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Current state of Root Analogue Implants (RAI): A systemic review

Master's Thesis

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Current state of Root Analogue Implant (RAI): A systemic review

Master thesis

The thesis was done

By student..	Supervisor..
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EVALUATION TABLE OF THE MASTER'S THESIS
OF THE TYPE OF SYSTEMIC REVIEW OF SCIENTIFIC LITERATURE

Evaluation: ....

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No.	MT parts	MT evaluation aspects	Compliance with MT requirements and evaluation		
			Yes	Partially	No
1	**Summary (0.5 point)**	Is summary informative and in compliance with the thesis content and requirements?	0.3	0.1	0
2		Are keywords in compliance with the thesis essence?	0.2	0.1	0
3	**Introduc-tion, aim and tasks (1 point)**	Are the novelty, relevance and significance of the work justified in the introduction of the thesis?	0.4	0.2	0
4		Are the problem, hypothesis, aim and tasks formed clearly and properly?	0.4	0.2	0
5		Are the aim and tasks interrelated?	0.2	0.1	0
6	**Selection criteria of the studies, search methods and strategy (3.4 points)**	Is the protocol of systemic review present?	0.6	0.3	0
7		Were the eligibility criteria of articles for the selected protocol determined (e.g., year, language, publication condition, etc.)	0.4	0.2	0
8		Are all the information sources (databases with dates of coverage, contact with study authors to identify additional studies) described and is the last search day indicated?	0.2	0.1	0
9		Is the electronic search strategy described in such a way that it could be repeated (year of search, the last search day; keywords and their combinations; number of found and selected articles according to the combinations of keywords)?	0.4	0.1	0
10		Is the selection process of studies (screening, eligibility, included in systemic review or, if applicable, included in the meta-analysis) described?	0.4	0.2	0
11		Is the data extraction method from the articles (types of investigations, participants, interventions, analysed factors, indexes) described?	0.4	0.2	0
12		Are all the variables (for which data were sought and any assumptions and simplifications made) listed and defined?	0.4	0.2	0
13		Are the methods, which were used to evaluate the risk of bias of individual studies and how this	0.2	0.1	0

		information is to be used in data synthesis, described?			
14		Were the principal summary measures (risk ratio, difference in means) stated?	0.4	0.2	0
15	**Systemiza-tion and analysis of data (2.2 points)**	Is the number of studies screened: included upon assessment for eligibility and excluded upon giving the reasons in each stage of exclusion presented?	0.6	0.3	0
16		Are the characteristics of studies presented in the included articles, according to which the data were extracted (e.g., study size, follow-up period, type of respondents) presented?	0.6	0.3	0
17		Are the evaluations of beneficial or harmful outcomes for each study presented? (a) simple summary data for each intervention group; b) effect estimates and confidence intervals)	0.4	0.2	0
18		Are the extracted and systemized data from studies presented in the tables according to individual tasks?	0.6	0.3	0
19	**Discussion (1.4 points)**	Are the main findings summarized and is their relevance indicated?	0.4	0.2	0
20		Are the limitations of the performed systemic review discussed?	0.4	0.2	0
21		Does author present the interpretation of the results?	0.4	0.2	0
22	**Conclusions (0.5 points)**	Do the conclusions reflect the topic, aim and tasks of the Master’s thesis?	0.2	0.1	0
23		Are the conclusions based on the analysed material?	0.2	0.1	0
24		Are the conclusions clear and laconic?	0.1	0.1	0
25	**References (1 point)**	Is the references list formed according to the requirements?	0.4	0.2	0
26		Are the links of the references to the text correct? Are the literature sources cited correctly and precisely?	0.2	0.1	0
27		Is the scientific level of references suitable for Master’s thesis?	0.2	0.1	0
28		Do the cited sources not older than 10 years old form at least 70% of sources, and the not older than 5 years – at least 40%?	0.2	0.1	0

Additional sections, which may increase the collected number of points					
29	**Annexes**	Do the presented annexes help to understand the analysed topic?	+0.2	+0.1	0
30	**Practical recommen-dations**	Are the practical recommendations suggested and are they related to the received results?	+0.4	+0.2	0
31		Were additional methods of data analysis and their results used and described (sensitivity analyses, meta-regression)?	+1	+0.5	0
32		Was meta-analysis applied? Are the selected statistical methods indicated? Are the results of each meta-analysis presented?	+2	+1	0
General requirements, non-compliance with which reduce the number of points					
33		Is the thesis volume sufficient (excluding annexes)?		15-20 pages (-2 points)	<15 pages (-5 points)
34		Is the thesis volume increased artificially?	-2 points	-1 point	
35		Does the thesis structure satisfy the requirements of Master's thesis?		-1 point	-2 points
36		Is the thesis written in correct language, scientifically, logically and laconically?		-0.5 point	-1 points
37		Are there any grammatical, style or computer literacy-related mistakes?	-2 points	-1 points	
38		Is text consistent, integral, and are the volumes of its structural parts balanced?		-0.2 point	-0.5 points
39	**General require-ments**	Amount of plagiarism in the thesis.	>20% (not evaluated)		
40		Is the content (names of sections and sub-sections and enumeration of pages) in compliance with the thesis structure and aims?		-0.2 point	-0.5 points
41		Are the names of the thesis parts in compliance with the text? Are the titles of sections and sub-sections distinguished		-0.2 point	-0.5 points

		logically and correctly?			
42		Are there explanations of the key terms and abbreviations (if needed)?		-0.2 point	-0.5 points
43		Is the quality of the thesis typography (quality of printing, visual aids, binding) good?		-0.2 point	-0.5 points
***In total (maximum 10 points):**					

***Remark:** *the amount of collected points may exceed 10 points.*

Reviewer's comments: ____
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Reviewer's name and surname Reviewer's signature

TABLE OF CONTENTS

SUMMARY

Objectives: The purpose of the present systemic review is to evaluate the survival rate of custom non-submerged implants placed in fresh extraction sockets. To compare the proposed protocols of manufacturing custom implants with emphasis on root analogue implants (RAI).

Methods: An electronic search was performed on PubMed, Google scholar and Cochrane library databases in order to identify prospective clinical studies and in vitro studies published from January 2007 to January 2017. Keywords that were used during the search: Root analogue zirconia implant, Root analogue implant, custom implant. A hand search was performed within the literature references. Studies were selected according to specific inclusion criteria.

Results: 269 articles were found of which 16 matched the inclusion criteria. 7 articles containing in total 23 Root analogue zirconia implants (RAZI) of which 6 were reported failure after 1 year follow up. 4 articles contained 219 titanium custom implants of which one implant failure was reported. Five *in vitro* studies of RAI in which the primary stability, CAD/CAM and different manufacturing methods were evaluated.

Conclusion: Adding targeted press-fit geometry or threads to the RAI will have a positive effect on stress distribution and lower concentration of bone stress and will provide a better primary stability.

Key words: Root analogue zirconia implant, Root analogue implant, custom implant

Data sources: PubMed, Google scholar, Cochrane library

Abbreviations: Root Analogue Implant (RAI)
Root Analogue Zirconia Implant (RAZI)
Root Analogue Titanium implant (RATI)
Direct Laser Metal Sintering (DLMS)
Yttrium-Partially Stabilized Zirconia (YPSZ)
Rapid Prototyping (RP)
Tessellation language files (STL)

INTRODUCTION

During the last years the field of dental implants has been improved tremendous. Combination of new alloys and coatings has had subsequently improved the success rate.

Conventional dental implants have been produced by machining titanium rods. By applying special coatings, osteointegration is accelerated and bone to implant contact increased. Surface modification as sandblasting, acid-etching, grit-blasting, anodization, discrete calcium-phosphate crystal deposition, coatings with biological molecules and chemical modification have been introduced[1].
The improved strength and flexibility of implant material have made it possible to create them narrower and smaller, to be placed in areas where space is scarce and bone amount is limited. The standard procedure often involves extraction and 6 months of healing of the alveolar bone. In this newly formed bone a new dental socket is drilled and prepared to accept the dental implant which is usually screwed in.

Problem with the current implants

Though the advancement of the technology has improved the implant success rate, it has not addressed all of the problems. Mainly the amount of bone that the implant needs is still often an issue. This is usually solved by bone augmentation or bone grafting which after a healing period will be prepared to accept the new dental implant.
A major advantage of an immediate implant placement is the decrease in treatment time with fewer surgical interventions leading to an improved quality of life and overall cost reduction. Also the possibility of less alveolar bone resorption and soft tissue regression due to early functional load[2]. Over the past 40 years, screw or cylinder-type implants have been used in most instances with no changes of the principle and only slight changes in design. The problem associated with immediate placement of these conventional implants is their incongruence with the extraction socket, necessitating the use of a barrier membrane and/or bone augmentation to prevent down growth of connective tissue or epithelium in between the implant and the socket[3]. To achieve stability during an immediate implant placement technique, the socket is widened to the same size disto-mesially and buccal-linguall to be incongruence with the cylindrical size for the implant. Placement of the implant 3-5 mm pass the anatomical alveolar socket is also performed to increase the stability during immediate implant placement[4]. During immediate implant placement gaps between the

implant and the alveolar socket could be present which are often filled with augmented material or bone particles. However in places where every millimeter is precious it is sometimes not possible for an immediate implant placement.
The conventional screw dental implant has a round cross section making it the same size both mesio-distally and buccal-lingually. However the cross sectional sizes of most anterior and premolar roots are larger buccal-lingually compared to mesio-distally. In some areas the space between the teeth does not allow implant placement, therefor smaller more narrower implants have been popular in the recent years.
Another disadvantage with the current conventional titanium implants is the aesthetic disadvantage as it can be seen from the thin buccal side of the gingival wall. Due to gradual bone loss the metallic color of the implant can shine through the gingiva and give it a grey color appearance. Titanium dental implants are well documented and still to this day the first choice, though the use of zirconia has been gradually advancing in the last 10 years.
As the RAI is a one-piece and one-stage implant, submerged healing is not an option. A proposed advantage of the RAI is the possibility to preserve the marginal alveolar bone and soft tissues; however no research has been done to conclude this.

Root analogue Implants

The first ever recorded RAI have been trailed by Hodosh et al. in 1969. The implant was made out of polymethylacrylate. This implant was not osteointegrated and no peri-implant was developed, instead the implant was encapsulated by soft tissue[5]. Root analogue titanium implants (RATI) are created by a combination of 3D scanning of the original tooth and rapid prototyping (RP). In 1992 Lundgren et al. reintroduced the idea of root analogue titanium implants, by evaluating them on beagle dogs. From the 32 RAI that were placed, 28 achieved osseointegration[6].
A system Re-implant® was developed in 1996 involving fabrication of root analogue titanium implants using CAD/CAM by kohal et al. The system required silicone impression of the dental socket and surgical guided preparation of the apical alveolar socket. The implant model was reconstructed with autopolymerizing acrylic and covered with special varnish prior laser scanning. The internal part of this implant was a conventional two part system making it possible for a healing cap placement, for a non-submerged healing. The outer part of the implant was 2nd grade titanium that was milled from the digital CAD/CAM laser scan. This system had a long fabrication period and the implant placement was done after 6-8 hours depending of the production time[7], [8].

In another study by kohal et al. different materials were compared and evaluated the three-dimensional finite element analysis. They analyzed stress distribution patterns in Re-Implant® implants made of commercially pure titanium (cpTi) and yttrium-partially stabilized zirconia (YPSZ). A porcelain-fused-to-metal (PFM) crown for a titanium implant and a ceramic crown for a zirconia implant were modeled and the stress levels were calculated according to the von Mises criteria. Zirconia Re-Implant implants presented a pattern of low, well-distributed stresses along the entire implant-to-bone interface. YPSZ implants had very similar stress distribution to cpTi implants. It was suggested that the zirconia (YPSZ) material was a viable esthetic alternatives, especially in maxillary anterior regions.[9]

However in a clinical investigation study in 2002 of the Re-implant®, 15 of a total of 31 (48%) titanium implants were lost within 9 months. 13 of the 15 implants were lost before prosthodontic reconstruction. Two implants were lost after insertion of the single crowns. Due to this high failure rate over a short time period the implant were not recommended for clinical application.[10]

SELECTION CRITERIA OF THE STUDIES. SEARCH METHODS AND STRATEGY

Fig. 1: Flowchart systemic review

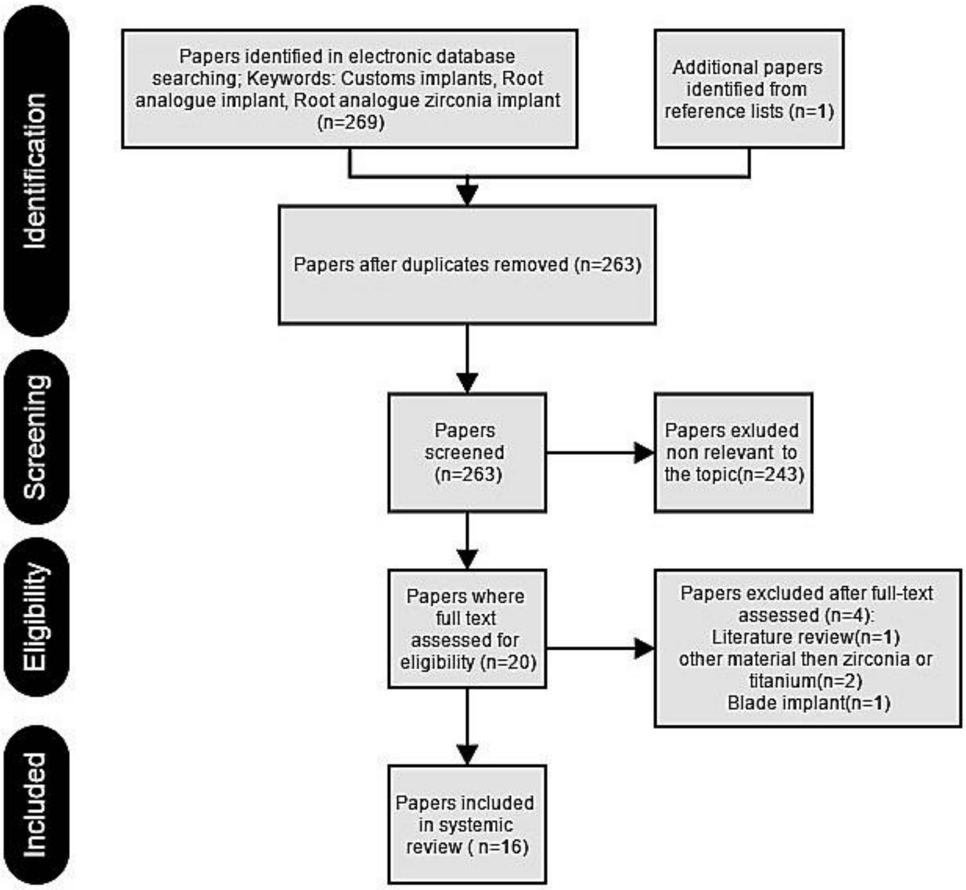

Table 1: Inclusion and exclusion criteria

Inclusion	Exclusion
Full text articles	Reviews, Overviews
DLMS implants	Custom abutment
Within 10 years	Older than 10 years
Articles written in English, German language	At least 1 year follow up
Human Case studies	Animal studies
In vitro studies	Blade implants
Novel studies	Materials other than titanium and zirconia
Clinical trials	

The systemic review was performed by using search engines PubMed, Google scholar and Cochrane library. The inclusion and exclusion criteria are listed in [Table 1]. The articles that were included were not older than 10 years. The search was performed within 5 years and within 10 years term as to compare the amount of published articles within those time limits. Five of the 16 articles were found between 5-10 years old, 11 articles were from the last 5 years. The final search was performed on January 21st of 2017. Using Google scholar search engine, "search in title" was selected within Google scholar advance menu as to reduce the amount of presented results from 57.754 results to 176. This function was also used for the keyword "custom implants" in PubMed search engine to reduce the amount of articles from 2351 to 16[Annex 1].

Table 1: Total amount of articles

Type of published article	Amount
A novel approach, finite element	5[11]–[15]
Case report, Zirconia	7 [2], [3], [16]–[20]
Case report, Titanium	4[21]–[24]

Reviews and overviews of the topic were excluded as they contain older perhaps non relevant information. After revising the titles and abstracts articles not related to the topic were excluded, the remaining articles were cross referenced for duplicates. Due to the lack of published articles within the topic, case reports were included. Root analogue implants both made out of titanium and zirconia were included as the procedure of fabrication and complications are similar. Including different materials of custom implants was done too evaluate their advantages and disadvantages. Custom made implants using the Direct Laser Metal Sintering (DLMS) technique were included as the fabrication method utilizes rapid prototyping similar to titanium RAI's. Exclusion of custom made abutment and custom blade implant. A follow up of at least one year was needed to assess the success rate for the case reports.

After further revising the 269 articles, only 16 articles met the inclusion criteria. Seven articles containing in total 23 Root analogue zirconia implants (RAZI) of which 6 reported implant failure after a 1 year follow up. Four articles contained 219 titanium custom implants of which one implant failure was reported. Five *in vitro* studies of RAI in which the primary stability, CAD/CAM and different manufacturing methods were evaluated.

No randomized control trials were found within the topic and the amount of published articles were limited. *In vitro* studies comparing the natural root and the fabricated RAI procedure and results were compared and reviewed. Finite element studies of RAI including von Mises were compared and reviewed. Success of single case reports and cases reports were reviewed and data extracted.

1. SYSTEMIZATION AND ANALYSIS OF DATA

1.1. Obtaining digital copy of the root

In the last few years, the application of digital technology in dentistry has become increasingly widespread with the introduction of CBCT scan technology, and considerable progress has been made in the development of computer-aided design/computer-aided manufacturing (CAD/CAM) techniques. CBCT has proven on multiple occasions to be an excellent candidate to obtain the 3D image, and DLMS technology for producing the titanium implant. DLMS is a fabrication process involves the laser-induced fusion of titanium micro particles, in order to build, layer-by-layer, the desired object[21].

By combining CBCT and the CAD/CAM technology it is possible to create more accurate anatomical identical prosthetic devices. The RAI can be manufactured prior extraction and placed directly after, reducing amount of visits and improving the patient's confidence. Another possibility is to acquire a digital copy of the root by laser scanning it post extraction. It is possible to modify the root anatomy by adding macro retentions with regular dental cement or reducing areas. The tooth can be repaired if there is a root fracture and modified by placing macro retention prior laser scanning[2], [3]. The mentioned method might exclude any inaccuracy that a CBCT might cause. However scanning and modifying the tooth post extraction will often result into a delayed implantation and a second surgical procedure is often needed.

Anssari Moin et al. mentioned the possibilities that these innovative techniques like CBCT could produce a customized dental root analogue implant as an alternative to the traditional threaded, straight or tapered implant systems intended to replace a missing tooth. In the study CBCT was used to scan the original tooth, titanium replica was produced by Selective Laser Melting (SLM). A negative 0.15 mm discrepancy has been found in the apical region between the original root and the produced titanium replica. This discrepancy was believed to be caused by the technology inability to distinguish between the dense bone and the apex[14]. The article shows prove of concept and the accuracy of the CBCT and its ability to obtain nearly identical tooth replica.

In a case study by F. G. Mangano et al. a computer tomographic (CT) datasets of a fractured first maxillary right premolar was acquired using a modern cone beam scanner (Veraviewepocs 3DR, Morita Corporation, Tokyo, Japan). After several data conversions software, the titanium RAI was constructed using DLMF device. After the extraction the RAI was placed and primary stability was

achieved[23], [25]. Though it is difficult process of data retrieval from a CT scan and a complex conversion method, the dental implant was accurate enough to achieve primary stability.
In a bigger study including 15 patients, F. G. Mangano et al evaluated the 1-year survival and success rate of root-analogue direct laser metal sintering (DLMS) implants. Computer tomographic datasets of the fractured teeth were acquired using a modern CBCT scanner (CS9300R, Carestream, Rochester, NY, USA). Multiple software conversions were needed to achieve the final three different standard tessellation language files (STL) with different size increments (0, 0.5, and 10 %) of the same RAI in case a smaller or larger size was necessary. The exact root analogue size of 0 % RAI's were placed under finger pressure and by subsequent gentle tapping with a hammer and a mallet[21]. This larger study showed that an exact copy of the root without size adjustment is sufficient to obtain a primary stability.
Anssari Moin et al. conducted an in vitro pilot investigation containing eleven single-rooted teeth from nine human cadaver mandibles. The mandibles were scanned with the use of a CBCT system (3D Accuitomo 170). The RAIs where constructed using rapid manufacturing technology using SLM technology (LayerWise NV, Dent-Wise Division, Leuven, Belgium). After a carefull extraction, the teeth were scanned using an optical system (Atos II SO; GOM GmbH, Braunschweig, Germany). The RAI's were smaller than the original teeth in all instances. Using a 3D iterative closest point registration algorithm (Aloimonos 2004), 3D models of the teeth and the optical scans of the RAIs were superimposed onto each other, and differences were quantified as mean (root mean square [RMS]). The discrepancy for the RMS, volumetric geometry, and surface area varied from 0.08 mm to 0.35 mm, 0.1% to 7.9%, and 1.1% to 3.8%, respectively. Anssari Moin concluded that "it has been demonstrated that the pre-emptive CAD/CAM-based RAI technique could potentially provide accurate dental implants for immediate implant placement. However, the influence of the different image artefacts on segmentation accuracy could be investigated as the study sample was confined to human cadaver mandibles"[13].
In another study by Anssari Moin et al. the accuracy of the printed zirconium RAI vs. the RAI CAD model vs. the optical scan of the natural tooth printing were compared. The results showed that the printed RAI has a 6.67% larger surface area, and 46.38% of the printed RAI has a greater distance than 0.1 mm from the original tooth representing a volumetrically larger copy. Measurement for the DLP 3D-printed RAI surface to be deviating from the CAD model, it is shown that 59.33% and 4.86% of the surface areas are exceeding the threshold distances of 0.1 and 0.5 mm. The greatest difference was in DLP 3D printed RAI compared to the original anatomy which was 0.86 mm

orientated in the apical region. In this study Anssari moin concluded that "The DLP 3D printing technology provides less accurate models then the commercially available technique for titanium implant production like SLM and DMS"[11], [14].
The published articles of Anssari Moin et al. show that it is possible to produce an accurate enough RAI. In both researches the apical part possesses a difficulty in obtaining the exact dimensions. All steps in the process of fabricating of a pre-emptively made RAI can result in geometrical deviations and structural imperfections. Consequently, these errors can lead to discrepancies in implant fit in the socket, lessened bone-to-implant contact, decreased mechanical engagement of the implant, or highly pressurized implant fit[13].

1.2. Modification of the custom implants

The great advantage of custom made implants made by rapid prototyping is the ability to modify the implant in any way the physician desires. Custom implant design can create new possibilities by designing an implant with the optimum depth and width. Next too size alteration mechanical retention and pressure reduction is often needed to increase the primary stability and reduce high pressure points.
Kohal et al. suggested modifying the RAI by widening the coronal part of the root analogue implant to compensate for the loss of periodontium after the extraction. However this modification led to fracturing of the thin buccal wall of the alveolar bone compromising the healing and subsequently failure of the implant[26].
David Anssari Moin et al preformed a study into RAI designs on alveolar bone stress. Design included five different types of designs; non-modified Standard, targeted press-fit Prism, targeted press-fit Fins, targeted press-fit Plug, and targeted press-fit Bulbs. The bone models were constructed using a homogenous isotropic linearly elastic material of 1mm inner cortical layer. Two loads were applied to simulate anterior bite force and evaluated. It was concluded that the design containing Fins or Bulbs had the most favourable results[12].
All articles suggested some sort of modification on the implant to relief pressure induced necrosis. An exact copy of the RAI may provide a good primary stability, however the RAI technique is based on the press-fit phenomenon. Pressure induced necrosis may cause intermediate time failure as the bone starts to resorb. It is caused due to subsequent uniform pressure-induced resorption simultaneously involving the entire alveolar surface[21]–[23].

Modification of the obtained root anatomy is difficult as there is no specialised software for that specific purpose. The digital modifications that were performed were done with a great variety of software to achieve the final STL file. Some authors modified the extracted tooth by adding macro retention on the original tooth with the usage of a dental cement to design the new implant prior obtaining a digital copy. Another great advantage of designing the implant is the ability to add prepared crown abutment with the desired step and inclination. Modifications were made by Patankar et al. on an extracted tooth with light cured composite material to form a post to receive crown after the implantation. Macro retentions were designed on the root surface with light cured flowable composite material. The macro retentions were placed only on the mesial and distal surface, adding them on the lingual and buccal side might cause a fracture of the thin alveolar bone[3].

Pirker et al. has pointed out that a perfectly identical implant would have good primary retention but might fail in the intermediate time. The uniform pressure caused by the RAI could potentially produce a negative effect on the alveolar bone causing resorption instead of osseointegration[2]. The conventional dental implant avoids this complication by having threads which cause areas of relieve. Reduction in the buccal and lingual face by 0.1-0.2 mm is advised to reduce the chance of fracture of the thin cortical bone during the insertion[17].

In a larger study by Pirker et al. the difference between modified and non-modified RAZI implants success rate was examined. It included 18 patients dividing them into 2 groups. Group A included 6 patients that got an unmodified RAZI, though primary stability was achieved all 6 implants failed within 26-128 day. Group B which consisted of 12 patients got the modified implants. The roots were modified with macroretention in the interdental space, and a diameter reduction of 0.1– 0.2 mm next to the buccal cortical bone. Only one implant failure was recorded and removed after 624 days[17]. With this study it has been shown the importance of proper design of a RAI. Though an exact root analogue implant is able to achieve good primary stability, they have a great failure rate due to lack of osseointegration and running the risk of fracturing the thin buccal wall.

Nair et al. created a custom zirconia implant for the use with the endpore dental implants system. The patient desired a metal free solution for his implant so a custom made zirconia implant was milled. The implant was placed after preparation of the alveolar bone using the endopore osteotomy burs[16].All of the articles containing RAZI implants were sandblasted and sintered for 8 Hours, this was done to achieve desired mechanical properties for greater retention.[2], [3], [17], [18] Laser forming methods allow the fabrication of functionally graded titanium implants with a, gradient of porosity perpendicular to the long axis. With DLMF, a porous surface structure for improved bone ingrowth capability is provided, eliminating the need for applying a thermally sprayed titanium coating on the implants. DLMF makes it possible to generate implants with a graded elasticity, incorporating a gradient of porosity, from the inner core to the outer surface[27], [28]. In a prospective clinical study by Carlo Mangano et al. the survival rate and the implant-crown success was evaluated. Two-hundred and one screw-type cylindrical implants were manufactured from titanium alloy (Ti-6Al- 4V) with a DLMF technique (TixOsR, Leader-Novaxa, Milan, Italy). The DLMF implants were made of master alloy powder with a particle size of 25–45 μm as the basic material. The implants were manufactured by the desired length and diameter. Though the involved implants were not RAI, the size and height of the implants were adopted to the alveolar bone classifying the implant as custom-made[29].

1.3. Manufacturing

Unlike zirconia RAI, titanium material for the RAI is well documented. DLMF is a technology in which a high-power laser beam is directed on a metal powder bed and programmed to fuse particles according to a CAD file, thus generating a thin metal layer. Apposition of subsequent layers gives shape to a desired 3D form with minimal post-processing requirements. With DLMF, it is possible to fabricate dental implants of different size and shape directly from CAD models.[23]

Trails using a different type of RAI fabrication methods have been done by David Anssari Moin et al. A high-end DLP 3D printing technology (under current development by ADMATEC Europe BV, Moergestel, the Netherlands) was used to fabricate the RAI from the CAD STL file. Unlike the milling technology this is an additive manufacturing technique in which solid 3D objects are built using a DLP projector to translate voxel data, so it is reproduced in liquid photopolymer, thereby light polymerizing the resin to solid[11]. The results were not optimal compared to the DLMS technique that is used for the fabrication of titanium RAI. It was mentioned that "perhaps the vault was in the resolution of the digital mirroring device which is a part of the DLP printer and the composition of the ceramic photopolymer. Fine-tuning the DLP 3D printing might resolve the problem" however during the study this was no performed.

The previous mentioned techniques all used DLMS to produce titanium root analogue implant (RATI). The RAZI are usually milled out of a solid zirconium dioxide block patankar et al. laser scanned the modified tooth and milled using a CAD CAM(Ivoclar vivadent-zenostar) using

“Ziecon by Jyoti Ceramic GmbH”[3]. However the articles containing RAZI the fabrication method was not explained in detail[2], [17]–[20].

1.4. Placement Timing and method

It has been greatly debated about the negative and positive sides of immediate implantation. Primary stability of an immediate implant is of great concern. RAI could potentially solve this problem as the implant should be in theory congruence with the alveolar socket.
During extraction of the affected tooth care should be taken into preserving the dental alveolar wall as this might influence primary stability. Francesco Guido Mangano et al. mentioned to perform a longitudinal extraction after periotomy avoiding orovestibular luxation. The loss of one of the cortical walls could compromise the correspondence between the custom-made RAI and the socket, reducing primary stability[21].
The presence of curved and divergent roots may represent another potential limitation of the RAI technique; in fact, this anatomical situation may render the placement of RAI difficult. However, the elasticity of alveolar bone may limit, at least to some extent, the negative impact of divergent root anatomy/curved roots, when RAI’s are placed.When atraumatic extraction cannot be performed, or bony walls of the socket are fractured, the placement of RAI should be avoided, and standard, commercially available implants/fixtures should be installed[18], [22].
In a case by Patankar et al. after extraction the extraction socket was cleaned by curettage and iodoform-cotton gauze was placed in the fresh socket. On the 3rd day the RAZI was placed under finger pressure[3]. In a clinical report by Pirker et al. RAZI was placed 4 days after extraction of the tooth. This small delay of implantation might have advantage so the body has the chance of removing any infected tissues in the socket. However a delay in implantation might have a negative effect on the placement of RAI implant as the socket might change its size[2]. In another clinical report by Pirker et al. the RAI was placed after 6 days, and even 7 days post tooth extraction[18], [19]. Though all of the RAI had a slight modified anatomy, it was is still possible to gently insert the implant by finger pressure and tap it firmly into place with a mallet.[2], [3], [17], [18] These cases show that the primary stability of an RAI can be achieved even up to several days of healing. The delay has small effect on the alveolar socket size and shape if the extraction was performed atraumatic.
Primary stability following implant placement is needed. When micromotion occurs, stem cells in the osseous wound differentiate to fibroblasts and form scar tissue around the implant, thus

inhibiting osseointegration[30]. Though in all of the reviewed articles the primary stability was always achieved, It was only confirmed by palpation and percussion as the conventional torqueing method could not be applied.[3]

1.5. Immediate implant placement in infected sites

Great concern with the immediate implant is the presence of an infection in the extracted socket. Presences of periodontitis could have influence on the survival of the immediate placed implant.
In a clinical report by Pirker et al. a maxillary right premolar was extracted which contained root caries indicating that there was some sort of bacterial infection process. The area of the apical paradontitis was cleaned by means of curettage, and an iodoform-soaked cotton gaze was placed in the socket. After 4 days the iodoform cotton gaze was removed, and the alveolar socket again curetted and flushed with sterile physiologic saline solution.[2]
In a different case by pirker et al. a fractured root was extracted and extra oral reconstructed. After addition of macroretention using dental cement, the tooth was laser scanned and a RAZI was manufactured.[19]
Also a combination of chronic apical periodontitis and root fracture has been treated with RAZI by pirker et al. The apical fracture was retrieved through a vestibular bone window keeping the alveolar border completely intact. After 7 days of healing the implant was placed with achieving primary stability.[18]
In a case study by Figliuzzi et al. a lateral incisor with a fractured non–restorable lateral right maxillary incisor was replaced by titanium DLMS RAI. In the article it was mentioned that "Prior to date, there were no studies reporting on these implants in the esthetic area of the anterior maxilla". Care was taken as to not damage the thin buccal wall which could influence the primary stability. At the 1-year follow-up control, the RAI was successfully in function. No biologic complications was reported[24].
Mangano FG, et al. performed a 1-year prospective study on 15 patients with titanium DLMS RAI. Fifteen patients (eight males, seven females; aged between 39 and 55 years, average 45.5) were selected for this study and 15 teeth were extracted. Seven were with root caries, and 5 with root fracture. Another 2 contained endodontic lesion and one with a failed root canal treatment. The result of the study concluded that "after 1 year after placement, no implants were lost, for an overall survival rate of 100 %. All implants were stable, with no signs of infection such as pain or suppuration"[21].

1.6. Tissue response

Pirker et al. stated that “after implantation there has been no change in marginal bone after 2 years of surveying”, however the measurement has been done only by radio graphical examination.[2] Pirker pointed out that bone level measurement by radiographic examination is limited. The dental implant is radiopaque and it is difficult to assess bone alteration radiographically. However in the same study it was noticed that the 58% of the 11 successful implants in the study showed no soft tissue retraction. Nonetheless some of the implants showed some soft tissue retraction up to 1.5 mm (0.5 ± 0.7, mean ± SD) within the first year[17].

Table 2: bone to implant contact

Reference	Crestal bone to implant contact (DIB)
(C. Mangano et al., 2012)	The 1-year mean (DIB) was 0.4±0.2 mm.
(F. G. Mangano et al., 2014)	The 1-year mean DIB was 0.7± 0.2 mm (median, 0.7; 95 % CI 95 %, 0.6–0.8).

C. Mangano et al. and F. G. Mangano et al. recorded the crestal bone to implant contact [Table 3]. In both studies after 1-year mean radiographic evaluation of the implants revealed a mean (± standard deviation) distance from the implant shoulder to the first crestal bone to implant contact (DIB). In the study containing 200 successful custom DLMS implants the DIB was 0.4±0.2 mm[29]. In a study including 15 successful RATI the DIB of 0.7± 0.2 mm was measured with the aim of an ocular grid[21].

2. Discussion

Lundgren et al. reintroduced the idea of RAI in 1992. He used a high grade titanium material, leading to osteointegration in 88 %. The authors concluded that this system osseointegrated with a high degree of predictability and the quality of bone-to- implant contact was high enough to function well[6].

In the reviewed articles that used zirconia as the preferred material over the titanium a yttria stabilized tetragonal zirconia polycrystal block(YZTP) were used[17]. It exhibits a very high flexural strength (900 to 1200 MPa), a favorable fracture toughness (KIC7 to 1 $MPam^{-1}$)[31].

In one reported case the patient insisted on a metal free solution so a zirconia was used to manufacture RAI[16]. Great concern grows lately regarding hypersensitivity and corrosion of the titanium implants. It has been mentioned that zirconia implants have a better esthetical quality when the implant shines through the thin buccal mucosal wall. As the RAI is intended for single rooted teeth its esthetical aspect is important. In a study comparing the peri-implant soft tissue of an titanium versus a zirconia implant. The tissue was compared with the reference tissue of a natural tooth. The zirconia implants had less color difference when compared with the titanium implants[32]. Diminished plaque accumulation and improved aesthetic giving the zirconia implants and advantage over the titanium[3].

In a systemic review about the osteointegration of zirconia Y-TZP implants. The results were comparable to or even better than titanium implants. Though the chosen studies were only on animals the mean bone-implant contact percentage was above 60% in almost all experimental groups. The Y-TZP implants may have the potential to become an alternative to titanium implants however it is stated that more research is needed [31].

A great advantage of titanium RAI produced by DLMF technique, is the possibility to control the porosity of each layer and consequently of the 3D model by changing the processing parameters, such as laser power and peak power, laser spot diameter, layer thickness, hatching pitch (or scan spacing), scan speed and scanning strategy, or by modifying the size of the original titanium particles[22], [29].

2.1. Implant survival and success criteria

Hodosh and colleagues published an article in 2002 proving that root-analogous titanium dental implants provided some initial success however portrayed poor success results (48%) after a 9 months follow-up. Owing to this high failure rate, the use of these titanium RAI was not recommended for clinical use[10].

The procedure for creating of RAI's has changed allot in the last few years. The usage of rapid prototyping technologies like DLMS and milling machines have come far in the last decade. From the 13 articles containing RAI implants, 7 articles contained in total 23 Root analogue zirconia implants (RAZI), 4 of the reviewed articles contained 219 Root analogue titanium implant (RATI) [Table 4].

A recent study by Francesco Guido Mangano included 15 RAI titanium implants. All of the 15 implants survived after 1 year follow-up, no implants were lost, for an overall survival rate of 100 %. It was stated that after 1 year "All implants were stable, with no signs of infection such as pain or of apical implantitis, as monitored by radiographs and soft tissue parameters; and no bleeding on probing"[21].

In the before mentioned prospective clinical study by Carlo Mangano et al. of 201 direct laser metal forming (DLMF) implants in different clinical applications. At the 1-year scheduled follow-up examination overall implant survival rate was 99.5%, with one implant loss (maxilla: 99.0%, 1 implant failure; mandible: 100.0%, no implant failures).Among the survived implants (200), five did not fulfil the success criteria, giving an implant-crown success of 97.5%[29].

Pirker et al. has published 4 case reports containing RAZI, all obtained a long term survival and a final prosthetic treatment[2], [17]–[19]. In a comparative study containing 18 patients Piker showed the necessity of modification of the RAI. Eleven of the 12 modified implants survived while all of the 6 unmodified failed[17]. With these case studies and the comparative study, Piker et al. published in total 15 RAZI that obtained a long term success and has shown the importance modifying of RAI.

Another two cases including RAZI were reported by Patankar et al. and Nair et al. In case of patankar et al. it was reported that "At 18 months follow-up, the patient presented with a stable implant, unchanged peri-implant marginal bone level and complete apical peri-implant ossification with no signs of peri-implantitis". And in case of Nair et al. at the follow up of two year patient presented with a stable implant, unchanged peri-implant and marginal bone level as monitored by radiographs and soft-tissue parameters, and no bleeding on probing was present. In all of the reviewed case studies it was stated that “no post-operative pain, bleeding, infection or swelling were noticed”[2], [3], [16].

Table 4: RAZI/RATI success rate

Reference	Implant type	Reason extraction	Element	Success/failure
(W. Pirker & Kocher, 2008)	Milled RAZI	Deep root caries and chronic apical paradontitis	maxillary right first premolar, FDI: 14#	At 2-year follow up the patient presented with a stable implant.
(W. Pirker & Kocher, 2009)	milled RAZI Group A: 6 unmodified Group B: 12 modified	Root caries, vertical or horizontal root fracture, endodontic lesions, and unsuccessful root canal treatment	18 patients with a single tooth gap anterior or premolar region	Group B: 5 failed implants Group A: 1 failed implant
(W. Pirker, Wiedemann, Lidauer, & Kocher, 2011)	Milled RAZI	Chronic apical periodontitis	Mandibular left first molar, FDI: 36#	At 24 months follow-up, the patient presented with a stable implant.
(Wolfgang Pirker & Kocher, 2011)	Milled RAZI	Fractured tooth	maxillary left second molar, FDI: 27#	At 3 years, the patient presented with a stable implant.
(F. G. Mangano, Cirotti, Sammons, & Mangano, 2012)	DLMF titanium RAI	Fractured non-restorable	Maxillary right first premolar FDI: 14#	At one year after placement, the RAI was still in function and stable.
(Figliuzzi, Mangano, & Mangano, 2012)	DLMF titanium RAI	Fractured non-restorable	Maxillary right second premolar FDI: 15#	At one year after placement, the RAI was still in function and stable. level and no peri-implant radiolucency.
(C. Mangano et al., 2012)	DLMS titanium custom implant	Not defined but exclusion active periodontal infections	Anterior (n=79) and Posterior (n=122) implants	One year follow up: 200(99.5%) survival rate One implant failed . 195(97.5%) classified implant- crown success Five implants (2.5%), could not fulfill the implant- crown success criteria
(Nair, Prithviraj, Regish, & Prithvi, 2013)	Milled partially stabilized zirconia Custom Implant	Delayed implant, healed socket	Mandibular Left first molar, FDI: 36#	At two years, the patient presented with a stable implant

(F. G. Mangano et al., 2014)	DLMS titanium RAI immediate	Root caries: 7 Vertical/horizontal root fracture: 5 Endodontic lesion 2 Unsuccessful RCT:1	Maxillary/Mandibular 15 premolars	At one year after placement overall survival rate of 100 %. All implants were stable
(F. Mangano, 2016)	DLMS titanium RAI	Fractured non-restorable	Maxillary right lateral incisor FDI: 12#	At one year after placement, the RAI was still in function and stable.
(Patankar, Kshirsagar, Patankar, & Pawar, 2016)	Milled RAZI	Root canal treated broken crown structure	Mandibular right first premolar: FDI: 44#	At 18 months follow-up, the patient presented with a stable implant

***2.2 In vitro* studies**

Moin et al. published *in vitro* studies containing the superimposed surfaces of the RAIs and the original tooth discrepancy for RMS, volumetric geometry, and surface area. Root mean square difference (RMS) is the mean distance between the two surfaces at anatomically corresponding locations. Additionally, maximum deviation between two surfaces (Hausdorff distance) was recorded. Surface area measurements of 11 RAI's showed an overall decrease (RMS) in surface area from 0.08 mm to 0.35 mm between the natural tooth and the RAI[13]. In a comparison metric study by Moin et al. in 2016, measured root RMS of 0.15 mm difference between the optical scan of the tooth compared with optical scan of 3D-printed DLP RAI [Table 5].

Moin et al. recorded a 6.33% surface area change for the RAI in comparison with the original tooth. And an increase of 0.27% surface area change when comparing the 3D surface model with optical scan of the original tooth.[14]In the study of 11 RAI implants the surface area change comparison between original tooth and RAI was between 1.1% and 3.8%.It was stated that "In every case, the volume of the socket was greater than the root part of the RAI ranging from 0.6% to 5.9% volume difference."[13]. The 3D-printed DLP RAI had a surface change of 6.76%[11].

Table 5: Surface change

Reference	RMS±SD(max hausdorff)		Surface area change (%)
(Anssari Moin, H Reference assan, and Wismeijer 2016)	Optical scan of the tooth vs optical scan of 3D-printed RAI		CAD model of the RAI vs Optical scan of the 3D-printed RAI
	% the surface exceeding the threshold distances of		% the surface exceeding the threshold distances of
	0.1 mm : 46.38%		0.1 mm : 59.33%
	0.5 mm : 1.55%		0.5 mm : 4.86 %
	RMS(SD) mm: 0.15(0.099)		RMS(SD) mm:0.18(0.090)
	Max errors(hausdorff distance in mm): 0.86		Max errors(hausdorff distance in mm) 0.66
	Surface area change (%): 6.67		Surface area change (%): 7.14
(Moin et al. 2014)	**RMS±SD(max hausdorff) mm Natural tooth vs RAI**		**Surface area change (%) between the original tooth and RAI.**
	0.171 ± 0.122(1.10)		1.1
	0.155 ± 0.112(1.11)		2.5
	0.098 ± 0.070(0.77)		3.8
	0.119 ± 0.086(1.87)		3.8
	0.14 ± 0.095(0.91)		2.3
	0.14 ± 0.088(1.01)		3.6
	0.098 ± 0.067(0.56)		1.3
	0.35 ± 0.20(1.06)		1.8
	0.13 ± 0.095(0.86)		1.4
	0.080 ± 0.043(0.31)		3.1
	0.099 ± 0.061(0.46)		1.7
(Moin et al. 2013)	**Surface area change (%) 3D surface model vs. Optical scan original tooth**	**Surface area change (%) Fabricated RAI vs. Optical scan original tooth**	**Surface area change (%) Fabricated RAI vs. 3D surface model**
	0.27	-6.33	-6.58

Moin et al. and Chen et al recorded the von Mises at the bone peri-implant interface as a quantity of stress level for the load transfer mechanism. Two loads were applied during the study of moin et al. The loads simulated anterior bite force: an oblique bucco-apical force with a magnitude of 300N set on 135∘ to the long axis of the implant and a vertical force in apical direction to the long axis of the implant with a magnitude of 150N. In the regions of the implant neck all designs exceeded the biological limit, inducing a risk to bone loss. The Standard design RAI exhibited the highest von Mises stress and highest minimum principal stress values [Table 6]. The highest magnitude of micromotion level was measured in the Prism 35 µm, 6.42 µm, design, 32.10 µm and 32.51 µm under vertical and oblique loading, respectively. Remarkably, the lowest levels of contact separation were measured in the Fins model followed by the Bulbs design under vertical and oblique forces: 5.45 µm, 6.25µm and 6.36 µm, 6.42µm. Micro displacement patterns were located at neck area in direction of the forces and in contra lateral direction in the apical area in all designs. It was concluded that "adding targeted press-fit geometry to the RAI Standard design, preferably Fins or Bulbs, will have a positive effect on stress distribution and lower concentration of bone stress and will provide a better primary stability for this patient case" [12]

In the finite element analysis by Chen et al. three dental implants were compared a cylindrical implant and two custom-made implants designed by reverse engineering technology, namely a root-analogue implant and a root-analogue threaded implant. The implants were loaded with occlusal force at 45° angle. The von Mises during immediate load was minor with a value of 9.08 MPa for the cylindrical design as the neck of the implant did not contact the cortical bone. Both the RI and RTI implants touched the cortical bone and produced maximum von Mises stresses concentrated in a small area in labial cortical bone of 151.92 and 139.03 MPa. In the cancellous bone, the cylinder implant produced a maximum stress of 33.50 MPa. In the simulation of osseointegrated implant the maximum von Mises were observed in crestal regions, with a maximum value of 91.99 Mpa for CI, 77.18 Mpa for RTI, and 56.59 MPa for RI. Within the article it has not been discussed about the micromotion of the immediate loaded implant. For the osseointegrated it was stated that "The CI model showed the most pronounced micro-motion of about 61 µm, while RI and RTI model showed smaller values of 47 and 48 µm, which indicated a slightly more reliable stability in the long term"

Table 6: Micromotion and Maximum von Mises (σt)

Study	Conditions					
(Anssari Moin, Hassan, & Wismeijer, 2016)	**Loading: 300N at 135°** **150N to the vertical axis of the implant** **(coefficient of friction = 0.3)**	**Model**	**Micromotion (μm) vertical loading**	**Micromotion (μm) oblique loading**		
		Standard	10.90	11.72		
		Prism	32.10	32.51		
		Fins	5.45	6.25		
		Plug	9.88	10.69		
		Bulbs	6.35	6.4		
			Vertical σ_t(MPa)	Oblique σ_t (MPa)		
		Standard	241	241		
		Prism	61	59		
		Fins	60	192		
		Plug	44	153		
		Bulbs	44	148		
(Chen, Zhang, Chen, & Zhang, 2017)	Loading: 100 N at 45° (coefficient of friction= 0.45 in immediate loading) conventional cylindrical implants (CI) Root-analogue implant (RI) root-analogue threaded implant (RTI)	Immediate loading				
		Type of bone	CI (Mpa)	RI (Mpa)	RTI (Mpa)	
		Cortical	9.08	151.92	139.03	
		Cancelous	33.50	10.07	9.23	
		Osseointegrated implant				
			CI (Mpa)	RI (Mpa)	RTI (Mpa)	
		Cortical	91.99	56.59	77.18	
		Cancelous	4.18	6.63	3.23	
		Type of implant	Micromotion Immediate loading (μm)		Micromotion Osseointegrated implant(μm)	
			Cortical	Cancellous bone	Cortical	Cancellous bone
		CI	38	71	61	59
		RI	190	174	47	45
		RTI	103	103	48	46

Conclusion

With the use of currently available technology it is very well feasible to create a RAI. It has been found that adding targeted press-fit geometry or threads to the RAI will have a positive effect on stress distribution and lower concentration of bone stress and will provide a better primary stability. Root analogue implants may have the potential to become an alternative to the conventional implants but cannot currently be recommended for routine clinical use, as no long-term clinical data are available. To properly evaluate their clinical performance, well-planned, controlled clinical trials with a long term follow-up must be performed.

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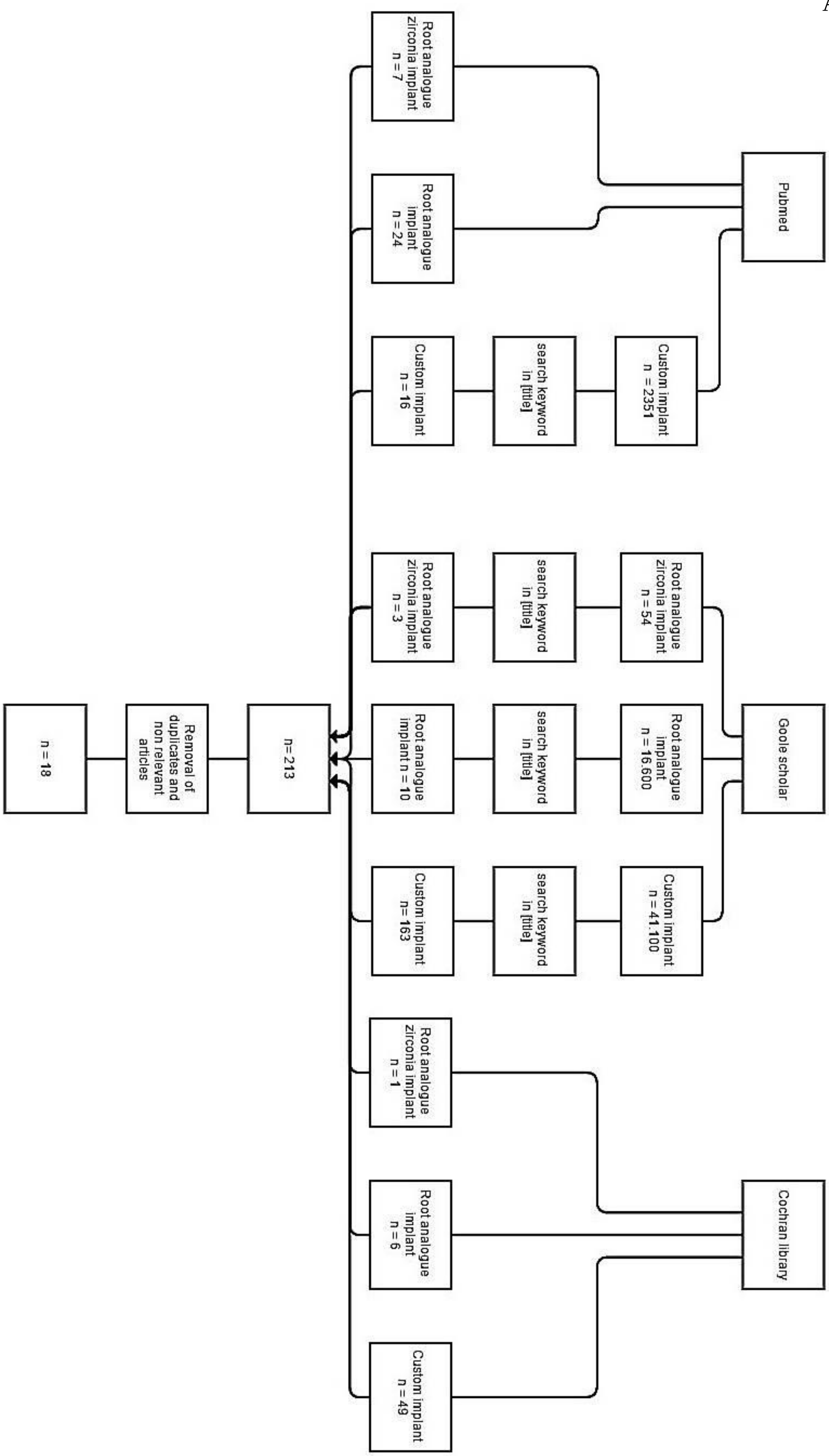
ANNEXES

Annex No. 1



Annex No. 2

INDIVIDUAL DEVELOPMENT PLAN FOR THE MASTER'S THESIS

Graduate student Roestam Banai, of the year 2017, and the group 15 of the integrated study programme of Odontology

Duration of studies from 2012 till 2017

Supervisor: Gyd. Marijus Leketas

MT title: Current state of Root Analogue Implants (RAI): A systemic review

MT annotation:
An electronic search on PubMed, Google scholar and Cochrane library databases

Aim of the work:

To evaluate the survival rate of custom non-submerged implants placed in fresh extraction sockets. Compare the proposed protocols of manufacturing custom implants with emphasis on root analogue implants (RAI).

Tasks of the work:

Perform a systemic review with the emphasis on root analogue implants using electronic databases. Evaluate the data within the selected articles.

Schedule of the works

No.	Description of MT task	Performance deadline	Done/not done (supervisor's evaluation and signature)
1	Perform electronic search	01-10-2016	
2	Acquire all the full articles	01-11-2016	
3	Select articles within the inclusion criteria	31-12-2016	
4	Perform Hand search	10-01-2016	
5	Review the articles and extract data	31-01-2017	
6	Create flowchart	28-02-2017	
7	Writing first draft	31-01-2017	
8	Writting final version	01-03-2017	
9	Correction of MT	07-03-2017	
10	Deadline MT	30-03-2017	

Graduate student's name, surname and signature ________________________________

Supervisor's name, surname and signature ____________________________________