioned satisfactory. The qualitative evaluation by the two oral surgeons was generally positive, although ergonomic challenges were identified. All study participants were examined after one year (n= 20 patients, 41 implants) and there were no implant loss. Peri-implant bone loss was less than 1mm and pocket depths less than 2mm for all implants. Generalization of the findings is limited by a small study sample.

Conclusions: Ergonomic challenges persist with optoelectronic CA-navigation devices. Clinicians should carefully consider these and other potentially critical issues in patient care.

Introduction

The ingenious innovation to combine three-dimensional (3-D) computed tomographic radiography with treatment planning software has facilitated the placement of dental implants with great accuracy[1]. New digital technologies now make possible 3-D guidance in real-time during the actual surgical intervention, termed computer-aided (CA-)navigation[2,3].

In late 2010, a manufacturer of image-guided surgery and medical image processing solutions (Claron Technology Inc., later renamed ClaroNav Inc., Toronto, Ontario, Canada) partnered with the University of Toronto with an intention to develop a CA-navigation device for dental implant surgery. The core components were to be their optoelectronic cameras and proprietary fiducial markers and software system (MicronTracker), which the manufacturer had developed successfully for other areas of medical surgery[4,5,6,7]. At the time, the existing CA-navigation devices for implant surgery demonstrated adequate accuracy[8,9,10], but sales were limited due to high initial equipment costs, shortcomings of the technology, and challenges associated with obtaining volumetric images prior to the spread of cone beam computed tomographic radiography (CBCT)[11]. These early CA-navigation devices used variants of algorithms for computing rotation matrices between point-to-point positions of fiducial markers registered by infrared (IR) cameras[12,13,14]. By 2010, however, advances in computer technology prompted the development of a new generation of optoelectronic CA-navigation devices[15], accelerated by the wide adoption of CBCT radiography in implant dentistry. To date, at least nine optoelectronic CA-navigation devices are commercially available (Table 1). While each of these products employs different technologies and has a diversity of designs and components (Figure 1), they ultimately rely on the use of “tracking fiducial markers,” i.e., objects are registered and their relative dynamic relations are tracked optoelectronically, and a “radiographical fiducial marker”, i.e., a fiducial marker registered in a CBCT scan. It should be noted that the aforementioned terms should be used for consistency because terms like “marker”, “tracking marker”, “fiducial marker” and “fiducial” are often used arbitrarily and may introduce confusion. A definition of a fiducial marker has recently been added in the last edition of the Glossary of Prosthodontics as “an object placed into an image and used as a reference; in radiology, a marker placed in a CBCT scan”.[16]

The technology employed by the existing optoelectronic CA-navigation devices on the market are based on either visible light or IR stereoscopic cameras (Figure 1). Four optoelectronic CA-navigation devices operate with either broad-spectrum light (DENACAM, Mininavident AG, Switzerland; Inliant, Navigate Surgical Technologies, Canada; Navident, ClaroNav, Toronto, Canada) or blue illumination (X-Guide, X-Nav Technologies, PA, USA). From a design perspective, the DENACAM device differs substantially from all other concepts by having miniaturized cameras mounted directly onto the surgical handpiece and the use of only one ceramic fiducial marker with engraved patterns. This CA-navigation device appears, however, to still be under development.

The remaining eight optoelectronic CA-navigation devices use stereo cameras further away from the fiducial markers. These differ by the type and position of the fiducial markers relative to the surgical field and to the surgical tool (Figure 1). IR cameras triangulate between active diodes (IGI-System, DenX Advanced Dental Systems), or between passive ball-shaped reflectors (AQ Navi Surgical Navigation System, Taiwan Implant Technology Company, Taiwan; ImplaNav, BresMedical, Australia). Another CA-navigation device employ the use of monochromatic laser light reflected by glass beads (IRIS-100 Implant Real-time Imaging System, EPED Incorporated, Taiwan). A common feature of these CA-navigation devices is that the fiducial markers are mounted on extenders away from the surgical field. Long arms may be good for fiducial marker visibility, but a drawback is the correlated inherent propensity for disturbance of the fiducial markers, especially if the extender is not made in a very stiff material.

The three optoelectronic CA-navigation devices based on broad-spectrum light appear to maintain a closer distance between the fiducial markers and the surgical work field. The Inliant device is based on cameras that track Braille-like 3x3 white dots in black boxes engraved into the actual surgical handpiece as well as on a barrel at the end of an arm affixed to the dentition. The Navident device includes cameras that track black and white divided circles on components affixed respectively to an intraoral splint and to the surgical handpiece by using universal adapters. X-Nav cameras track 2-D barcodes on a barrel mounted to an intraoral splint and on a funnel-like sleeve fitted over the surgical handpiece. Interestingly, the promotional material of both Inliant and X-Nav, as well as the videos uploaded by

some of the users of these optoelectronic CA-navigation devices demonstrate several unconventional configurations of the implant surgeon's seating relative to the patient position, the light, and the camera location versus the computer screen position. We speculate that these variations may be forced by the fiducial markers of these optoelectronic CA-navigation devices being located in more confined areas, making them easily inadvertently concealed by a change of the handgrip during the surgery. Moreover, all optoelectronic logic circuits are more or less affected by the qualities of the ambient lightning, as well as by sudden changes of light intensity caused e.g., by a bright LED light of particular wavelength from a surgeon's headlamp. It is unknown which photosensors are being used in the identified optoelectronic CA-navigation devices, and the development of new logic circuits is at an unprecedented pace currently[17].

An effectual optoelectronic CA-navigation device must achieve high accuracy, while ensuring that the individual components of the CA-navigation device are designed to facilitate standard operating procedures in the surgical environment. Moreover, optoelectronic navigation devices that require continuous direct line-of-sight in the usually confined dental surgical suite must meet several additional ergonomic challenges including enabling clinician interaction with the navigation device without violating the sterile operating environment[18]. The proposed prototype CA-navigation device would need to meet these challenges and more, to demonstrate its superiority to conventional guided surgery. Once satisfactory trueness and precision for obtaining correct implant site osteotomies had been obtained under simulated conditions[19], the project proceeded to field test the prototype CA-navigation device under realistic clinical conditions in an investigational pilot clinical trial.

The aim of the investigational pilot clinical trial was to demonstrate the safety and effectiveness of a prototype optoelectronic CA-navigation device in comparison with the conventional method of planning and conducting dental implant surgery. The null hypothesis was that the use of the prototype CA-navigation device would not lead to more surgical, biological and prosthetic adverse events, including inappropriate positioning of the dental implants.

Materials and methods

The Research Ethics Board of the University of Toronto (Ref. 2012-#28344) approved the study protocol, patient information letters and case report forms (CRFs). The authorization for investigational testing of the prototype CA-navigation device was obtained from Health Canada (ref. Therapeutic Products Directorate, 2013-207594). The pilot clinical trial was initially planned as a small RCT with two parallel study arms, each involving 2 x 5 study participants: prototype CA-navigation vs. conventional laboratory surgical guide, compliant with the CONSORT guidelines. However, hardware and software challenges encountered during the implant surgeries warranted modification of the prototype CA-navigation device components and the user interface of the software. At the completion of the trial, the intention-to-treat (ITT) status deviated markedly from the per-protocol (PP) situation: as detailed in the results section, it was not possible in four situations to proceed with CA-navigation due to technical challenges with the prototype CA-navigation device encountered during implant surgery. Subsequently, an amendment in the study protocol to increase the number of study participants by 10 was approved by Health Canada (ref. Therapeutic Products Directorate, 2013-207594) and the Research Ethics Board of the University of Toronto (ref. 2013-#28344). The additional study participants underwent dental implant surgeries using the prototype CA-navigation device. At completion, the investigational pilot clinical trial consisted of a small RCT with only 3 study participants having had implants placed with the prototype CA-navigation device, and a case series of n=10 study participants having had implants placed with the prototype CA-navigation device.

Study participants

Study participants were recruited from the pool of patients referred to the University of Toronto Graduate Prosthodontics clinic. Patients with single tooth loss or small edentulous spaces were eligible for study participation. Interested potential study participants were informed regarding the requirements and procedures of the clinical trial, the nature of the proposed treatment, the potential benefits, risks, and possible complications of the proposed treatment, and alternative treatment options. They were also advised of the schedule of prescribed follow-up visits for ongoing care and data collection, and that they could withdraw from the study at any time without

consequences. Once written consent had been obtained, a Staff Prosthodontist verified that the participant satisfied the inclusion and exclusion criteria for study participation (Table 2). Additional exclusion criteria applicable during the implant surgery were insufficient bone volume for implant placement, or a lack of primary stability at the time of Stage 1 surgery. In these instances, the study participant would be withdrawn from the study.

Prototype CA-navigation device

Akin to other optoelectronic CA-navigation devices the investigational device consisted of four basic elements to enable real-time integration of the virtual position of a surgical tool into a virtual surgical environment: i) a digital virtual surgical field obtained using computed tomographic radiography; ii) a plan of the dental implant location within the virtual surgical field; iii) a registration mapping between the virtual and real surgical fields obtained through calibration; and iv) a dynamic tracking and navigation of the surgical tool used for osteotomy relative to the real surgical field.

i) Digital virtual surgical field

A radiographic template was made from a white thermoplastic polymer (Naviplast, ClaroNav Inc., Canada) conformed to the patients' diagnostic casts as follows: once heated with hot water, the polymer was moulded to the diagnostic stone cast holding one or more radiopaque teeth in their planned positions and cooled down in cold water. A rigid handle containing a radiographical fiducial marker was affixed anteriorly with a cyanoacrylate glue. The radiographic template was positioned intraorally and checked for adequate fit and stability before CBCT imaging (MercuRay, Hitachi Medical Systems, Tokyo, Japan).

ii) Plan of dental implant location within the virtual surgical field

The digital tomogram was exported from the CBCT in a DICOM file format and imported into the prototype CA-navigation device for planning of the surgical implant placement. The software planning module of the CA-navigation device enable the clinician to determine the desired implant size, location and angulation using the planned positions of the radiopaque teeth as a guide for prosthodontically-driven treatment planning.

iii) Registration mapping between the virtual and real surgical fields

Sections of the radiographic template were removed to enable surgical instrument access at the designated implant sites. After confirming that the fit and stability of the remaining parts of the radiographic template against the dentition was satisfactory, a component covered by fiducial markers and containing a calibration peg was affixed to the protruding rigid handle. Another component with fiducial markers was clamped securely to the surgical handpiece (Figure 2).

The calibration to register the spatial relationship between the surgical field and the tip position and angulation of the drill was done by first placing the head of the surgical handpiece onto the calibration peg located on the extension from the intraoral template and then by placing the tip of the precision drill on a calibration dimple on the same extension (Figure 3). Once calibrated, the software provided 2-D visualizations of the drill relative to the CBCT image of the patient's anatomy from three perspectives, and two reticles separately depicting the tip position and angulation of the drill relative to the planned location. Recalibration was done change from precision to twist and between different twist drills. Calibration was verified regularly during surgery by placing the tip of the drill against an intraoral anatomical landmark to confirm the correct position in the virtual anatomy displayed on the computer screen.

iv) dynamic tracking and navigation of the surgical tool

Dynamic tracking and navigation of the surgical tool is accomplished by utilizing a stereoscopic camera and fiducial markers that maintain a rigid relationship to the surgical field and to the surgical tool used for osteotomy. The operator's navigation of the surgical tool relative to the pre-planned implant site location can then be guided by both visual and auditory means.

Pre-operative procedure

The study participants underwent standard clinical examination procedures, including medical history taking, diagnostic photography, impression making, and complete extra/intra-oral examination. Additionally, a surgical guide made from heat-cured conventional polymethyl-methacrylate (PMMA) was fabricated on articulated stone casts in the laboratory for all the study participants. The PMMA surgical guide was kept in a stainless steel bowl filled with 60% alcohol until ready for intraoral use.

Randomization of the first ten study participants

Study participants were allocated to the study arms following a randomization list that had been generated by an independent researcher. Each study participant was assigned a unique participant number and the allocation code was kept in a numbered sealed opaque envelope. The opaque envelope was opened an hour prior to the implant surgery, to enable time for setup of the prototype CA-navigation device in the operating room. The envelopes were retained for later patient allocation verification against the randomization list. Participants allocated to the control study arm had implants placed using a conventional laboratory-fabricated surgical guide, while the prototype CA-navigation device was intended for use for the participants allocated to the experimental group.

Surgical procedure

All implant surgeries were performed by two experienced, board certified prosthodontists. Prophylactic antibiotics were prescribed in dosage appropriate to the medical condition of the patient, and the implant surgery was performed under local anesthesia. A full-thickness mucoperiosteal flap was raised in the edentulous space. The osteotomies were prepared according to the implant manufacturers' instructions for one-stage delayed function dental implant surgery. Primary stability was assessed both by manual torque wrench and resonance frequency analysis (Osstell, Maryland, USA). A healing abutment of sufficient length to just clear the marginal soft tissue was inserted, and tension-free primary closure was obtained. The study participants were prescribed analgesics per patient preference (ibuprofen 600 mg or acetaminophen 500 mg) and mouth rinse (0.12 % chlorhexidine rinse twice per day for 1 week). The patients were provided written post-operative oral hygiene and home care instructions.

During the use of the prototype CA-navigation device, the surgeon could deviate from the pre-planned implant site if circumstances or new discoveries made during the surgery dictated a more optimal placement of the dental implant. In such case, the modification from the virtual plan was recorded on the CRF.

Restorative procedures

Restorative procedures were initiated a minimum of three months after implant placement and after osseointegration of the implant had been confirmed by

radiographic evaluation and implant stability (Osstell, Maryland, USA). Polyvinyl siloxane (Aquasil, Dentsply, Woodbridge, ON) was used for final impression-making, the opposing arches were captured with alginate (Jeltrate, Dentsply, Woodbridge, ON), and bite registration was made with Blu-Mousse (Parkell Inc., Edgewood, New York, USA). All restorations were fabricated at one dental laboratory (LHM Dental Studios, Toronto, Canada) and were predominantly CAD/CAM milled titanium veneered with porcelain. Some were lab-cemented monolithic zirconia on stock titanium bases. Most restorations were screw-retained, but one was cement-retained on a custom titanium abutment. All restorative work was done by the supervised residents of the Graduate Prosthodontics program.

Follow-up assessments

The study participants were recalled for clinical examination at 6 months and 12 months after placement of the final restoration. Implant stability, probing depth, bleeding on probing, and oral hygiene were recorded. Standard periapical radiographs were taken using the same type of film and radiographic exposure settings.

Radiographic measurements

The periapical radiographs were digitized and the bone level measurements were completed by a blinded independent assessor using a public domain image processing software (ImageJ, U.S. National Institutes of Health, Bethesda, MD, USA). Vertical distances in millimeters from the implant shoulder to the most apical initial point of first visible bone contact were measured for both interproximal sites. Misalignments of the film plane relative to the implant long axis were accounted for by calibrating the software for each measurement to the known implant length.

Primary and secondary outcomes

Primary

Any adverse surgical events were recorded on the CRF immediately after implant surgery. Any adverse events were recorded during the immediate healing period up to 10 days and during the healing period up to 3 months. Any adverse events during the restorative treatment was also recorded, as well as at the one-year consultation.

Secondary

The surgeon completed immediately following the surgery a Likert-type questionnaire. On a scale from 0 to 4 the clinician recorded their perception of the ease of use of the software, to which extent computer screen guidance was required, judgment of the accuracy of the implant placement, and the time needed for surgery. The ease of use and screen guidance was scored as very simple - simple - challenging – difficult; implant accuracy was scored as excellent – good – inaccurate – very inaccurate; planning time & surgery time was scored as compressed - normal – delayed – very delayed while insertion of the implant and the positioning of the implant was scored as “facilitated” versus “not facilitated”.

Whether the dental implant positioning was considered optimal for clinical restoration was determined by having 4 blinded certified prosthodontists independently assessing de-identified sets of clinical photographs and matched peri-apical radiographs of implants placed with and without the use of the investigational CA-navigation device. The categorization was dichotomous, i.e., optimal = no modifications would be needed to restore the implant, alternatively, suboptimal = may be clinically acceptable , but modification (slight or major) would need to be considered.

The peri-implant characteristics included marginal bone levels and peri-implant mucosa condition and were measured at both the subject- and implant-levels.

Statistical considerations

Because this was a pilot clinical trial, no power calculations were made. The initial sample size of 2x5 study participants was determined principally to comply with Health Canada requirements for investigational testing of medical devices.

All statistical analyses were done using SPSS statistical software version 18 (SPSS Inc., Chicago, IL, USA). Parametric and non-parametric analyses when appropriate were used to test for statistical differences regarding (I) radiographic bone loss from loading date, and, (II) the nature and time-to-event of any biological and/or technical complications.

Results

Ten study participants were recruited in the original RCT trial and they underwent dental implant surgery between April and June 2013. The study amendment included ten additional study participants who underwent implant surgery between January

and June 2014. No participants were excluded due to insufficient bone volume for dental implant placement. In the initial RCT trial, the average age was 52 years (ranging between 30 and 66 years), with 7 female and three male study participants. The respective demography in the subsequent case series study was 52 years (range 29 to 69 years), involving 8 females and two males.

The implants were restored by single crowns in a single tooth gap (n=20) or a bound edentulous space (n=6). Seven fixed partial prostheses were placed in bound edentulous spaces; (2 units on 2 implants (n=3), 3 units on 2 implants (n=2), 3 units on 3 implants (n=1) and 4 units on 3 implants (n=1)) (Table 3). There were no distal extension situations or anterior edentulous spaces in the mandible, and the majority of implants were placed in the posterior mandible (Table 4).

In the RCT trial, the placed implants were either Osseospeed TX (n=11, Astra, Dentsply, Gothenburg, Sweden), Replace Select Ti-Unite (n=8, Nobel Biocare AG, Kloten, Switzerland) or Straumann Bone-level SLActive implants (n=6, Straumann USA, Andover, USA). In the subsequent case series study, all were Straumann bone level (n=8) or tissue-level (n=8) implants, with one exception (Table 5). All implants (n=41) achieved an acceptable primary stability (>35Ncm insertional torque and ISQ>65 measured immediately post-surgically).

The two surgeons judged that, in most situations, the prototype CA-navigation device according to the Likert-type questionnaire scored “good” for ease of use and guidance provided by the computer screen, the accuracy was assigned the highest Likert score, and planning time and surgery time required scored “normal”. The surgeons also reported that the insertion of the implant was facilitated with the investigational prototype CA-navigation device compared to the conventional approach (Figure 4). In no situations did the investigational prototype CA-navigation device interfere with the drilling protocol specified by the implant manufacturers. However, in two instances, a right-handed surgeon needed to employ his left hand in order to successfully place the implants because the prototype component on the surgical handpiece was bulky and made it difficult to follow the manufacturer’s drilling protocols in these specific cases. There were no situations where the surgeon due to new discoveries made during the surgery had to deviate from the pre-planned implant site to place an implant in a more optimal position.

Inadequate performance of a component of the prototype CA-navigation device led in four situations to the surgeon abandoning CA-navigation and to proceed with using the laboratory-fabricated surgical guide as guidance.. The two reasons were because of poor fit of the intraoral template (n=3 patients, 7 implants), or because a discrepancy was noted between the computer screen and the anatomy intraorally (n=1 patient, 3 implants). In two of these situations, intraoral templates had been fabricated for CA-navigation in both jaws, and the surgeon was able to place the implants according to this procedure in one of the jaws (Table 3).

The independent assessment of the clinical photographs and radiographs identified 26 implants that were considered optimal placements. Sixteen implants showed minor deviations from an optimal position. Ten of these had been placed with use of a laboratory-fabricated surgical guide, while 6 had been placed by use of the prototype CA-navigation device. None of the implants were judged to exhibit any major deviations from optimal position, and all could be restored without any technical challenges (Figure 5).

All study participants were present for clinical and radiological examination at the 1-year follow-up consultation. The post-loading interproximal bone loss was in all cases less than 1 mm. Peri-implant pocket depths were measured using a standard periodontal probe and were less than 2 mm for all implants (n=41). Three out of 17 and 18 implants respectively in the conventional group and the prototype group revealed bleeding upon probing (Table 6). There were no signs or symptoms of complications associated with the final implant-supported prostheses.

Health Canada issued in May 2014 a medical device license for the prototype CA-navigation device and the product has subsequently been labeled as Navident (ClaroNav, Toronto, Ontario, Canada).

Discussion

A major challenge with any optoelectronic CA-navigation device is that the view between the stereoscopic camera and the fiducial markers needs to be constant. Operators and assistants must therefore be vigilant and avoid positioning themselves or any surgical instrument in the line-of-sight between the camera and

the fiducial markers in the operation field. A momentary loss of line-of-sight is in itself not problematic provided that the software can resume its functions immediately. Such interruptions in some early-generation optoelectronic devices developed for tracking mandibular 3-D movements[20] led to total software “freeze”, which obviously must not happen during a surgery. In this respect, the prototype CA-navigation device used in the current investigational pilot clinical trial functioned adequately and regained operations immediately. To what extent the current CA-navigation devices on the market meet this requirement must be assessed in the intended sterile environment with a realistic setup and realistic computer interaction (Table 1).

An alternative to avoid the ergonomical issues with optoelectronic tracking is to use some form of physical component to measure 3-D space. One device for dental implant surgery that was approved by FDA in 2016 is the Neocis Guidance System (www.neocis.com), There are no clinical data regarding the performance of this CA-navigation device.

It is wise to remember that CA-navigation devices presented at trade fairs and on promotional videos are likely being run on a high-end computer. The manufacturers have established minimum specifications for computer performance, but for the end-user to fairly assess the real-world performance of a CA-navigation device, the CA-navigation software must be installed and run on the user’s designated computer to verify the adequacy of the hardware to meet the significant computational demands of the software.

At this time, it is unknown how the new generation of different CA-navigation devices (Table 1) perform in terms of real-world clinical efficacy. To the authors’ knowledge, there are no studies that have compared navigation devices head-to-head in a clinical environment. We have identified only one paper with clinical data, which is a summary of 100 patient cases treated by 3 very experienced oral surgeons using the X-Nav device[21]. One of their conclusions likely applies to all optoeletronic CA-navigation devices, i.e., that implant surgeons will need to adapt to a new cognitive approach to surgery by trusting both that preplanning has been done correctly and that the navigation device works properly.

Indeed, surgeons must be persuaded that the use of a CA-navigation device can lead to improved patient care, an issue that encompasses considerations of the

potential for optimization of implant placement and/or less time required for the surgeon and patient in the surgical suite. In the current study, the surgeons' judgements of practical usability and user friendliness of the components of the prototype CA-navigation device improved over time (Figure 4), although we recognize the potential bias introduced by the learning by experience and adopting novel operating procedures throughout the study period. One of the surgeons expressed that even if the use of an optoelectronic CA-navigation device can result in a successful surgical outcome, it must be miniaturized before mostly non-ambidextrous surgeons will integrate such device into their surgical suite.

Beyond the variations in design and componentry of CA-navigation devices as well as technical specifications of the hardware and software, all devices depend critically on the accuracy of the calibration between the volumetric CBCT image and reality, i.e., the jaw being operated on. A first prerequisite is that the position of the radiographical fiducial marker(s) relative to the tissues as recorded in the volumetric radiograph must be consistent at all times. Ideally, the radiographical fiducial marker(s) should not be disturbed or removed until the implant surgery has been completed. While this is impractical, there are risks created otherwise, because accurate repositioning may be problematic or even impossible under certain circumstances. An added dimension is that if the clinician relies on a third-party centre for CBCT radiography, the staff there may not recognize the critical need for an exact positioning of the template that contains a radiographical fiducial marker(s).

The manufacturers have developed different solutions for avoiding mobility of templates in partially-dentate patients, which include full jaw or quadrant size tightly fitted occlusal splints or clips attached to adjacent teeth (Figure 1). Assuring a firm position of a template in a fully edentulous jaw is more challenging, apart from adopting an approach used in complex robotic surgery to embed dispersed miniscrews into bone before CBCT and subsequently calibrate the navigation device versus the screw heads with a digital mechanical positioning probe[22]. While the accuracy is excellent and supported by multiple papers in the craniomaxillofacial surgery literature, some may question the need for such invasive approach to place dental implants. One paper report a variant of the concept, whereby four screws are embedded into the alveolar ridge before the CBCT recording and a tracking plate

named “e-clip” (X-Nav technologies) is fitted to the screws following a subperiostal incision[23].

Radiographic templates and surgical guides or occlusal splints made from polymers may deform due to inadvertent exposure to excessive heat during handling or in storage. Some of the existing navigation devices include the use of a thermoplastic proprietary polymer, which raises questions about both biocompatibility as well as deformation resistance. One should recognize that certain polymers are vulnerable to dimensional changes during conventional sterilization procedures. It has therefore been proposed that hydrogen peroxide-based plasma sterilization should be used for medical devices made from thermoplastic materials[24].

A rigid study design was adopted rather than case series, to minimize potential detection bias. The sample size was not determined by estimated power calculation because investigational testing of new medical devices follows national regulatory requirements. These vary from country to country, but in general, regulatory agencies receive specified data from manufacturers and following a risk assessment versus considerations of effect size, grant permissions to proceed with clinical trials. Health Canada granted permission to undertake a limited pilot RCT, based on data submitted from the manufacturer (ref. Therapeutic Products Directorate, 2013-207594). Yet, the unanticipated practical problems encountered during the initial test period illustrates how translatory research from promising in vitro data to pragmatic use under realistic circumstances may not always be predictable. The ethical and statistical alternatives under the circumstances were to not recruit more study participants, or to expand the sample size of the RCT or to proceed with a single cohort study. The research ethics board of the University of Toronto endorsed our judgement to switch study design from RCT and granted permission to proceed with another ten study participants.

The focus of this study was to determine whether the prototype CA-navigation device enabled the surgeon to achieve clinically acceptable implant positions, and not to measure the precise extent of deviations from the planned placement. For this pilot study, a relative simple way of assessing the position of the dental implants was selected. The rational was that given that the development of the prototype CA-navigation device under investigation was at a relatively early stage, and considering that the patients would not benefit from a post-operative CBCT scan, it was

determined that the additional radiation exposure was not warranted from a research ethics perspective. The decision was based on the belief that minor deviations from an optimal placement can be corrected by an individualized CAD/CAM abutment or crown. In future studies, greater precision in the determination of the post-operative implant location relative to the virtual plan may be obtained by one of two methods: post-operative CBCT; and, intraoral digital optical scan using an implant-specific scan body[25], [26].

A further rationale for undertaking safety pilot studies of innovative CA-navigation devices prior to measuring accuracy is that there is currently no unitary understanding of accuracy in the clinical application of CA-navigation technologies[27], and the terminology used for describing accuracy remains confusing[28],[29]. Future studies are required to identify the extent of deviations from the virtually-planned intended implant placement and determine whether these deviations stem from problems with the actual CBCT, or are related to the sequence of DICOM-file export-import transfer, virtual implant planning, placement of the tracking devices, clinical operatory setting factors including light, or the surgeon performance.

Conclusions

No surgical adverse events were experienced while placing dental implants guided by the prototype CA-navigation device. All implants healed without any biological adverse events and were positioned in the jaw that enabled the placement of a prosthetic superstructure. The oral surgeons' perception of ease of use of the prototype CA-navigation device was generally positive. Extrapolation to generalized clinical use is limited by a restricted sample size and deliberate selection of only study participants with single tooth loss or small edentulous spaces. Ergonomic challenges persist with optoelectronic CA-navigation devices and clinicians should carefully consider these potentially critical issues in patient care.

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Table 1. Current commercially available optoelectronic computer-aided navigation devices for surgical placement of dental implants

Introduced	Device	Manufacturer	www	FDA-approved
2017	Adens-NAVI	U&I Adens Dental Clinic, Taiwan	www.adens.com	-
2014	AQ Navi Surgical Navigation System	Taiwan Implant Technology Company, Taiwan	www.titc-dental.com	-
2016	DENACAM	Mininavident AG, Swtizerland	www.mininavident.com	-
2001	IGI-System (AKA DenX)	DenX Advanced Dental systems, Israel	www.image-navigation.com	K023424-2003
2016	ImplaNav	BresMedical, Australia	www.bresmedical.com	-
2015	Inliant	Navigate Surgical Technologies Technologies, Canada	www.inliant.com	-
2015	IRIS-100 Implant Real-time Imaging System	EPED Incorporated, Taiwan	www.eped.com.tw	-
2014	Navident	ClaroNav Inc., Canada	www.claronav.com	K161406-2016
2014	X-Guide Dynamic 3D Navigation	X-Nav Technologies, PA, USA	www.x-navtech.com	K150222 - 2015

Table 2. Inclusion and exclusion criteria of study participants.

Eligibility Criteria	
Inclusion Criteria	Patient at least 18 years or older
	Single tooth loss or small edentulous spaces
	Edentulous at least 3 months before date of implant surgery
	Eventual previous GBR/GTR procedures done at least 6 months prior to implant surgery
Systemic Exclusion Criteria	Chronic routine prophylactic use of antibiotics
	Prolonged use of steroids
	Hematologic disorders, neoplastic disease requiring radiation or chemotherapy, renal failure, metabolic bone disorder or uncontrolled endocrine disorders
	Use of any investigational drug or device within the 30-day period immediately prior to implant surgery
Local Exclusion Criteria	Remaining intraoral infection
	Local inflammation, including untreated periodontitis
	History of local irradiation therapy
	Presence of osseous lesions
	Mucosal disease such as erosive lichen planus
	Parafunction: severe bruxism or clenching
	Insufficient bone for the procedure

Table 3. Implant location and superstructure provided to the study participants in the parallel RCT trial (n=5+5 participants with 10+15 implants), and the case series study (n=10 participants with 16 implants).

		RCT TRIAL				CASE SERIES	
		Conventional, n=5 participants with 10 crowns on 10 implants		Prototype, n=5 participants with 3 jaws, 3 crowns and 5 FDPs on 15 implants		Prototype, n=10 participants with 11 jaws, 14 prostheses on 16 implants	
INDICATION	Jaw	Implant	Prosthesis	Implant	Prosthesis	Implant	Prosthesis
SINGLE TOOTH GAP	Max	1	C	1	C*	6	CCCCCC
	Mand	3	CCC	2	C**+C***	6	CCCCCC
EDENTULOUS SPACE ANTERIOR	Max	4	CCCC	0	-	0	-
	Mand	0	-	0	-	0	-
EDENTULOUS SPACE POSTERIOR	Max	2	CC	5	4u-3i 3u-2i***	0	-
	Mand	0		7	2u-2i* 2u-2i** 3u-3i****	4	2u-2i 2u-2i
TOTAL		10	10	15	8	16	14

C = Crown, FDP = Fixed dental prosthesis, u= unit, i = implant

* CA-navigation planned for single implant in the maxilla and two adjacent implants in the mandible. The intraoral template in the mandible did not adapt to the teeth, so the laboratory-fabricated surgical guide was used to place 2 implants. (case #170096)

**CA-navigation planned for a single implant plus two adjacent implants. The intraoral template did not adapt to the teeth intraorally, so the laboratory- fabricated surgical guide was used to place all 3 implants. (case #161515)

*** CA-navigation planned for two adjacent implants in the maxilla and a single implant in the mandible. The intraoral template in the maxilla did not adapt to the teeth intraorally, so the laboratory- fabricated surgical guide was used to place 2 implants. (case #172481)

**** CA-navigation planned for three adjacent implants. A discrepancy was noted between computer screen and anatomy intraorally, so the laboratory- fabricated surgical guide was used for surgical guidance to place 3 implants. (case #143045)

Table 4. Distribution of implant locations in the RCT trial (n=25 implants) and in the case series study (n=16 implants, *cursive*).

Number of implants placed per location															Sum
# implants	0	0	0&3	2&*2*	1&*0*	0	1&0	1&0	1&0	*0*	*2*&*1*	2&*0*	2&*0*	1&*0*	13 &*6*
Maxilla tooth#:	17	16	15	14	13	12	11	21	22	23	24	25	26	27	
Mandible tooth#:	47	46	45	44	43	42	41	31	32	33	34	35	36	37	
# implants	0	2&*3*	2&*1*	0	0	0	0	0	0	0	1&*0*	3&*1*	3&*4*	1&*1*	12 &*10*

Table 5. Different implant systems, lengths (mm) and diameters (mm) used in the RCT trial (n=25) and in the case series study (n=16, cursive).

	LENGTH (mm)	**8**	**9**	**10**	**11**	**13**	**n**
DIAMETER (mm)	**ASTRA OSSEOSPEED TX (11 & *0*)**						
3.5		3	1	-	1	-	**5 & *0***
4.0		0	0	-	4	-	***4 & 0***
5.0		0	1	-	1	-	**2 & *0***
	NOBEL REPLACE TAPERED GROOVY (8 & *1*)						
3.5		0	-	2	-	3	**5 & *0***
4.3		1	-	1 & *1*	-	0	**2 & *1***
5.0		1	-	0	-	0	**1 & *0***
	STRAUMANN BONE-LEVEL SLACTIVE (6 & *8*)						
3.3		*1*	-	1	-	-	**1 & *1***
4.1		*1*	-	4 & *6*	-	-	***4 & 7***
4.8		0	-	1	-	-	**1 & *0***
	STRAUMANN STANDARD PLUS (TISSUE LEVEL) (0 & *8*)						
3.3		*1*	-	-	-	-	**0 & *1***
4.1		*3*	-	*0*	-	-	**0 & *3***
4.8		*2*	-	*1*	-	-	**0 & *3***
	n	**5 & *8***	**2 & *0***	**9 & *8***	**6 & *0***	**3 & *0***	**25 & *16***

Table 6. Radiological and clinical changes noted at the clinical examination 1 year after implant placement.

Clinical variable:	**Conventional surgical guide (n= 20 implants)**	**Investigational prototype CA-navigation device (n=21 implants)**
Radiographic bone loss: 0-1 / >1 – 2 / >2 (mm)	20 / 0 / 0	21 / 0 / 0
Pocket depth: 0-1 / >1 – 2 / >2 (mm)	11 / 9 / 0	13 / 8 / 0
Oral hygiene (Excellent/Good/Fair/Poor)	8 / 7 / 5 / 0	9 / 7 / 5 / 0
Bleeding on probing (Yes/No)	3 / 17	3 / 18

Legends to figures

Figure 1. Current commercially available computer-aided navigation devices based on optoelectronic technology for surgical placement of dental implants. (All pictures received from the manufacturers or downloaded from their respective website)

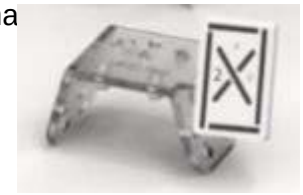
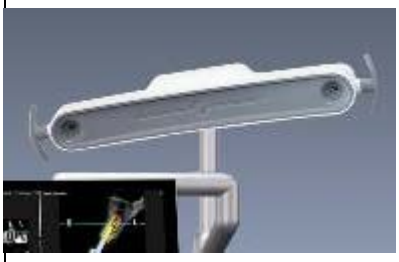
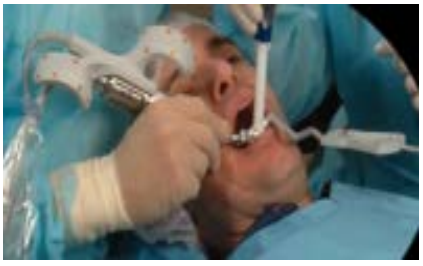
Figure 2. Top row: Fiducial markers on component attached to the anterior part of the intraoral splint (two different prototype designs shown). Centre row: Fiducial markers on component clamped to the handpiece (two different prototype designs shown). The bottom picture illustrates one arrangement of the computer screen as seen from the surgeon's perspective. (The design of the prototype components differ from the marketed product)

Figure 3. Calibration of the spatial relationship between the fiducial markers on the component clamped to the handpiece and to those on the component attached to the intraoral splint. First step is by positioning the head of the handpiece onto a peg projecting from the component attached to the intraoral splint and next placing the tip of the twist drill, alternatively the actual implant before its endosseous placement, on a designated spot on the same component. (The design of the prototype components differ from the marketed product)

Figure 4. Assessment of the practical usability of the investigational prototype CA-navigation device, as judged by the surgeons immediately following implant placement. Ease of use and Screen guidance: Very simple (green) - Simple (light green) - Challenging (grey) - Difficult (red). Implant accuracy: Excellent (dark green) - Good (light green). Planning time & Surgery time: Compressed (green) - Normal (light green) - Delayed (grey). Insertion of the implant and the Positioning of the implant facilitated (green) or not facilitated (red). Left column within each criteria represent the feedback in the initial RCT trial (n=5 implants*) while the right column represent the feedback in the succeeding case series study (n=16 implants).

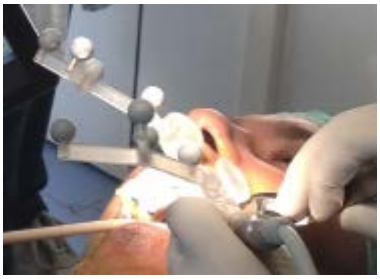
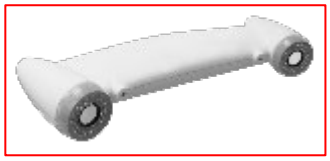
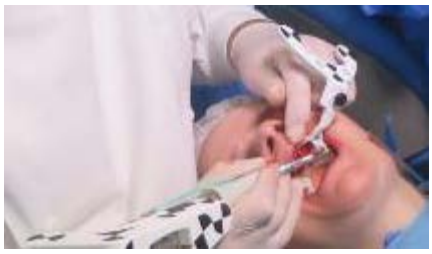
Figure 5. All implants placed by use of the investigational prototype CA-navigation device (n=21), radiographs taken 12 months after implant placement. The implants considered as not optimally placed with regard to the platform or apex position of the implant, or its angulation are framed in grey (n=6).

Figure 1. Current commercially available computer-aided navigation devices based on optoelectronic technology for surgical placement of dental implants. (All pictures received from the manufacturers or downloaded from their respective website)

	Light / Camera Source	Fiducial markers attached to the surgical handpiece & relative to the surgical field
Adens-NAVI (2017 IDS*) Prototype stage. Camera & fiducial marker concept is unknown.		No photographs available.
AQ Navi (2014) IR camera. Reflective balls mounted on plastic extensions clamped to a handpiece & on a curved plastic arm affixed to an occlusal splint on the surgical jaw ("CT Plate")		
DENACAM (2017 IDS*) Optical camera on a handpiece. Engraved ceramic marker is fixated to adjacent teeth by a clip (“DENAMARK”) or affixed to an occlusal splint on the surgical jaw (“DENATRAY”)		No clinical photographs. Intraoral clip with ceramic fiducial ma 
IGI-System (2001) IR camera. Active diodes (i.e., wired) on a plastic case clamped to a handpiece & on a plate affixed to bent metal arm affixed to an intraoral splint on the surgical jaw		

* IDS = International Dental Trade Fair, Cologne. Presentation of product.

Commercial status is unknown.

ImplaNav (2016) IR camera. Reflective balls mounted on polycarbonate frames respectively clamped to a handpiece and connected to the patient via an occlusal tray (partially edentulous case) or an implant-supported plate (edentulous case) on the surgical jaw.		
Inliant (2015) Optical camera. 2-D data matrices engraved on a handpiece & on a metal cylinder attached to a clip (“FiducialMarker”) fixated to adjacent teeth in the surgical jaw		
IRIS-100 (2015) IR camera with dual-laser pointers. Reflective spots on a plastic casing fitted over a handpiece & on a plastic sheath on adjustable arm affixed to an occlusal splint on the surgical jaw (“Occlusal guide”)		
Navident (2014) Optical camera. Geometric patterns on a plastic sheath clamped to a handpiece & on a curbed plastic component affixed to an occlusal splint on the surgical jaw (“NaviStent”)		
X-Nav (2014) Optical camera. 2-D data matrices engraved in autoclavable metal casings fitted over a handpiece & on extension from a clip fixated to teeth in the surgical jaw using a chair-side impression material (“X-clip”) or fixated		

to the surgical jaw bone for edentulous patients (“E-clip”)		

1

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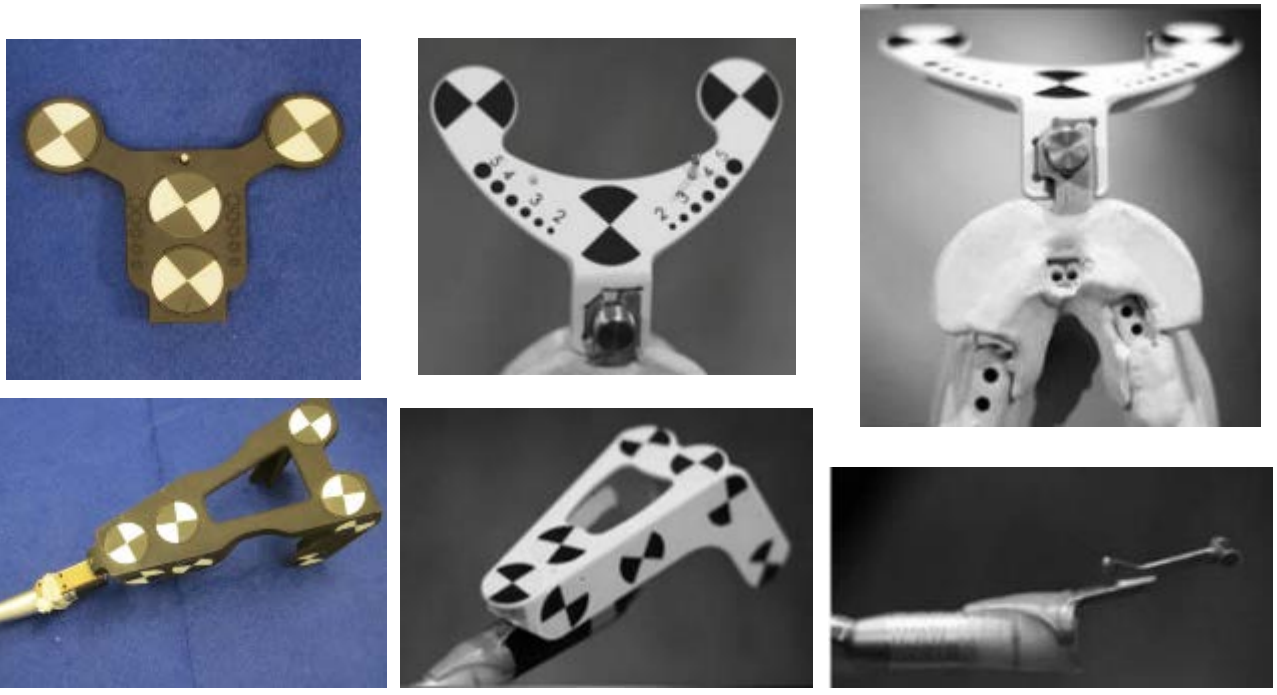

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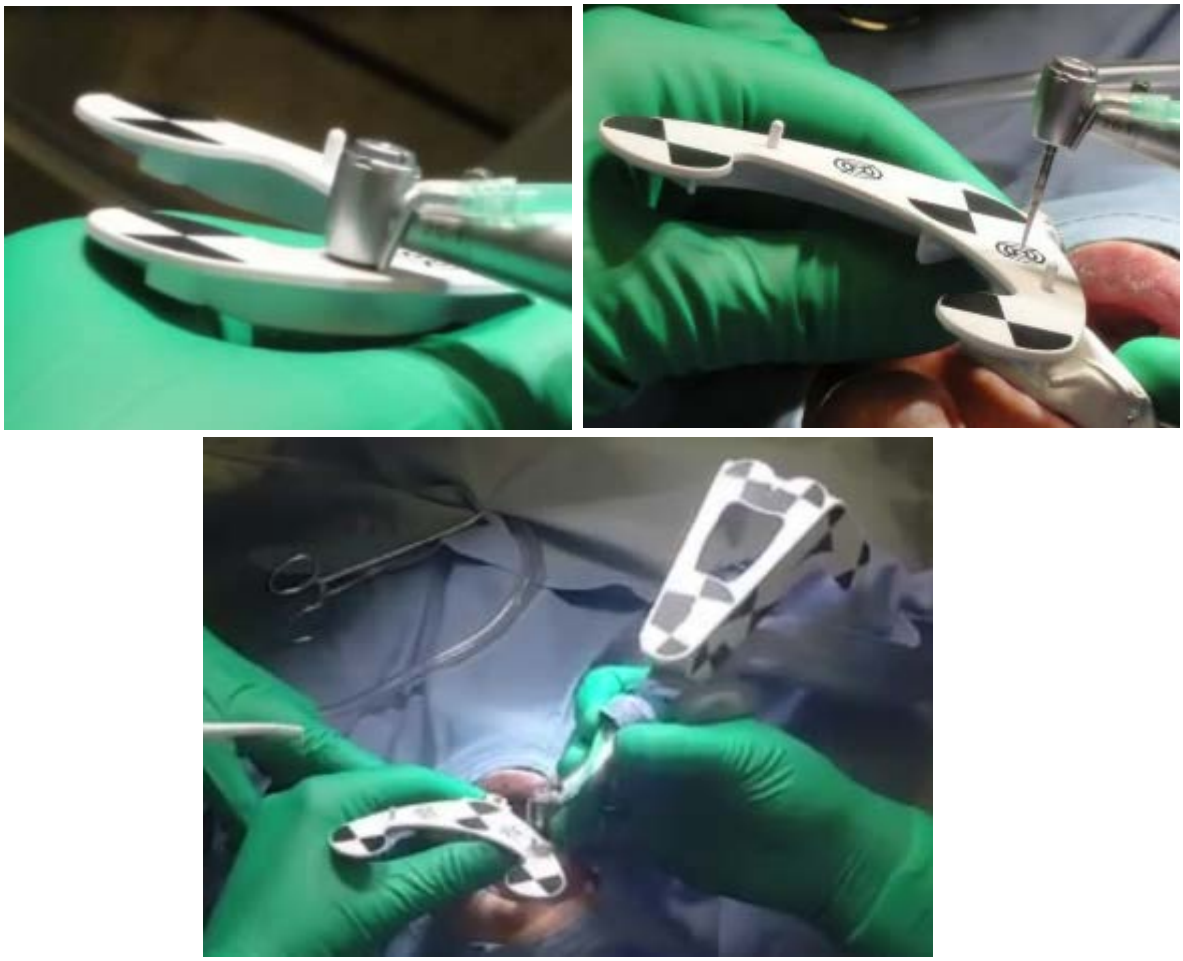

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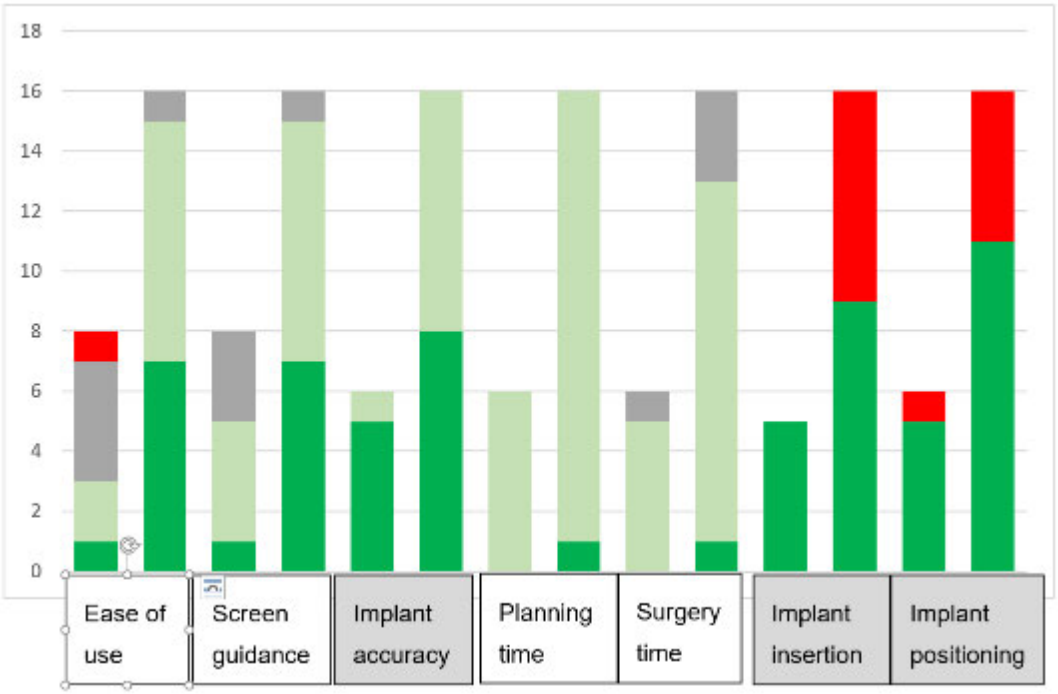
*Eight evaluations, include 3 surgeries where implants could not be placed by use of the prototype CA-navigation device



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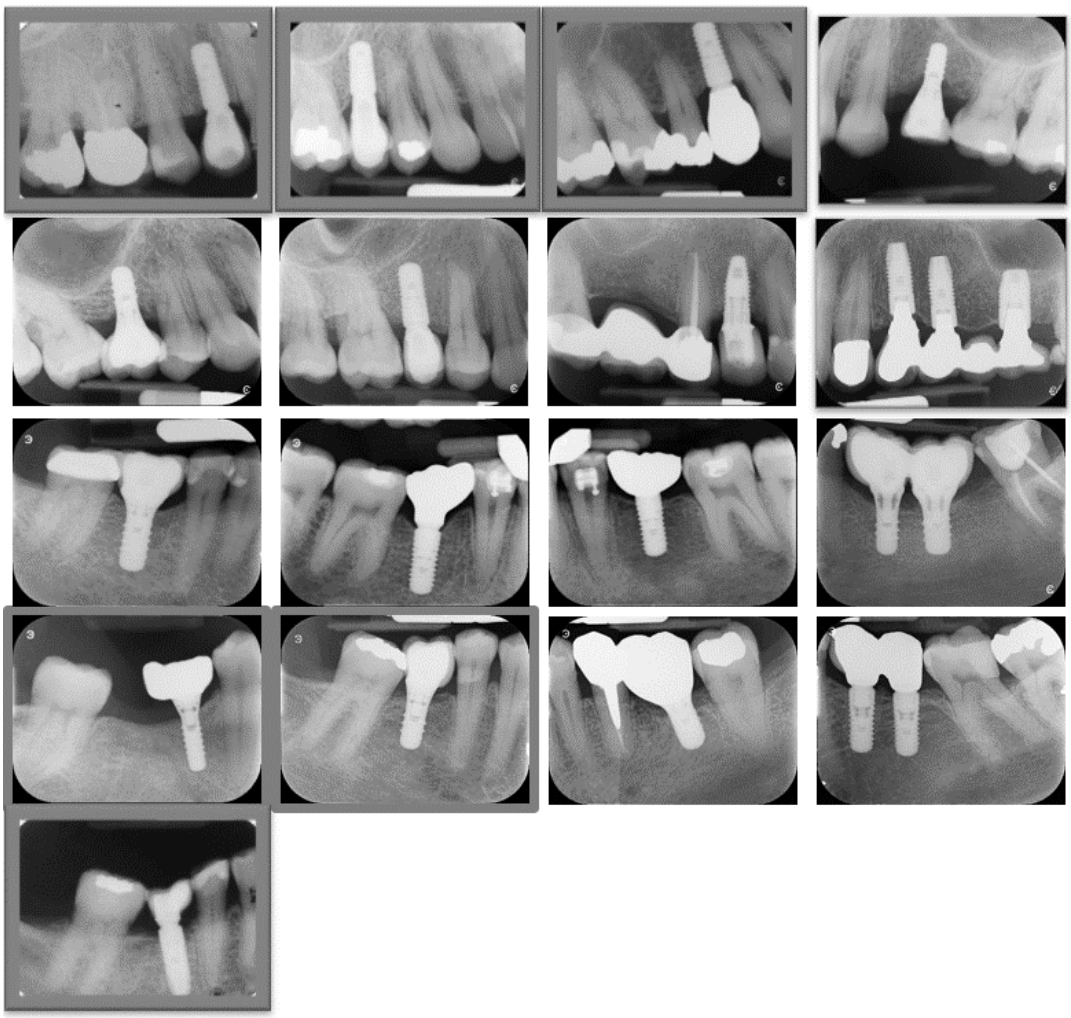

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