IJBPAS, October, 2020, 9(10): 2816-2833

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

MECHANICAL PROPERTIES AND BIOLOGICAL IMPLICATIONS OF TITANIUM-ZIRCONIUM DENTAL IMPLANTS: A STRUCTURED REVIEW

NALLURI S[*1] AND NALLASWAMY D[2]

1: Post Graduate Student, Department of Prosthodontics, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Chennai, India

2: Director of Academics, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Chennai, India

***Corresponding Author: Sathvik Nalluri: E Mail:** sathvik3@gmail.com;

Ph.No. +91-9940680939

Received 20th March 2020; Revised 23rd April 2020; Accepted 14th May 2020; Available online 1st Oct. 2020

https://doi.org/10.31032/IJBPAS/2020/9.10.5326

ABSTRACT

Objectives

This structured review was performed to analyse the mechanical properties and biological implications of the Titanium-Zirconium alloy and to associate the findings with human bone parameters.

Materials and methodology

A thorough search was done in Medline/ PubMed databases, Cochrane library, IEEE Xplore, Google scholar to search for articles on Titanium-Zirconium Implants upto February 2019. The structured review was performed in accordance with PRISMA/PICO requirements.

Results

Total number of articles collected from the search was 8 out of which 2 were included from hand searched articles. The studies included in the review evaluated the mechanical properties and biological implications of Titanium-Zirconium alloy with varying proportions of zirconium.

Conclusion

Titanium-Zirconium is a popular alloy that started off as an alternative for Commercially pure Titanium (Cp Ti) and Ti-6Al-4V(TAV) dental implants. Claims have been made that the Ti-Zr alloy is superior in strength and more biocompatible to Cp Ti and TAV. It has been implied that different concentrations or ratios of Zirconium complexed with titanium change the mechanical and biological properties of the material. Currently Ti 13-17Zr is the most popular alloy for dental implant. Hence in this review, we have attempted to evaluate the mechanical properties and biological implications of Ti-Zr, based on various studies done with different ratios of Ti-Zr.

Keywords: Titanium-Zirconium, Zirconium-Titanium, mechanical properties, cytotoxicity, tensile strength

1. INTRODUCTION

Titanium (Ti) is the most biocompatible and nontoxic biomedical material **[1]**. Pure Ti was first used for medical application in the 1960s **[2]**. Commercially pure Ti(Cp Ti) and TiNi, Ti-6Al-4V(TAV), Ti-6Al-7Nb are among the materials currently being used for this purpose **[2, 3]**. But then researchers discovered the strength of Ti to be too low which impeded its wide application. It has been reported that the gradual release of aluminium and vanadium ions from the surface of Ti-6Al-4V alloy into the surrounding fluid causes local adverse tissue reactions and immunological responses **[4]**. Therefore, an increasing number of researchers were devoting themselves to search for alternative Ti alloys to replace CP–Ti in implant use **[5]**. The need to develop an implant material which has improved mechanical strength while retaining biological properties of existing titanium alloys **[6]** culminated in to the invention of Titanium-Zirconium alloy.

The development of new Ti–Zr alloys for medical devices was first established in 1995 when **[7]** investigated this new alloy for its suitability as a biomedical implant **[7]**. Zirconium (Zr) and Ti belong to the IVb group in the periodic table, thus possessing similar chemical properties **[3]**. Zirconium is considered a neutral element when added to a solid solution with titanium because it has an identical allotropic transformation with a similar phase transition temperature. When in a solid solution with titanium, in both α and β phases, it promotes hardening and slows the speed of phase transformation. This element has great solubility in both crystalline phases of titanium and can form alloys of various proportions, with proportional increases in mechanical strength (such as tensile strength, hardness, and flexural strength) and improvement in corrosion potential **[3]**. Earlier studies have shown that the formation of solid solutions with zirconium can decrease the α′ martensitic transformation temperature of titanium **[3, 8]**. The addition of zirconium can also decrease the melting temperature of titanium, which can reduce the cost of casting and swaging **[3]**. It was found that Zr offers a superior corrosion resistance over most other alloying systems across a wide range of environments and Zr also shows an acceptable mechanical strength and satisfactory biocompatibility **[9]**.

Improved mechanical properties of Ti-Zr compared to Ti need to be supported by improved biological characteristics to result in better osseointegration and implant success. Literature has reported poor cell adhesion and cell proliferation of Ti-Zr in comparison to Ti **[10]**. Literature evidence demonstrates positive correlation between the levels of Zirconium and alkaline phosphatase levels. Owing to the negative biological effects reported, it is very important to further look into the evidence available on the biological implications of addition of zirconium to titanium.

2. MATERIALS AND METHODS

This review was done in accordance with the PRISMA guidelines which were laid down by **[10]**. The structured search question was framed using PICO method given by **[11]**. The search strategy was then formulated using the same search question. The structured question was then used to formulate the search strategy.

SEARCH QUESTION: At what concentration of Zirconium in TiZr alloy are the mechanical and biological properties closest to human bone?

SEARCH STRATEGY:

The search strategy included searching MEDLINE/ PubMed, Google Scholar, Scholar's portal, IEEE database. PICO search terms were used are mentioned below.

P- zirconium titanium, zirconium titanium alloys, zirconium titanium implants, titanium zirconium alloys, titanium zirconium implants, zr ti, zr ti implants, ti zr, roxolid, narrow diameter implants.

I- compressive strength, tensile strength, shear strength, fatigue, cyclic fatigue, fatigue strength, biomechanics, hardness, hardness number, surface roughness, sla, slactive, acid etching, sand blasting, density, corrosion, corrosion resistance, mechanical properties, elastic modulus, modulus of elasticity, biomaterials.

O- osseointegration, cell adhesion, cell attachment, cellular attachment, osteoblasts, fibroblasts, macrophages, cytotoxicity, biocompatibility, cytocompatibility, histochemistry, mesenchymal cells, cell differentiation.

HAND SEARCHED ARTICLES:

In order to complete the search the following journals were hand searched for articles on the subject of interest from January 1970 to January 2019

- Journal of Prosthetic Dentistry
- Clinical Oral Implant Research
- Journal of Prosthodontics
- Journal of Biomaterial Applications
- Journal of Alloys and compounds
- Journal of Material Sciences

This research was supplemented by cross checking the reference lists of the selected studies and review articles to locate additional papers that could meet the eligibility criteria fixed for this study. Also, the "grey literature" was investigated by means of direct contacts with the authors.

INCLUSION CRITERIA:

- Articles with studies on Titanium-Zirconium alloy or implants and the mechanical properties and biological implications.
- Outcome measures included are mechanical properties
- In vitro studies included
- Studies answering the PICO questions
- In vivo Animal studies are included
- Studies with various compositions of Ti-Zr

EXCLUSION CRITERIA:

- Review studies
- Case reports
- Surface treatments and treated
- Alloys of Ti-Zr with other metals
- Studies where ratios of composition of Ti-Zr is not mentioned
- Clinical studies with mechanical properties evaluated

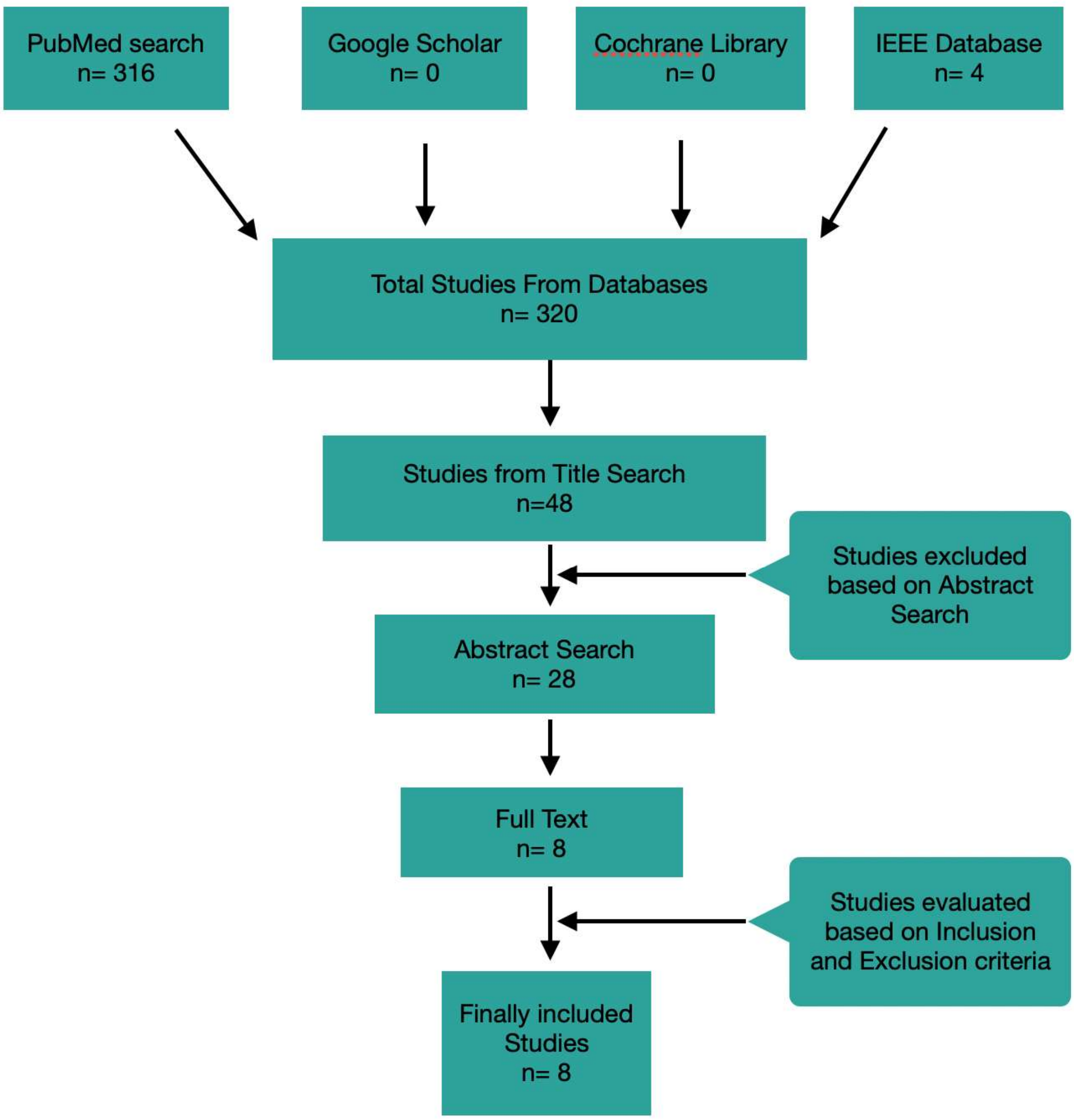

Figure 1: Flowchart showing search strategy

Search	Add to builder	Query	Items found	Time
#36	Add	Search **cell attachment**	43711	23:41:36
#35	Add	Search **cell adhesion**	197074	23:41:25
#34	Add	Search **osseointegration**	12635	23:41:13
#33	Add	Search **bio materials**	13190	23:40:49
#32	Add	Search **modulus of elasticity**	22200	23:40:27
#31	Add	Search **elastic modulus**	18583	23:40:04
#30	Add	Search **mechanical properties**	94583	23:39:51
#29	Add	Search **corrosion resistance**	2937	23:39:32
#28	Add	Search **corrosion**	14726	23:39:14
#27	Add	Search **density**	648822	23:39:05
#26	Add	Search **sand blasting**	171	23:38:45
#25	Add	Search **acid etching**	10102	23:38:36
#24	Add	Search **slactive**	142	23:38:13
#23	Add	Search **sla**	2817	23:38:04
#22	Add	Search **surface roughness**	14137	23:37:57
#21	Add	Search **hardness number**	1333	23:37:18
#20	Add	Search **hardness**	20872	23:37:07
#19	Add	Search **biomechanics**	35032	23:36:58
#18	Add	Search **fatigue strength**	8048	23:36:48
#17	Add	Search **cyclic fatigue**	1875	23:36:37
#16	Add	Search **fatigue**	98020	23:36:18
#15	Add	Search **shear strength**	13710	23:36:01
#14	Add	Search **tensile strength**	30686	23:35:54
#13	Add	Search **compressive strength**	12340	23:35:44
#12	Add	Search **narrow diameter implants**	238	23:34:58
#11	Add	Search **roxolid**	26	23:34:44
#10	Add	Search **Ti Zr alloy**	28	23:34:34
#9	Add	Search **TiZr alloy**	47	23:34:24
#8	Add	Search **Ti Zr**	1611	23:34:12
#7	Add	Search **zi ti implants**	9	23:34:01
#6	Add	Search **zi ti**	34	23:33:34
#5	Add	Search **titanium zirconium alloys**	450	23:33:29
#4	Add	Search **titanium zirconium implants**	724	23:32:52
#3	Add	Search **zirconium titanium alloy**	530	23:32:16
#2	Add	Search **zirconium titanium implants**	724	23:31:55
#1	Add	Search **zirconium titanium**	1860	23:31:31
#51	Add	Search **(((((((((((osseointegration) OR cell adhesion) OR cell attachment) OR cellular attachment) OR cell culture) OR osteoblasts) OR fibroblasts) OR macrophages) OR cytocompatibility) OR histochemistry) OR mesenchymal cells) OR cell differentiation) OR cytotoxicity**	1924120	23:53:03
#50	Add	Search **((((((((((((((((((compressive strength) OR tensile strength) OR shear strength) OR fatigue) OR cyclic fatigue) OR fatigue strength) OR biomechanics) OR hardness) OR hardness number) OR surface roughness) OR sla) OR slactive) OR acid etching) OR sand blasting) OR density) OR corrosion resistance) OR mechanical properties) OR elastic modulus) OR modulus of elasticity) OR bio materials**	941903	23:51:30
#49	Add	Search **((((((((((zirconium titanium) OR zirconium titanium implants) OR zirconium titanium alloy) OR titanium zirconium implants) OR titanium zirconium alloys) OR zi ti) OR zi ti implants) OR Ti Zr) OR TiZr alloy) OR Ti Zr alloy) OR roxolid) OR narrow diameter implants**	3384	23:49:04
#48	Add	Search **cytotoxicity**	173814	23:44:33
#47	Add	Search **cell differentiation**	477466	23:43:42
#46	Add	Search **mesenchymal cells**	92551	23:43:32
#45	Add	Search **histochemistry**	477821	23:43:18
#44	Add	Search **cytocompatibility**	2995	23:43:05
#43	Add	Search **biocompatibility**	29085	23:42:52
#41	Add	Search **macrophages**	249556	23:42:26
#40	Add	Search **fibroblasts**	244970	23:42:15
#39	Add	Search **osteoblasts**	41760	23:42:07
#38	Add	Search **cell culture**	397946	23:41:59
#37	Add	Search **cellular attachment**	46168	23:41:49
#73	Add	Search **(((((((((((((zirconium titanium) OR zirconium titanium implants) OR zirconium titanium alloys) OR titanium zirconium implants) OR titanium zirconium alloys) OR zr ti) OR zr ti implants) OR Ti Zr) OR roxolid) OR reduced diameter implants) OR TiZr alloy) OR Ti Zr Alloy)) AND ((((((((((((((((((((compressive strength) OR tensile strength) OR shear strength) OR fatigue) OR cyclic fatigue) OR fatigue strength) OR biomechanics) OR hardness) OR hardness number) OR surface roughness) OR sla) OR slactive) OR acid etching) OR sand blasting) OR density) OR corrosion) OR corrosion resistance) OR mechanical properties) OR elastic modulus) OR modulus of elasticity) OR bio materials)) AND ((((((((((((((osseointegration) OR cell adhesion) OR cell attachment) OR cellular attachment) OR cell culture) OR osteoblasts) OR fibroblasts) OR macrophages) OR cytotoxicity) OR biocompatibility) OR cytocompatibility) OR histochemistry) OR mesenchymal cells) OR cell differentiation)**	316	14:48:44

Figure 2: PICO terms used to search in the PubMed database

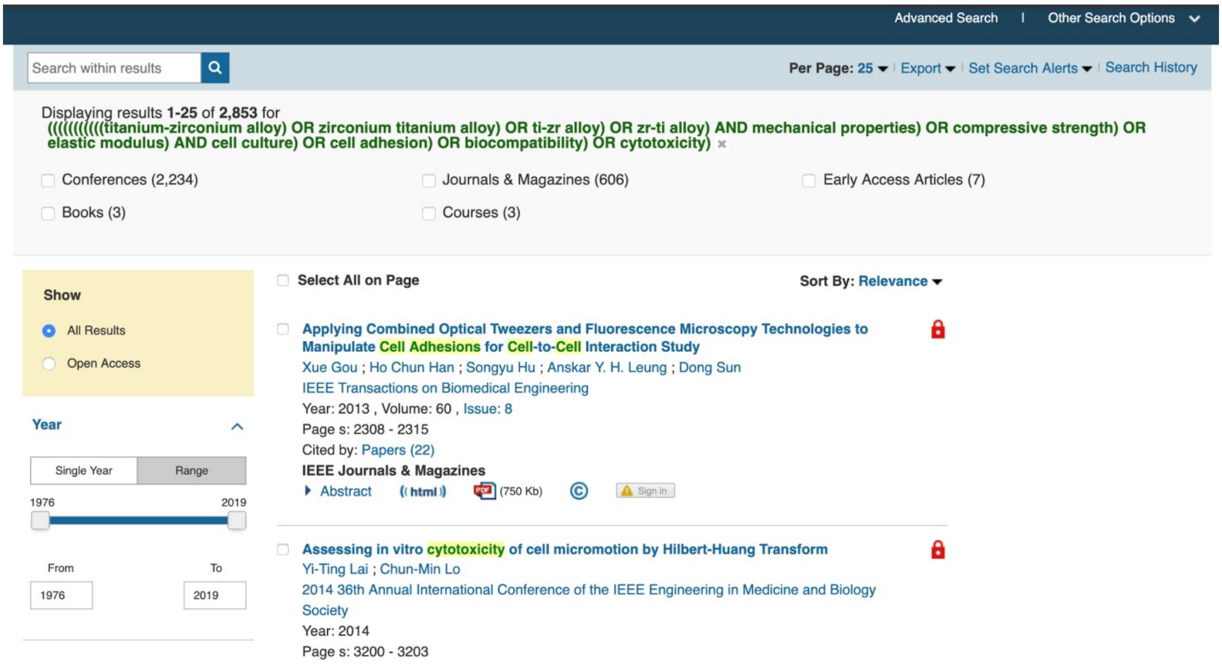

Figure 3: Search results from IEEE Xplore Digital Library

3. RESULTS

A total of 316 articles were obtained from the database search. Out of these 316 articles, 26 articles were selected after title exclusion. Two more articles were added by hand search which made a total of 28 articles. After this, a full text evaluation of these 28 articles was done; of which only 8 were included into the structured review based on the inclusion criteria. The data was extracted independently by two examiners. Where resolution was not possible, a third review author was consulted.

After data extraction, the studies were sorted based on predetermined inclusion and exclusion criteria. Studies rejected at this or subsequent stages were recorded in the table of excluded studies, and reasons for exclusion recorded the data extraction forms were piloted on several papers and modified as required before use. All authors were contacted for clarification or missing information.

From the reviewed 8 articles, mechanical properties and biological implications were extracted using data extraction table. 6 out of 8 studies have done biocompatibility and cytotoxicity tests and 7 out of 8 have done tests on mechanical properties. Compressive strengths of varying concentrations of TiZr were evaluated only in one study.

S.No	Author	Groups	Biological Implication				
1	Wang et al (2018)	Ti 5Zr	Medium	Type of cells	Cell adhesion	Alkaline phosphate activity	Osteocalcin
		Ti 15Zr	RPM 160 Suppiments	Murine osteoblast cells (MG-63)	Values not mentioned		NA
		Ti 25Zr				No	
		Ti 35Zr					
		Ti 45Zr					
2	Akimoto et al (october 2016)	Ti 30Zr					
		Ti 50Zr	5.85 gl NaCl + 10/0 gl lactic acid and Fusayama artificial saliva	NA	NA	NA	NA
		Ti 70Zr					
		Cp Ti					
		Zr pure					
3	Lotz et al	Grade 4 titanium					
	April 2016	Ti 13-17Zr	DEME & MSC growth medium	Normal Human Osteoblasts	No	Yes	No
4	Lee et al	Ti 10Zr					
		Ti 20Zr	Alpha MEM	Mouse osteoblasts; MC3T3-E1	Values not mentioned	Yes	Yes
		Ti 30Zr					
		Ti 40Zr					
		Ti 50Zr					
		Ti 60Zr					
		Ti 70Zr					
		Ti 80Zr					
		Ti 90Zr					
5	Correa et al*	Ti 5Zr					
	Sept 2013	Ti 10Zr	Alpha MEM	Mouse osteoblasts; MC3T3-E1	yes	No	
		Ti 15Zr					
6	Sista et al	Ti					
	2010	Ti 50Zr	Alpha MEM	Mouse osteoblasts; MC3T3-E1	27%	Yes	
					35%		
7	Corderio et al*	Cp Ti					
	July 2018	TAV	Alpha MEM	Mouse osteoblasts; MC3T3-E1		No	Yes
		Ti 5Zr					
		Ti 10Zr					
		Ti 15Zr					
		Cp Ti					
		TAV					
		Ti 5Zr					
		Ti 10Zr					
		Ti 15Zr					
8	Chen et al	Ti					
	March 2008	Zirconium	Simulated body fluid	NA	NA	NA	No
		Ti 50Zr					

Figure 4: Data extraction table showing Biological implications

S.No	Author	Groups	Mechanical Property										
			Surface	Compressive Strength	Tensile strength	Hardness	Elastic Modulus	Poisons ratio	Strain	Contact Angle	Roughness	Corrosion resistance	Removal torque
1	Wang et al (2018)	Ti 5Zr	Normal	1200 Mpa	NA	473 HVN	NA	NA	NA	NA	NA	NA	NA
		Ti 15Zr											
		Ti 25Zr											
		Ti 35Zr											
		Ti 45Zr		1599.8 MPa		525 HVN							
2	Akimoto et al (october 2016)	Ti 30Zr	800 grit SiC	No	NA	NA	NA	NA	NA	NA	NA		NA
		Ti 50Zr										Pitting corrosion	
		Ti 70Zr											
		Cp Ti											
		Zr pure											
3	Lotz et al	Grade 4 titanium	SlActive	No	NA	NA	NA	NA	NA	0°	NA	NA	NA
	April 2016	Ti 13-17Zr	SlActive							0°			
4	Lee et al	Ti 10Zr		No	705 MPa	NA		NA	8.7%	NA	NA	NA	NA
		Ti 20Zr	No										
		Ti 30Zr			980 MPa				6.0%				
		Ti 40Zr											
		Ti 50Zr			820 MPa				4.3%				
		Ti 60Zr											
		Ti 70Zr			835 MPa				5.6%				
		Ti 80Zr											
		Ti 90Zr											
5	Correa et al*	Ti 5Zr	Polished and acid etched	No	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Sept 2013	Ti 10Zr											
		Ti 15Zr											
6	Sista et al	Ti	Anodized	No	NA	NA	NA	NA	NA	68.31°	0.20 µm	NA	NA
	2010	Ti 50Zr								63.85°	0.17 µm		

Figure 5: Data extraction table showing Mechanical Properties

S.No	Author	Groups						Mechanical Property					
		Ti 70Zr			835 MPa				5.6%				
		Ti 80Zr											
		Ti 90Zr											
5	Correa et al*	Ti 5Zr	Polished and acid etched	No	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Sept 2013	Ti 10Zr											
		Ti 15Zr											
6	Sista et al	Ti	Anodized	No	NA	NA	NA	NA	NA	68.31°	0.20 µm	NA	NA
	2010	Ti 50Zr								63.85°	0.17 µm		
7	Cordeiro et al*	Cp Ti	Machined	No	NA	186.25 HVN	102.96 GPa	NA	NA	NA	NA	NA	NA
	July 2018	TAV				352.62 HVN	139.88 GPa						
		Ti 5Zr				436.25 HVN	123.30 GPa						
		Ti 10Zr				421.20 HVN	137.29 GPa						
		Ti 15Zr				422.20 HVN	124.31 GPa						
		Cp Ti	Double etched			212.50 HVN							
		TAV				395.40 HVN							
		Ti 5Zr				458.76 HVN							
		Ti 10Zr				386.45 HVN							
		Ti 15Zr				483.45 HVN							
8	Chen et al	Ti	120, 240, 600, 1200 grit (SiC)	No	NA	NA		NA	NA	NA	1.2, 1.0, 0.6, 0.2 µm	NA	NA
	March 2008	Zirconium	120, 240, 600, 1200 grit (SiC)								1.2, 1.0, 0.6, 0.2 µm		
		Ti 50Zr	120, 240, 600, 1200 grit (SiC)								1.2, 0.6, 0.4, 0.2 µm		

Continued.. Figure 5: Data extraction table showing Mechanical Properties

Table 1: Risk of bias

S. No	Study Title	Randomisation	Allocation concealment	Blinding	Risk of bias
1	Microstructure, mechanical properties, and preliminary biocompatibility evaluation of binary Ti–Zr alloys for dental application	No	No	No	High
2	Evaluation of corrosion resistance of implant-use Ti-Zr binary alloys with a range of compositions	No	No	No	High
3	Comparable responses of osteoblast lineage cells to microstructured hydrophilic titanium–zirconium and microstructured hydrophilic titanium	No	No	No	High
4	Titanium -Zriconium binary alloyas dental implant material: Analysis of the influence of compositional change on mechanical properties and in vitro biologic response	No	No	No	High
5	The effect of the solute on the structure, selected mechanical properties, and biocompatibility of Ti–Zr system alloys for dental applications	No	No	No	High
6	The influence of surface energy of titanium-zirconium alloy on osteoblast cell functions in vitro	No	No	No	High
7	Characterization of chemically treated Ti-Zr system alloys for dental implant application	No	No	No	High
8	Effect of Surface Roughness of Ti, Zr, and TiZr on Apatite Precipitation From Simulated Body Fluid	No	No	No	High

4. DISCUSSION

The current structured review, reviews 8 articles on titanium zirconium alloys. In the collected articles, mechanical properties of various compositions / ratios of titanium zirconium were given. However the exclusions were not statistically significant and so larger studies with stronger design are required to provide conclusive evidence. A Meta-analysis could not be performed with the studies included, as the outcome parameters measuring the mechanical properties were different in all the studies.

4.1 MECHANICAL PROPERTIES:

Mechanical properties define the quality of the implant and its close approximation to the bone.

4.1.1 COMPRESSIVE STRENGTH

In a study by **[12]**, they have evaluated the effect of increasing concentrations of Zirconium in TiZr alloy. The study showed that as the ratio of zirconium increases the compressive strength increases. In all the included studies this is the only study where compressive strengths were evaluated. Ti–Zr alloys consist of alpha and beta phase with lamellar shapes which increases the compressive strength as the concentration of Zr increases.

4.1.2 TENSILE STRENGTH

Tensile strength is the property that resists the plastic deformation of metal. Higher the tensile strength the lesser plastic deformation happens while torque loading a dental implant. In the study by **[13]**, the tensile strengths of Ti10Zr, Ti30Zr, Ti50Zr, Ti70Zr were studied with an Instron-type universal testing machine. There is an increase in the tensile with a ratio of Ti30Zr upto 980 Mpa, which was also the result given by **[14]**. The rise in tensile strength was seen till 30% concentration of Zirconium and a gradual drop was seen as the Zr concentration increases beyond 30%. Grade 4 Titanium has a tensile strength of 970 Mpa as studied by **[15]** which put Ti 30Zr closest to it.

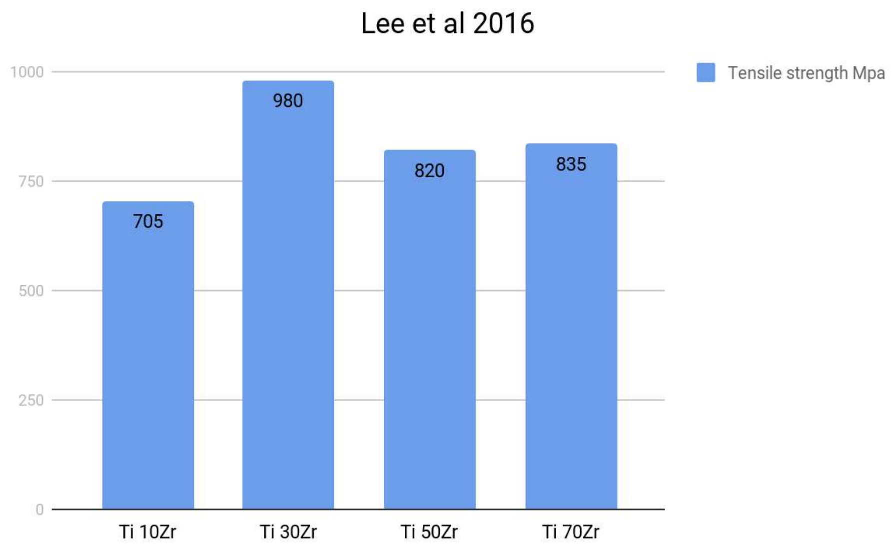

Figure 6: Graphical representation of the effect of variation in the proportion of zirconium in Ti-Zr alloy on the tensile strength

4.1.3 ELASTIC MODULUS

Elastic modulus is an important property to implant materials and it should be comparable to that of bone tissue to prevent bone atrophy and to stimulate its remodeling by the effective load transfer and uniform stress distribution **[16, 17]**. It is an important factor whether the stress shielding (i.e. insufficient loading of bone due to the large difference in elastic modulus between the implant device and its surrounding bone) occurs or not **[1, 3, 18]**. It is reported that the elastic modulus of human bone ranged from 4.4 to 28.8 GPa **[1]**. According to **[12]**, the elastic modulus of Cp Ti shows an elastic modulus of 103 GPa while the series of Ti–Zr alloys exhibited lower elastic modulus ranging from 53.5 GPa for Ti–35Zr to 59.3

GPa for Ti–5Zr which is much closer to human bone. **[13]** also presented in his study that elastic modulus of Ti 45-50Zr showed 85 GPa where Cp Ti showed more than 120 GPa. In the study by **[19]** there is an imbalance in the graph of elastic modulus comparing TAV, Cp Ti and Ti-xZr, where TAV showed highest elastic modulus

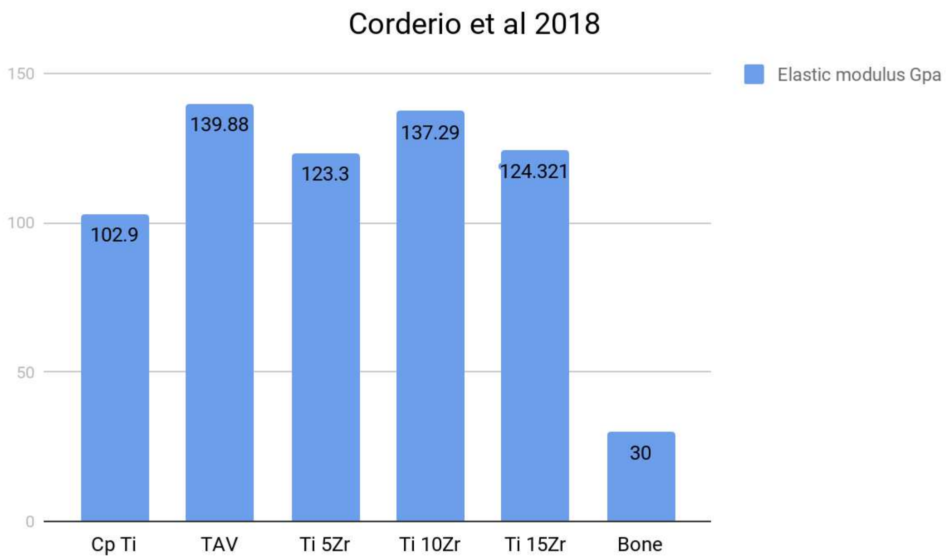

Figure 7: Graphical representation of the effect of variation in the proportion of zirconium in Ti-Zr alloy on the elastic modulus

4.1.4 HARDNESS

Of the included articles only 2 studies performed Vickers Hardness test on various concentrations of TiZr. As per **[19]**, there is an increase in the hardness of the alloy at Ti5Zr and a gradual decrease from beyond. In another study by **[13]**, the vickers hardness test results shows an increase from Ti10Zr to Ti40Zr and a gradual drop till Ti90Zr. The TiZr ingot used in the previous study is 2 mm thickness whereas the later one is 1 mm thickness showing increased hardness for narrow diameter implants.

4.1.5 SURFACE ROUGHNESS

Roughness of the implant is assessed after it undergoes surface treatment. The surface roughness of the implant changes based on the type of surface treatment and the material with which the implant is made. Hardness also places a roll in surface the treatments as the higher the value the harder it is to abrade a surface. **[20]** in his study used different grits of Silicon Carbide abrasive (SiC) and ground the implant samples. This study was performed comparing Ti, Zr and Ti50Zr, where the results showed no significant difference in the surface roughness when treated with different grits of SiC. Only

Ti50Zr showed a slight lower microns of roughness comparably. A study was done on Anodization of Ti50Zr by **[21]** also showed increase in the surfaces roughness. Ti50Zr shows a roughness of 0.17µm on anodization. On comparison, Ti50Zr showed better surface roughness on anodization (0.17µm) compared to SiC grit abrasives (0.2µm).

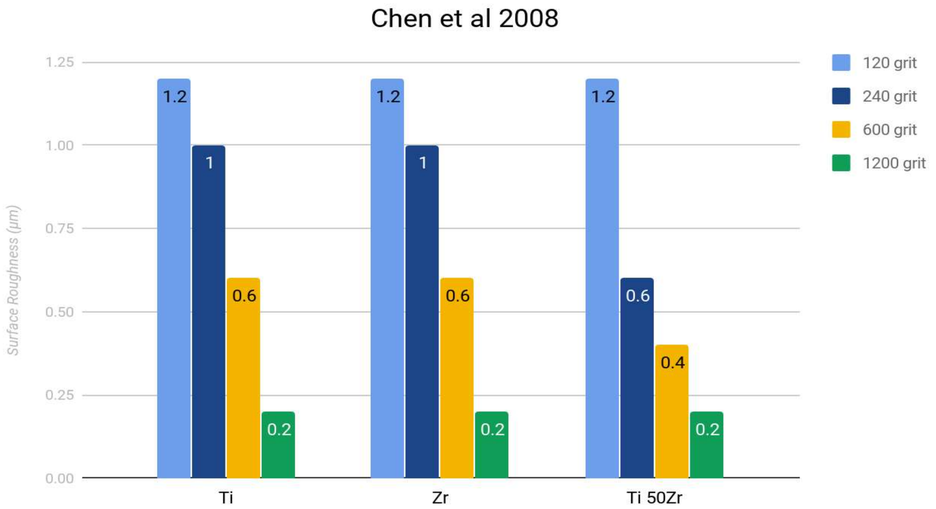

Figure 8: Variation in the surface roughness depending on the different grits of Silicon Carbide used to abrade the surface of Ti-Zr alloy

4.2. BIOLOGICAL IMPLICATIONS

Biocompatibility is the second important property as the lack of it is a failure of the material. The properties considered for the structured review are, cell attachment, cell differentiation, cell viability etc were evaluated. Of the 8 included studies, 6 articles showed cell culture results.

4.2.1 CELL ATTACHMENT / ADHESION

It is the first criteria we looked into in biological implications. In all the included studies cell attachment was assessed by osteoblasts of which 4 studies used mouse osteoblasts, 1 study used Murine osteoblasts and 1 used Normal Human Osteoblasts (NHO). **[12]** mentioned that no adverse effects were seen on biocompatibility and cytotoxicity testing with osteoblasts on various compositions of TiZr. In **[13]** study, density of cell attachment was high on Ti30Zr on a 4 hour culture and shifted to Ti10Zr at 24 hour. Impaired cell adhesion and spreading were noticeable with a higher Zr concentration among all the alloys. **[22]** showed in his study that the biocompatibility of Cp-Ti slightly decreases with the addition of Zr. This means that the Zr has slightly affected the biocompatibility of Cp-Ti. But the advantage of using Zr to enhance the mechanical properties of Cp-Ti outweighs this slight decrease in biocompatibility.

4.2.2 ALKALINE PHOSPHATASE

ALP is linked to the membrane via glycosylphosphatidylinositol (GPI) anchors by means of posttranslational modification. Tissue-nonspecific alkaline phosphatase (TNAP) is expressed on the cell membrane of hypertrophic chondrocytes, osteoblasts, and odontoblasts, and is also concentrated on the membranes of the matrix vesicles budding from these cells **[23, 24]**. Rise in alkaline phosphatase is the measure of cell differentiation. These levels were evaluated in 3 studies. As per **[10]** there were minimal but comparable values of alkaline phosphatase between Ti SL Active and TiZr SL Active, but significant difference with the Tissue culture polystyrene (TCPS) which is the control group. In **[13]** study, the alkaline phosphatase levels were high on Ti10Zr on day 7 and high on Ti50Zr on day 12 culture. A study by **[21]** also showed an increase in ALP levels with addition Zirconium to titanium.

Table 2: Levels of evidence

S. No	Study	Type	Level
1	Microstructure, mechanical properties, and preliminary biocompatibility evaluation of binary Ti–Zr alloys for dental application	In vitro study	Level 5
2	Evaluation of corrosion resistance of implant-use Ti-Zr binary alloys with a range of compositions	In vitro study	Level 5
3	Comparable responses of osteoblast lineage cells to microstructured hydrophilic titanium–zirconium and microstructured hydrophilic titanium	In vitro study	Level 5
4	Titanium -Zriconium binary alloyas dental implant material: Analysis of the influence of compositional change on mechanical properties and in vitro biologic response	In vitro study	Level 5
5	The effect of the solute on the structure, selected mechanical properties, and biocompatibility of Ti–Zr system alloys for dental applications	In vitro study	Level 5
6	The influence of surface energy of titanium-zirconium alloy on osteoblast cell functions in vitro	In vitro study	Level 5
7	Characterization of chemically treated Ti-Zr system alloys for dental implant application	In vitro study	Level 5
8	Effect of Surface Roughness of Ti, Zr, and TiZr on Apatite Precipitation From Simulated Body Fluid	In vitro study	Level 5

5. CONCLUSION

Based on the structured review, TiZr has shown better mechanical properties. The elastic modulus of TiZr is much closer to that of human bone when compared with Cp Ti which makes it a better implant material. The biocompatibility and cytotoxicity of TiZr is comparatively lesser than Cp Ti which is overlooked due to the need for implants with better mechanical properties.

REFERENCES

[1] Geetha, M. *et al.*, 2009. Ti based biomaterials, the ultimate choice for orthopaedic implants – A review. *Progress in Materials Science*, 54(3), pp.397–425. Available at: http://dx.doi.org/10.1016/j.pmatsci.2008.06.004.

[2] Long, M. & Rack, H.J., 1998. Titanium alloys in total joint replacement—a materials science perspective. *Biomaterials*, 19(18), pp.1621–1639. Available at: http://dx.doi.org/10.1016/s0142-9612(97)00146-4.

[3] Ho, W.-F. *et al.*, 2008. Structure, mechanical properties, and grindability of dental Ti–Zr alloys. *Journal of Materials Science: Materials in Medicine*, 19(10), pp.3179–3186. Available at: http://dx.doi.org/10.1007/s10856-008-3454-x.

[4] Eisenbarth, E. *et al.*, 2004. Biocompatibility of beta-stabilizing elements of titanium alloys. *Biomaterials*, 25(26), pp.5705–5713.

[5] Eisenbarth, E. *et al.*, 1996. Influence of the surface structure of titanium materials on the adhesion of fibroblasts. *Biomaterials*, 17(14), pp.1399–1403.

[6] Naganawa, T. *et al.*, 2004. In Vitro Biocompatibility of a New Titanium-29Niobium-13Tantalum-4.6Zirconium Alloy With Osteoblast-Like MG63 Cells. *Journal of Periodontology*, 75(12), pp. 1701 – 1707. http://dx.doi.org/10.1902/jop.2004.75.12.1701.

[7] Kobayashi, E. *et al.*, 1995. Mechanical properties of the binary titanium-zirconium alloys and their potential for biomedical materials. *Journal of biomedical materials research*, 29(8), pp.943–950.

[8] Hsu, H.-C. *et al.*, 2009. The structure and mechanical properties of as-cast Zr–Ti alloys. *Journal of Alloys and Compounds*, 488(1), pp.279–283. http://dx.doi.org/10.1016/j.jallcom.2009.08.105.

[9] Murray, J.L., 1987. *Phase diagrams of binary titanium alloys*, Asm Intl.

[10] Lotz, E.M. *et al*., 2017. Comparable responses of osteoblast lineage cells to microstructured hydrophilic titanium-zirconium and micro-structured hydrophilic titanium. *Clinical oral implants research*, 28(7), pp.e51–e59.

[11] Schardt, C. *et al*., 2007. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC medical informatics and decision making*, 7, p.16.

[12] Wang, B. *et al*., 2019. Microstructure, mechanical properties, and preliminary biocom-patibility evaluation of binary Ti–Zr alloys for dental application. *Journal of Biomaterials Applications*, 33(6), pp.766–775. http://dx.doi.org/10.1177/0885328218811052.

[13] Lee, T. *et al*., 2016. Titanium-Zirconium Binary Alloy as Dental Implant Material: Analysis of the Influence of Compositional Change on Mechanical Properties and In Vitro Biologic Response. *The International Journal of Oral & Maxillofacial Implants*, pp.547–554. http://dx.doi.org/10.11607/jomi.4349.

[14] Akimoto, T. *et al*., 2018. Evaluation of corrosion resistance of implant-use Ti-Zr binary alloys with a range of compositions. *Journal of biomedical materials research. Part B, Applied biomaterials*, 106(1), pp.73–79.

[15] Elias, C.N. *et al*., 2015. Mechanical properties, surface morphology and stability of a modified commercially pure high strength titanium alloy for dental implants. *Dental Materials*, 31(2), pp.e1–e13. at: http://dx.doi.org/10.1016/j.dental.2014.10.002.

[16] Niinomi, M., Nakai, M. & Hieda, J., 2012. Development of new metallic alloys for biomedical applications. *Acta biomaterialia*, 8(11), pp.3888–3903.

[17] Nune, K.C. *et al*., 2017. Osteoblast cellular activity on low elastic modulus Ti–24Nb–4Zr–8Sn alloy. *Dental Materials*, 33(2), pp.152–165. Available at: http://dx.doi.org/10.1016/j.dental.2016.11.005.

[18] Sumner, D.R. & Galante, J.O., 1992. Determinants of stress shielding:

design versus materials versus interface. *Clinical orthopaedics and related research*, (274), pp.202–212.

[19] Cordeiro, J.M. *et al*., 2018. Characterization of chemically treated Ti-Zr system alloys for dental implant application. *Materials science & engineering. C, Materials for biological applications*, 92, pp.849–861.

[20] Chen, X. e*t al*., 2008. Effect of surface roughness of Ti, Zr, and TiZr on apatite precipitation from simulated body fluid. *Biotechnology and bioengineering*, 101(2), pp.378–387.

[21] Sista, S. *et al*., 2011. The influence of surface energy of titanium-zirconium alloy on osteoblast cell functions in vitro. *Journal of biomedical materials research. Part A*, 97(1), pp.27–36.

[22] Correa, D.R.N. *et al*., 2014. The effect of the solute on the structure, selected mechanical properties, and biocompatibility of Ti–Zr system alloys for dental applications. *Materials Science and Engineering: C*, 34, pp.354–359. Available at: http://dx.doi.org/10.1016/j.msec.2013.09.032.

[23] Hoshi, K. *et al*., 1997. Immunolocalization of tissue non-specific alkaline phosphatase in mice. *Histochemistry and cell biology*, 107(3), pp.183–191.

[24] Miao, D. & Scutt, A., 2002. Histochemical localization of alkaline phosphatase activity in decalcified bone and cartilage. *The journal of histochemistry and cytochemistry: official journal of the Histochemistry Society*, 50(3), pp.333–340.