Chapter 5
Oxide Bioceramics: Inert Ceramic Materials in Medicine and Dentistry

J. Li and G.W. Hastings

5.1 Introduction

Single oxide ceramics, e.g. aluminium oxide (Al_2O_3, alumina) and zirconium dioxide (ZrO_2, zirconia), are bioceramics of an inert nature. An inert ceramic does not form a bonding to bone similar to those bioceramics of bioactive nature. Alumina bioceramics are in the pure aluminium oxide form, whereas zirconia bioceramics are partially stabilized by additional oxides, e.g. yttrium oxide, calcium oxide or magnesium oxide.

Oxide ceramics exhibit superior mechanical properties, corrosion and wear resistance. Since the oxides are the highest oxidation state of the metal, they are stable even in the most invasive industrial and biomedical environments. Alumina and zirconia are utilized as load-bearing hard tissue replacements and fixation implants in dentistry and surgery.

5.2 Short History

Although the use of alumina as implants can be traced back to the 1930s as described by Hulbert *et al.* (1) (Table 5.1), the extensive use of alumina since the 1980s has depended on new powder processing technology enabling grain size reduction of the sintered ceramics from 10 micrometers down to 2 micrometers (Figure 5.1, microstructure of alumina). This significantly improves the performance of the

J. Li (✉)
Centre for Oral Biology, Karolinska Institute, Huddinge S 141–4, Sweden

G.W. Hastings
Institute of Materials Research and Engineering, Singapore, Singapore

Table 5.1 Evaluation of oxide ceramic implants: alumina and zirconia

1932	First suggestion of application of alumina ceramics in medicine	Rock (2)
1963	First orthopaedic bone substitute application	Smith (3)
1964	First dental implant of alumina	Sandhaus (4)
1970	French hip prosthesis: Alumina ceramic ball and cup	Boutin (5)
1974	German hip prosthesis	Mittelmeier (6)
1977	28 mm alumina ball	Shikita (7)
1981	Alumina total knee prosthesis	Oonishi *et al.* (8)
1982	FDA approval for non-cemented alumina ceramic cup and ball and CoCrMo-stem of Mittelmeier type	
1986	First zirconia ball of 32 mm	Lord *et al.* (9)
1993	First dental implant of zirconia	Akagawa *et al.* (10)
1995	First zirconia dental post	Meyenberg *et al.* (11)
1996	First zirconia inlay	Johansson (12)
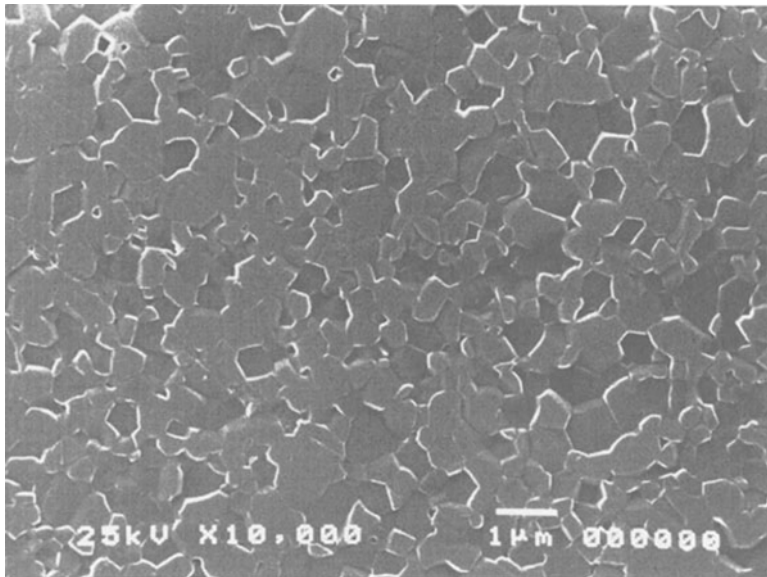
Figure 5.1 SEM micrograph of dense alumina, etched in boiling H_3PO_4 for 6 minutes to show the microstructure.

alumina ceramic hip balls. Alumina and partially stabilized zirconia are currently in extensive use as implants in consequence of their high strength, excellent corrosion and wear resistance and stability, non-toxicity and biocompatibility *in vivo*. A summary of alumina- and zirconia-based implants is presented in Table 5.2. The most established example is in the total hip endoprosthesis with a combination of metallic stem, ceramic ball and ultra high molecule weight polyethylene (UHMWPE)

Table 5.2 Biomedical applications of oxide ceramics

Materials	Applications	References
Alumina	Hip ball & cup	Clarke and Willmann (13)
	Knee joint	Oonishi *et al.* (8)
	Bone screws	
	Dental implant	Kawahara (14)
	Dental crowns & brackets	Sinha *et al.* (15)
Zirconia	Hip ball	Christel (16)
	Dental implants	Akagawa *et al.* (10)
	Dental post, brackets and inlay	(10, 11), Keith *et al.* (17)

acetabular cup. A ten year clinical success rate better than 90% is reported for the cemented total hip endoprosthesis.

Dental implants of polycrystalline alumina were suggested by Sandhaus in Germany (4). Type Tübingen was produced by Frialit in the 1970s. These devices have not been generally accepted, due to the fracture failure of the implants, particularly for those of polycrystalline type produced in the early 1970s. The single crystal sapphire type, introduced in Japan by Kawahara in the 1970s (18) is, however, still being used and a recent 10-year clinical follow-up report from Sweden showed a 92% success rate (19) for the single crystal dental implants.

Alumina and zirconia ceramics are also being used for alveolar ridge reconstruction (20), maxillofacial reconstruction, as ossicular bone substitutes (21), and in ophthalmology (22), knee prosthesis (8), bone screws as well as other applications as dental biomaterials, such as dental crown core, post, bracket and inlay (23, 24).

5.3 Material Properties and Processing

5.3.1 Materials properties

Although alumina is chemically more stable it is mechanically weaker than zirconia, and the phase changes or transformation mechanisms in zirconia produce a unique ceramic material having much higher strength and higher fracture toughness compared with alumina and other ceramics. The excellent mechanical properties of zirconia allow the design of hip balls of smaller diameter in order to reduce the wear of the UHMWPE cup with expected increased long-term clinical performance as a result.

The chemical stability of alumina is related to its phase stability, whereas the phase changes of zirconia result in degradation in strength and wear resistance. Release of substances from zirconia and alumina implants to the surrounding tissue is very low and neither local nor systemic effects have been reported.

Aluminium oxide: alumina

Aluminium oxide is produced by heating its hydrates. At least seven forms of alumina have been reported, but six of these forms have traditionally been designated 'gamma alumina'. When heated above 1200°C, all other structures are irreversibly transformed to the hexagonal alpha-alumina, corundum, a close-packed arrangement of oxygen ions. Thus alphaalumina is the only stable form above 1200°C and by far the most commonly used of structural ceramics. Alpha-alumina is thermodynamically stable and is crystallographically identical with the single crystal ruby and sapphire ceramics. Each aluminium ion is surrounded by six oxygen ions, three of which form a regular triangle on one side, the other three form a similar triangle on the other side, with the two planes of the triangles being parallel and the triangles being twisted 180° (25).

Physical and mechanical properties

Table 5.3 and 5.4. Resulting from a strong chemical bond between the Al and O ions, as expected from the value of heat of formation (-400K cal/mol), Al_2O_3 has a high melting point, the highest hardness among known oxides, and high mechanical strength (26).

Table 5.3 Engineering Properties of Alumina and Zirconia (At 25 °C)*

Property	Al_2O_3	ZrO_2**
Physical		
Crystallography	Hexagonal	Tetragonal***
a(Å)	4.76	3.64
c(Å)	13.0	5.27
Space group	D^6_{Ba}	$P4_2/nmc$
Melting point (°C)	2040	2680
Density (g/cm³)	3.98	6.08
Grain size (µm)	1–6	0.54
Hardness (GPa)	22	12.2
Modulus of elasticity, (GPa)	366	201
Poisson's ratio	0.26	0.30
Thermal coefficient of expansion 25–200 °C	6.5	10.1
Mechanical		
Flexural strength (MPa)	551	1074
Compressive Strength (MPa)	3790	7500
Tensile strength (MPa)	310	420
Fracture toughness (MPa $m^{1/2}$)	4.0	6–15

* Sources: refs 26, 44 and 45
** Zirconia presented is the yttria-partially stabilized material
*** Most of the medical-grade zirconia is partially stabilized tetragonal zirconia

Table 5.4 Properties of medical-grade ceramic materials according to the standards to the standards and the manufacturer's technical date – alumina and zirconia

Property	Alumina according to ISO-6474 ASTM F 603–83 DIN 58 8353	Frialit bioceramic alumina	Zirconia according to ISO/DIS 13356	Prozyr® zirconia
Purity (%)	>99.5	>99.5	>99.5*	>95
Density (g/cm^3)	>3.9	>3.98	>6.0	6
Porosity (%)	0	**	0	0
Grain size (µm)	<4.5	>2.5	<0.6	<1
Microhardness (GPa)	23	23	—	13
Young's modulus (GPa)	380	380	—	220
Flexural strength (MPa)	>400	>450	>900	>920
Biaxial flexural strength (MPa)	250	—	>550	—
Impact strength (cm MPa)	>40	>40		124
Fracture toughness (MPa m$^{1/2}$)				10
Wear resistance (mm^3/h)	0.01	0.001		__
Corrosion resistance (mg/m^{2}d)	<0.1	<0.1	—	—

* $ZrO_2 + HfO_2 + Y_2O_3$
** Not available.

Chemical properties

Alumina is chemically stable and corrosion resistant. It is insoluble in water and very slightly soluble in strong acids and alkalies. Therefore, practically no release of ions from alumina occurs at a physiological pH level, 7.4.

Wear resistance

Arising from the chemical stability and high surface finish and accurate dimensions, there is a very low friction torque between the alumina femoral heads and the acetabular cup, leading to a low wear rate. Combinations of ceramic head/UHMWPE cup and ceramic head/ceramic cup were tested and compared to the metal head/UHMWPE cup. The wear resistance of the ceramic head/UHMWPE cup combination over metal/UHMWPE has improved from 1.3 to 34 times in the laboratory and from three to four times clinically (27, 28). No alumina wear particles from retrieved ceramic/UHMWPE were found, whereas UHMWPE wear particles from microns to millimetres in size were found in the retrieved surrounding tissues. However, from the ceramic/ceramic combination, ceramic particles resembling 'fine grains and great fragments in the ranges from 0.5 to 10 micrometers diameter, with the predominant size of about 1 micrometer' were found in the surrounding tissue (29). The advantage of ceramic/ceramic combination over ceramic/UHMWPE is, therefore, doubtful. For wear tests, we refer to ISO-6474 ASTM F-603.

Clinical performance

The fracture of ceramic balls in ceramic: UHMWPE combination has been virtually zero. Fritsch and Gleitz (30) published a failure analysis on 4341 alumina ceramic heads articulating with 2693 alumina ceramic and 1464 polymer sockets implanted over 20 years (1974 to 1994), and concluded that the use of ball type neckless heads brought the fracture rate close to zero. The success rate of 10 years foliow-up is normally above 90% for the 'elderly' patient population. Stem and cup loosening are the causes of failure, where the consistent wear debris from UHMWPE and bone cement remain the problems.

Zirconium dioxide: zirconia

Zirconia ceramics are termed polymorphic because they undergo several transformations on cooling from a molten state to room temperature. It exhibits three well-defined polymorphs, the monoclinic, tetragonal and cubic phases and a high pressure orthorhombic form also exists. The monoclinic phase is stable up to about 1170°C where it transforms to the tetragonal phase, stable up to 2370°C, while the cubic phase exists up to the melting point 2680°C. A large volume change of 3 to 5% occurs when zirconia is cooled down and transforms from the tetragonal to the monoclinic phase.

Partially stabilized zirconia (PSZ) and tetragonal zirconia polycrystals (TZP)

The volume change due to phase transformation is sufficient to exceed elastic and fracture limits and causes cracking of the zirconia ceramics. Therefore, additives such as calcia (CaO), magnesia (MgO) and/or yttria (Y_2O_3) must be mixed with zirconia to stabilize the material in either the tetragonal or the cubic phase. PSZ is a mixture of cubic and tetragonal and /or monoclinic phases, whereas TZP is 100% tetragonal (phase diagram Figure 5.2). Both PSZ and TZP are suggested for medical implant applications. Yttria-TZP ceramics have a strength and fracture toughness approximately twice that of alumina ceramics used in the biomedical field. This makes zirconia heads less sensitive to stress concentrations at the points of contact with metal cones.

Physical and mechanical properties

Zirconia ceramics have a high density because of heavy zirconium ions, and a low microhardness and elastic modulus, together with high strength and fracture toughness compared to other ceramics including alumina. The superior mechanical strength provides the possibilities for producing ceramic ball heads of size below 32 mm.

Figure 5.2(a) Part of the equilibrium phase diagram for the system ZrOz-CaO. Css refers to the cubic solid-solution phase, Tss to the tetragonal solid-solution phase, and Mss to the monoclinic solid-solution phase (ref. 21).
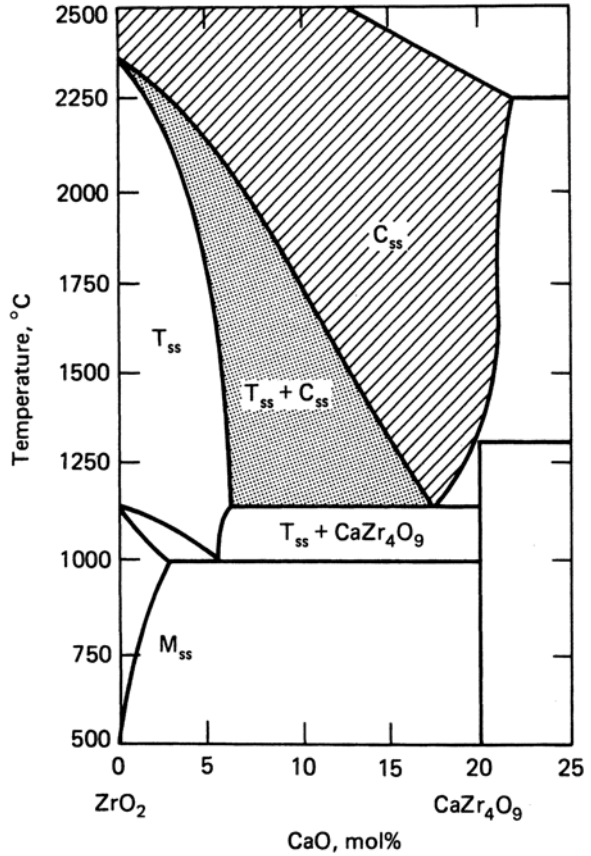
Figure 5.2(b) Y_2O_3–ZrO_2 phase diagram: the addition of less than 5% of Y_2O_3 to ZrO_2 allows the sintering of a fully tetragonal material (t=tetragonal phase; m=monoclinic phase; c=cubic phase) (ref. 16).
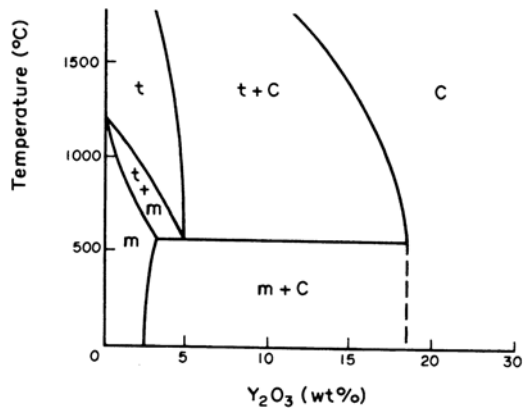
Fracture toughness mechanisms:

Garvie *et al*. were the first to realize the transformation toughening mechanism for zirconia ceramics. Increase of both strength and fracture toughness can be obtained by utilizing the tetragonal-monoclinic phase transformation of metastable tetragonal grains induced by the presence of the stress field ahead of a crack (31). The volume change and the shear strain developed in the martensitic reaction were recognized as opposing the opening of the crack and therefore acting to increase the resistance to crack propagation.

Wear resistance and chemical stability:

The published results of *in vitro* wear tests demonstrated that zirconia has a superior wear resistance. Saikko (32) showed no wear of zirconia femoral heads on his hip simulator wear test against 10.9 mm UHMWPE cup, and Praveen Kumar *et al.* (33) demonstrated the high wear resistance of zirconia against UHMWPE and the superiority of zirconia ceramics even over alumina ceramics in terms of low wear and low friction. A significant reduction in the wear rate of zirconia ball heads compared to the metal ball heads was reported on a pin-on-disc wear test and on a hip simulator (34). However, there are two potential limitations for the use of zirconia as bioceramics: degradation and radiation. It is known that the phase transformation is accelerated in aqueous environment, but little is known about how this phase transformation will occur in biological environment, particularly under dynamic loadings. A warning against steam resterilization has been issued in the UK. Radioactive U-235 impurity was detected in some 'pure zirconia', both alpha- and gamma-irradiation were measured from zirconia femoral balls. Although the radioactivity was low, more work is required to verify this matter (13).

Clinical performance

The surface degradation of the zirconia balls due to the phase transformation under loading seems to be a problem, although no significant change in mechanical strength was reported in some long-term *in vivo* and *in vitro* studies (35, 36). Seriously, catastrophic failure of modular zirconia ceramics femoral head components after total hip arthroplasty was reported (37). Since zirconia femoral heads have a short clinical history and few clinical results are available, more investigation is required to eliminate the factors which impair the clinical stability of zirconia ceramics under loading.

5.3.2 Materials processing

An advanced ceramic is processed in such a way that the structure of the materials on different levels, including atomic, electronic, grain boundary, microstructural and macrostructural, is under strict control. In the manufacturing processes, emphasis is placed on producing dense ceramics with a fine microstructure. However, other factors such as chemical composition, the nature and distribution of the impurities, crystal structure, grain size, and defects are also of importance to the performance of the ceramic materials. Three basic processes are involved in the production of fine ceramic components, namely: 1. powder technology, 2. densification or sintering and 3. machining. Both alumina and zirconia hip balls are produced by compacting fined-grained powder (green bodies), and sintering at 1500–1700 °C and finally grinding or lapping to obtain a high surface finish and sphericity (Ra<0.02 μm).

5.4   Biocompatibility of Oxide Bioceramics

No materials placed within a living tissue can be considered to be completely inert. However, oxide bioceramics, by their very nature, do not suffer from corrosion or degradation in biological environments, as metals or plastics do. Ceramics, having molecular structures completely different from those of living tissues, are generally stable inside the living body and provide a high degree of acceptance by the apposition to the surrounding tissue as shown by *in vitro* and *in vivo* studies Ichikawa *et al*. observed no adverse soft tissue responses to zirconia and alumina implants after 12 months of implanation (38). Takamura *et al*. reported that alumina and zirconia did not possess chronic toxicity to mice (39), whereas Steflik *et al*. found a biological seal at the alumina dental implant and epithelium interface (40). However, oxide bioceramics do not form a chemical bond to bone tissue and are therefore defined as inert biomaterials. Oxide bioceramics are defined as inert biomaterials.

The ASTM standards (F 748/82, 763/82) and ISO standards No 10993 have set the guidance for biological testing of biomaterials for orthopaedic application. The materials should be tested in soft tissue as well as in hard tissue environments, for both short-term and long-term experiments. A summary of recommended biological testing is presented in Table 5.5. Both alumina and zirconia have shown nontoxicity and good biocompatibility according to the tests. Testing results for zirconia made by a French Company are shown in Table 5.6. Although some serious problems occurred with zirconia balls, the basic biocompatibility of the zirconia remains. Soft tissue and bone responses to zirconia and alumina were studied in our lab: no adverse tissue reaction to these ceramics were found. The patterns of tissue-materials interface after 1 month implantation in muscle and femur of rat are shown in Figure 5.3.

Table 5.5 Guidance for Biologic Evaluation Tests of the Implant Device in Contact to bone Tissue (According to ISO 10993–1:1992 (E))

Biological tests	Contact duration		
	A-limited (>24 h)	B-prolonged (<24 h to 30 days)	C-permanent (<30 days)
Cytotoxity	x	x	x
Sensitisation	x	x	x
Irritation/Intracutaneous Reactivity	x	x	x
Irritation/Intracutaneous	x		
Genotoxicity		x	x
Implantation		x	x
Chronic toxicity			x
Carcinogenicity			x

The related tests see ISO standards from No. 10993–1 to 10993–6

Table 5.6 Biological evaluations of zirconia ceramics (Prozyr®, Ceramiques Desmarquest, France)

| Biocompatibility	Standard used	Results
Short-term *in vivo* biocompatibility	ASTM F 763/82	Very good
In vitro biocompatibility	ASTM F 748/82	
Cell culture cytotoxicity	PRS 90.702	Good cytocompatibility
Mutagenicity	Ames test Micronucleus test	No mutagenic activity
Systemic injection acute toxicity	ASTM F 750/82	According to standard
Intracutaneous injection	ASTM F 749/82 ASTM F720/81	No irritation
Sensitization	Magnusson	No sensitization

5.5   Applications

5.5.1   Orthopaedic applications

The dominating application of alumina and zirconia is as hip balls as well as cups of total femoral prosthesis. The neckless hip balls are the most popular design. In 1981, Oonishi *et al*. (8) reported on the use of an alumina ceramic total knee prosthesis. High alumina ceramic middle ear implants (Frialit) are used clinically in Europe since 1979 (21). An opthalmological implant device consisting of a combination of a single crystal alumina optional cylinder and a polycrystalline alumina holding ring was introduced clinically in 1977 (22). Kawahara (12) has reported extensively on single crystal alumina bone screws.
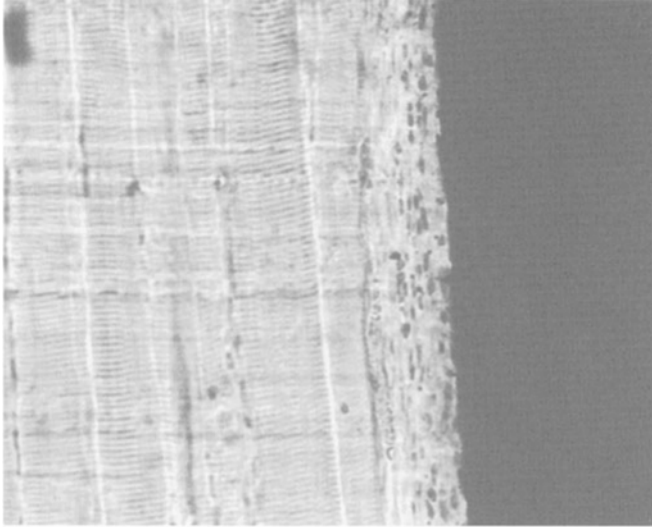
(a)

Figure 5.3(a)   Optical micrograph of alumina and soft tissue interface.
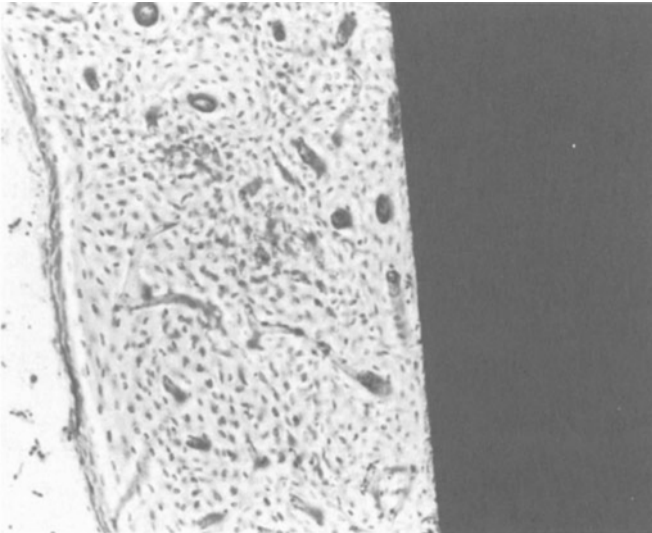
(b)

Figure 5.3(b)   Zirconia and bone interface 1 month after implantation. Arrows are pointing to the interfaces.

Table 5.7 Ceramic manufacturers known for their bioceramic productions

Manufacturer	Country	Primary Materials	Secondary Materials	Trade Names Al_2O_3 (ZrO_2)
Astroment	USA	ZrO_2	Al_2O_3	
Ceraver	France	Al_2O_3	ZrO_2	
Cerasiv	Germany	Al_2O_3	ZrO_2	Biolox
Desmarquest	France	ZrO_2		(Proyzr)
HiTech	France	ZrO_2	Al_2O_3	
Kyocera	Japan	Al_2O_3	ZrO_2	Bioceram
Metoxit	Switzerland	ZrO_2		
Morgan Matroc	England	ZrO_2	Al_2O_3	
NGK	Japan	ZrO_2		
Biocare	Sweden	Al_2O_3		Procera
Unitek	USA	Al_2O_3		Transcend 2000
Maillefer	Switzerland	ZrO_2		

5.5.2 Dental applications

Alumina and zirconia ceramics have been utilized for root analogue, endosteal screws, blades and pin-type dental implants. The root and blade form dental implants used during the 1970s tended to fracture after a few years in function (41, 42) (Brose *et al*., 1987, Driskell, 1987). Although initial testing of these polycrystalline alumina materials showed adequate mechanical strength, the long-term clinical results demonstrated functional limitations related to material properties and implant design. However, single crystalline alumina showed mechanical strength superior to that of polycrystalline alumina. It allows a much higher load. One-stage dental implants of single crystalline alumina are used clinically with a high success rate. McKinnery (43) had also reported on single crystal alumina blade and screw dental implants. Dental implants of zirconia have not been widely used clinically although zirconia has a similar mechanical strength and a much higher fracture toughness in addition to lower cost of production compared to single crystalline alumina. The term dental implant is used only for materials in contact with bone and soft tissue (14). Alumina and zirconia are also used in other dental applications, alumina ceramic crowns, Procera® (23), zirconia dental post, (10) and recently a dental inlay of zirconia was introduced (11). Orthodontic brackets made of oxide ceramics were also produced, tested and used clinically. Unfortunately, tooth surface damage was observed when the brackets were taken away (15). Modification of the debonding technique is under developing.

5.6   Manufacturers and Their Implant Products

Clarke and Willmann (13) make a comprehensive summary about the bioceramic manufacturers (Table 5.6). Some dental companies are included.

5.7 Problems and Future Prospects

Hip balls of polycrystalline alumina have a minimum size limitation to ca. 28 mm due to strength limitations. A reduced ball size might have two positive effects on the applications: reduced wear and better suitability (smaller) for Asian patients. Although single crystalline alumina might overcome the strength limitation, the cost of manufacturing is unreasonably high and in addition, some processing problems remain. Zirconia, on the other hand, has a high strength and high fracture toughness, but it suffers from potential biodegradation. Therefore, the future research and development will focus on the understanding of degradation mechanisms of zirconia in the body and the improvement of stability of this material. Of course, combinations, such as alumina/zirconia composite and even non-oxide ceramic, such as nitrides and carbides, ought also to be investigated.

References

1. Hulbert, S.F., Bokros, J.C., Hench, L.L., Wilson, J. and Heimke, G. In *Ceramics in Clinical Applications*, ed. by Vincenzini, P. Elsevier, Amsterdam, 1987, pp. 3–27.
2. Rock, M. German Patent 583 589, 1933.
3. Smith, L. *Arch. Surg.* 1963; **87: 653**–661.
4. Sandhaus, S. British Patent 1083769, 1967.
5. Boutin, P. *Presse Med.* 1971; **79**: 639.
6. Mittelmeier, H. Z. *Orthop. Ihre Grenzgeb* 1974; **112** : 27.
7. Shikita, T. Paper presented at the XIV World Congress of SICOT, Kyoto, Japan, October 15–20, 1978.
8. Oonishi, H., Okabe, N., Hamaguchi, T. and Nabeshima, T. *Orthopaedic Ceramic Implants I*, 1981; 11–18.
9. Lord, G. *et al.* Paper presented at the Harrington Arthritis Research Centre Symposium, November 18–21, 1990.
10. Akagawa, Y. *et al. J. Prosthet. Dent.* 1993; **69**: 599–604.
11. Meyenberg, K.H., Luthy, H. and Scharer, P. *J. Esthet. Dent.*, 1995; **7**(2): 73–80.
12. Johansson, B. *Tandläkartidningen* 1996; 14746–749.
13. Clarke, I.C and Willmann, G. In *Bone implant Interface* ed. H.V. Cameron,Hugh U., Mosby, 1994, pp. 222.
14. Kawahara, H. In *Encyclopedic handbook of biomaterials and bioengineering* ed. by Wise, Donald L. *et al.* Marcel Dekker, Inc., New York, 1995, pp. 1469–1524.
15. Sinha, P.K., Rohrer, M.D., Nanda, R.S. and Brickman, C.D. *American J. Orthodont & Dentofacial Orthop*, 1995; **108**: 455–63.
16. *Christel, P.S.* In *Condse Encyclopedia of Medical & Dental Materials*, ed. by Williams, D.F., Pergamon Press, Oxford, 1990, pp. 375–379.
17. Keith, O., Kusy, R.P. and Whitley, J.Q. *American J. Orthodont. & Dentofacial Orthop.*, 1994; **106**(6): 605–614.
18. Kawahara, H. *Orthopaedic Ceramic Implants 1*,1981; 1–10.
19. Fartash, B. Single Crystal Sapphire Dental Implants: Experimental and Clinical Studies. PhD thesis, Karolinska Institute, Sweden, 1996.
20. Hammer, N.B., Topazian, R.G., McKinney, P.V. and Hulbert, S.F. *J. Dent. Res.* 1973; **52**: 356–361.

21. Jahnke, K. *Biomaterials in Otology* , Martinus Nijhoff, The Hague, 1984:205–209.
22. Polack, F.M. and Heimke, G. *Ophthalmology*, 1980; **87**(7): 693–698.
23. Andersson, M. and Odén, A. *Acta Odont. Scand.*, 1993; **51**: 59–64.
24. Kittipibul, P. and Godfrey, K. *American J. Orthodont & Dentofadal Orthopedics*, 1995; **108**(3): 308–315.
25. Heimke, G. In *Metal and Ceramic Biomaterials* Vol I Structure, ed. by Ducheyne, P. and Hastings, G.W. CRC Press Inc., Boca Raton. Florida, 1984, pp. 41–42.
26. Miyayama. M. *et al.* In *Ceramics and Glass, Engineered Materials Handbook* Volume 4, ASM International, 1991, pp. 748–757.
27. Griss, P. In *Functional Behavior of Orthopaedic Biomaterials 11*, Ch 2, 1984.
28. Jager M. and Plitz, W. *Triobology of aluminium ceramics, Symposium of Biomaterials*, pp. 114–122, 1981.
29. Willert, H.G. *et al.* In *Implant Retrieval: Material and Biological Analysis*, ed. by Weinstein. A., Gibbons, D., Brown, S. and Ruff, W. 1981.
30. Fritsch, E.W. and Gleitz, M. *Clin. Orthop. & Related Res.*, 1996; **328**: 129–136.
31. Garvie, R.C, Hannink, R.H. and Pascoe, R.T. *Nature*, 1975; **258**: 703.
32. Saikka, V.O. *Acta Orthop. Scand.*, 1995; **66**(6): 501–506.
33. Kumar, P. *et al. J. Biomed. Mater. Res.*, 1991; **25**: 813–828.
34. Derbyshire, B. *et af. Medical Eng. & Phys.*, 1994; **16**(39): 229–36.
35. Shimizu, K. *et al.* J. Biomed. Mater. Res., 1993; **27**: 729–734.
36. Cales, B., Stefani, Y. and Lilley, E. *J. Biomed. Mater. Res.*, 1994; **28:** 619–624.
37. Hummer, C.D., Rothman, R.H. and Hozack, W.J. *J. Arthroplasty* , 1995; **10**(6): 848–850.
38. Ichikawa, Y. *et al. J. Prosthet. Dent.* 1992; **68**: 322–6.
39. Takamura, K. *et al. J. Biomed. Mater. Res.*, 1994; **28** : 583–589.
40. Steflik, D., McKinney Jr R.V. and Koth, D. In *Bioceramics: Materials characteristics versus in vivo behavior*, ed. by Ducheyne, P. and Lemons, J.E. *Ann. N. Y. Acad. Sci.* **523**, pp. 4–18.
41. Brose, M. *et al. J. Dent. Res.*, 1987; **66**: 113.
42. Driskel, T.D. *J. Calif Dent. Assoc.*, 1987; 16–25.
43. Mckinney, R.V. and Koth, D.L. *J. Prosthet. Dent.*, 1982: **47** : 69–84.
44. Park, J.B. and Lakes, R.S. *Biomaterials: an Introduction*, 2nd edition, Plenum Press, New York, 1992.
45. Bajpai, P.K. and Billotte, W.G. In *The Biomedical Engineering Handbook*, ed.by Bronzino, J.D. CRC Press, 1995, pp. 552–580.