

Investigational Clinical Trial of a Prototype Optoelectronic Computer-Aided Navigation Device for Dental Implant Surgery

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Purpose: New digital technologies enable real-time computer-aided (CA) three-dimensional (3D) guidance during dental implant surgery. The aim of this investigational clinical trial was to demonstrate the safety and effectiveness of a prototype optoelectronic CA-navigation device in comparison with the conventional approach for planning and effecting dental implant surgery. **Materials and Methods:** Study participants with up to four missing 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 a prototype device study arm in a randomized trial. The next 10 participants received implants using the prototype device. All study participants were restored with fixed dental prostheses after 3 (mandible) or 6 (maxilla) months healing, and monitored over 12 months. The primary outcome was the incidence of any surgical, biologic, or prosthetic adverse events or device-related complications. Secondary outcomes were the incidence of positioning of implants not considered suitable for straightforward prosthetic restoration (yes/no); the perception of the ease of use of the prototype device by the two oral surgeons, recorded by use of a Likert-type questionnaire; and the clinical performance of the implant and superstructure after 1 year in function. Positioning of the implants was appraised on periapical radiographs and clinical photographs by four independent blinded examiners. Peri-implant bone loss was measured on periapical radiographs by a blinded examiner. **Results:** No adverse events occurred related to placing any implants. Four device-related complications led to a switch from using the prototype device to the conventional method. All implants placed by use of the prototype device were in a position considered suitable for straightforward prosthetic restoration ($n = 21$). The qualitative evaluation by the surgeons was generally positive, although ergonomic challenges were identified. All study participants were present for the 1-year examination ($n = 20$ patients, 41 implants, 32 superstructures), and no complications or failures with any implants or superstructures were revealed. The peri-implant bone loss was less than 1 mm for all implants. **Conclusion:** Within the limitations of this trial, the prototype device provided placement of dental implants without adverse events. INT J ORAL MAXILLOFAC IMPLANTS 2018;33:679–692. doi: 10.11607/jomi.6351

Keywords: clinical trials, computer-aided, cone beam computed tomography, investigational, phase I, surgery, surgical techniques, therapies

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The ingenious innovation to combine three-dimensional (3D) computed tomographic radiography with treatment planning software has facilitated the placement of dental implants with great accuracy.¹ New digital technologies now make 3D guidance possible 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, later renamed ClaroNav) 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

Table 1 Current Commercially Available Optoelectronic Computer-Aided Navigation Devices for Surgical Placement of Dental Implants

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

system (MicronTracker), which the manufacturer had developed successfully for other areas of medical surgery.⁴⁻⁷ At the time, the existing CA-navigation devices for implant surgery demonstrated adequate accuracy,⁸⁻¹⁰ but sales were limited due to high initial equipment costs, shortcomings of the technology, and challenges associated with obtaining volumetric images prior to the widespread use of cone beam computed tomographic (CBCT) radiography.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.¹²⁻¹⁴ 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 designs and components (Fig 1), they ultimately rely on the use of tracking fiducial markers; ie, objects are registered, and their relative dynamic relations are tracked optoelectronically. It should be noted that the terms “marker”, “tracking marker”, and “fiducial” are often used arbitrarily as synonyms for “fiducial marker”. The latest edition of the Glossary of Prosthodontics Terms has defined a fiducial marker as “an object placed into an image and used as a reference; in radiology, a marker placed in a CBCT scan”.¹⁶

The optoelectronic CA-navigation devices that are currently available on the market (Table 1) implement technologies based on either visible light or IR stereoscopic cameras, and the majority have been launched within the last 3 years (Fig 1). From a design perspective, one optoelectronic device (DENACAM, Mininavident) differs substantially from the other products by consisting of 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 other eight optoelectronic devices use stereo cameras further away from the fiducial markers. A common feature of these 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 of a very stiff material. Besides the light source, the devices also differ by the type and position of the fiducial markers relative to the surgical field and to the surgical tool (Fig 1). Devices based on IR cameras triangulate between either active diodes (IGI-System, DenX Advanced Dental Systems), or passive ball-shaped reflectors (AQ Navi Surgical Navigation System, Taiwan Implant Technology Company; ImplaNavi, BresMedical). Another device uses monochromatic laser light reflected by glass beads (IRIS-100 Implant Real-time Imaging System, EPED Incorporated). Two devices operate with use of broad-spectrum light (Inliant, Navigate Surgical Technologies; Navident, ClaroNav) and one with use of blue illumination (X-Guide, X-Nav Technologies). These three devices (Inliant, Navident, X-Guide) maintain a closer distance between the fiducial markers and the surgical work field. Inliant uses cameras that track Braille-like 3 × 3 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. Navident has cameras that track black and white divided circles on components affixed to both an intraoral splint and the surgical handpiece by using universal adapters. X-Guide makes use of cameras that track two-dimensional (2D) barcodes on a barrel mounted



Fig 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). (a, b, d, f, h, j, l, n, p) Light/camera source. (c, e, g, i, k, m, o, q) Fiducial markers attached to the surgical handpiece and relative to the surgical field. (a) Adens-NAVI (2017 IDS): Prototype stage. Camera and fiducial marker concept is unknown. (b, c) AQ Navi (2014): IR camera. Reflective balls mounted on plastic extensions clamped to a handpiece and on a curved plastic arm affixed to an occlusal splint on the surgical jaw ("CT Plate"). (d, e) DENACAM (2017): 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"). (e) No clinical photographs. Intraoral clip shown with ceramic fiducial marker. (f, g) IGI-System (2001): IR camera. Active diodes (ie, wired) on a plastic case clamped to a handpiece and on a plate affixed to bent metal arm affixed to an intraoral splint on the surgical jaw. (h, i) 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. (j, k) Inliant (2015): Optical camera. 2D data matrices engraved on a handpiece and on a metal cylinder attached to a clip ("FiducialMarker") fixated to adjacent teeth in the surgical jaw. (l, m) IRIS-100 (2015): IR camera with dual-laser pointers. Reflective spots on a plastic casing fitted over a handpiece and on a plastic sheath on adjustable arm affixed to an occlusal splint on the surgical jaw ("Occlusal guide"). (n, o) Navident (2014): Optical camera. Geometric patterns on a plastic sheath clamped to a handpiece and on a curved plastic component affixed to an occlusal splint on the surgical jaw ("NaviStent"). (p, q) X-Guide (2014): Optical camera. 2D data matrices engraved in autoclavable metal casings fitted over a handpiece and on extension from a clip fixated to teeth in the surgical jaw using a chairside impression material ("X-clip") or fixated to the surgical jaw bone for edentulous patients ("E-clip"). IDS = International Dental Trade Fair, Cologne. Presentation of product. Commercial status is unknown.

to an intraoral splint and on a funnel-like sleeve fitted over the surgical handpiece.

An effective 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.¹⁷ 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,¹⁸ the project proceeded to field test the prototype CA-navigation device under realistic clinical conditions in an investigational clinical trial.

The aim of the investigational clinical trial was to assess for regulatory purposes 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, biologic, 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 investigational clinical trial was initially planned as a small randomized controlled trial (RCT) with two parallel study arms, each involving 2×5 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, in four situations, it was not possible to proceed with CA-navigation due to technical challenges with the prototype CA-navigation device 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 clinical trial consisted of a small RCT with only three 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 (no more than four missing teeth in total) 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 implant surgery were insufficient bone volume for implant placement, or a lack of primary stability. In these instances, the study participant would be withdrawn from the study.

Prototype CA-Navigation Device. Akin to other optoelectronic CA-navigation devices, the prototype device consisted of four basic elements to enable real-time integration of the virtual position of a surgical tool into a virtual surgical environment: (1) a digital virtual surgical field obtained using computed tomographic radiography; (2) a plan of the dental implant location within the virtual surgical field; (3) a registration mapping between the virtual and real surgical fields obtained through calibration; and (4) a dynamic tracking and navigation of the surgical tool used for osteotomy relative to the real surgical field.

1. *Digital virtual surgical field:* A customized radiographic stent was fitted to each patient. This template consisted of a horseshoe-shaped, white, thermoplastic polymer (Naviplast, ClaroNav) that had a metal fiducial marker embedded in it. The template was customized for each patient by heating it in hot water and adapting it to the diagnostic stone cast of the patient. In the edentulous space where the implant was to be planned, a radiopaque denture tooth was positioned with another strip of thermoplastic polymer to hold it in place on top of the template. The radiographic template was positioned intraorally and checked for adequate fit and stability before CBCT imaging (MercuryRay, Hitachi Medical Systems).
2. *Plan of dental implant location within the virtual surgical field:* The digital tomogram was exported from the CBCT machine in a DICOM file format and imported into the prototype CA-navigation device for planning of the surgical implant placement. The

Table 2 Inclusion and Exclusion Criteria of Study Participants**Eligibility criteria**

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

GBR/GTR = guided bone regeneration/guided tissue regeneration.

software planning module of the CA-navigation device enables 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.

3. *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 were 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 (Fig 2). The calibration to register the spatial relationship between the surgical field and the tip position and angulation of the drill was accomplished 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 (Fig 3). Once calibrated, the software provided 2D 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, as well as a

scale to show proximity to the planned implant depth. Recalibration was done every time the bur was changed (for instance, from the precision drill to the 2.0-mm 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.

4. *Dynamic tracking and navigation of the surgical tool:* Dynamic tracking and navigation of the surgical tool was accomplished by utilizing a stereoscopic camera and fiducial markers to maintain a rigid relationship between the planned virtual surgical field and the real surgical field/real surgical tool used for osteotomy. The operator's navigation of the surgical tool relative to the preplanned implant site location can then be guided by both visual and auditory means.

Preoperative Procedure

The study participants underwent standard clinical examination procedures, including medical history taking, diagnostic photography, impression making, and complete extraoral/intraoral 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.

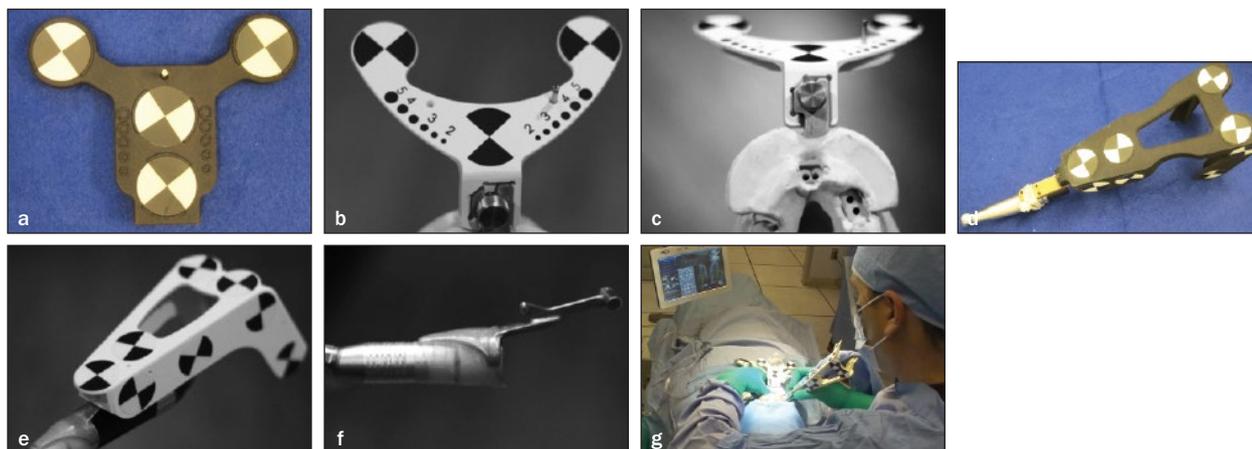


Fig 2 (a to c) Fiducial markers on component attached to the anterior part of the intraoral splint (two different prototype designs shown). (d to f) Fiducial markers on component clamped to the handpiece (two different prototype designs shown). (g) One arrangement of the computer screen as seen from the surgeon's perspective. (The design of the prototype components differs from the marketed product.)



Fig 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, or alternatively, the actual implant before its endosseous placement, on a designated spot on the same component. (The design of the prototype components differs from the marketed product.)

Randomization of the First 10 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). 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 mouthrinse (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 preplanned 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 3 (mandible) or 6 (maxilla) months after implant

placement and after osseointegration of the implant had been confirmed by radiographic evaluation and measurement of implant stability by use of resonance frequency analysis (Osstell). The clinicians were graduate students in prosthodontics. Polyvinyl siloxane (Aquasil, Dentsply) was used for final impression-making, the opposing arches were captured with alginate (Jeltrate, Dentsply), and bite registration was made with Blu-Mousse (Parkell). All restorations were fabricated at one dental laboratory (LHM Dental Studios) and were predominantly computer-aided design/computer-assisted manufacturing (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 definitive 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. The clinical examiner was more often than not different from the graduate student in prosthodontics who had fabricated the superstructure, but he or she was not blinded to the patient chart history.

Radiographic Measurements

The periapical radiographs were digitized and bone level measurements were completed by a blinded independent examiner using public domain image processing software (ImageJ, U.S. National Institutes of Health [NIH]). 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. The intraobserver reliability based on 10 repeat measurements was excellent, with intraclass correlation = 1.

Primary and Secondary Outcomes

Primary. Any adverse surgical events were recorded on the CRF immediately after implant surgery. Any adverse events during the immediate healing period up to 10 days and during the healing period up to 3 months were recorded. Any adverse events during the restorative treatment and 1-year follow-up were also recorded.

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

Whether the positioning of the individual dental implants was considered suitable for straightforward prosthetic restoration or not was determined by having four board-certified prosthodontists independently assessing de-identified sets of clinical photographs and matched periapical radiographs. The examiners were blinded for whether the implants had been placed with the prototype device or conventional surgical guide. The categorization was dichotomous, optimal or suboptimal (ie, 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). Consensus was determined by a forced majority decision among the four examiners.

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 an investigational clinical trial, no power calculations were made. The initial sample size of 2 × 5 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). Parametric and nonparametric analyses when appropriate were used to test for statistical differences regarding (1) radiographic bone loss from loading date, and (2) the nature and time-to-event of any biologic and/or technical complications.

RESULTS

Ten study participants were recruited in the original RCT, and they underwent dental implant surgery between April and June 2013. The study amendment included 10 additional study participants who underwent implant surgery between January and

Table 3 Implant Location and Superstructure Provided to Study Participants in Parallel RCT (n = 5 + 5 Participants with 10 + 15 Implants) and Case Series Study (n = 10 Participants with 16 Implants)

Indication	Arch	RCT				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	
		Implant	Prosthesis	Implant	Prosthesis	Implant	Prosthesis
Single tooth gap	Max	1	C	1	C ^a	6	CCCCCC
	Mand	3	CCC	2	C ^b +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 ^c	0	–
	Mand	0		7	2u-2i ^a	4	2u-2i
					2u-2i ^b		2u-2i
					3u-3i ^d		
Total		10	10	15	8	16	14

C = crown; FDP = fixed dental prosthesis; RCT = randomized controlled trial; max = maxilla; mand = mandible; u = unit; i = implant.
^a 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 two implants (case #170096).
^b 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 three implants (case #161515).
^c 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 two implants (case #172481).
^d 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 three implants (case #143045).

Table 4 Distribution of Implant Locations in RCT (n = 25 implants) and in Case Series Study (n = 16 Implants)

	Number of implants placed per location														Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
RCT	0	0	0	2	1	0	1	1	1	0	2	2	2	1	13
CS	0	0	3	2	0	0	0	0	0	0	1	0	0	0	6
Maxilla tooth No.	17	16	15	14	13	12	11	21	22	23	24	25	26	27	
Mandible tooth No.	47	46	45	44	43	42	41	31	32	33	34	35	36	37	
RCT	0	2	2	0	0	0	0	0	0	1	3	3	1	12	
CS	0	3	1	0	0	0	0	0	0	0	1	4	1	10	

FDI tooth-numbering system.
 RCT = randomized controlled trial; CS = case series study.

June 2014. No participants were excluded due to insufficient bone volume for dental implant placement. In the initial RCT, the mean 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 women and two men.

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

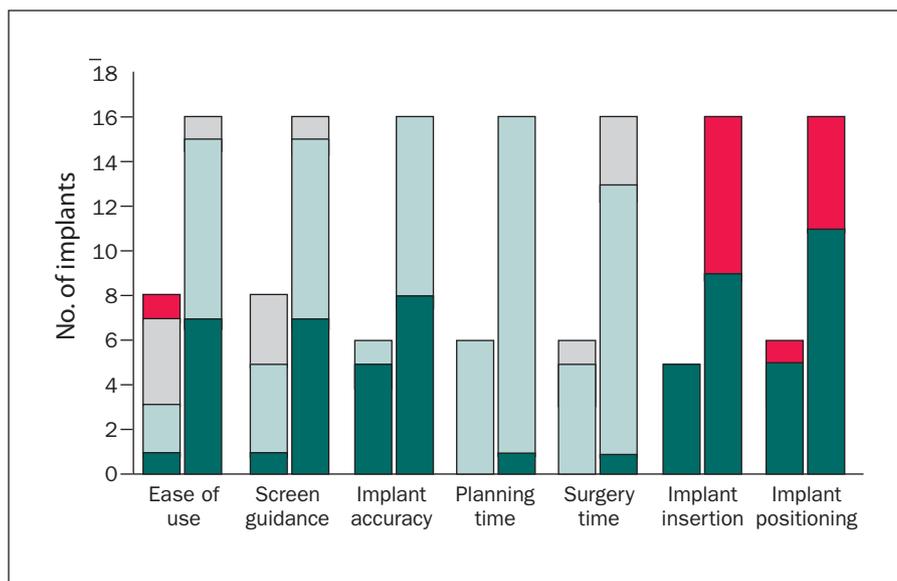
3). There were no distal extension situations or anterior edentulous spaces in the mandible, and the majority of implants were placed in the posterior mandible (Table 4).

In the RCT, the placed implants were either Osseospeed TX (n = 11, Astra, Dentsply), Replace Select Ti-Unite (n = 8, Nobel Biocare), or Straumann Bone-Level SLActive implants (n = 6, Straumann 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 (> 35 Ncm insertional torque and implant stability quotient [ISQ] > 65 measured immediately postsurgically).

Table 5 Different Implant Systems, Lengths, and Diameters Used in RCT (n = 25) and in Case Series Study (n = 16, cursive)

Diameter (mm)	Length (mm)					n
	8	9	10	11	13	
Astra Osseospeed TX (11 and 0)						
3.5	3	1	–	1	–	5 and 0
4.0	0	0	–	4	–	4 and 0
5.0	0	1	–	1	–	2 and 0
Nobel Replace Tapered Groovy (8 and 1)						
3.5	0	–	2	–	3	5 and 0
4.3	1	–	1 and 1	–	0	2 and 1
5.0	1	–	0	–	0	1 and 0
Straumann Bone-Level SLActive (6 and 8)						
3.3	1	–	1	–	–	1 and 1
4.1	1	–	4 and 6	–	–	4 and 7
4.8	0	–	1	–	–	1 and 0
Straumann Standard Plus (Tissue Level) (0 and 8)						
3.3	1	–	–	–	–	0 and 1
4.1	3	–	0	–	–	0 and 3
4.8	2	–	1	–	–	0 and 3
n	5 and 8	2 and 0	9 and 8	6 and 0	3 and 0	25 and 16

Fig 4 Assessment of the practical usability of the prototype device, as judged by the surgeons immediately following implant placement. Ease of use and Screen guidance: Very simple (*green*), Simple (*light green*), Challenging (*gray*), Difficult (*red*). Implant accuracy: Excellent (*dark green*), Good (*light green*). Planning time and Surgery time: Compressed (*green*), Normal (*light green*), Delayed (*gray*). Implant insertion and Implant positioning: facilitated (*green*) or not facilitated (*red*). Left column within each criteria represents the feedback in the initial RCT trial (n = 5 implants [8 evaluations, including 3 surgeries where implants could not be placed by use of the prototype CA-navigation device]), while the right column represents the feedback in the succeeding case series study (n = 16 implants).



The two surgeons judged that, in most situations, according to the Likert-type questionnaire, the prototype CA-navigation device scored “good” for ease of use and guidance provided by the computer screen, “excellent” for implant placement accuracy, and “normal” for the planning time and surgery time required. The surgeons also reported that the insertion of the implant was facilitated with the prototype device compared with the conventional approach (Fig 4). In no situation did the one prototype 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 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 had to deviate from the preplanned implant site to place an implant in a more optimal position.

In four situations, inadequate performance of a component of the prototype device led to the surgeon abandoning CA-navigation and proceeding with using



Fig 5 All implants placed by use of the prototype 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 marked with an asterisk (*) ($n = 6$).

the laboratory-fabricated surgical guide as guidance. The two reasons were poor fit of the intraoral template ($n = 3$ patients, 7 implants), and discrepancies noted between the virtual surgical field and the intraoral anatomy ($n = 1$ patient, 3 implants). In two of these situations, intraoral templates had been fabricated for CA-navigation in both arches, and the surgeon was able to place the implants according to this procedure in one of the arches (Table 3).

The independent assessment of the clinical photographs and radiographs identified 26 of the 41 implants considered as optimal placements, while 16 showed minor deviations from an optimal position. Ten of the implants demonstrating minor deviations had been placed with the use of a laboratory-fabricated surgical guide, while six had

been placed by use of the prototype device. None of the implants were judged to exhibit any major deviations from the optimal position. All the implants had been restored without any adverse events during the fabrication process (Fig 5).

All study participants were examined clinically and radiologically 1 year after implant loading. The postloading 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 in the conventional group and the prototype group, respectively, revealed bleeding upon probing (Table 6). There were no signs or symptoms of complications associated with the definitive implant-supported prostheses.

Table 6 Radiologic and Clinical Changes Observed at the Clinical Examination 1 Year After Implant Loading

Clinical variable	Conventional surgical guide (n = 20 implants)	Prototype 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

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

DISCUSSION

Optoelectronic CA-navigation devices for dental implant surgery hold great promise, but at present, are not without their shortcomings. A major challenge with any optoelectronic CA-navigation device is that the line-of-sight between the stereoscopic camera and the fiducial markers must be clear at all times. Operators and assistants must therefore be vigilant and avoid positioning themselves or any surgical instrument in this line-of-sight. A momentary loss of line-of-sight is in itself not usually problematic, provided that the software can accommodate brief interruptions and resume its functions immediately. Such interruptions in some early-generation optoelectronic devices developed for tracking mandibular 3D movements¹⁹ 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 clinical trial functioned adequately and regained operations immediately. To what extent the other 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).

Moreover, all optoelectronic logic circuits are more or less affected by the qualities of the ambient lighting, as well as by sudden changes of light intensity or wavelength caused, eg, by reflections or by direct bright LED light from a surgeon’s headlamp. The type of photosensors adopted in existing optoelectronic CA-navigation devices is proprietary information, concurrent with the development of new logic circuits currently occurring at an unprecedented pace.²⁰ Interestingly, 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 appear in some promotional material of optoelectronic CA-navigation devices and are corroborated by videos uploaded to the internet by users. The authors of the present study speculate that these adaptations 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.

The ergonomic issues created by the need to keep this line-of-sight clear may be avoided by using some form of physical component to measure 3D space. One device for dental implant surgery that was approved by the U.S. Food and Drug Administration (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 also 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 in real time.

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. The authors have identified only one paper with clinical data, which is a summary of 100 patient cases treated by three very experienced oral surgeons using the X-Nav device.²¹ One of their conclusions likely applies to all optoelectronic CA-navigation devices, ie, 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 present study, the surgeons' judgments of practical usability and user-friendliness of the components of the prototype CA-navigation device improved over time (Fig 4), although the authors 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 a 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, ie, the arch being operated on. A first prerequisite is that the position of the radiographic fiducial marker(s) relative to the tissues as recorded in the volumetric radiograph must be consistent at all times. Ideally, the radiographic 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 center for CBCT radiography, the staff there may not recognize the critical need for an exact positioning of the template that contains a radiographic fiducial marker(s).

Attempting to control the intraoral aspects of the preparatory imaging, the manufacturers have developed different solutions for avoiding mobility of templates in partially dentate patients through full-jaw or quadrant-sized tightly fitted occlusal splints or clips attached to adjacent teeth (Fig 1). Ensuring a firm position of a template in a fully edentulous arch 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 an invasive approach to place dental implants. One paper reported 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 subperiosteal incision.²³

Inherent in many of these technical approaches is that 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 a case series in order 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 after having received 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 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 illustrate how translating 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 recruit more study participants, 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 the authors' judgment to switch study design from RCT and granted permission to proceed with another 10 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 investigational clinical study, the authors selected a relatively simple way of assessing the clinical suitability of the position of the dental implants with regard to straightforwardness of placing a superstructure. The rationale 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 postoperative 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 abutment or crown. In future studies, greater precision in the determination of the postoperative implant location relative to the virtual plan may be obtained by one of two methods: postoperative CBCT and intraoral digital optical scan using an implant-specific scan body.^{25,26}

A further rationale for undertaking safety 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 in medicine,²⁷ and that 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's performance.

CONCLUSIONS

No surgical adverse events were experienced while placing dental implants guided by the prototype CA-navigation device. A rigid study design was adopted rather than a case series in order to minimize potential detection bias. 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.

ACKNOWLEDGMENTS

The clinicians and staff in the prosthodontic graduate clinic who were involved in this study are thanked for their dedication and efforts; Janet deWinter has excelled as study coordinator for the trial. The implant surgeries were performed by Drs Joseph Fava and Mark Lin. Dental laboratory support and consultation was acquired from Dr Romeo Paculanan. The prosthodontic treatments and follow-up clinical examinations were undertaken by Drs Kinga Baskai, Waad Kheder, Hung-Wen Lee, Hooman Mohandesan, David Powell, and Eszter Somogyi-Ganss. This study was sponsored by Claron Technology Inc, Toronto, Ontario, Canada, through a research agreement with the University of Toronto Innovations and Partnerships Office

(Operating grant #490569) and Dr Asbjørn Jokstad as the principal investigator. The authors reported no conflicts of interest related to this study.

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