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A REVIEW OF EXPANDABLE DENTAL IMPLANTS

Juan José Londoño^{a,1}

Email: juanjose.londono@pxgroup.com

Antonio Manuel Ramos^b

Email: a.amos@ua.pt

Santiago Alberto Correa^c

Email: scorrea5@eafit.edu.co

Corresponding Author: Michel Mesnard^a

Email: michel.mesnard@u-bordeaux.fr

^a *Institut de Mécanique et d'Ingénierie, Université de Bordeaux, Talence, France*

^b *Center for Mechanical Technology & Automation, Department of Mechanical Engineering, University of Aveiro, Aveiro, Portugal*

^c *Bioengineering Research Group, Department of Mechanical Engineering, Universidad EAFIT, Medellín, Colombia*

¹ Present address: R&D, PX Services, La Chaux-de-Fonds, Switzerland

Review of expandable dental implants

Abstract

In the last few years the dental implants market has grown both in developed and developing countries, and is associated with high aesthetic expectations and well-being. Although the success rate of commercial implants is high, some problems associated with a lack of initial stability, marginal bony resorption, and periodontal health, remain, especially with immediate placement and loading. The market offers different designs of dental implants, but cylindrical and tapered devices that are fixed to the bone via an external thread are dominant. One lesser-known but potentially useful design is the expandable dental implant (EDI). This paper presents a review of expandable dental implants that encompasses a survey of the literature, published patents, and available commercial devices. We found 15 articles: prospective human trials (n = 4), human case reports (n = 3), published independent discussions of other articles (n = 2), three big animal trials (n = 3), and in silico studies (n = 3). A total of 73 published patents were found and two expandable dental implants are commercially available to date. We propose a classification system that differentiates between the expansion mechanism and the origin of the expanding action. Some expandable designs have been shown to provide good primary stability, but evidence to date is limited. We encourage future clinical and biomechanical studies to clarify and optimise the potential benefits of these implants.

Keywords: dental implant, new concepts, expandable, primary stability, immediate loading

Introduction

The world market for dental implants was worth US \$4380 million in 2018 and is expected to nearly double by the year 2026.¹ Endosseous (endosteal) dental implants (ODI) make up 80% of that market and are now the main technique used to replace missing teeth or bear a fixed or removable prosthesis.¹ These implants have a high success rate and provide improved functional and aesthetic results compared with other prostheses that replace absent teeth.² The success of ODI depends on multiple variables some of which are shown in Figure 1,^{3,4} and a combination of these determines the mechanical engagement of the implant with the bone immediately after implantation - that is, the primary stability.

It has been shown that micro-displacements below 50 - 125 μm do not interfere with bony repair, and in pure titanium and titanium alloy implants lead to gradual osseointegration.⁵ Higher micro-displacements allowed by inadequate primary stability result in the interposition of fibrous tissue and early loss of the implant.⁵⁻⁷ Early (48 hours - 3 months), conventional (3 - 6 months), and delayed (after 6 months) protocols for the loading of ODI take into account a healing period after implantation when the implant is not functionally loaded.⁸ In this way micro-displacements are minimised, osseointegration occurs, and secondary stability is achieved (secondary stability being the biological anchoring of the ODI to the bone).

In contrast to the aforementioned protocols, immediate loading (IL) does not wait for secondary stability to develop before functional loading of the implant, and thus relies solely on high primary stability to avoid large micro-displacements in the initial period after implantation. IL is becoming more common in clinical practice because it has several advantages, such as a reduction in soft tissue trauma (as no re-entry surgery is necessary), and faster aesthetic and functional results that translate into higher patient satisfaction.⁹ However, it is restricted to cases in which the amount and quality of the bone will allow high primary stability.¹⁰ In the past the use

of ODI with longer and wider diameters than would be necessary for conventional protocols has been suggested to extend the use of IL to suboptimal sites. This, however, is not always sufficient to achieve adequate primary stability, and may not even be an option given the anatomical restrictions and increased risk of larger surgical areas being affected.

Expandable dental implants (EDI) are implants that can increase in geometrical dimension (usually the diameter) after implantation in bone. They were introduced as an option to deliver high primary stability in constrained sites and to extend the use of IL.¹¹⁻¹³ Furthermore, in conjunction with conventional loading protocols they could allow implant placement in sites in which traditional ODI are contraindicated (for example, low bone density, highly resorbed jaw ridge, or osteoporosis). The concept of expandable implants has been successfully implemented in other medical applications such as spinal body fusion,¹⁴ and the stabilisation of ankle and humeral shaft fractures.¹⁵⁻¹⁷ Even though early clinical reports show acceptable success rates,^{11,12} and new EDI patents are currently being applied for, the literature and commercially available devices remain scarce.

The objectives of this review are to present the current state of EDI in the literature (including patents and the market), to propose a classification for EDI, and to identify the potential future for this kind of implant.

Methods

Two electronic searches in the National Library of Medicine's database MEDLINE were performed in July 2020 through the search engine PubMed with no date restrictions. Search one used the terms [expandable OR expanding OR expansion] AND implant AND [tooth OR dental] NOT [[palatal OR maxillary OR ridge OR bone] AND expansion]. Search 2 used [[expandable

implant] AND [tooth OR dental]]. Additionally, the references and the citing articles for each relevant paper were checked to meet the inclusion criteria.

Studies regarding any aspect of EDI with full texts available (including animal or human trials, in vitro or ex vivo experiments, technical notes on the design or working mechanisms of the devices, biomechanical studies and simulations, and even published commentaries on other studies) were included. Studies that did not meet the eligibility criteria were excluded. The systematic methodology is depicted in Figure 2 according to the PRISMA guidelines.

The search for patents was performed directly in the Patentoscope database from the World Intellectual Property Organization (WIPO), which indexes patents from many national offices including the United States Patent and Trademark Office (USPTO), the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), and the National Intellectual Property Administration of the People's Republic of China (CNIPA). No date restriction was imposed on the search results. The relevant patents were categorised according to our proposed EDI classification. We also surveyed the market for commercially available EDI, and gathered information on their design, indicated use, and regulatory status from the manufacturer's published technical specifications and from their market notifications. To facilitate comparison and discussion of the human and animal trials, we used the dental implant placement and loading protocol nomenclature described by Gallucci et al¹⁸ (Table 1).

Results

EDI literature

The systematic literature search found 10 unique articles that met the inclusion criteria. Seven additional documents also met the inclusion criteria after inspection of the referenced and citing articles. Table 2 summarises the 15 articles that were analysed in the review (4 prospective

human trials, 3 human case reports, 2 published independent discussions of other articles, 3 animal trials, and 3 finite elements biomechanical studies).^{11-13,19-30}

EDI patents

Appendix A (online only) shows the results of the search for patents, which included 73 patents from 17 different countries including other members of the patent family (same patent but published in a different patent office). The patents ranged from 1941 - 2019. Figure 3 shows the number of patents published by decade according to the proposed classification.

Type-FI EDI was the most common type found in 60% of the patents, and type RI was the second most common, present in about one-third. Only about 5% of the reviewed patents explored type FS. Type RS was not described in any of the reviewed patents.

Commercial EDI

Only two EDI are available commercially. The first is currently marketed as Ultratooth³¹ (Biodent Inc) but was initially sold as Sargon Immediate Load Implant (Sargon Enterprises Inc). The second has the trademark Pyramidion³² (Dentack Implants Ltd) but was originally named Quad by the same company. A summary of the characteristics of these commercial EDI from their respective websites and 510(k) premarket notices can be found in Table 3. Figure 4 shows the initial and expanded geometry of both commercial implants.

EDI classification

Based on the EDI concepts found in the patents and the literature, we identified two independent aspects that determine the functionality across all types. The first refers to the type of mechanism for the expansion. If it is a rigid body mechanism - that is, it is composed of rigid elements that move relative to each other, we call it 'R' ('rigid'), but if it is compliant or partially

compliant – that is, its working system relies on the elastic deformation of at least one element to press against the bone around the implant, we name it 'F' ('flexible').

The second independent aspect relates to the way in which the expansion mechanism is activated. If it is activated by the input of an external force after implantation, we call it 'I' ('input'). One commonly found example in the reviewed patents is the turning of a screw. Alternatively, if the mechanism is activated by the release of stored energy we call it 'S' ('stored'). The only kind of stored energy in the implants from the reviewed literature and patents was strain energy, but this category could also include other types such as stored energy. Strain energy can be placed on the device before implantation or by the implantation procedure itself (as the surgeon pushes the implant inside the drilled bone or socket). We propose that all EDI should be classified by both aspects and that the letter that identifies the expansion mechanism is used first, resulting in FI, RI, FS, and RS types. However, no RS-type EDI was found in any of the searches. Figure 5 exemplifies the classification of three implants found in the patent search, which fall under different types according to the proposed classification system.

Discussion

In a recent systematic review, Gallucci et al¹⁸ showed that IL protocols for ODI, combined with any placement protocol (immediate, early, or late) are not yet clinically well documented or scientifically and clinically validated. Furthermore, they point out that although immediate and late placement combined with IL protocols, have been sparsely documented, the clinical success rates are not homogeneous, ranging from 87% - 100%. The enduring unpredictability of immediate placement is shown by this and by the fact that strict criteria for case selection were applied in most of the reviewed articles. This means that there is probably a selection bias towards the easiest cases to treat and the patients with the least associated risk factors.²⁰ In the case of ODI for fixed prostheses, Chen et al³³ showed in their meta-analysis of randomised

controlled trials, that IL protocols were associated with a higher incidence of implant failure when compared with conventional loading. The achievement of reliable clinical outcomes with immediate placement and IL protocols by means of improved initial stability has been the main driving force for inventors and manufacturers to develop EDI. However, evidence that suggests that any type of EDI improves initial stability over ODI, and that it translates to higher clinical success in immediate placement and IL protocols, is limited. We could not find a single randomised controlled trial or retrospective study on EDI; all the human trials are prospective. The only studies that directly compared the stability of EDI with conventional ODI were animal trials or finite elements analyses.

The first finite element analysis of EDI was by Pierrisnard et al²⁵ who compared a type-FI EDI, an implant with a locking pin, and cylindrical implant design in different cancellous bone densities. They showed that the implants had better stability (lower maximum displacements) than the control cylindrical implants, but the stability of the locking pin implant was even better than the EDI. The EDI behaved better than the control and locking pin implants in stress distribution, as this was less concentrated around the neck and was spread more evenly from the neck to the apex of the implant. The finite element analysis of the type-FI EDI by Xiao et al²³ compared four ODI designs (conventional cylindrical threaded, apical tapered, neck-tapered, and EDI) in mandibular bones with normal and osteoporotic mechanical properties, and showed some improvement in load distribution with EDI in osteoporotic bone. The high stress areas were smaller and the maximum equivalent stress in the cortical bone lower. Nevertheless, the neck-tapered implant showed better stability in both normal and osteoporotic bone and a similar stress distribution as the EDI. It is important to note that the study's boundary conditions of bonded contact between the implant and bone represented a 'healed' state, and that cancellous bone also grew in the inner part of the EDI. A more accurate analysis of primary stability should simulate the conditions immediately after implantation, as the primary concern is to understand

how the EDI affects primary stability when the implant is not osseointegrated (friction contact conditions), or there is no bone in the inner part of the expandable mechanism and the bone has been compressed around the expanding section.

In the third finite element study, Xiao et al²² focused on the optimisation of the expansion angle and expansion length ratio. For their model, which is similar to the Ultratooth (Biodent Inc) commercial implant, they found that the optimal expansion angle lay between 1.5° and 2.5°, and an expansion length ratio of between 1/3 and 1/2 yielded the best stability in osteoporotic bone. The Ultratooth implant has an expansion length ratio of 1/2, and the expansion angle can be graduated between these values.

Huré et al²⁴ compared the implant stability quotient (ISQ) and bony growth of a type-FI EDI against a locking pin implant in a dog model. The type-FI implant is similar to the Ultratooth design in which the expansion is done in the apical end, and the locking-pin implant consists of a traditional ODI with two transversal holes into which titanium rods are inserted after implantation. They found that there was no difference in ISQ immediately after implantation, but the locking-pin implant had developed a significantly higher ISQ by the end of the 12-week study.

Regarding bony growth around the implants no statistical difference was found. In another animal study, Xiao et al¹¹ compared the ISQ, bony growth, and pull-out force of an FI EDI with a tapered ODI in an osteoporotic sheep model. They found no difference in ISQ after 12 weeks of implantation. The bone-implant contact and pull-out force were increased in the EDI but, as explained in their discussion, this can be a consequence of an increase in the surface area available for osseointegration where new bone grows on the fissures and expanding elements. Although no implant failed, the authors mentioned that F1 EDI can generate the fracture of

trabecular bone as it expands and becomes more brittle and prone to fatigue failure as the internal strains increase at the expanding section.

Lynde et al²⁹ implemented a type-RI EDI in a dog model. This was the only study of this type, and of all the animal studies it had the lowest success rate (26%). The researchers pointed out that the thin expanding wing of this specific design did not effectively compress the bone around the implant, and the wings were prone to incomplete expansion and fracture. Furthermore, there was no way of holding the implant in place while the internal screw was rotated to engage the expansion mechanism. This clearly shows a lack of appropriate tools for the task and highlighted the fact that the implantation of EDI might have special requirements. To be successful, the implant and the placement procedure should be integrated from the beginning of the design process.

Three prospective human clinical trials for type-FI EDI showed overall success rates ranging from 93.3% to 96%. Jo et al¹¹ presented the biggest sample with placement of 286 Ultratooth implants. They reported a higher success rate for immediately-placed EDI (98.9%) than for those placed late (93.9%), and attributed this to higher bone metabolism in the fresh extraction sockets. They also reported a higher success rate for immediate (96.3%) than conventional loading (90%), and attributed it to the strong anchoring provided by the expansion mechanism and the immediate intermittent mechanical stimulation by the occlusive force that stimulates fast osseointegration. Despite the high success rates, they mentioned that 208 of the 286 implants had to be re-expanded after some days of implantation because of a loss of primary stability and development of micromotion. This is a potential issue for types FI and RI EDI, as the expansion relies on the expanded mechanism being locked in place after input of the external force. If the mechanism relies on friction to maintain stability of the expanded mechanism after activation, cyclic loading of the implant by mastication and thermal stress from the ingestion of cold and hot

fluids could loosen it. This common need for re-intervention can also imply higher associated costs and risks of implant failure if the micromotion is not fixed in a timely manner.

Type-FS implants could potentially avoid this issue as they rely on their internal energy to stay expanded and they could potentially consist of a single part with sufficient elastic properties. Samet²¹ placed 23 Pyramidion short EDI implants (7 mm long) in patients with some resorption of the alveolar ridge but healed bone. A 91% success rate was reported with a conventional loading protocol (4C). In a prospective human trial, Reich et al¹² reported a 93% success rate for the Pyramidion EDI with high initial and secondary stability in a slightly larger sample (30 implants).

The most recent study involving EDI, also by Reich et al,¹⁹ expanded on their previous trial with a total of 104 followed-up implants (112 before dropouts). They reported implant success rates of 94.7% in the mandible (2 implants lost) and 83.6% in the maxilla (4 implants lost), and a prosthetic success rate of 100%. These studies on the Pyramidion EDI have exploited the added primary stability of the implant to avoid the need for vertical augmentation of alveolar bone, which is usually indicated in short dental implants, thus saving time and money, and discomfort for the patients.

It is, however, important to note that none of the human trials compared EDI with conventional ODI. This lack of information is critical for accurate assessment of the benefits or deficits that EDI could provide. Another concern about EDI is that it could be easier for bacteria to leak through the inner expansion mechanism and travel to the apical region in the cancellous bone. This was reported by Jo et al,¹¹ as they found evidence that bacteria-laden oral fluids had passed to the apical part of the implant and caused lesions. Although this was not reported in any of their patients, Samet²¹ and Reich et al¹² also mentioned this possibility, as it has been

shown that modern implant-abutment connections do not have the capacity to prevent microbial leakage completely.^{34,35}

It is interesting to notice that the EDI studied in finite elements analyses and in animal and human trials have been limited to those that expand in the apical part, and that no devices that expand in the middle or above the middle point have been explored, even though some patents show that kind of contraption.

Conclusions

As one of the aims of this review we have proposed a classification for EDI. This can help to differentiate the clinical and biomechanical results that have been, and will be, published. Most of the patents describe type-FI EDI and both the commercially available devices are of this type. As there is a vast range of EDI concepts and indicated applications, a first step towards a better understanding of their effects on primary stability could be a well-structured and realistic biomechanical analysis that compares type FI, RI, and FS implants with leading dental implants in different bone scenarios, and is optimised to account for differences in osseointegration, marginal bony resorption, and associated complications. When promising designs are found, animal and human studies could be the next step.

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Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

Not required

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Figure legends

Fig. 1. Variables influencing stability and ultimate success of the dental implant.^{16,17}

Fig. 2. PRISMA diagram of sytematic search of literature on expandable dental implants (EDI).

Fig. 3. Number of patents for expandable dental implants (EDI) published/decade according to the proposed EDI classification.

Fig. 4. Diagrams of the commercially available expandable dental implants (EDI) and their methods of expansion: a) Ultratooth (Biodent Inc) in which the inner screw (in blue) is rotated to displace the nut upwards (in orange) and expand the apical part of the implant; b) Pyramidion (Dentack Implants Ltd) in which a disc (in orange) is pushed in the apical direction by an external tool (not shown) to expand the apical part of the implant.

Fig. 5. Illustrative example of the classification system for EDI: a) Type FI: the internal screw (in blue) is rotated after implantation to expand the flexible middle section (in orange) (based on patent US/6227860); b) Type RI: the internal screw (in blue) is rotated after implantation to slide the anchoring elements (in orange) against the bone (based on patent US/5013242); c) Type FS: the implant is pushed into the bone and the thinner part flexed inward to push against the bone after the implant is released (based on patent US/2721387).

Implant

Implant attribute

- Material
- Surface treatment or coating
- Diameter
- Length
- Taper angle
- Screw presence and type
- Other geometrical parameters

Clinical procedure

- Number of surgical steps
- Healing time before loading
- Overheating at drilling site
- Insertion depth
- Insertion torque
- Drilling sequence
- Use of grafting material

Patient

Lifestyle

- Smoking or tobacco chewing
- Alcohol consumption
- Bruxism
- Diet
- Oral hygiene

Medical condition

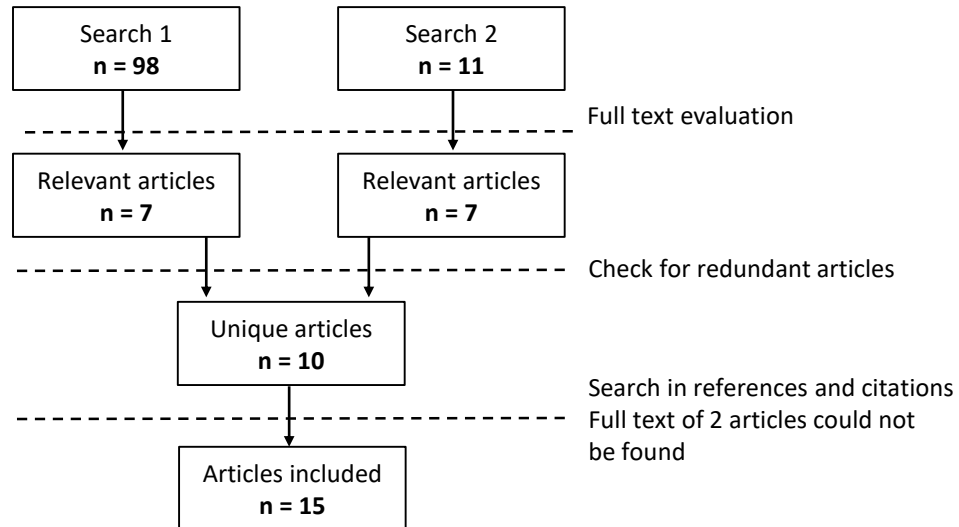
- Diabetes
- Osteoporosis
- Anemia
- Infection
- Use of bisphosphonates

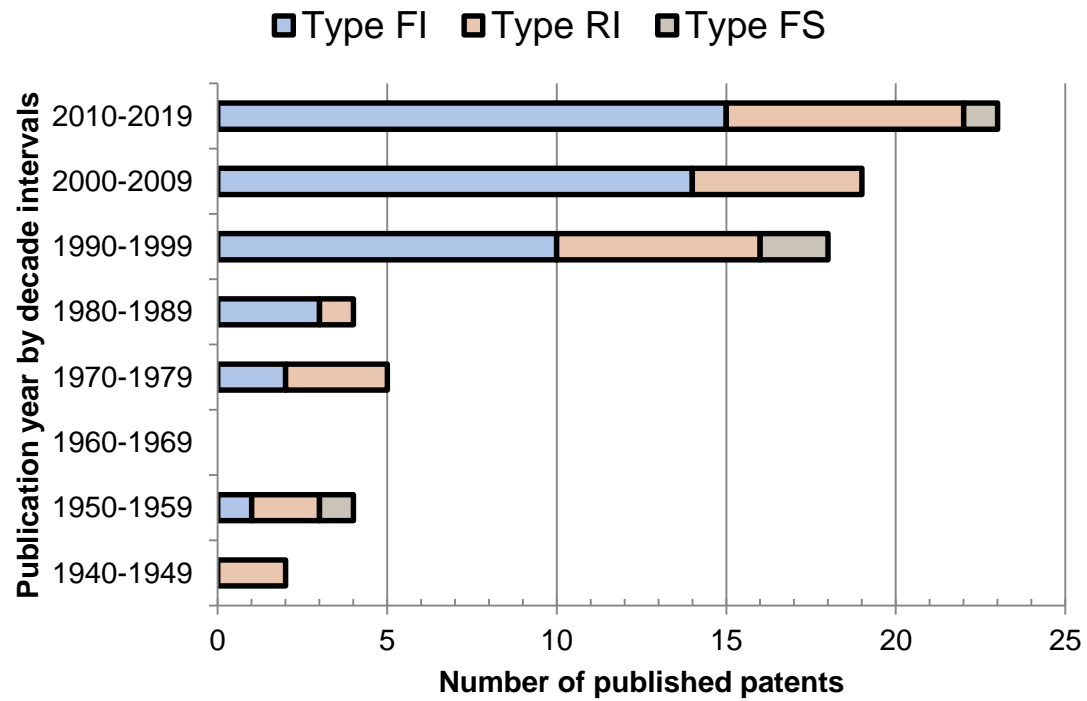
Anatomical

- Bone density
- Bone shape and volume
- Jaw type
- Position in the jaw

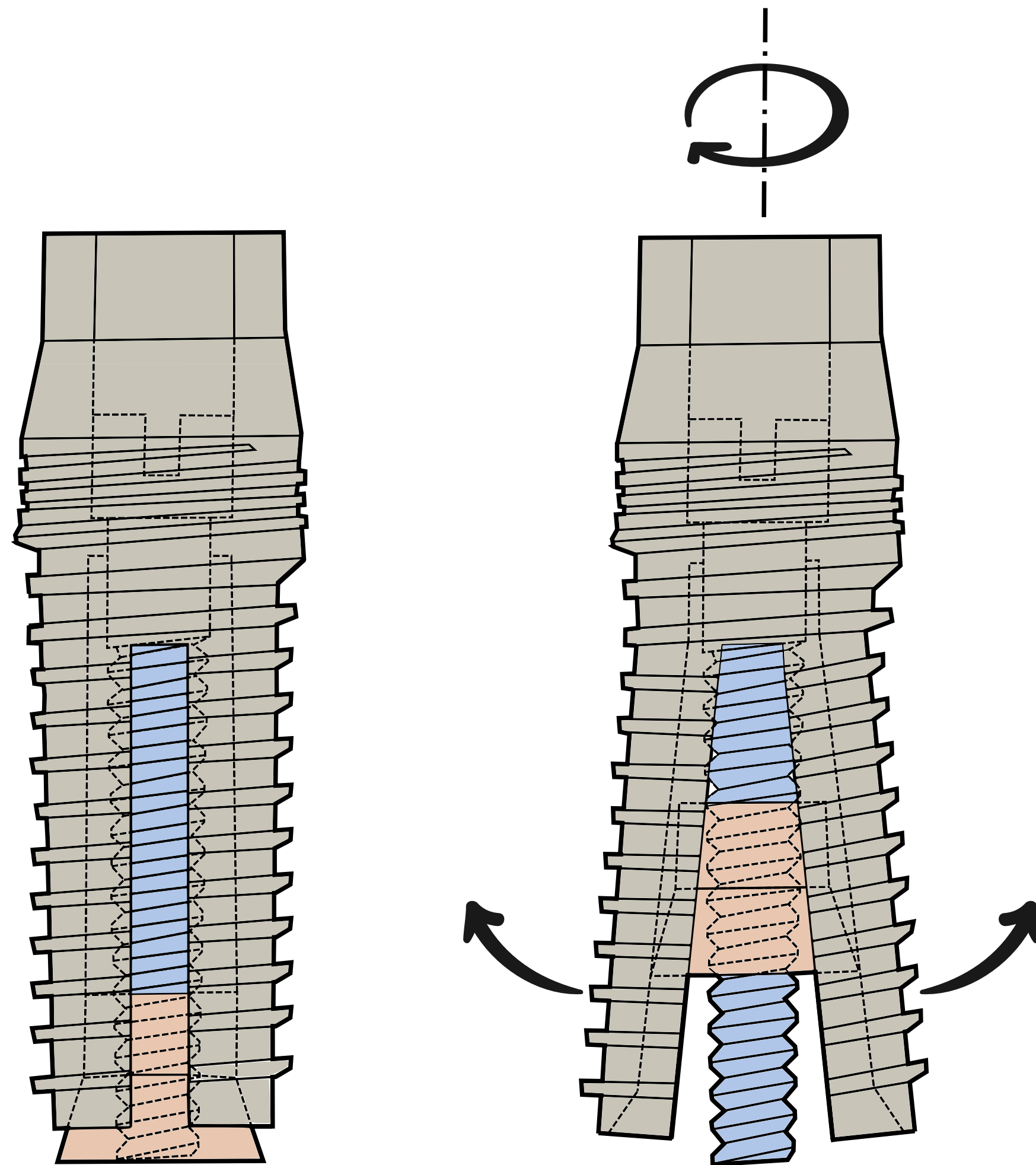
Demographic

- Age
- Gender



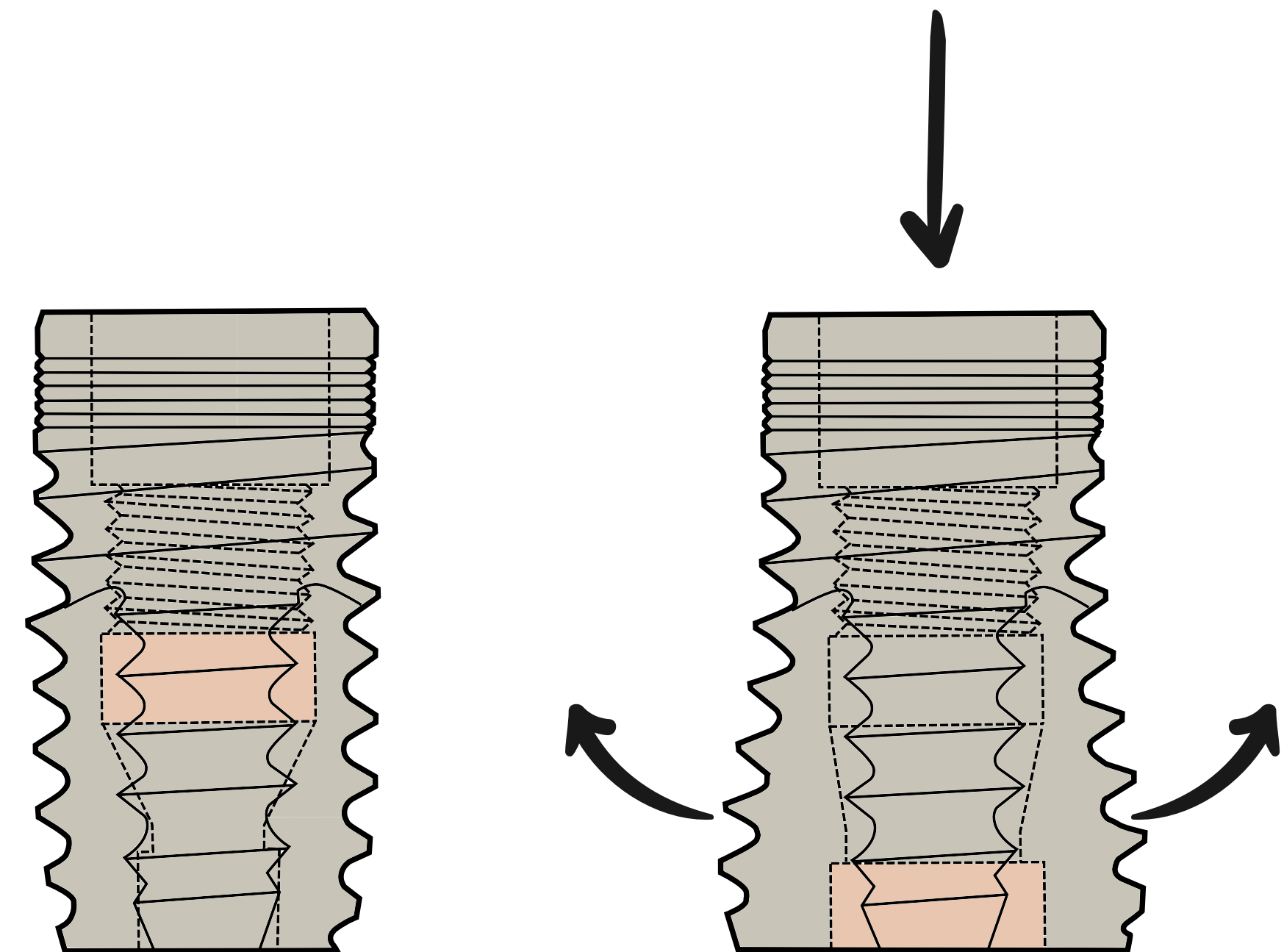


Ultratooth



a)

Pyramidion

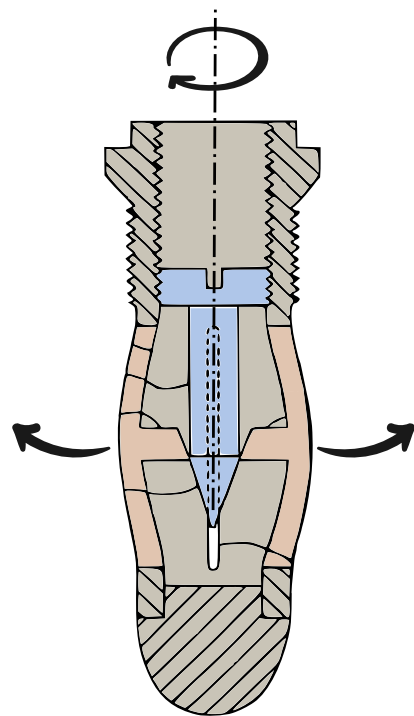


b)

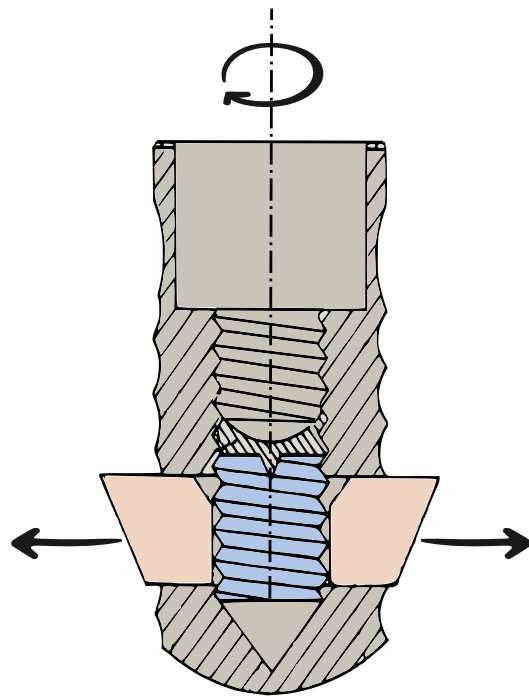
FI

RI

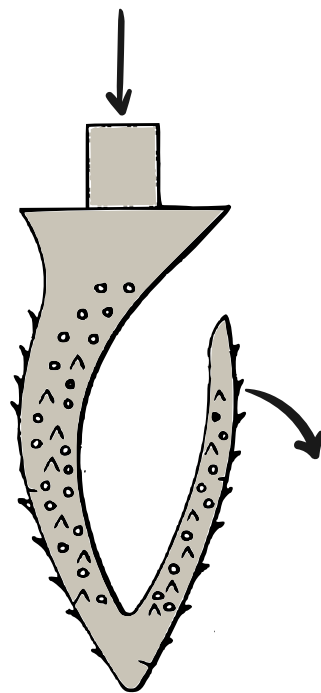
FS



a)



b)



c)

Table 1.

Nomenclature for implant placement and loading protocols for expandable dental implants (EDI).

Placement protocol	Loading protocol		
	Immediate (< 1 week)	Early (1 week – 2 months)	Conventional (> 2 months)
Immediate (same day)	1A	1B	1C
Early (4 -16 weeks)	2-3A	2-3B	2-3C
Late (>6 months)	4A	4B	4C

Table 2.

Summary of articles regarding expandable dental implants (EDI).

First author, year, and reference	Type of study	No. of EDI placed/ EDI type	Placement and loading protocol : No. of implants placed	Follow up time	Conclusions
Reich 2020 ¹⁹	Prospective human trial	104/FI	4C:104	Up to 4.5 years	Overall survival rates in the maxilla and mandible: 1-year survival of 86.8% and 98.0%, respectively, 2-year survival of 84.9% and 96.1%, respectively, and 3-year survival of 84.9% and 96.1%, respectively
Brignardello-Petersen 2018 ²⁰	Discussion on Reich et al ¹⁰	----/FI	----	----	Short EDI should be directly compared with regular short implants, regular length implants, and bone augmentation before deciding between them
Reich 2017 ¹²	Prospective human trial	30/FI	4C : 30	3 years	Success of 93.3%. High initial and secondary stability

Samet 2014 ²¹	Prospective human trial	23/FI	1C : 1 4C : 22	Up to 3 years	Success of 91%. No periapical pathologies
Xiao 2013 ¹³	Prospective animal trial	12/FI	----	12 weeks	EDI increased bone-implant contact and increased osseointegrated surface area compared with tapered implant
Xiao 2013 ²²	Finite element analysis	----/FI	----	----	For apically expanding EDI, the optimal expansion angle is between 1.5° and 2.5° and the expansion length is between 2/6 and 3/6 of the implant body
Xiao 2011 ²³	Finite element analysis	----FI	----	----	Better stress distribution for the EDI than cylindrical implant
Huré 2004 ²⁴	Prospective animal trial	9/FI	----	3 months	Higher secondary stability for locking pin system than for EDI
Pierrisnard 2002 ²⁵	Finite element analysis	----FI	----	----	Better stress distribution and slightly higher initial stability for the EDI than cylindrical implant
Jo 2001 ¹¹	Prospective human trial	286/FI	1A : 82 1C : 8 4A : 164 4C : 32	Up to 40 months	Success of 96% in the maxilla and 94.8% in the mandible
Langstaff 2001 ²⁶	Single human case report	1/FI	1A : 1	52 months	Successful immediate loading
Allen 1999 ²⁷	Discussion on Nowzari et al ²⁸	----FI	----	----	Single case report not clinically relevant to draw conclusions
Nowzari 1998 ²⁸	Single human case report	1/FI	1A : 1	9 months	Successful immediate loading
Lynde 1996 ²⁹	Prospective animal trial	27/FI	----	12 weeks	Flawed implant design with breaking expandable parts. Must be improved before human trial
Lazarof 1992 ³⁰	Single human case report	2/FI	1A : 2	8 weeks	Successful immediate loading

Table 3.

Comparison of two commercially available expandable dental implants (EDI).

	Ultratooth™	Pyramidion™
Manufacturer	Biodent Inc.	Dentack Implants Ltd.
Country	USA	Israel
Location	Posterior or anterior / maxilla or mandible	Posterior or anterior / atrophic maxilla or mandible
Indicated loading protocol	Immediate implant placement and loading	Delayed, conventional or immediate (only when good primary stability is achieved). 5 and 6 mm implants only for delayed loading
Diameter (mm)	3.9	3.75 4.1
Length (mm)	10, 13, 16	7, 8 5, 6, 7, 8
Material	Ti-6Al-4V ELI	Body: Ti-6Al-4V ELI, Foils: titanium
Surface	Alumina grit blasting and acid etching	Titanium oxide blasting and acid etching
FDA 510(k) #	K981141, K961005	K152188, K180859
FDA 510(k) Year	1996, 1999	2016, 2018
Related literature	9,26–28,30	10,19,21
Related patents	WO/1997/024996	WO/2008/029215
EDI classification	FI	FI

Appendix A (online only)

EDI patents found in the database search.

Office	Publication number	Year of publication	Applicant Country	Also published as	Type
United States of America	US/2258207	1941	United States of America		RI

United States of America	US/2449522	1948	United States of America	RI
United States of America	US/2721387	1955	United States of America	FI,FS
United States of America	US/2745180	1956	United States of America	RI
United States of America	US/2857670	1956	United States of America	RI
United States of America	US/3497953	1970	United States of America	RI
United States of America	US/3738008	1973	United States of America	RI
United States of America	US/3708883	1973	United States of America	FI
United States of America	US/3905107	1975	United States of America	RI
Russian Federation (USSR data)	SU/00728855	1977	Russian Federation	FI
United States of America	US/4220712A	1980	Italy	FI
Germany	DE/000003326710	1985	Germany	FI
United States of America	US/4588381	1986	Italy	DK/511083 EP/0114955 ES/283485 ES/287490 PT/77696 IT/1159829 FI
Germany	DE/000003819172	1989	Germany	RI
United States of America	US/5004421	1991	United States of America	FI

United States of America	US/5013242	1991	Switzerland	EP/0317688	RI
United States of America	US/5141435	1992	United States of America		FI,RI
United States of America	US/5197881	1993	United States of America		RI
United States of America	US/5219287	1993	Japan		FS
United States of America	US/5470230	1995	United States of America		FI
WIPO	WO/1995/031152	1995	United States of America	AU/1995024785 CA/2188940 EP/0760635 JP/2000504233 US/08242258 US/5931674	FI
WIPO	WO/1996/035393	1996	Germany	DE/19517459 EP/0784456 US/6007337	FI
WIPO	WO/1996/022061	1996	United States of America	AU/1996048989 CA/2186028 EP/0752834 US/08376013	FS
South Africa	ZA/1996/03718	1997	Germany		FI
WIPO	WO/1997/024996	1997	United States of America	AU/1997010783 CA/2241926 CN/1207028 EP/0877578 EP/1281372 JP/1999501856 KR/1019990076811 MX/PA/a/1998/005423 NO/19983047 SG/54750 US/08590275	FI
Germany	DE/000019705571	1998	Germany		FI

United States of America	US/5725378	1998	Taiwan		RI
				AU/1997043055 CA/2266126 CN/1230880 CZ/PV1999-893 EP/1014899 IL/128695 JP/2001505081 KR/1020000044042 MX/PA/a/1999/0023 45 NO/19991228 RU/02195894 TR/1999/00545 US/20020040243 US/20020116066 US/6129763	
WIPO	WO/1998/0107 22	1998	France		FI
WIPO	WO/1998/0095 81	1998	Germany	AU/1997042945 DE/19635619 EP/1006926	FI
United States of America	US/5849004	1998	United States of America		RI
United States of America	US/5951288	1999	United States of America		FI
United States of America	US/5890902	1999	United States of America		RI
European Patent Office	EP/1018319	2000	Switzerland		RI
United States of America	US/6042380	2000	Israel		FI
WIPO	WO/2000/0060 37	2000	Germany		RI
United States of America	US/6227860	2001	Japan	JP/2000157558	FI
United States of America	US/6332778	2001	South Korea	KR/1020000056128	FI

United States of America	US/6350126	2002	Argentina		FI
South Korea	KR/1020020072632	2002	South Korea		RI
WIPO	WO/2002/062256	2002	Hungary	AU/2002232029	RI
WIPO	WO/2003/057066	2002	United States of America	AU/2002326370 EP/1465543 US/10034344	FI
WIPO	WO/2003/055403	2003	South Korea	AU/2002367158 KR/1020010088231	FI
United States of America	US/20030124488	2003	United States of America		FI
Spain	ES/2216692	2004	Spain		FI
WIPO	WO/2004043281	2004	United States of America	AU/2003291735 US/10292182	FI
WIPO	WO/2006/112955	2006	United States of America	AU/2006237638 EP/1868516 NZ/562505 US/11107610	FI
WIPO	WO/2008/029215	2008	Israel	EP/2076206 ES/2594862 IL/177848 KR/1020090053846 US/20090208905	FI
Japan	JP/1999033039	2008	Japan		FI
United States of America	US/20080208264	2008	United States of America		FI
South Korea	KR/100925661	2009	South Korea		FI
United States of America	US/20090125071	2009	United States of America		RI

United States of America	US/20100304333	2010	United States of America		RI
WIPO	WO/2010/053767	2010	United States of America	EP/2378999 ES/2662943 US/20100114314 US/20120129132	FI
Spain	ES/2341069	2011	Spain		FI
China	CN/101690679	2011	China		FI
WIPO	WO/2011/017523	2011	South Korea	KR/1020120096926 US/12536948	FI,FS
United States of America	US/20110269103	2011	United States of America		FI
WIPO	WO/2011/143346	2011	United States of America		FI
WIPO	WO/2011/033498	2011	Israel	EA/201270229 EP/2480162 IL/218427 IN/1843/DELNP/2012 US/20120270181	FI
WIPO	WO/2012/024445	2012	United States of America		RI
WIPO	WO/2012/045787	2012	France	EP/2603163 ES/2632347 US/20140148864	FI
France	FR/2970641	2012	France		RI
United States of America	US/20130260338	2013	United States of America		RI
China	CN/104068942	2014	China		FI
WIPO	WO/2014/164923	2014	New Zealand	EP/2967763 US/20160022386	RI

United States of America	US/20140363787	2014	Italy		RI
United States of America	US/20140356812	2014	United States of America		FI
WIPO	WO/2015/068945	2015	South Korea	CN/105705111 KR/1020130134052 US/20170119503	FI
China	CN/106073916	2016	China		FI
United States of America	US/20160278886	2016	United States of America		FI
WIPO	WO/2016/060962	2016	New Zealand; United States of America	CA/2964912 JP/2017534423 US/20170239020	RI
China	105997278	2018	China		FI
WIPO	WO/2019/152869	2019	United States of America		FI
