Mechanical and Microstructural Properties of Monolithic Zirconia

Crown Fracture Resistance and Impact of Low-Temperature Degradation

Keisuke Nakamura

Department of Prosthetic Dentistry/Dental Materials Science
Institute of Odontology
Sahlgrenska Academy at University of Gothenburg

UNIVERSITY OF GOTHENBURG

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keisuke@m.tohoku.ac.jp

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To my father, Osamu and my mother, Mieko

To my family; Ai and Mizuki

ABSTRACT

Mechanical and Microstructural Properties of Monolithic Zirconia: Crown Fracture Resistance and Impact of Low-Temperature Degradation

Keisuke Nakamura
Department of Prosthetic Dentistry/Dental Materials Science, Institute of Odontology, Sahlgrenska Academy at University of Gothenburg, Göteborg, Sweden

Zirconia has been widely used in dentistry to improve the strength of ceramic restorations maintaining aesthetics. In addition, zirconia is increasingly being used for monolithic crowns without veneering porcelain. However, there is a lack of scientific information regarding whether or not monolithic zirconia crowns can function with sufficient durability, especially in the molar regions. The overall aim of this thesis was to analyze factors that would affect mechanical and microstructural properties of monolithic zirconia crowns.

Material testing was performed to evaluate the influence of sintering temperature, additional heat treatment, coloring procedure and autoclaving-induced low-temperature degradation (LTD) on the biaxial flexural strength of zirconia. Additional heat treatment did not reduce the strength, but the strength was found to decrease as the sintering temperature increased. The tooth-colored zirconia possessed equivalent strength to the non-colored zirconia. In addition, X-ray diffraction analysis and scanning electron microscopy showed that the tooth-colored zirconia had higher resistance to LTD.

Crown fracture testing showed that the fracture resistance of the monolithic zirconia crowns with an occlusal thickness of 0.5 mm was significantly higher than that of lithium disilicate crowns with an occlusal thickness of 1.5 mm. The types of cements did not significantly affect the fracture resistance of monolithic zirconia crowns. When subjected to autoclaving-induced LTD, the fracture resistance of the monolithic zirconia crowns significantly decreased. By contrast, cyclic loading with a load of 300 N for 240,000 cycles did not significantly affect the fracture resistance of the crowns.

The knowledge obtained by the laboratory studies performed suggests that monolithic zirconia crowns with a minimal thickness of 0.5 mm will have the capability of being applied to the molar region with sufficient durability, providing there is a properly controlled fabrication process to avoid unexpected degradation of the material.

Keywords: zirconia, flexural strength, microstructure, fracture resistance, monolithic crown, low-temperature degradation, phase transformation
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LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Nakamura, K., Adolfsson, E., Milleding, P., Kanno, T., Örtengren, U. (2012) Influence of grain size and veneer firing process on the flexural strength of zirconia ceramics. *Eur J Oral Sci* 120: 249-254

II. Nakamura, K., Harada, A., Ono, M., Shibasaki, H., Kanno, T., Niwano, Y., Adolfsson, E., Milleding, P., Örtengren, U. (2015) Effect of low-temperature degradation on the mechanical and microstructural properties of tooth-colored 3Y-TZP ceramics. Submitted for publication.

III. Nakamura, K., Harada, A., Inagaki, R., Kanno, T., Niwano, Y., Milleding, P., Örtengren, U. (2015) Fracture resistance of monolithic zirconia molar crowns with reduced thickness. *Acta Odont Scand*, E-pub ahead of print

IV. Nakamura, K., Mohat, M., Nergård J.M., Lægreid, S.J., Kanno, T., Milleding, P., Örtengren, U. (2015) Effect of cements on fracture resistance of monolithic zirconia crowns. Submitted for publication.

V. Nakamura, K., Harada, A., Kanno, T., Inagaki, R., Niwano, Y., Milleding, P., Örtengren, U. (2015) The influence of low-temperature degradation and cyclic loading on the fracture resistance of monolithic zirconia molar crowns. Submitted for publication.

Appendix

Nakamura, K., Kanno, T., Milleding, P., Örtengren, U. (2010) Zirconia as a dental implant abutment material: A systematic review. *Int J Prosthodont* 23: 299-309

CONTENT

ABBREVIATIONS

CAD/CAM	computer aided designing and computer aided manufacturing
CIP	cold isostatic pressing
FDP	fixed dental prosthesis
IF	infiltration technique
HIP	hot isostatic pressing
LTD	low-temperature degradation
Micro-CT	micro-computed tomography
NC	non-colored zirconia
PM	powder mixing method
PSZ	partially stabilized zirconia
SEM	scanning electron microscope
XRD	X-ray diffraction
XRF	X-ray fluorescence
Y-TZP	yttria stabilized tetragonal polycrystals
3Y-TZP	3 mol.% yttria stabilized tetragonal polycrystals

1 INTRODUCTION

All-ceramic restorations have been widely applied in dentistry to obtain improved aesthetics compared with metal-ceramic restorations (Pjetursson et al., 2007; Sailer et al., 2007b; Pieger et al., 2014). The optical properties of ceramics, especially porcelain (feldspathic ceramic), make it possible to replicate natural tooth color (Giordano, 2006; Vult von Steyern, 2013). In addition to aesthetic perspective, all-ceramic restorations are thought to be preferable to restorations containing metal structure to avoid adverse reactions, such as toxicity and hypersensitivity (Vamnes et al., 2004; van Noort et al., 2004; Hensten and Gjerdet, 2013). Although the risk of allergy caused by metal-ceramic restorations may be relatively low, chemical inertness of ceramics are still beneficial (Anusavice, 2013b). However, ceramics are generally inferior to metal in terms of strength, and are mechanically brittle, which limited the application of all-ceramic restorations (Vult von Steyern, 2013).

In this context, oxide ceramics with higher strength than other types of dental ceramics have been introduced. Although the optical property of oxide ceramics are inferior to porcelain, they are still aesthetic material compared to metals. In the early 1990s, alumina (aluminum oxide, Al_2O_3) that possesses flexural strength of about 650 MPa (Zeng et al., 1996; Itinoche et al., 2006) found use in dentistry (Andersson and Oden, 1993; Prestipino and Ingber, 1993a; b). Alumina was mainly applied to framework of single crowns and dental implant abutments (Odman and Andersson, 2001; Andersson et al., 2003; Zitzmann et al., 2007). However, alumina still had a risk of fracture both during laboratory work and in clinical use (Andersson et al., 2001; Walter et al., 2006) though alumina prostheses functioned biologically as well as aesthetically. Thus, zirconia (zirconium dioxide, ZrO_2) with higher strength (900-1200 MPa) (Christel et al., 1989; Kosmac et al., 1999; Guazzato et al., 2005) has been applied as an alternative material. The development of computer aided design/computer aided manufacturing (CAD/CAM) technology (Manicone et al., 2007; Denry and Kelly, 2008) has made zirconia

popular in dentistry. Currently, zirconia has overtaken alumina as the preferred dental ceramic material. Furthermore, because of the development of translucent tooth-colored zirconia ceramics, zirconia has found increased use for monolithic restorations without veneering material, also called full-contour zirconia (Christensen, 2011). However, there is a lack of scientific information if newly developed monolithic zirconia restorations can function with sufficient durability, especially in the molar regions. Therefore, this thesis was designed to obtain scientific information on dental monolithic zirconia crowns.

1.1 Zirconia ceramics

1.1.1 Microstructure

Crystalline structure

Zirconia has a polymorph form which consists of monoclinic, tetragonal and cubic phase (Figure 1). At room temperature, zirconia adopts a monoclinic structure and transforms into tetragonal phase at 1170°C, followed by a cubic phase at 2370°C (Scott, 1975; Chevalier et al., 2009). When pure zirconia without stabilizers is sintered at a temperature of above 1170°C, tetragonal phase is generated. During subsequent cooling, the phase transformation from tetragonal to monoclinic occurs. This phase transformation is accompanied by 3-5% volume expansion of the crystalline phase, which generates stress in the sintered material. Since the stress induces severe cracking in the material upon cooling, pure zirconia cannot be used as a bulk material.

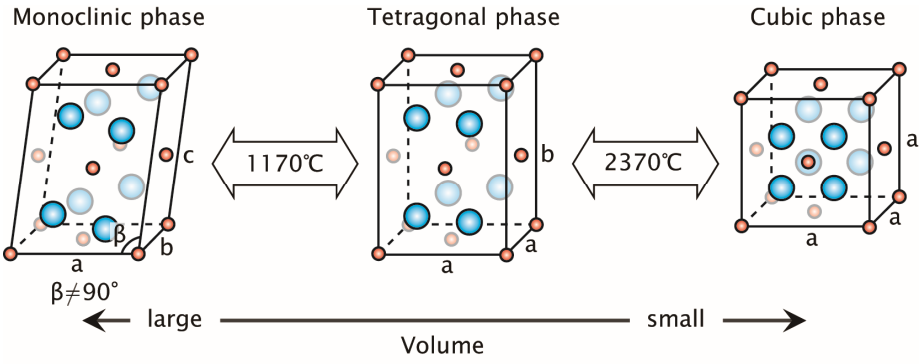

Figure 1. Schematic of temperature-dependent crystalline structure of zirconia. Red spheres = Zr, Blue spheres = O. The figure is modified from (Hannink et al., 2000; Anusavice, 2013b).

The instability of tetragonal and cubic phase in zirconia at room temperature is attributed to smaller ionic radius of Zr^{4+} (0.84 Å) in comparison with O^{2-} (1.38 Å), which results in oxygen overcrowding and displacement of oxygen atoms due to repulsive forces of the anions (Estell and Flengas, 1970; Shannon, 1976; Chevalier et al., 2009). The oxygen overcrowding can be relieved by introducing oxygen vacancies in the crystalline structure and/or by expanding the lattice size (Fabris et al., 2002; Chevalier et al., 2009). For instance, oxygen vacancies can be created by doping with a lower valence cation (*e.g.* Ca^{2+}, Mg^{2+} and Y^{3+}), and the lattice can be expanded by doping with an oversized cation, such as Ce^{4+} (0.97 Å) and Y^{3+} (1.019 Å) (Shannon, 1976). Thus, the addition of metal oxides, such as CaO, MgO, CeO_2, and Y_2O_3, to pure zirconia can stabilize tetragonal and/or cubic phase at room temperature (Garvie and Nicholson, 1972; Garvie et al., 1984; Piconi et al., 1998; Ban et al., 2008). Of these stabilizers, yttria (Y_2O_3) is the most frequently used for dental applications (Denry and Kelly, 2008). When stabilized with 3 mol.% yttria, zirconia is composed of metastable tetragonal phase. This type of material is referred to as yttria-stabilized tetragonal zirconia polycrystals (3Y-TZP). The stabilized zirconia (hereafter referred to as "zirconia") can be used as a bulk material.

Stress-induced transformation toughening

The metastable tetragonal phase in zirconia contributes not only to the application of the material as a bulk at room temperature but also to the resistance against crack propagation. When exposed to mechanical stress, the metastable tetragonal phase transforms to monoclinic phase (Hannink et al., 2000). Since the phase transformation is accompanied by the volume expansion of grains, compressive stress is generated in localized areas around micro-cracks (Kelly and Ball, 1986), resulting in arrested crack propagation (Figure 2). This phenomenon is known as stress-induced transformation toughening, which was first reported by Garvie et al. (1975). Thus, zirconia ceramics can exhibit flexural strength of ≥ 900 MPa and fracture toughness of approximately 5-10 MPa·m$^{1/2}$ that is higher than that of alumina (3.5-4 MPa·m$^{1/2}$) (Piconi and Maccauro, 1999; Anusavice, 2013b).

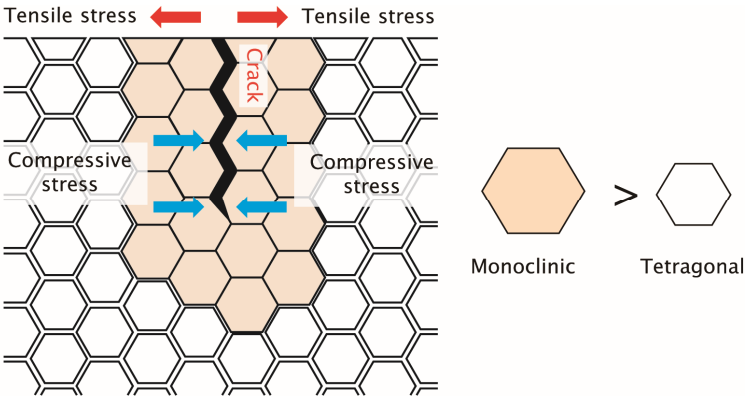

Figure 2. Schematic of stress-induced transformation toughening in zirconia. Compressive stress generated by volume expansion as a result of phase transformation arrests crack propagation. The figure is modified from (Piconi and Maccauro, 1999; Anusavice, 2013b).

Surface condition-related strength

It has been demonstrated that flexural strength of zirconia can be additionally augmented by surface grinding and sandblasting (Kosmac et al., 1999; 2000; Guazzato et al., 2005). Such treatments generate compressive stress only on the surface of material as a result of the phase transformation from metastable tetragonal to stable monoclinic phase,

which can counteract against crack propagation. The improvement in flexural strength depends on the severity of the surface treatment. Exsessive surface treatement, expecially grinding, decreases the flexural strength as well as reliability of the material (Kosmac et al., 2000; Curtis et al., 2006), suggesting that the flaws created by the treatment may prevail against the positive effect of compressive stress generated. In addition, it has been demonstrated that reverse transformation from monoclinic to tetragonal can occur in sandblasted or ground material when subjected to annealing, resulting in the decrease of flexural stregnth (Kosmac et al., 2000; Guazzato et al., 2005). Although grinding and sandblasting increase the initial strength, they are not used for that purpose, at least in dentistry, because they may deteriorate durability of the material. However, these evidences clearly show that the mechanical property of zirconia depends in large part on its unique crystalline phase transformation.

1.1.2 Low-temperature degradation (LTD)

Mechanism of LTD

The metastable tetragonal phase spontaneously transforms into the monoclinic phase in a humid atmosphere even without mechanical stress, which begins at the surface and enters the bulk of the material. This process is often referred to as low-temperature degradation (LTD) or aging (Chevalier et al., 2007). As shown in Figure 3, nucleus is first formed at a specific grain that is more susceptible to the phase transformation because of a disequilibrium state, such as large grain size, lower content of stabilizer and the presence of residual stresses (Chevalier, 2006). Although the mechanism of the phase transformation caused by water molecules has not been fully elucidated (Lughi and Sergo, 2010), following steps are proposed (Yoshimura et al., 1987; Lawson, 1995; Chevalier et al., 2009):

1) Chemical adsorption of H_2O on ZrO_2 surfaces
2) Formation of Zr-OH bond disrupting Zr-O-Zr bond
3) Penetration of OH^- and/or O^{2-} into the inner part by grain boundary diffusion
4) Filling of oxygen vacancies by OH^- and/or O^{2-}
5) Reduction of the oxygen vacancies destabilizing tetragonal phase

Since the transformation is accompanied with volume expansion of the crystalline structure, surface uplift and micro-cracks are introduced. The micro-cracks then allow water to penetrate into the bulk causing the cascade of events where further phase transformation occurs one after another. Finally, major cracks are generated leading to a catastrophic failure of the material.

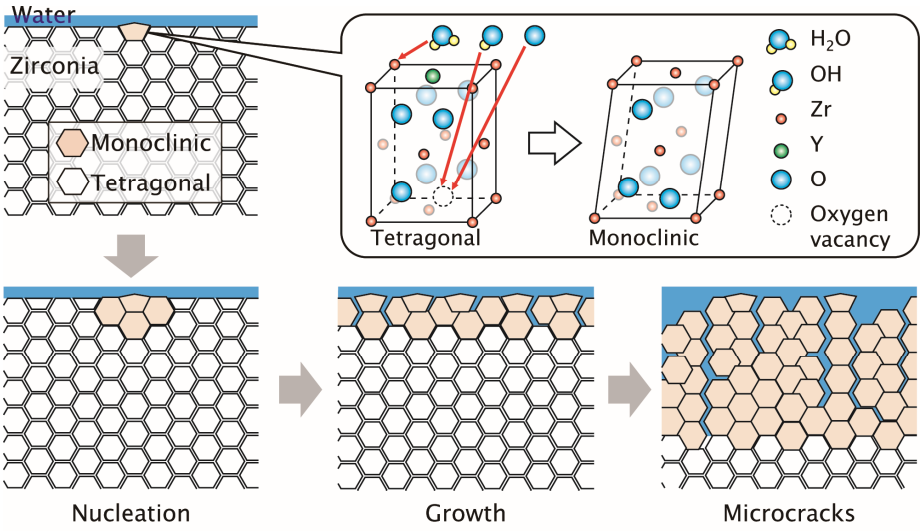

Figure 3. Schematic of progress of LTD. Nucleus is formed where water destabilizes the tetragonal phase by filling the oxygen vacancy with OH^- and/or O^{2-}. The transformed zone grows with the water penetration resulting in the generation of micro-cracks. The figure is modified from (Chevalier, 2006; Chevalier et al., 2009)

LTD-related problems in orthopedics

LTD in zirconia was firstly reported in an *in vitro* study performed by Kobayashi et al. (1981). Since then, substantial studies on this issue have been conducted, and it was found that LTD progresses most rapidly at temperatures

of 200-300°C (Yoshimura, 1988; Lawson, 1995). Thus, it was considered that the influence of LTD on biomaterial of zirconia at 37°C would be limited or negligible until 2001, when several hundreds of zirconia ball used for orthopedic femoral heads in certain batches failed as a result of LTD. Chevalier et al. (2007) described the incidence and discussed that LTD might be accelerated by a combination of lower density and residual stresses that were generated as a result of sintering in a tunnel furnace and drilling of the zirconia balls after sintering. Besides those dramatic failures, the influence of LTD on zirconia heads was also reported in other studies. Haraguchi et al. (2001) reported that zirconia heads retrieved from patients were suffered from surface roughening, and showed an increase of monoclinic phase after only 3- and 6-year use. Clarke et al. (2003) also reported that an increase of monoclinic phase was observed in a retrieved zirconia head after 8-year use whereas another retrieved zirconia heads after 10-year use showed minimum phase transformation. These findings suggest that LTD of zirconia can also occur at body temperature, and the susceptibility to LTD will vary with products produced by different processes and/or the service conditions.

Requirements for zirconia implants to avoid LTD

It has been established that the stability of tetragonal phase, and in turn susceptibility to LTD, depends on several material properties, such as density, purity, grain size, and type and content of stabilizer (Clarke et al., 2003; Chevalier et al., 2007; Lughi and Sergo, 2010). Therefore, requirements for the physical and chemical properties of Y-TZP used for surgical implants have been established and are given in ISO 13356:2008 “Implants for surgery – Ceramic materials based on yttria-stabilized tetragonal zirconia (Y-TZP)” (Table 1).

Table 1. Requirements for zirconia ceramic used for surgical implants given in ISO 13356:2008

	Unit	Requirement
Density	g/cm^3	≥ 6.00
Grain size (linear intersection distance)	µm	≤ 0.4
Chemical composition:	mass %	
$ZrO_2 + HfO_2 + Y_2O_3$		≥ 99.0
Y_2O_3		4.5-6.0
HfO_2		≤ 5
Al_2O_3		≤ 0.5
Other oxides		≤ 0.5

Density

If density of Y-TZP is low (*i.e.* presence of open porosity in the material), water can more easily penetrates resulting in acceleration of LTD (Chevalier et al., 2007). Density of the final product is affected by manufacturing process, such as forming, sintering and pressing. At the first step of forming, zirconia power is compacted to form a green body by cold isostatic pressing (CIP), which achieves greater uniformity of compact by application of pressure from multiple directions. CIP increases density of the green body that will affect the density of final product. After forming and milling (if applicable), the green body is sintered to densify and solidify the material. Sintering is essentially a removal of the pores, and as such, is accompanied with shrinkage of the material (Richerson, 2006a). Heat is the primary source for the movement of the atoms, and commonly used sintering temperature for zirconia is 1350-1550°C with dwell times between 2 and 5 h (Denry and Kelly, 2008). In general, sintered zirconia is additionally subjected to hot isostatic pressing (HIP) (Clarke et al., 2003; Munoz-Saldana et al., 2003). HIP is performed in a special furnace applying heat and pressure simultaneously to further densify the material (Richerson, 2006a). By controlling these processes, density of 6.00 g/cm^3 that is > 98% of theoretical density calculated to be 6.10 g/cm^3 can be achieved.

Grain size

With increased grain size, tetragonal phase in Y-TZP becomes less stable and more susceptible to LTD (Tsukuma et al., 1984; Munoz-Saldana et al., 2003; Chevalier et al., 2004). Thus, a reduction of the grain size improves the phase stability of the tetragonal phase. However, this will also reduce the stress-induced transformation resulting in lower fracture toughness (Swain, 1986; Cottom and Mayo, 1996). The grain size in a zirconia material depends on both raw material and manufacturing process (Scott, 1975; Chevalier et al., 2004). The finer the powders and the lower the sintering temperature, the smaller the grain size becomes (Lawson, 1995). However, when sintering temperature is too low, zirconia is not densified sufficiently (Munoz-Saldana et al., 2003). Therefore, the raw materials and the sintering process used should be selected in a suitable way to avoid grain coarsening.

Stabilizer

The susceptibility of zirconia to LTD is influenced by the concentration of stabilizer. In the case of yttria-stabilized zirconia, the susceptibility decreases with the increase of yttria (Masaki, 1986; Chevalier et al., 2009). However, the increased phase stability also restricts the stress-induced transformation decreasing fracture toughness and strength (Lange, 1982; Kondoh et al., 2004; Chevalier et al., 2009). Thus, biomedical grade zirconia, especially used in the field of orthopedics, is stabilized with 3 mol.% yttria (≈ 5 wt.%) where sufficient resistance to LTD is obtained while maintaining the high mechanical properties (Chevalier et al., 2009). Still, 3Y-TZP is susceptible to LTD when density and grain size are not controlled properly. In this context, ceria (CeO_2) has attracted an interest because ceria-stabilized zirconia possesses much higher resistance to LTD than 3Y-TZP (Chevalier et al., 2009). Since Ce^{4+} is a tetravalent cation, and stabilizes zirconia by relieving oxygen crowding through dilatation of the cation network, doping with Ce^{4+} does not generate oxygen vacancies that will destabilize tetragonal phases when filled with OH^- and/or O^{2-} in the process of LTD. Recently, an improved material based on ceria-stabilized zirconia (ceria-stabilized tetragonal zirconia polycrystals

/alumina nanocomposites; Ce-TZP/Al_2O_3) that possess compatible strength and higher fracture toughness compared to 3Y-TZP has been introduced in the field of dentistry (Miyazaki et al., 2013). Another stabilizer used for dental application is magnesia (MgO). Magnesia-stabilized zirconia consists of tetragonal precipitates in a cubic matrix, which is so-called partially stabilized zirconia (PSZ). Since water molecule diffusion is slow in the cubic matrix, the tetragonal precipitates experience less contact with water molecules. Thus, the progression rate of LTD is also slow (Chevalier et al., 2009). However, the application of magnesia-stabilized zirconia as a dental material is limited because of the lower strength and the need of higher sintering temperature (Denry and Kelly, 2008).

1.1.3 Biological property

Biomaterials including zirconia should not be responsible for inflammatory, allergic, mutagenic and carcinogenic reactions. The first attempt to use zirconia as a biomaterial was made in 1969 in the field of orthopedics (Piconi and Maccauro, 1999). Since then, the biocompatibility of zirconia has been studied with both *in vitro* and *in vivo* tests.

In vitro biocompatibility test

In vitro tests using various types of cells indicated that powders and solid samples of zirconia are not cytotoxic (Dion et al., 1994; Torricelli et al., 2001; Lohmann et al., 2002; Bachle et al., 2007). It has also been reported that zirconia does not induce inflammatory cytokine release (TNF-α, IL-1 and IL-6) from monocytes and fibroblast-like cells (Hisbergues et al., 2009). Although some studies showed that zirconia powders induced apoptotic cell death in macrophage, the cytotoxicity of zirconia is less than or equal to those of alumina and titanium (Catelas et al., 1999; Piconi and Maccauro, 1999; Nkamgueu et al., 2000; Hisbergues et al., 2009), suggesting that the cytotoxicity is negligible. Furthermore, it has been demonstrated that zirconia are not mutagenic or carcinogenic (Covacci et al., 1999; Silva et al., 2002).

In vivo biocompatibility test

In vivo tests on biocompatibility of zirconia have been performed with various animal models and various forms of the material (Hisbergues et al., 2009). It has been reported that zirconia is encapsulated with thin fibrous tissue when implanted in soft tissue, such as muscles and subcutaneous, suggesting that foreign body reaction is not severe and the material is biocompatible. (Garvie et al., 1984; Christel et al., 1989; Ichikawa et al., 1992). In addition, zirconia dental implants can establish direct bone implant interface (Akagawa et al., 1993; Akagawa et al., 1998; Kohal et al., 2004; Depprich et al., 2008) as can titanium, which is known as osseointegration firstly reported by Brånemark (1969). Furthermore, the soft tissue integration established around dental zirconia implants/abutments are similar to that around titanium implants/abutments (Kohal et al., 2004; Welander et al., 2008; Tete et al., 2009). A human histologic study also demonstrated that inflammatory infiltrate around zirconia healing caps was smaller than that around titanium healing caps (Degidi et al., 2006). Thus, zirconia is regarded as a bioinert ceramic with a high chemical stability *in vivo* (Yamamuro, 2004), and there is a general agreement on the absence of local or systemic toxic effects after the implantation of zirconia (Piconi and Maccauro, 1999).

Bacterial adhesion

It was indicated that zirconia might accumulate less plaque than titanium based on the studies performed before 2010 (Nakamura et al., 2010). For instance, Scarano et al. (2004) demonstrated that the percentage of the zirconia disk surface covered with bacteria after exposure to the oral environment for 24 h was significantly lower than that of titanium despite that the both disks had similar surface roughness. This finding was supported by Rimondini et al (2002). Since infection is one of the major causes of dental lesions, this property of zirconia restorations was considered beneficial to avoid secondary problems. However, according to recent *in vitro* and *in vivo* studies that were well designed, there seems to be only small or no difference in bacterial adhesion and colonization between zirconia and titanium (Salihoglu et al., 2011; Egawa et al., 2013; Hahnel et al., 2014; Nascimento et al., 2014). There

also seems to be only little difference between zirconia and other dental ceramics, such as alumina, porcelain and glass ceramics (Rosentritt et al., 2009; Bremer et al., 2011; Yamane et al., 2013). Although additional benefits may not be expected in terms of plaque accumulation, zirconia can be applied to dental restorations as can other dental ceramic materials.

1.2 Dental application of zirconia

1.2.1 Fabrication of zirconia dental prostheses

Of zirconia-containing ceramics, Y-TZP is the most widely used in dentistry though other types are also available; Mg-PSZ (*e.g.* Denzir-M, Dentronic AB, Sweden), Ce-TZP/Al_2O_3 (*e.g.* NanoZir, Panasonic, Japan) and zirconia-toughened alumina (*e.g.* In-Ceram Zirconia, VITA Zahnfabrik, Germany) (Denry and Kelly, 2008; Anusavice, 2013b). Y-TZP has been used for orthodontic brackets, endodontic posts, implant fixtures, implant abutments, crowns and fixed dental prostheses (FDP) (Springate and Winchester, 1991; Nothdurft and Pospiech, 2006; Manicone et al., 2007; Wenz et al., 2008; Nakamura et al., 2010). Custom-made Y-TZP prostheses, such as implant abutments, crowns and FDPs, can be fabricated using dental CAD/CAM system in which machining of Y-TZP block is performed according to digital data created by a computer software (Beuer et al., 2008; Miyazaki et al., 2009; Li et al., 2014). Currently, two different machining processes are available; 1) hard machining of fully sintered blocks and 2) soft machining of pre-sintered blocks followed by final sintering (Denry and Kelly, 2008). The blocks used in hard machining are fully sintered at 1400-1500°C followed by HIP. The advantage of hard machining is that HIPed Y-TZP with higher density can be used, and the prostheses do not show dimensional change throughout the process (*i.e.* no shrinkage) because sintering has already been performed. However, it has been demonstrated that HIP cannot close subsurface flaws generated during processing resulting in no improvement of strength (Scherrer et al., 2013). Thus, it is indicated that HIPed and non-HIPed material are equivalent from a clinical point of view (Vult von Steyern, 2013). In addition, the hard machining takes longer milling time, and causes higher wear of cutting

tools than soft machining because of the hardness of the blocks. Thus, hard machining is not widely used but there are several systems adopting hard machining (*e.g.* Denzir, Cadesthetics AB, Sweden; KaVo Everest BIO ZH-Blank, KaVo Dental, Germany). The blocks for the soft machining are usually compacted by CIP followed by pre-sintering at around 900°C to obtain adequate hardness for handling as well as to retain sufficient machinability. Since final sintering at 1350-1550°C is performed after machining process, enlarged restoration is milled to compensate the shrinkage of 20-25%. The development of CAD/CAM technology enables to precisely compensate the shrinkage and to fabricate restorations with clinically acceptable fit (Bindl and Mormann, 2007; Att et al., 2009; Biscaro et al., 2013). Examples of systems adopting soft machining are Lava Zirconia (3M/ESPE, USA), Cercon (Dentsply, USA), Procera Zirconia (NobelBiocare, Sweden), and IPS e.max ZirCAD (Ivoclar/Vivadent, Schaan, Liechtenstein).

1.2.2 Implant abutments

Titanium has a dominant position as an abutment material as well as a fixture material in implant therapy (Lindhe and Berglundh, 1998; Linkevicius and Apse, 2008). Today, however, requirements for high aesthetic treatments are very common. In this context, zirconia has been considered as an alternative material for implant abutments. Several *in vitro* studies showed that zirconia abutments could be applicable at least in the anterior region, where the physiological maximal biting forces are 300 N (Yildirim et al., 2003; Butz et al., 2005; Att et al., 2006b; a; Gehrke et al., 2006). Animal studies and a human histologic study suggest that soft tissue integration is formed around zirconia as well as titanium, and as such, zirconia is applicable for dental implant abutment material (Kohal et al., 2004; Degidi et al., 2006; Welander et al., 2008). Systematic reviews revealed that zirconia abutments applied for both anterior and posterior region could function without fracture, at least in mid-term (3-5 years) (Nakamura et al., 2010; Zembic et al., 2014a). In addition, Zembic et al. (Zembic et al., 2014b) has recently reported that none of the zirconia abutments supporting single restorations were fractured after 11 years of use. However, another recent clinical study reported that 2 out of 12 zirconia

abutments fractured when tightening, suggesting the necessity of careful handling procedures (Carrillo de Albornoz et al., 2014). Furthermore, it should be noted that there are only limited numbers of clinical studies (Nakamura et al., 2010; Zembic et al., 2014a). Due to the risk of fracture and the limited number of well-performed scientific studies, the indication of zirconia abutments may be restricted to single-implant supported restoration in the aesthetic zone. Controlled clinical trials with long-term follow-up periods are needed to expand the indications of zirconia abutments in the future.

1.2.3 Zirconia-based prostheses

Laboratory studies suggest that zirconia-based crowns and FDPs are applicable in the molar regions in terms of fracture resistance. Sundh and Sjögren (2004) demonstrated that zirconia-based crowns with cores that were designed to be anatomic shape showed higher fracture resistance than those with cores with a uniform thickness of 0.5 mm. Still, even the crowns with a 0.5 mm core showed a mean fracture load of 2200 N, which is higher than maximal bite force in the molar regions (Waltimo and Kononen, 1994; Waltimo et al., 1994). High fracture resistance of zirconia-based crowns have also been reported by other researchers (Akesson et al., 2009; Beuer et al., 2009). Concerning zirconia-based FDPs, it is suggested that 3- and 4-unit zirconia-based FDPs possess load-bearing capacity to be applied in the molar regions (Tinschert et al., 2001; Kohorst et al., 2007). However, the increase in the number of pontics seems to decrease the load bearing capacity (Mahmood et al., 2013). Thus, it may be necessary to augment the load bearing capacity by increasing the diameter of the connector, which has been reported to influence the fracture resistance more than the core thickness (Ambre et al., 2013).

Clinical performance of zirconia-based crowns and FDPs has been studied. According to the latest systematic reviews (Larsson and Wennerberg, 2014; Le et al., 2015), cumulative 5-year survival rates for tooth-supported zirconia-based crowns and FDPs were 95.9% and 93.5%, respectively, which are comparable to metal-ceramic restorations. Furthermore, slightly higher cumulative 5-year survival rates for implant-supported zirconia-based crowns

(97.1%) and FDPs (100%) were reported. Bulk fracture of the crowns appears to be quite uncommon. In total, only three catastrophic failures of the crowns were reported in the reviewed studies. In the case of the FDPs, zirconia framework fracture occurred but was not so frequent. However, the risk for fracture of the veneering porcelain (*e.g.* chipping) seems to higher for zirconia-based prosthesis compared to metal-ceramic restorations (Sailer et al., 2007a; Larsson et al., 2010; Vigolo and Mutinelli, 2012; Larsson and Vult Von Steyern, 2013).

1.2.4 Monolithic zirconia

Due to the normal color of Y-TZP (*i.e.* bright white), its application in prosthetic dentistry was limited to implant abutments or frameworks of prostheses until recently. The development of translucent tooth-colored zirconia, however, enables the fabrication of monolithic zirconia restorations without veneering material, also referred to as full-contour zirconia restorations (Beuer et al., 2012). Thus, the demand for tooth-colored zirconia ceramics is increasing. Tooth-like color can be given to zirconia by adding coloring pigments, such as metal oxides (Cales, 1998; Shah et al., 2008). There are mainly two techniques to add these coloring pigments to zirconia used in dentistry. One is referred to as infiltration technique in which a zirconia prosthesis milled from a non-colored and pre-sintered zirconia block is immersed in a coloring liquid or a coloring liquid is applied to the material using a brush before sintering (Hjerppe et al., 2008; Shah et al., 2008). The other is a powder mixing method in which zirconia powder is mixed with coloring pigments before zirconia block formation (Cales, 1998; Kaya, 2013).

The drawback of fractures occurring in the veneering porcelain of zirconia-based restorations, as mentioned earlier, can be overcome through the use of monolithic zirconia crowns. Other advantages of monolithic zirconia crowns may be limited amounts of defects due to fabrication with CAD/CAM technique using a material with high homogeneity. The fabrication with CAD/CAM technique may also reduce production time and cost. By contrast, there is a concern about the wear of the opposing teeth by monolithic zirconia

crowns because zirconia is harder than enamel and other dental ceramics. However, recent studies demonstrated that polished zirconia showed lower wear rate on enamel and steatite, which is often used as a substitute for human enamel, than other dental materials, such as metal alloy, veneering porcelain and lithium disilicate (Preis et al., 2011; Miyazaki et al., 2013; Stawarczyk et al., 2013). In addition, Stober et al. (2014) demonstrated that the antagonistic enamel wear by monolithic zirconia crowns after 6 months of clinical use would be acceptable.

Since zirconia has high strength, it is expected that monolithic zirconia molar crowns may withstand bite force even if the crown thickness is thinner than conventional all-ceramic crowns. This could be beneficial because tooth substances can be more preserved. When a tooth is restored with a conventional all-ceramic crown, irrespective of the materials used, it is recommended that axial and occlusal reduction of the preparation should be 1.5 and 2.0 mm, respectively (Milleding, 2012). The reason is to obtain sufficient strength of the reconstruction and space for veneering. It has been demonstrated that monolithic lithium disilicate crowns for posterior teeth with reduced occlusal thickness showed more fatigue failures than those with a thickness of ≥ 1.5 mm (Dhima et al., 2014). Since zirconia has higher flexural strength (> 1000 MPa) (Piconi and Maccauro, 1999) than lithium disilicate (about 400 MPa) (Holand et al., 2000; Kang et al., 2013), the fracture resistance of monolithic zirconia molar crowns may be acceptable even at a reduced thickness. Still, there are few available data regarding the matter.

Even if monolithic zirconia crowns seem to have sufficient fracture resistance, the importance of the cement cannot be underestimated. It has been demonstrated that the supporting materials, such as abutment materials and cement, will influence the fracture resistance of all-ceramic crowns (Mormann et al., 1998; Yucel et al., 2012). That is, if the abutment material shows increased elastic properties and/or low compressive strength, the fracture resistance of all-ceramic crowns becomes lower. As for type of cement used, it is suggested that the compressive strength is of importance since it will support the reconstruction. Indeed, Bindl et al. (2006) demonstrated that the

fracture resistance of monolithic all-ceramic crowns made of feldspar ceramic, leucite glass-ceramic and lithium disilicate glass-ceramic increased by using a polymer resin-based cement with a compressive strength of 320 MPa compared to zinc phosphate cement (121 MPa). In addition to the compressive strength, it is suggested that the crown-cement interface plays an important role in the fracture resistance of all-ceramic crowns (Scherrer et al., 1994; Behr et al., 2003). The weaker the bond the lower the fracture resistance becomes. It is, however, difficult to treat zirconia for an optimal micromechanical adhesion to polymer resin-based cement because of the structure of this oxide ceramic (Papia et al., 2014). Even though adhesion between zirconia and polymer resin-based cement is not well established, the high compressive strength of the polymer resin-based cement may be of importance to give the crown-cement-tooth complex the ability to withstand forces in the molar region. There is little information about the influence of compressive strength of the cement on the fracture resistance of monolithic zirconia crowns.

It is known that the durability of all-ceramic restorations is influenced by repeated exposure to cycles of stress during normal mastication (Anusavice, 2013a). Thus, laboratory fatigue tests with mechanical cycling are often performed to predict the durability (Attia and Kern, 2004). Furthermore, in the case of monolithic zirconia crowns, LTD may affect the durability. However, the influence of fatigue and LTD on monolithic zirconia restorations has not been studied yet. When the zirconia core is veneered with dental porcelain (*i.e.* zirconia-based restorations), zirconia is not directly exposed to the oral environment or to saliva. Thus, the influence of LTD could be limited. However, monolithic zirconia crowns will be directly exposed to saliva. Therefore, it is reasonable to assume that LTD may occur. In addition, cyclic loading and LTD together may reduce the fracture resistance of monolithic zirconia crowns though there are few available data regarding this issue.

1.3 Challenges

Monolithic zirconia restorations have been developed as a new alternative, and the demand for monolithic zirconia restorations has rapidly increased (Christensen, 2011). However, there seems to be a lack of scientific information. Currently, only a few clinical reports with a small sample size and short-term outcome are available (Batson et al., 2014; Stober et al., 2014). Even the information from laboratory studies seems to be limited. In order to evaluate the advantages and disadvantages of monolithic zirconia restorations, more laboratory studies should be conducted to obtain more scientific knowledge before clinical studies are performed. In particular, the influence of LTD in relation to some fabrication processes of monolithic zirconia restorations, such as sintering, additional firing process and coloring procedure, on the mechanical and microstructural properties of zirconia should be studied in detail. Furthermore, there is little information about the appropriate tooth preparation and choice of cement for monolithic zirconia crowns, which may affect fracture resistance of the crowns. Based on the background, this thesis was designed to provide scientific evidence for the use of monolithic zirconia restorations.

2 AIM

The overall aim of this thesis was to analyze factors that affect 1) mechanical and microstructural properties of 3Y-TZP, and 2) fracture resistance of monolithic zirconia crowns.

The specific aims of the studies included in this thesis were:

Study I: To study the influence of grain size on strength when 3Y-TZP with different grain sizes were exposed to an additional heat treatment which mimicking the veneering process.

Study II: To evaluate the effects of LTD induced by autoclaving on mechanical and microstructural properties of tooth-colored 3Y-TZP shaded by infiltration technique and powder mixing method.

Study III: To analyze the relationship between fracture load of monolithic zirconia crowns and axial/occlusal thickness.

To evaluate the fracture resistance of monolithic zirconia crowns with reduced thickness in comparison with that of monolithic lithium disilicate crowns with regular thickness.

Study IV: To investigate the effect of the cements on fracture resistance of monolithic zirconia crowns in relation to their compressive strength.

Study V: To analyze the kinetics of LTD in zirconia used for monolithic crowns.

To evaluate the influence of LTD and cyclic loading on the fracture resistance of monolithic zirconia crowns.

3 MATERIALS AND METHODS

The series of laboratory studies was conducted to evaluate mechanical and microstructural properties of zirconia in relation to dental applications, especially monolithic crowns. The test methods used in Study I-V are summarized in Table 2.

Table 2. Summary of the test methods

	I	II	III	IV	V
Treatment					
Heat treatment	○				
Autoclaving-induced LTD	○	○			○
Mechanical cycling					○
Mechanical test					
Biaxial flexural test	○	○			
Three-point bending test			○		
Compression test			○	○	
Vickers hardness test		○			
Crown fracture testing (load-to-failure test)			○	○	○
Microstructural analysis					
SEM[*1]	○	○		○	○
XRD[*2]		○			○
Other analyses					
XRF[*3]		○			
Color analysis		○			
Surface roughness measurement		○			
Micro-CT[*4]			○	○	

[*1] scanning electron microscopy, [*2] X-ray diffraction analysis, [*3] X-ray fluorescence analysis and [*4] X-ray micro computed tomography

3.1 Sample preparation

3.1.1 Specimens for material testing (Study I-V)

Disc-shaped specimens of zirconia were prepared for biaxial flexural strength test according to ISO 6872:2008 “Dentistry – Ceramic materials” (Study I and II). Eighty (n = 10 per group) and 162 (n = 18 per group) specimens were used in Study I and II, respectively. Green bodies of 3Y-TZP were prepared by cold

isostatic pressing at 200 MPa followed by pre-sintering at 900°C for 2 h. Commercial powder (TZ-3YSB-E, Tosoh, Tokyo, Japan) was used for the non-colored specimens (NC, Study I and II) and the tooth-colored specimens shaded by infiltration technique (IF, Study II). Another type of tooth-colored specimens shaded by powder mixing method (PM, Study II) was prepared from commercial pre-colored and ready-mixed powder (TZ-Yellow-SBE, Tosoh) that is designed to contain Fe_2O_3 as a coloring pigment. The green bodies were cut to be disc-shaped specimens. To shade the specimens in IF group, the non-colored discs were dipped in commercial coloring liquid with a shade of A3.5 (Lava Plus Zirconia Dyeing Liquid, 3M/ESPE, St. Paul, MN) for 2 min according to the manufacturer's instructions. Subsequently, the specimens used in Study I were sintered at 1425, 1500 or 1575°C while those used in Study II were sintered at 1500°C. One side of the disc-shaped specimen was thoroughly polished using 1-μm diamond suspensions whereas the other side was used as sintered. The density of the specimens were determined by Archimedes method.

Bar-shaped specimens were prepared from composite resin blocks (Lava Ultimate, 3M/ESPE), which were used as a die material, for evaluation of mechanical property. The composite resin block were cut to be 22.3 × 2.0 × 2.0 mm for three-point bending test (n = 5) and 15 × 15 × 15 mm for measurement of Poisson's ratio (n = 6). The former specimens were polished using #1000 silicon carbide paper.

Cylindrical-shaped specimens of the cements tested were prepared for compressive strength test (Study IV). Zinc phosphate cement (ZPC; De Trey Zinc, Dentsply, York, PA, USA), glass-ionomer cement (GIC; Fuji I, GC, Tokyo, Japan), self-adhesive polymer resin-based cement (SRC; RelyX Unicem2, 3M/ESPE) and polymer resin-based cement (RC; Panavia F2.0, Kuraray Noritake Dental, Tokyo, Japan) were used. RC was tested in both dual cure mode (RC-D) and pure chemical cure mode (RC-C). When light curing was needed throughout the study, a light curing unit (Bluephase, Ivoclar/Vivadent) was used at an irradiance of 1370 ± 50 mW/cm^2 controlled using Bluephase meter (Ivoclar/Vivadent) at each occasion. Ten specimens

from each cement were produced in a mold of polytetra-fluoroethene (PTFE) with the inner dimension of 4 mm in diameter and a height of 6 mm. The cements were mixed according to the manufacturers' instructions and was introduced into the PTFE mold placed on a glass-plate covered with a polyethylene film. The upper surface was treated as the lower end by coverage using the same film with glass plate on top and the cement was left to set. When applicable, the cement was light cured through the glass plate from above for 2 s, after which the plate was removed and continued light curing was performed for 40 s. For RC-D and RC-C, a droplet consisting of a mixture of ED primer A and B (Kuraray Noritake Dental) was added to the cement to get proper chemical cure. After curing, the end surfaces of each specimen were polished using #400 silicon carbide paper to remove excess cement and to ensure a surface perpendicular to the load direction.

Sixty bar-shaped specimens of zirconia were prepared for kinetic analysis of autoclaving-induced LTD (Study V). Specimens with dimensions of 17 × 7 × 1.8 mm were cut from the zirconia blocks (Lava Plus Zirconia, 3M/ESPE) using an Isomet 4000 (Buehler, Lake Bluff, IL, USA). The specimens were sintered at 1450°C for 2 h according to the manufacturer's instructions. After sintering, the dimensions of the specimens were 13.5 × 5.5 × 1.5 mm. One side of the specimens was polished using 1-μm diamond suspensions. The specimens were subjected to autoclaving as mentioned below, and then they were cut in the middle vertically in the direction of the long axis. One piece of the specimens was used for XRD and the other was used for SEM.

3.1.2 Specimens for crown fracture testing (Study III, IV and V)

Abutment tooth model

Plastic tooth models of mandibular right first molar (A5A-500, NISSIN, Kyoto, Japan) were used to prepare different types of abutments. The tooth model was prepared with a chamfer finish line (width: 0.5, 0.7 and 1.0 mm) (Figure 4a). The total occlusal convergence angle was finally finished using a milling machine (F3 ergo, DeguDent GmbH, Hanau-Wolfgang, Germany) to be 10°

(Figure 4a). The prepared tooth models were scanned using a digital scanner (LavaScan ST, 3M/ESPE) made for a dental CAD/CAM system (Lava System, 3M/ESPE). The chamfer width was measured at the central part of mesial, distal, buccal and lingual surfaces using a CAD software (Lava Design 5.50, 3M/ESPE). Preparation and measurement were repeated until the defined chamfer width with an error range of 50 μm or less was obtained. The occlusal surface was prepared to be V-shape to ensure as equal thickness as possible for the occlusal ceramic (Figure 4b). The prepared and non-prepared tooth models were scanned to evaluate the reduction of occlusal surface using the CAD software. The vertical distance was defined as the occlusal reduction, and measurements were performed at 10 different points (Figure 4c). The minimal reduction of occlusal surface was defined to be 0.6, 1.1 and 1.6 mm resulting in a minimal occlusal thickness of the crowns of about 0.5, 1.0 and 1.5 mm including the cement space (70 μm). Nine abutments were prepared and coded as follows; C0.5/O0.5, C0.5/O1.0, C0.5/O1.5, C0.7/O0.5, C0.7/O1.0, C0.7/O1.5, C1.0/O0.5, C1.0/O1.0 and C1.0/O1.5 (Figure 5). The first 2 digits express the chamfer width and the last 2 the minimal occlusal thickness. In addition, an abutment with facetted occlusal shape (chamfer width of 0.5 mm/occlusal reduction of 0.6 mm) was prepared (C0.5/O0.5f, Figure 5). All abutments were scanned and dies were milled from composite resin blocks (Lava Ultimate) using the CAD/CAM system at the 3M Education Center (Tokyo, Japan).

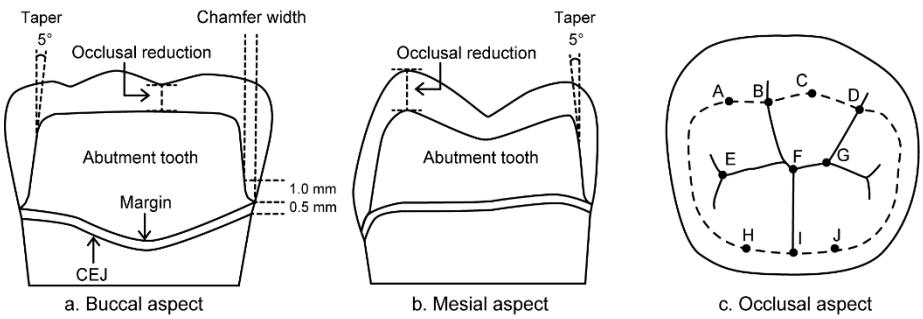

Figure 4. Schematic illustration of the abutment tooth 46 (a, b) and measurement points for occlusal reduction (c). Occlusal reduction was measured as the vertical distance between the prepared and non-prepared tooth models at 10 different points (A-J). The minimal occlusal thickness was obtained at B, F and I. CEJ: cement enamel junction.

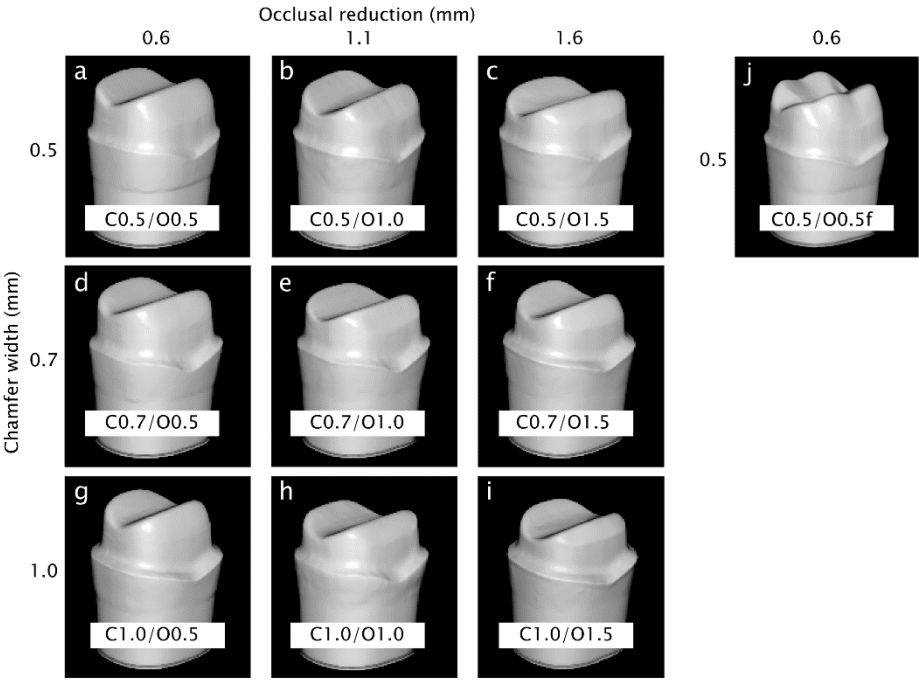

Figure 5. Scanned abutment images of (a) C0.5/O0.5, (b) C0.5/O1.0, (c) C0.5/O1.5, (d) C0.7/O0.5, (e) C0.7/O1.0, (f) C0.7/O1.5, (g) C1.0/O0.5, (h) C1.0/O1.0, (i) C1.0/O1.5 and (j) C0.5/O0.5f.

Crown fabrication

The dies were scanned, and crowns were designed by double scan technique in which additional scanning of the non-prepared tooth model was performed to obtain an identical outer shape for each type of dies. The cement space was fixed at 70 μm for all samples according to the default setting of the CAD/CAM software (Lava Design 5.50 CAD software, 3M/ESPE). Thus, the minimum thickness of the crown at the occlusal surface was expected to be 0.5, 1.0 and 1.5 mm following subtraction of cement space from occlusal reduction. Monolithic zirconia crowns were milled from pre-sintered zirconia blocks (Lava Plus Zirconia, 3M/ESPE). Coloring was performed using zirconia dyeing liquid (A2, 3M/ESPE) followed by final sintering. The fabrication process was performed at the Lava Milling Center (Dental Digital Operation, Osaka, Japan). After sintering, margin adjustment was performed manually using a dental micromotor (Ultimate 500, Nakanishi, Tochigi, Japan) and

grinding point (CeraPro, Edenta, AU/SG, Switzerland). Polishing was done using polishing points (StarGloss, Edenta) and wheel brush together with polishing agent (Zircon-Brite, Dental Ventures of America, Corona, CA, USA). All types of crowns were tested in Study III while only C0.5/O0.5 was used in Study IV and V (n = 6/group in all studies). The groups of tested crowns are displayed in Table 3.

Table 3. The groups of monolithic crowns tested

Code of the group	Chamfer width (mm)	Minimal occlusal thickness (mm)
0505	0.5	0.5
0510	0.5	1.0
0515	0.5	1.5
0705	0.7	0.5
0710	0.7	1.0
0715	0.7	1.5
1005	1.0	0.5
1010	1.0	1.0
1015	1.0	1.5
0505f*	0.5	0.5
1015e.max press	1.0	1.5

*: C0.5/O0.5f was fabricated on the die with the facetted occlusal surface.

Monolithic lithium disilicate crowns (IPS e.max press, Ivoclar/Vivadent) were fabricated on the C1.0/O1.5 die (C1.0/O1.5e.max press) as a control group in Study III (n = 6). A mold of the non-prepared tooth was produced using a silicone impression material (Exafine, GC, Tokyo, Japan). A spacer (Thickness: 70 μm, SureSpacer, GC) and a separator were applied onto the die surfaces. The mold was fit to the die and molten wax was poured into the mold to obtain the identical outer shape of the non-prepared tooth, *i.e.* also identical to the monolithic zirconia crowns. Subsequent investment, pressing and glazing were performed according to the manufacturer's instructions.

Cementation

In Study III and V, the crowns were cemented to the dies using a polymer resin-based cement (Panavia F2.0) with chemical cure mode (RC-C) according to

the manufacturer's instructions. A static load of 20 N was applied for 5 min using a universal testing machine (AI-GS, Shimadzu Kyoto, Japan). Excessive cement was removed immediately after loading and Oxyguard (Kuraray Noritake Dental) was applied around the margin. In Study IV, the crowns were cemented to the dies using ZPC, GIC, SRC, RC-D and RC-C. The cements were prepared and mixed according to the manufacturers' instructions as described above. A static load of 20 N was applied until the cement had set in a universal testing machine (Zwick/Roell, Ulm, Germany). For ZPC, GIC and RC-C, the crowns were subjected to the static load for 15 min. For the crowns cemented with SRC and RC-D, the static load was held for 4 min while the cement was light cured from five different directions for 40 s (total: 200 s).

3.1.3 Heat treatment (Study I)

To evaluate the influence of veneer firing process on the strength of zirconia, the specimens were subjected to additional heat treatment before performing the strength test. Ten disc-shaped specimens sintered at different temperatures were heat-treated five times in a porcelain furnace (Multimat C; Dentsply, Konstanz, Germany) mimicking the standard veneering process (liner firing: 930°C, dentin firing 1: 910°C, dentin firing 2: 900°C, glaze firing: 890°C, and corrections: 850°C). Additional ten specimens sintered at 1500°C were also subjected to the heat treatment followed by autoclaving.

3.1.4 Autoclaving-induced LTD (Study I, II and V)

Accelerated aging test was performed with autoclaving at 134°C under 0.2 MPa, which induces LTD in zirconia (Chevalier, 2006). In Study I, the specimens sintered at 1500°C with or without the heat treatment were subjected to autoclaving for 10 h (n = 10/group). In Study II, the specimens from each group (NC, IF and PM) were subjected to autoclaving for 10 and 100 h (n = 18/group). In Study V, bar-shaped specimens were autoclaved for 10, 20, 30, 40, 50, 100, 150 and 200 h for kinetic analysis on LTD (n = 6/group), and the monolithic zirconia crowns (C0.5/O0.5) were subjected to autoclaving for 10, 50 and 100 h (n = 6/group) before cementation. In addition, to evaluate

the effect of autoclaving followed by mechanical cyclic loading on fracture resistance of the crown, six monolithic zirconia crowns were autoclaved for 100 h before cementation.

3.1.5 Mechanical cycling (Study V)

The monolithic zirconia crowns with or without autoclaving were cemented to the dies (n = 6/group). Subsequently, they were subjected to mechanical cyclic loading using a servo-hydraulic testing machine (FastTrack 8800, Instron, Norwood, MA, USA). A 2-mm-thick urethane rubber sheet (Kokugo, Tokyo, Japan) was interspersed between the indenter and the occlusal surface to avoid contact damage. The load was vertically applied on the occlusal surface of the crown-die sample via the indenter with a diameter of 10 mm between 50 and 300 N for 240,000 cycles at a frequency of 10 Hz in distilled water. After cyclic loading, the crowns were examined using a stereomicroscope (A60 S, Leica Microsystems GmbH, Wetzlar, Germany) to inspect whether the crowns fractured during cyclic loading.

3.2 Material testing

3.2.1 Biaxial flexural strength test (Study I and II)

Biaxial flexural strength was measured in a piston-on-three-ball test according to ISO 6872:2008 "Dentistry – Ceramic materials". In Study I, the test was performed using Lloyd LRX (Lloyd Instruments, Fareham, UK) while the test in Study II was performed using AG-IS (Shimadzu). The disc-shaped specimen was positioned centrally on three steel balls with diameter of 3 mm, positioned 120° apart on a support circle. The polished surface of the specimen was positioned in the tensile stress zone while the unpolished surface was loaded with a flat punch with a diameter of 1.4 mm, at a cross-head speed of 1 mm/min until fracture. The maximum load (N) was recorded and the biaxial flexural strength (MPa) was calculated according the following equations:

$$\sigma = -0.2387P(X - Y)/b^2$$

where σ is biaxial flexural strength (MPa), P is maximum load (N), L is length of support span (mm), and b is specimen thickness (mm). X and Y are determined as follows:

$$X = (1 + v)ln(r_2/r_3)^2 + [(1 - v)/2](r_2/r_3)^2$$

$$Y = (1 + v)[1 + ln(r_1/r_3)^2] + (1 - v)(r_1/r_3)^2$$

in which v is Poisson's ration (0.25), r_1 is the radius of support circle (mm), r_2 is the radius of loaded area (mm) and r_3 is the radius of specimen (mm).

3.2.2 Three-point bending test (Study III)

Flexural strength and modulus of elasticity of die material (Lava Ultimate) was measured in a three-point bending test according to ISO 4049:2009 "Dentistry – Polymer based restorative materials". The specimens were loaded at a crosshead speed of 0.5 mm/min and with a 15-mm support span in a universal testing machine (AG-IS). Flexural strength and modulus of elasticity were calculated using the following equations:

$$\sigma = 3FL/2bh^2$$

where σ is flexural strength (MPa), F is maximum load (N), L is length of support span (mm), b is specimen width (mm), and h is specimen thickness (mm).

$$E = [F_1/d] \times [L^3/4bh^3]$$

where E is modulus of elasticity (MPa), F_1/d (N/mm) is the slope of the linear portion of load-deflection line, L is the length of support span (mm), b is specimen width (mm), and h is specimen thickness (mm).

3.2.3 Compression test (Study III and IV)

Poisson's ratio of die material (Lava Ultimate) was evaluated using a universal testing machine with video extensiometer (Zwick/Roell). The specimens were loaded at a crosshead speed of 0.5 mm/min. Poisson's ratio was calculated as follows:

$$v = \varepsilon_1 / \varepsilon_2$$

where v is Poisson's ratio, ε_1 is horizontal deformation ratio (%) and ε_2 is vertical deformation ratio (%).

Compressive strength of the cements was tested according to ISO 9917:2004 "Dentistry – Water-based cements". The specimens were loaded at a crosshead speed of 0.75 mm/min using a universal testing machine (Zwick/Roell). The compressive strength was calculated according to the following equation:

$$Fc = P/\pi(d/2)^2$$

where Fc is compressive strength (MPa), P is maximum load (N), π is circle ratio and d is the diameter of the specimen.

3.2.4 Vickers hardness test (Study II)

The specimens for hardness measurement were randomly selected from those used in the biaxial flexural strength test. Nine specimens from each group were subjected to the micro-Vickers hardness test. Indentation was produced on the polished surface under a load of 9.8 N for 15 s in a digital micro-hardness tester (MVK-H2, Mitutoyo/Akashi, Kawasaki, Japan).

3.2.5 SEM analysis (Study I, II and V)

The average grain size were determined by linear intercept method using a scanning electron microscope (SEM, EM-3000, Topcon, Tokyo, Japan) according to ASTM E112-13 "Standard test methods for determining average grain size". In Study I and II, six specimens for SEM analysis were randomly selected from those used in the biaxial flexural strength test. In Study V, six specimens were prepared and used for the grain size analysis. The specimens were thermally etched at a temperature 50°C below the sintering temperature for 30 min. The polished surface was coated with a gold layer and imaged.

The penetration depth of the monoclinic phase as a result of LTD was measured in a cross section of the specimens. In Study II, fifteen specimens were randomly selected from those used in the biaxial flexural test were used while specimens prepared for the kinetic analysis of LTD were used (n = 6/group). The specimens were embedded in an epoxy resin and the cross-sectional surface was polished. The specimens were then coated with a 15-nm

gold layer and imaged. Three micrographs were taken for each specimen at randomly selected areas. The deepest distance of the transformed zone in each image was measured using the image processing program (ImageJ, The Research Services Branch of the NIH). The mean value of penetration depth of the monoclinic phase was regarded as the representative value of the specimen.

3.2.6 XRD analysis (Study II and V)

Crystalline phase on the surface of the specimens was analyzed with XRD. In Study II, six specimens were randomly selected for the analysis from those used in the biaxial flexural test. In Study V, specimens subjected to autoclaving with different treatment time were analyzed (n = 6/group). XRD data were collected with a θ-2θ diffractometer (X'Pert MPD, PANalytical) using Cu-Kα radiation. Diffractograms were obtained from 27° to 33°, at scan speed of 0.3°/min and a step size of 0.02°. The monoclinic phase fraction, *Xm*, was calculated using the Garvie and Nicholson method (1972),

$$Xm = [Im(-111) + Im(111)]/[Im(-111) + Im(111) + It(101)]$$

where *It* and *Im* represent the integrated intensity of the tetragonal (101), and monoclinic (111) and (−111) peaks.

The integrated intensity of each peak was calculated using HighScore Plus software (PANalytical). The monoclinic phase fraction is expressed as the percentage of tetragonal phase that was transformed to the monoclinic phase.

3.2.7 XRF analysis (Study II)

In Study II, the chemical composition of nine specimens randomly selected from each color group (before autoclaving) was analyzed with XRF spectroscopy (Axios PW440/40, Panalytical, Tokyo, Japan). The quantitative analysis was conducted using UniQuant5 software (Panalytical).

3.2.8 Color analysis (Study II)

The specimens with or without autoclaving were subjected to color analysis performed using a portable colorimeter (ShadeEye NCC, Shofu, Kyoto, Japan) and the CIE (Commission Internationale de I'Eclairaga) $L^*a^*b^*$ colorimetric system in Study II. A color is expressed in the CIE system with three parameters, L^*, a^* and b^*, which represent lightness (0 to 100), green-red value (-60 to 60) and blue-yellow value (-60 to 60), respectively. The analysis was performed in triplicate for each specimen, and the mean value was regarded as the representative value of the specimen. Color difference (ΔE) between the specimens with or without 100 h of autoclaving was calculated as follows:

$$\Delta E = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$$

where ΔL^*, Δa^*, and Δb^* represent the differences in L^*, a^*, and b^* between the specimens with or without 100 h of autoclaving.

3.2.9 Surface roughness measurement (Study II)

Surface roughness of randomly selected six specimens per group was measured using a surface profilometer (Surfcom 130A, Tokyo Seimitsu, Tokyo, Japan). The stylus with a tip diameter of 2.5 μm moved across the polished surface for a distance of 2.5 mm, and mean arithmetic roughness (Ra) was recorded. Cutoff value and resolution of recorded data were 0.08 mm and 0.001 μm, respectively.

3.3 Crown fracture testing

3.3.1 Micro-CT analysis (Study III and IV)

The evaluation of crown thickness was performed non-destructively with micro-CT before cementation. In Study III, all of the monolithic zirconia crowns and monolithic lithium disilicate crowns were subjected to micro-CT analysis (ScanXmate-D225RSS270, Comscantecno, Kanagawa, Japan). The conditions for analysis were as follows: voltage; 200 kV (zirconia) vs. 90 kV (lithium disilicate), current; 200 μA (zirconia) vs. 220 μA (lithium disilicate),

resolution (voxel size) 14.9 µm. ImageJ (The Research Services Branch of the NIH), an image processing program, was used for analysis. The thickness was measured at the same points with those used for the evaluation of the abutments as shown in Figure 4c.

In Study IV, three crowns and dies were randomly selected, and the crowns seated onto the dies without cement were subjected to the analysis under the same measuring conditions. Cement space as well as crown thickness was evaluated based on the micro-tomographs. The vertical distance between the inner surface of crowns and the occlusal surface of the die was regarded as the cement space. The cement space was measured at the same points with those used for the evaluation of the abutments as shown in Figure 4c.

3.3.2 Load-to-failure test (Study III, IV and V)

The test was performed in a universal testing machine (Figure 6, AI-GS for Study III and V, and Zwick/Roell for Study IV) with a 10 kN load cell. A custom-made spherical indenter (Ø = 10 mm) of type 304-stainless steel was placed in the central fossa of the occlusal surface. A urethane rubber sheet (Kokugo, Tokyo, Japan) (Thickness = 2 mm, Shore A Hardness = 90) was interspersed between the indenter and the occlusal surface to avoid contact damage (Oilo et al., 2013). A preload of 20 N was applied vertically to the crown followed by compressive loading at a crosshead speed of 0.5 mm/min until fracture.

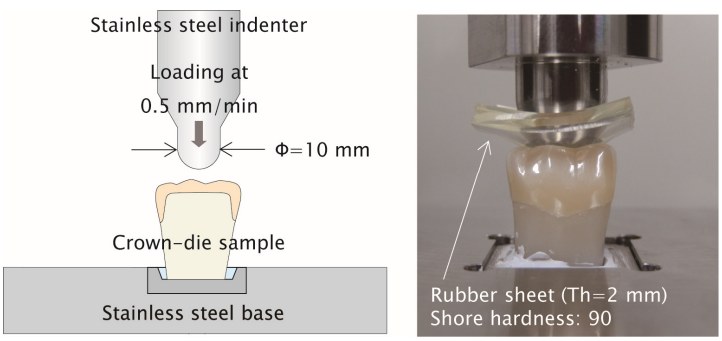

Figure 6. Illustration of load-to-failure test

In Study IV, fracture analysis was performed with SEM (Sigma, Carl Zeiss Microscopy, Jena, Germany) on two randomly selected samples from each group after the load-to-failure test. In Study V, fragments of the crowns in each group were selected for SEM analysis (EM-3000), and the monoclinic phase in the cross-section was observed as previously described.

3.3.3 Statistical analysis

Statistical analyses were performed using JMP Pro 11.0.0 software (SAS Institute, Cary NC, USA). Differences within and between the groups were analyzed with analysis of variance (ANOVA) or two-way ANOVA followed by Tukey-Kramer HSD multiple comparison test. The influence of the axial and occlusal thickness on the fracture resistance of monolithic zirconia crowns was assessed by multiple regression analysis (Study III). The representative thickness of the axial wall and occlusal surface for each crown, calculated as an average of 4 measuring points and as an average of minimal thickness at the measuring points of B, F and I (Figure 4c), respectively, were used for the multiple regression analysis. In any cases, the level of significance was set at 5%. In addition, the variability of the biaxial flexural strength (Study I and II) was analyzed by Weibull statistics using the following equations;

$$Pf(\sigma) = 1\text{-}exp[-(\sigma/\sigma_0)m]$$

where $Pf(\sigma)$ is probability of failure, σ is fracture strength, σ_0 is characteristic strength ($P1(\sigma)$ = 63.2%) that is a representative strength value in Weibull distribution, and m is Weibull modulus. The failure probability was calculated using the following equation;

$$Pf = (i - 0.5)/n,$$

where i is ranking and n is number of specimens.

Accordingly, following equation was derived;

$$lnln[1/(1 - Pf)] = mln\sigma\text{-}mln\sigma_0,$$

Thus, plotting $lnln[1/(1 - Pf)]$ against $ln\sigma$ provides a slope (m: Weibull modulus) and an intercept (σ_0: characteristic strength).

4 RESULTS

4.1 Material testing

4.1.1 Chemical and physical properties

Density (Study I, II and V)

The density of the 3Y-TZP specimens sintered at 1425, 1500 and 1575°C (Study I) reached 6.06, 6.07 and 6.07 g/cm^3, respectively. The density for NC, IF and PM (Study II) were 6.07, 6.08 and 6.08 g/cm^3, respectively. The specimens milled from commercial blocks (Lava Plus Zirconia) and used for kinetic analysis (Study V) also showed a density of 6.08 g/cm^3.

Chemical composition (Study II)

The chemical composition of each colored zirconia as well as of the non-colored zirconia analyzed by XRF is shown in Table 4. IF contained Er_2O_3 and Fe_2O_3, and PM contained Fe_2O_3 while such metal oxides were not detected in NC.

Table 4. Chemical composition of colored and non-colored 3Y-TZP

	wt.%					
	NC		**IF**		**PM**	
	Ave	SD	Ave	SD	Ave	SD
ZrO_2	92.99	0.28	92.68	0.18	92.98	0.19
Y_2O_3	4.99	0.02	4.93	0.02	4.97	0.03
HfO_2	1.62	0.04	1.61	0.02	1.63	0.03
Al_2O_3	0.07	0.03	0.06	0.03	0.07	0.03
Er_2O_3	N.D	-	0.46	0.10	N.D	-
Fe_2O_3	N.D	-	0.07	0.01	0.14	0.02
Others	0.33		0.19		0.21	

N.D: not detected

Color (Study II)

Some parameters were slightly affected by 100 h of autoclaving, depending on the group. The ΔE (after 100 h of autoclaving) for NC, IF and PM was 1.40, 0.78 and 1.35, respectively.

Surface roughness (Study II)

The mean *Ra* of each group was ≤ 0.015 μm regardless of autoclaving or not. Two-way ANOVA showed that the coloring techniques and the autoclaving did not significantly affect the surface roughness.

Biaxial flexural strength (Study I and II)

In Study I, biaxial flexural strength of 3Y-TZP showed tendency to decrease with the increase of sintering temperature though there was no statistical difference between the groups (Figure 7). After the heat treatment simulating the veneering process, the biaxial strength obtained was almost the same as that obtained for the corresponding specimens not exposed to the thermal cycles (Figure 7). The mean value of the biaxial flexural strength of the specimens sintered at 1500°C was 1152 MPa. When subjected to the heat treatment, 10 h of autoclaving and the combination of the two, the mean value of the strength became 1163, 1139 and 1087 MPa, respectively.

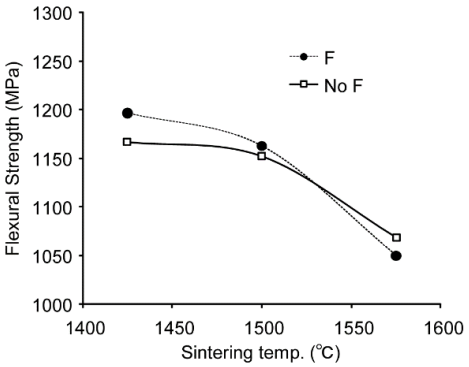

Figure 7. Influence of sintering temperature and heat treatment on biaxial flexural strength of 3Y-TZP. F: five thermal cycles, No F: no additional heat treatment.

Biaxial flexural strength, characteristic strength and Weibull modulus of the non-colored and colored 3Y-TZP (NC, IF and PM tested in Study II) are summarized in Table 5. Two-way ANOVA showed that the autoclaving significantly affected the biaxial flexural strength but the coloring techniques did not. In NC and PM, the mean value of biaxial flexural strength decreased with autoclaving time. In the case of IF, the mean value of the strength after 10 h of autoclaving increased while after 100 h of autoclaving the increased value of the strength decreased becoming almost the same with that without autoclaving. This tendency was also confirmed with the characteristic strength calculated by Weibull statistics (Table 5). When the strengths of the specimens were compared between the groups, IF showed significantly higher value than NC after 10 h of autoclaving ($p < 0.05$), and IF and PM showed significantly higher value than NC after 100 h of autoclaving ($p < 001$). Weibull plot for each group is shown in Figure 8. Small variations in Weibull modulus (*m*) was recorded when the 0 h and 10 h of autoclaving were compared, while *m* increased to above 30 for all materials exposed to 100 h of autoclaving (Table 5).

Table 5. Biaxial flexural strength and Weibull analytical results

	NC			IF			PM		
Autoclaving time	**0 h**	**10 h**	**100 h**	**0 h**	**10 h**	**100 h**	**0 h**	**10 h**	**100 h**
Mean value of strength (MPa)	1121	1030	1012	1081	1153	1077	1150	1113	1058
Characteristic strength (MPa)	1195	1094	1030	1139	1198	1095	1220	1171	1074
Weibull modulus	10.8	9.1	30.6	9.3	13.4	33.1	8.3	9.6	35.2

Characteristic strength: the strength that corresponds to a failure probability of 63.2% calculated in Weibull statistics.

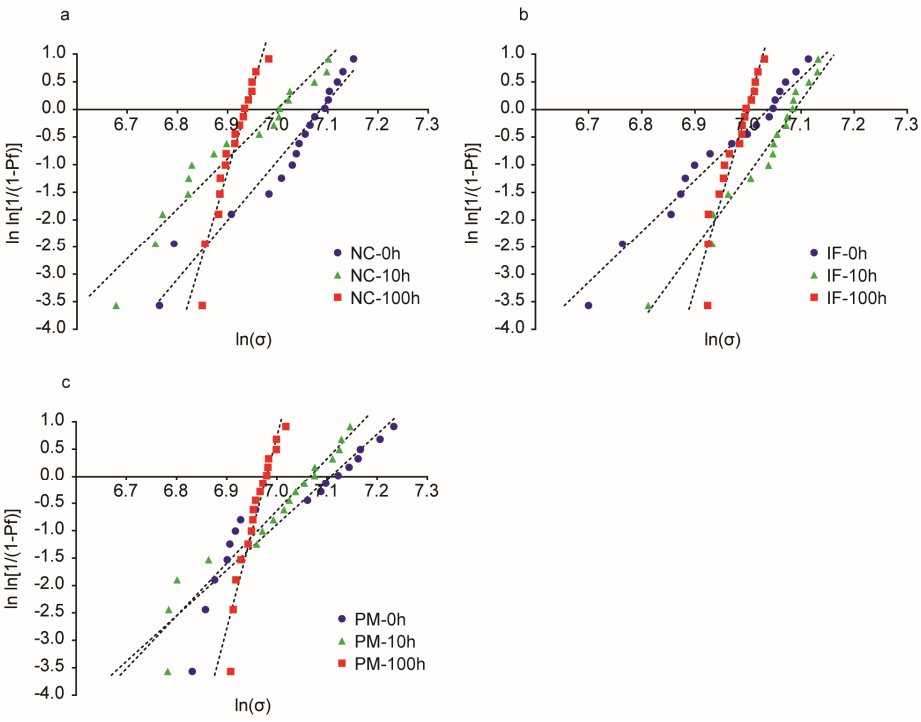

Figure 8. Weibull plot for (a) NC, (b) IF and (c) PM with or without 10 and 100 h of autoclaving. NC: non-colored zirconia, IF: zirconia shaded by infiltration technique, PM: zirconia shaded by powder mixing.

Vickers hardness (Study II)

Two-way ANOVA showed that the Vickers hardness was significantly affected by coloring, autoclaving and the combination of the two. The post hoc test revealed that there was no significant difference between the groups (NC, IF and PM) when they were not subjected to autoclaving. After 100 h of autoclaving, PM and IF showed significantly higher hardness than NC ($p < 0.01$). In addition, PM showed significantly higher hardness than IF ($p < 0.05$).

4.1.2 Microstructural property

Grain size (Study I, II and V)

The grain size of the 3Y-TZP specimens sintered at 1425, 1500 and 1575°C (Study I) were 0.30, 0.42 and 0.63 μm, respectively (Figure 9). There were significant differences between each group ($p < 0.01$). The grain size for NC, IF and PM (Study II) were 0.37, 0.43 and 0.44 μm, respectively. There was significant difference between NC and IF, and NC and PM ($p < 0.01$). The grain size of Lava Plus Zirconia used for kinetic analysis (Study V) was 0.32 μm.

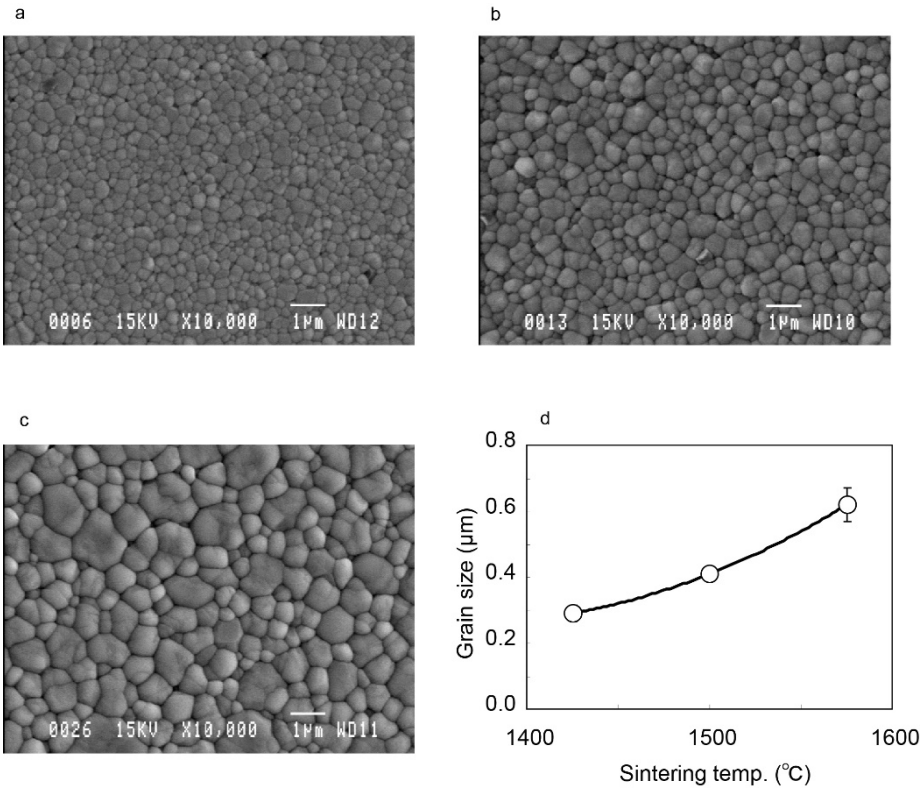

Figure 9. SEM images of 3Y-TZP after thermal etching. The specimens were sintered at (a) 1425°C, (b) 1500°C and (c) 1575°C. Relationship between grain size and sintering temperature is displayed in (d).

Monoclinic fraction (Study II and V)

In Study V, only the *It*(101) peak was observed by XRD analysis when the 3Y-TZP specimens (Lava Plus Zirconia) were not autoclaved. However, the *It*(101) peak was attenuated and the peaks of the monoclinic phase [*Im*(-111) and *Im*(111)] appeared when autoclaved (Figure 10a). Based on the calculations, the monoclinic fraction increased with autoclaving time from 0% (below the detection limit) at 0 h to approximately 70% after 50 h of autoclaving, and then reached a plateau (Figure 10b).

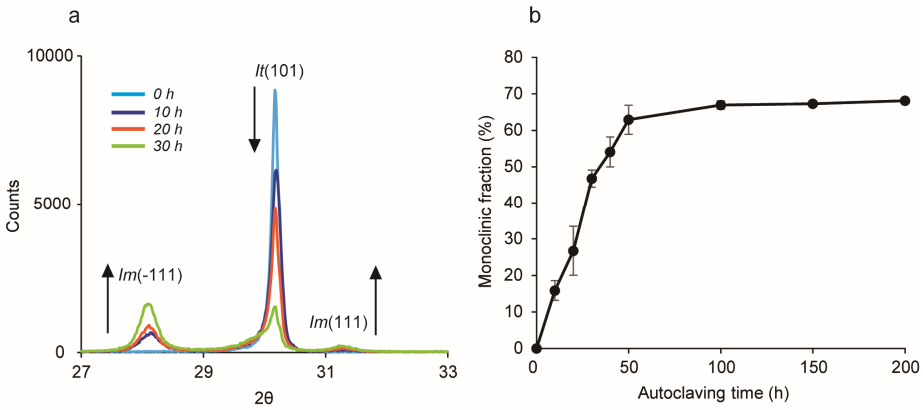

Figure 10. (a) Representative XRD spectra and (b) changes in monoclinic fraction with an increase in the autoclaving time. Each value is the mean with SD (n = 6).

In Study II, without autoclaving, the monoclinic phase could not be detected by XRD regardless of the color group. When the specimens were subjected to autoclaving, the monoclinic phase on the surface was detected by XRD, and increased with autoclaving time. The results are summarized in Figure 11. Two-way ANOVA showed that the monoclinic fraction on the surface was significantly affected by coloring, autoclaving and the combination of the two. The post hoc test revealed that IF and PM showed significantly lower monoclinic fraction than NC after 10 and 100 h of autoclaving. In addition, IF showed significantly lower monoclinic fraction than PM after 100 h of autoclaving.

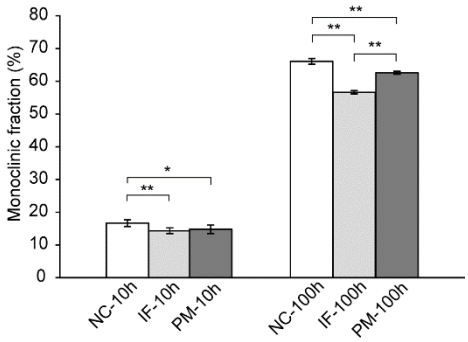

*Figure 11. Monoclinic fraction on the surface of the zirconia specimens autoclaved for 10 and 100 h. Each value represents the mean with SD (n = 6). *: $p < 0.05$, **: $p < 0.01$. NC: non-colored zirconia, IF: zirconia shaded by infiltration technique, PM: zirconia shaded by powder mixing.*

Penetration depth of monoclinic phase (Study II and V)

In Study V, when the 3Y-TZP specimens (Lava Plus Zirconia) were not subjected to autoclaving, there were no clear signs of a phase transformation in the SEM images (Figure 12). When autoclaved, a limited region of the zirconia changed phase (the transformed zone). In the transformed zone, grains that were affected by LTD were pulled out during polishing in contrast to non-transformed zirconia as shown in the SEM images of the cross-sectional surface (Figure 12). The depth of the transformed zone increased with autoclaving time and reached 31.4 μm after being autoclaved for 200 h (Figure 12).

In Study II, the SEM analysis of the cross sections showed that the monoclinic spots were detected after 10 h of autoclaving, and a layer of transformed zone was observed after 100 h of autoclaving though no monoclinic phase was detected in the specimens without autoclaving. The colored 3Y-TZP (IF and PM) showed significantly smaller depth of transformed zone than NC after 100 h of autoclaving (Figure 13). In addition, PM showed significantly smaller depth than IF.

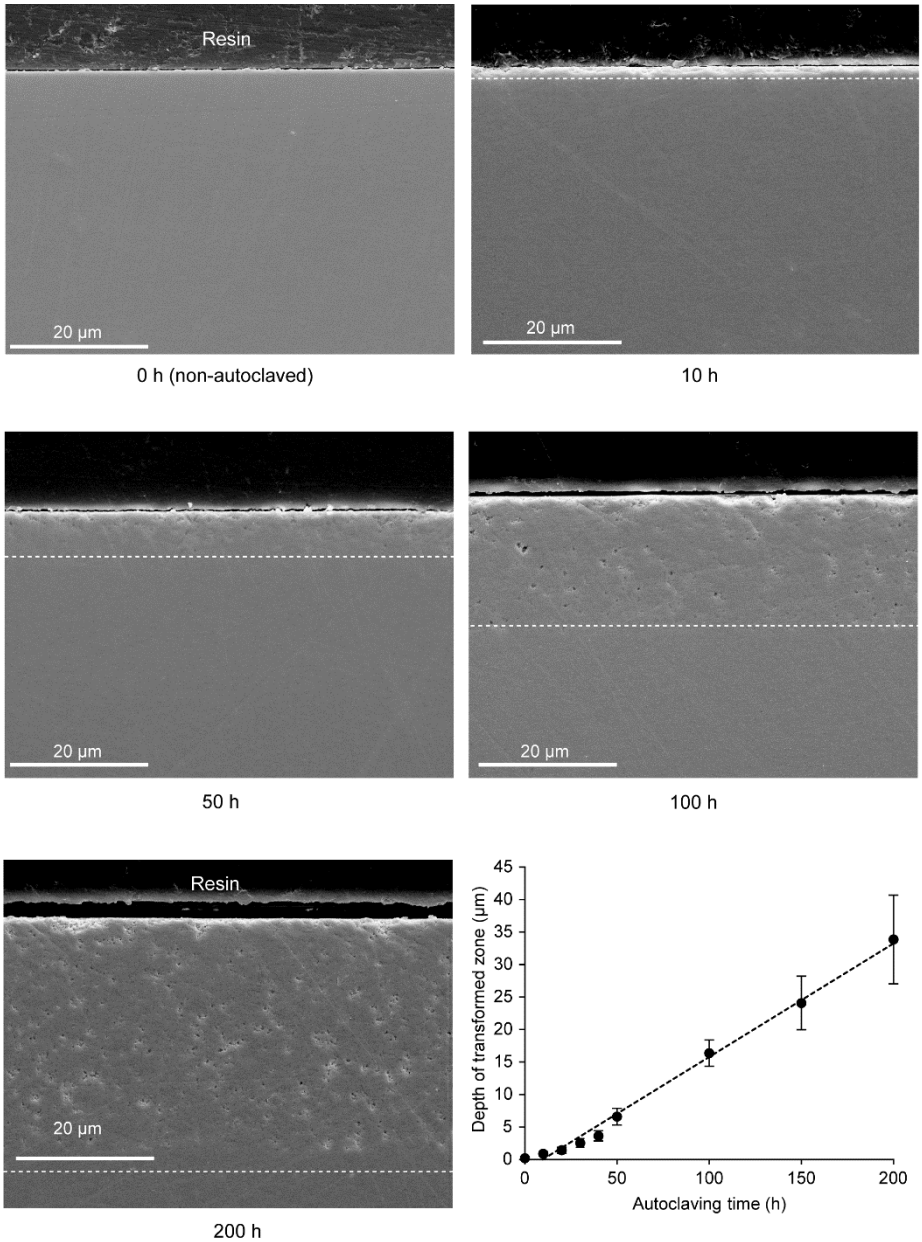

Figure 12. The depth of the transformed zone with representative SEM images of cross section of the zirconia specimens autoclaved for 0-200 h. Each value represents the mean with SD (n = 6)

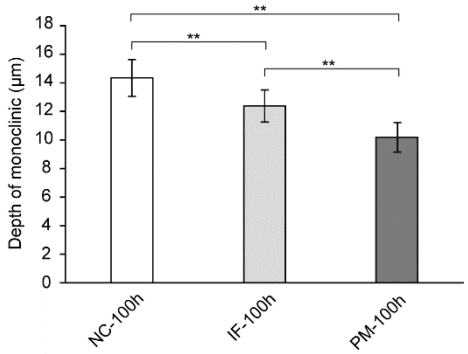

*Figure 13. The penetration depth of the monoclinic phase in non-colored and colored zirconia autoclaved for 100 h. Each value represents the mean with SD (n = 6). **: p < 0.01. NC: non-colored zirconia, IF: zirconia shaded by infiltration technique, PM: zirconia shaded by powder mixing.*

4.2 Crown fracture testing

4.2.1 Evaluation of die material and cements

The mean values of the flexural strength, the modulus of elasticity and the Poisson's ratio of the die material evaluated in Study III were 196 MPa, 10.73 GPa and 0.43, respectively.

The compressive strengths of ZPC (45.4 ± 15.7 MPa) and GIC (81.0 ± 12.4 MPa) were significantly lower than those of SRC (212.6 ± 27.3 MPa), RC-D (161.8 ± 53.3 MPa) and RC-C (183.4 ± 33.2 MPa). In addition, SRC showed significantly higher compressive strength than RC-D.

4.2.2 Micro-CT analysis

Crown thickness

The axial and occlusal thicknesses of the monolithic crowns tested in Study III are summarized in Table 6. The cement space in the occlusal surface of the monolithic zirconia crowns tested in Study IV was in the range of 112–144 μm

depending on the measuring points though it was designed to be 70 μm in the CAD/CAM software.

Table 6. Axial and occlusal thickness of crowns evaluated by micro-CT analysis. Each value represents the mean with SD (n = 6) given within the parentheses.

	Axial thickness (mm)				Occlusal thickness (mm)									
	m	**d**	**b**	**l**	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**
C0.5/O0.5	0.84 (0.02)	0.71 (0.02)	0.75 (0.02)	0.70 (0.01)	1.00 (0.01)	0.50 (0.01)	1.03 (0.02)	0.64 (0.02)	0.62 (0.03)	0.50 (0.01)	0.64 (0.01)	1.08 (0.01)	0.57 (0.01)	1.03 (0.02)
C0.5/O1.0	0.81 (0.02)	0.72 (0.02)	0.79 (0.02)	0.72 (0.02)	1.44 (0.01)	1.05 (0.01)	1.50 (0.02)	1.14 (0.01)	1.08 (0.01)	1.06 (0.01)	1.23 (0.01)	1.47 (0.01)	1.07 (0.01)	1.56 (0.01)
C0.5/O1.5	0.78 (0.02)	0.72 (0.01)	0.78 (0.03)	0.69 (0.02)	1.96 (0.01)	1.45 (0.02)	1.97 (0.01)	1.53 (0.03)	1.64 (0.01)	1.52 (0.02)	1.67 (2.02)	2.02 (0.02)	1.49 (0.02)	2.00 (0.03)
C0.7/O0.5	1.02 (0.01)	0.87 (0.02)	0.95 (0.02)	0.91 (0.02)	1.19 (0.01)	0.61 (0.01)	1.17 (0.01)	0.74 (0.01)	0.65 (0.01)	0.59 (0.00)	0.69 (0.02)	1.13 (0.01)	0.06 (0.02)	1.19 (0.01)
C0.7/O1.0	1.13 (0.03)	0.90 (0.02)	0.94 (0.04)	0.94 (0.02)	1.49 (0.01)	0.99 (0.01)	1.57 (0.01)	1.17 (0.02)	1.07 (0.01)	1.11 (0.02)	1.26 (0.02)	1.66 (0.01)	1.11 (0.01)	1.66 (0.01)
C0.7/O1.5	1.04 (0.02)	0.93 (0.02)	1.00 (0.02)	0.94 (0.01)	1.94 (0.01)	1.43 (0.02)	2.01 (0.02)	1.56 (0.02)	1.72 (0.02)	1.51 (0.02)	1.60 (0.02)	2.18 (0.03)	1.59 (0.02)	2.05 (0.02)
C1.0/O0.5	1.33 (0.02)	1.22 (0.02)	1.23 (0.03)	1.12 (0.02)	1.16 (0.02)	0.55 (0.01)	1.03 (0.02)	0.72 (0.02)	0.84 (0.02)	0.56 (0.01)	0.67 (0.01)	1.41 (0.02)	0.65 (0.01)	1.24 (0.01)
C1.0/O1.0	1.35 (0.02)	1.22 (0.02)	1.20 (0.05)	1.15 (0.02)	1.60 (0.03)	0.99 (0.01)	1.49 (0.02)	1.20 (0.02)	1.25 (0.02)	1.02 (0.02)	1.15 (0.01)	1.74 (0.03)	1.10 (0.01)	1.71 (0.02)
C1.0/O1.5	1.32 (0.03)	1.24 (0.01)	1.23 (0.03)	1.14 (0.03)	2.13 (0.02)	1.51 (0.02)	1.96 (0.02)	1.64 (0.03)	1.66 (0.02)	1.50 (0.02)	1.62 (0.02)	2.32 (0.02)	1.70 (0.02)	2.28 (0.02)
C0.5/O0.5f	0.88 (0.01)	0.66 (0.01)	0.81 (0.02)	0.66 (0.01)	0.46 (0.01)	0.45 (0.01)	0.55 (0.02)	0.48 (0.02)	0.60 (0.01)	0.50 (0.01)	0.56 (0.02)	0.55 (0.03)	0.54 (0.01)	0.57 (0.01)
C1.0/O1.5 e.max press	1.30 (0.05)	1.30 (0.04)	1.39 (0.06)	1.33 (0.05)	2.51 (0.16)	1.55 (0.14)	1.96 (0.13)	1.70 (0.11)	1.70 (0.18)	1.48 (0.13)	1.57 (0.18)	2.32 (0.16)	1.69 (0.13)	2.18 (0.15)

m: mesial, d: distal, b: buccal, l: lingual, A-J correspond to the measuring points shown in Figure 4c.

4.2.3 Fracture resistance of monolithic zirconia crowns

In Study III, one out of 6, 4 of 6, and 4 of 6 crowns from the group of C0.5/O1.5, C0.7/O1.5, and C1.0/O1.5, respectively, did not fracture even at 10 kN. As shown in Figure 14, there were significant differences in the fracture load between the crowns of various thickness. Based on the measurement of crown thickness (Table 6) and the fracture load, multiple regression analysis was performed, and the following statistical prediction formula was calculated.

That is, $F = 3295 + 657 \times A + 3465 \times O$

where F is the fracture load (N), A is the axial thickness (mm), and O is the occlusal thickness (mm).

Adjusted coefficient of determination was 0.711. It was revealed that the occlusal thickness significantly affected the fracture load ($p < 0.01$) whereas the axial thickness did not ($p = 0.2828$).

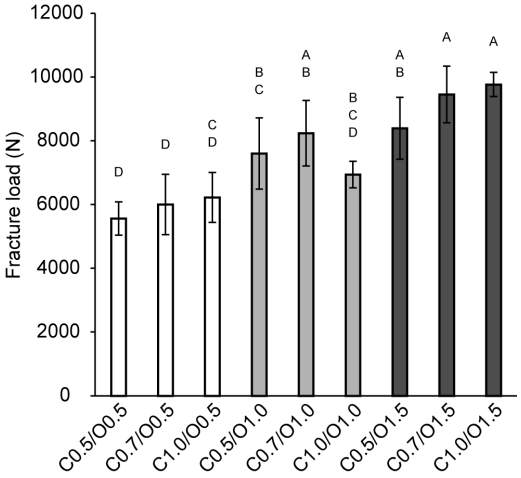

Figure 14. Fracture load of the monolithic zirconia crowns tested. Each bar represents the mean with SD (n = 6). Different letters above the bars show significant differences (p < 0.05).

Although the reduction of occlusal thickness decreased the fracture resistance of monolithic zirconia crown, the fracture load of C0.5/O0.5 (5558 ± 522 N) and C0.5/O0.5f (4597 ± 532 N) was significantly higher than that of C1.0/O1.5e.max press (3147 ± 409 N) (Figure 15). Between the two types of monolithic zirconia crowns (V-shape and facetted shape), C0.5/O0.5f showed significantly lower fracture load than C0.5/O0.5.

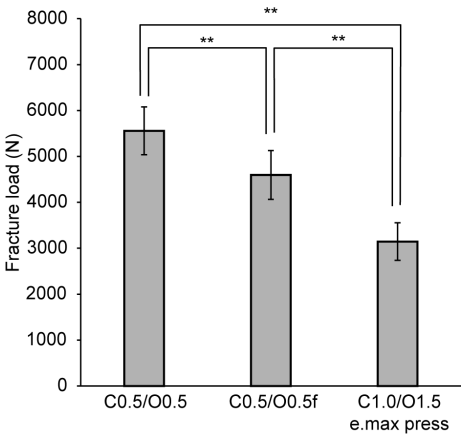

*Figure 15. Comparison of fracture load of monolithic zirconia crown with reduced thickness (C0.5/O0.5 and C0.5/O0.5f) with that of lithium disilicate crown (C1.0/O1.5e.max press). Each value represents the mean with SD (n = 6). **: p < 0.01*

The results of Study IV in which load-to-failure test was performed using the monolithic zirconia crowns cemented with various types of cements are shown in Figure 16. There were no significant differences in fracture resistance between the different cement groups.

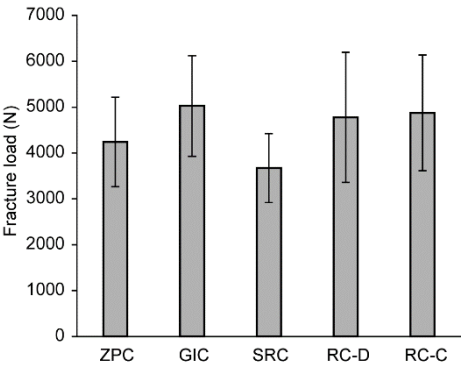

Figure 16. Fracture resistance of C0.5/O0.5 monolithic zirconia crowns cemented to dies using different cements. ANOVA revealed that there was no statistical difference between the groups. ZPC: zinc phosphate cement, GI: glass-ionomer cement, SRC: self-adhesive resin-based cement, RC-D: resin-based cement (dual cure mode), RC-C: resin-based cement (chemical cure mode).

Fractographic analysis revealed that there were no signs of Hertzian cone cracks at the occlusal surface. In all cases, primary fracture origin was located at the occlusal surface (Figure 17).

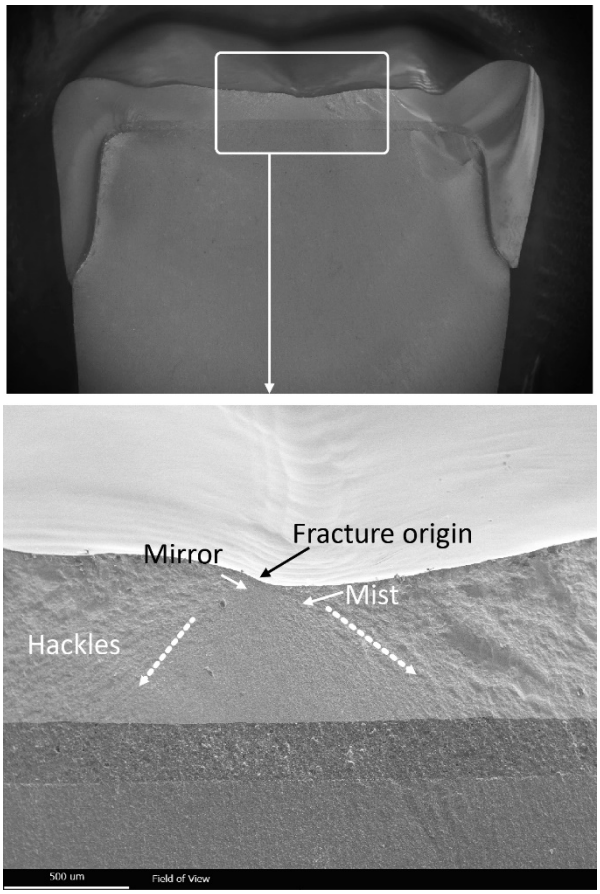

Figure 17. Representative micrograph and SEM image of fractured monolithic zirconia crown. The fractographic features (i.e. fracture mirror, mist and hackles) indicated that the fracture origin was located at occlusal surface. The dotted lines indicate the direction of the fracture wave.

Study V showed that the fracture load of the monolithic zirconia crowns significantly decreased from 5683 N without autoclaving to 3975 N after autoclaving for 100 h (Figure 18). After cyclic loading, no signs of fracture were observed using stereomicroscopic analysis. Thus, all of the crown-die

samples subjected to cyclic loading were subsequently tested in a load-to-failure test. As shown in Figure 18, cyclic loading did not significantly affect the strength of the crowns tested. This was regardless of whether autoclaving was performed. The SEM analysis of the cross sections of randomly selected fractured crowns showed that autoclaving generated a monoclinic phase (the transformed zone) on the outer and inner surfaces whereas cyclic loading without autoclaving did not. No quantitative analysis of the transformed zone was performed since the fractures did not occur exactly at the same location, direction, or angle in each crown, which would affect the measurement.

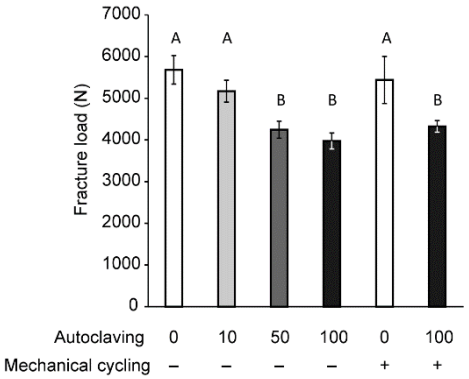

Figure 18. The fracture load of C0.5/O0.5 monolithic zirconia crowns with or without autoclaving and mechanical cycling. Each value represents the mean with SD (n = 6). The different letters above the bars show significant differences (p < 0.01). Numbers displayed in the row of Autoclaving represent treatment time (h). Mechanical cycling was performed with 240,000 cycles between 30 and 300 N.

5 DISCUSSION

5.1 Discussion of method

5.1.1 Biaxial flexural strength test

Flexural strength is considered as one of the most important properties for brittle dental materials as they are much weaker in tension than in compression (Ban and Anusavice, 1990; Vallittu and Kononen, 2013). In the ISO 6872:2008, three flexural strength tests are accepted for dental ceramic materials test; three-point bending test, four-point bending test and biaxial flexure test. Uniaxial flexural tests (three- and four-point bending test) are, however, influenced by the edge flaws and defects in test specimens, known as "edge effect" (Ban and Anusavice, 1990; Wagner and Chu, 1996). Due to the edge effect, the strength values obtained in the uniaxial flexural tests are lower than those of biaxial flexural test in some cases (Shetty et al., 1981; Ban and Anusavice, 1990). In biaxial flexural test, disc specimens are loaded with a flat punch at the center, and tensile stress is generated on the opposite sides. Consequently, the cracks propagate from the center toward the edges and as such, the edge effect can be eliminated (Ban and Anusavice, 1990; Wagner and Chu, 1996). Therefore, in Study I and II, biaxial flexural strength test was performed with piston-on-three-ball test method given in the ISO 6872:2008. As the mechanical evaluation was performed on polished specimens, stresses caused by defects related to the sample preparation at the surface exposed to tensile stresses were assumed to be limited.

5.1.2 Load-to-failure test

Laboratory load-to-failure tests often induce contact damage at the loading point causing Hertzian cone crack (Webber et al., 2003; Sundh and Sjogren, 2004; Akesson et al., 2009), which is rarely observed as a primary damage for catastrophic failure in a clinical situation (Kelly, 1999; Scherrer et al., 2008; Oilo and Gjerdet, 2013). The stress distribution that creates Hertzian cone cracks is thought to be different from clinical condition, and as such, the fracture resistance of crowns may be overestimated in laboratory tests (Kelly,

1999). Several test methods have been proposed in order to simulate clinical fracture (Kelly, 1999; Oilo et al., 2013) though standardized test method has not been established yet. Firstly, it is necessary to avoid contact damage of the steel indenter. For that purpose, it is recommended that a spherical indenter with a large diameter (≥ 10 mm) be used (Kelly, 1999). In addition, it has been demonstrated that a rubber sheet with a thickness of 2-3 mm interspersed between the indenter and crown can further assure a broad even contact resulting in clinically relevant fracture (Oilo et al., 2013; Oilo et al., 2014b). Secondary, the test samples should be prepared as close to clinical restorations as possilbe to reproduce the clinically relevant stress distribution (Kelly, 1999). Also, it is recommended that a polymer resin-based material, which has similar mechanical properties as dentin, be used as a die material (Kelly, 1999).

In this context, the preparation of materials and load-to-failure test were performed according to the proposed recommendations (Kelly, 1999; Oilo et al., 2013). Fractographic analysis (Study IV) revealed that no Hertzian cone cracks occurred, suggesting that the test conditions could successfully avoid the contact damage. Concerning the sample preparation, the crowns with anatomic shape were prepared and cemented to the dies mimicking the clinical situation as much as possible. Since the monolithic zirconia crowns and dies were fabricated with CAD/CAM technique, the samples with the identical shape for each group could be obtained. This would contribute to reducing errors related to laboratory tests. In addition, the mechanical properties of die material (Lava Ultimate) were evaluated in Study III, and confirmed that the modulus of elasticity was in the range of those reported for dentin (Kinney et al., 2003) as well as those for polymer resin-based materials used in earlier studies (Scherrer and de Rijk, 1993; Yucel et al., 2012). It was also demonstrated that the Poisson's ratio of the die material in use (0.43) was found to be close to that of wet (*i.e.* vital) dentin (0.38-0.45) (Kinney et al., 2003; Kinney et al., 2004).

The difference in the Poisson's ratio as well as in the modulus of elasticity between the monolithic zirconia crown and die material (Poisson's ratio: 0.33 for zirconia vs 0.43 for Lava Ultimate, Modulus of elasticity: 220 GPa for

zirconia vs 11 GPa for Lava Ultimate) might give rise to stress build-up, eventually leading to material fracture. Oilo et al. (Oilo and Gjerdet, 2013; Oilo et al., 2013; Oilo et al., 2014a) demonstrated that the fractures of all-ceramic crowns seen in the clinical situation and replicated in an in vitro experimental study originated from the cervical parts probably as a result of hoop stress due to volumetric changes of the abutment material at loading. In the present study and contrary to their findings, the fractures in the monolithic zirconia crowns initiated from the occlusal surface, verified by fractographic features displayed in SEM images of the fracture surfaces. The divergence in results may in specific be referred to differences in the crown and abutment materials as well as in the test methods used. A thicker interspersed sheet and use of a larger diameter of the spherical indenter than were used in the present study would cause a greater reduction and leveling out of the loading factor. Lack of information on *e.g.* the mechanical properties of the epoxy material used for the abutments and certain loading factors make a direct comparison of results difficult.

It should be noted that the load-to-failure test with single loading does not necessarily reflect clinical situations since few clinical fractures occur during a single-loading (Anusavice, 2013a). Still, load-to-failure test can be used as the initial step for evaluation of new materials or concepts (Sornsuwan et al., 2011) since it will allow a standardization of certain factors that are difficult to standardize in the clinic. At least, the fracture load obtained in the single load-to-failure test should be greater than maximal bite force with safety margin.

To simulate a more realistic clinical situation, fatigue tests with or without load-to-failure test may be conducted. Clinically, all-ceramic crowns fail through slow crack growth as a result of many cycles of stress, so-called fatigue failure (Anusavice, 2013a; Vallittu and Kononen, 2013). Fatigue tests for all-ceramic crowns have been performed mainly with mechanical cycling, thermal cycling and thermo-mechanical cycling. However, no standardized fatigue test for crowns and FDPs has been established yet. For instance, mechanical cycling was performed under different conditions in terms of size of indenter (Ø = 2.5-12 mm), load (50-750 N), frequency (1-20 Hz) and cycles (10^4-10^6

cycles) (Rosentritt et al., 2006; Zahran et al., 2008; Guess et al., 2010; Preis et al., 2012; Johansson et al., 2014). It is reported that average chewing force, maximum bite force in molar region and frequency of mastication varies from 50 to 150 N, from 400 to 890 N and from 0.89 to 1.57 Hz, respectively (Youssef et al., 1997; Schindler et al., 1998; Anusavice, 2013a). Kelly et al. (2010) reported that the influence of frequency on the results of mechanical cycling test was small, and suggested that the test could be performed at 20 Hz. Regarding the cycles, it is estimated that cycles of mastication per day is about 2700 resulting in 10^6 cycles per year (Wiskott et al., 1995). However, since not all chewing cycles are active, this number should be reduced by a factor ranging between 5 and 20. If the factor of 5 is used, these become 200,000 cycles/year (Wiskott et al., 1995). Another research group also estimated that 1.2×10^6 cycles corresponded to 5 year (240,000 cycles/year) (Rosentritt et al., 2006). Based on the background, mechanical cycling test was performed 300 N for 240,000 cycles at a frequency of 10 Hz in water to simulate 1 year of clinical service in Study V.

5.1.3 Autoclaving-induced LTD

An accelerated LTD test by autoclaving has been proposed to estimate the phase transformation of zirconia *in vivo*. The ISO 13356:2008 requires that zirconia ceramics used for surgical implants should not show > 20% of monoclinic phase after 5 h of autoclaving at a temperature of 134°C and a pressure of 0.2 MPa. It was calculated that 1 h of autoclaving at 134 °C theoretically corresponded to 3–4 years *in vivo* (Chevalier et al., 1999; Chevalier, 2006). Based on this estimation, the LTD caused by 10–200 h of autoclaving in the present study would correspond to 30–600 years at body temperature. However, as suggested by Lughi and Sergo (2010), estimations of *in vivo* phase transformation might contain large errors. The estimation was based on the assumption that the transformation rate obtained in accelerated tests at 100–300 °C follows the same Arrhenius-like trend down to a body temperature of 37 °C. Therefore, an extended autoclaving time was adopted so that LTD might sufficiently cover the possible lifetime in the oral cavity.

5.2 Discussion of results

5.2.1 Mechanical and microstructural properties of 3Y-TZP

Influence of sintering, veneer firing process and coloring

Sintering temperature of 3Y-TZP used in dentistry varies between 1350 and 1550 °C depending on the manufacturers (Denry and Kelly, 2008). When veneering is needed, fully sintered material is subjected to additional firing processes. Even monolithic zirconia restorations may be subjected to such heat treatment for glazing or for veneering when they are used in an FDP composed of both monolithic and veneered crowns. Thus, the influence of sintering temperature and additional heat treatment on the flexural strength of 3Y-TZP was investigated in Study I. It was confirmed that the higher the sintering temperature the larger the grain size became as reported previously (Elshazly et al., 2011). The biaxial flexural strength showed a tendency to decrease as grain size increased while the strength seemed not to be influenced when exposed to the veneering firing process. Some previous studies reported that a significant reduction of the strength was observed after the first firing (Guazzato et al., 2005; Oilo et al., 2008). In the previous studies, the specimens were prepared by grinding whilst the specimens used in the present study were polished. Polishing is a gentle material removal procedure that can produce an almost stress free surface without phase transformation compared to grinding. It has been suggested that, as an effect of elevated temperature such as during the veneering process, the monoclinic grains at the surface will return to its tetragonal phase resulting in removal of the compressive surface stresses (Guazzato et al., 2005). This would be a probable explanation why the heat treatment used for veneering reduced the strength of the ground zirconia ceramics but not that of polished ones. In spite of the fact that the zirconia specimens used in the present study included various grain sizes, the heat treatment did not affect the mechanical strength of the polished zirconia specimens.

In Study II, a coloring liquid designed to provide shade A3.5, which is the strongest A shade color in the Lava System (3M/ESPE), was used for IF. It is expected that a stronger shade, which would require a larger amount of additive, would influence the behavior of the zirconia material to a larger extent. The ability to detect such a change from the evaluated material properties would thus be increased. For the same reason, PM was fabricated without dilution of color by adding non-colored zirconia powder to obtain a maximal shade. There were no significant difference in density and grain size between the different color groups. XRF analysis revealed that IF contained Fe_2O_3 and Er_2O_3, while PM contained Fe_2O_3, both of which are well-known coloring pigments (Yashima et al., 1995; Guo and Xiao, 2012). Although the chemical composition of NC, IF, and PM were similar except for the coloring pigments, it should be noted that the zirconia powder used in PM was a different product compared to the powder used for NC and IF. Therefore, the difference in properties between PM and the others may have arisen because of the difference in raw materials and the different coloring techniques used. The biaxial flexural strength of the colored and non-colored 3Y-TZP tested in Study II was close to those recorded in Study I as well as in other studies (Guazzato et al., 2005; Pittayachawan et al., 2007). Comparing the strengths of NC and IF, which were made from the same zirconia powder, the IF process had a tendency to decrease the specimen strength, although there was no statistical difference in the strengths of all materials tested. It was also demonstrated that there was no significant difference in Vickers hardness between the groups. Thus, it is suggested that the coloring of 3Y-TZP will not affect the mechanical and microstructural properties as long as the concentration of color pigment used was low.

Influence of LTD

In Study II, the influence of LTD on the properties of the non-colored and colored 3Y-TZP was studied. The color of the non-colored and colored 3Y-TZP was slightly affected by the LTD. This was likely caused by the phase transformation at the surface of the specimens, which would change its optical reflection. According to critical marks of color change quantified by the

National Bureau of Standards (NBS, USA) (Nimeroff, 1968), the NBS units of color difference can be calculated using the following formula: NBS unit = ΔE × 0.92. Therefore, the NBS units for NC, IF and PM were calculated to be 1.28, 0.71, and 1.24, respectively. These NBS units in the range between 0.5 and 1.5 were classified as 'slight', meaning that the observed color changes were not severe. Furthermore, Gross and Moser (Gross and Moser, 1977) reported that ΔE values in the range of 0–2 represent color differences are imperceptible to the human eye. Thus, it is suggested that the color of the colored and non-colored 3Y-TZP is relatively stable even when affected by LTD.

No change in the surface roughness of the non-colored and colored 3Y-TZP was detected even after 100 h of autoclaving, which may have been due to the stylus of the profilometer used in the present study. Because the tip diameter of the stylus (2.5 μm) used was much larger than the grain size, any change in height over a short distance caused by individual grains may not have been detected as was done in a previous study where an optical interferometer was used to demonstrate LTD-induced surface coarsening (Gremillard et al., 2013). Although the results should be interpreted with respect to the limitation in methodology, it is suggested that the deterioration of the surface roughness was of a level that cannot be detected by a stylus type surface analyzer. However, as reported previously (Gremillard et al., 2013), it is assumed that the surface affected by LTD might be more worn than a non-affected surface. This issue should be studied further in terms of the surface wear of monolithic zirconia crowns.

When LTD was induced by autoclaving, the biaxial flexural strength of 3Y-TZP was significantly affected. The mean strength of IF increased after 10 h of autoclaving, but after 100 h of autoclaving, a similar strength to that of the untreated material was obtained. In contrast, the strength of NC and PM decreased with autoclaving time. This trend was also confirmed by the characteristic strength calculated by Weibull statistics, which is the representative value of Weibull distribution. When zirconia is subjected to autoclaving, the amount of monoclinic phase increases with time (Chevalier et al., 1999). At the beginning, superficial phase transformation generates

compressive stress in the surface layer, which resists crack propagation (Virkar et al., 1987; Kim et al., 2009; Siarampi et al., 2014), resulting in an increase in strength. Further generation of monoclinic phase causes micro-cracks, which act as defects (Swain and Rose, 1986) causing a decrease in strength. Thus, the initial increase in the strength of IF was probably caused by superficial phase transformation. One of the possible reasons for the difference in strength between IF and NC would be the phase transformation rate, as shown by the XRD analysis. Deduced from this, the colored 3Y-TZP had a significantly lower monoclinic fraction than the non-colored material after 100 h of autoclaving. Similarly, SEM analysis revealed that the penetration depth of the monoclinic phase in the colored 3Y-TZP was significantly smaller than that in the non-colored material. The reduced phase transformation rate of the colored 3Y-TZP might be attributed to the presence of Fe^{3+} and Er^{3+}, which may form a solid solution with ZrO_2 and thus act as additional dopants (Li et al., 1994; Khor and Yang, 1997). The results of the present study suggest that coloring pigments such as Fe_2O_3 and Er_2O_3 give zirconia a higher resistance to LTD by retarding the phase transformation from tetragonal to monoclinic phase. It has previously been demonstrated that the stability of the tetragonal phase increases with the concentration of trivalent dopants (Yashima et al., 1995; Khor and Yang, 1997). In the present study, IF was found to contain Fe_2O_3 and Er_2O_3 at concentrations of 0.07 wt.% (0.06 mol.%) and 0.46 wt.% (0.15 mol.%), respectively, and PM contained Fe_2O_3 at a concentration of 0.14 wt.% (0.11 mol.%). Thus, the total amount of trivalent dopants in the colored 3Y-TZP was slightly increased (3 mol.% Y_2O_3 + coloring pigments) compared with that of the non-colored 3Y-TZP. This may have caused the higher resistance of the colored zirconia to the LTD. As for grain size, IF and PM showed significantly larger grain size than NC, as previously reported (Guo and Xiao, 2012). However, the average grain sizes of the colored 3Y-TZP were still below 0.5 μm. Although, in general, zirconia becomes less stable and more susceptible to LTD as the grain size increases (Tsukuma et al., 1984; Munoz-Saldana et al., 2003; Chevalier et al., 2004), the retarding effect of the coloring pigments on the phase transformation upon LTD may have prevailed against the negative effect of the increased grain size.

The LTD obtained after 100 h of autoclaving also significantly deteriorated the hardness. This finding is identical to that of a previous study, which demonstrated that the Vickers hardness of 3Y-TZP decreased with autoclaving time (Elshazly et al., 2011). Although the non-autoclaved specimens did not show any significant differences in hardness between the different color groups, the colored 3Y-TZP showed a higher resistance to the deterioration in hardness. The depth of the hardness indentations was around 16 μm in the materials exposed to 100 h of autoclaving, and the decrease in the Vickers hardness was well correlated to the penetration depth of the monoclinic phase. NC, which had the largest monoclinic phase penetration depth, showed the lowest hardness, while PM with the smallest depth exhibited the highest hardness.

Weibull modulus (*m*) is used to characterize the distribution of flaws in ceramic materials (Afferrante et al., 2006; Richerson, 2006b). Higher values of *m* indicate a narrower defect size distribution. Most ceramics are reported to have *m* in the range of 5–15, whereas metals exhibit values in the range of 30–100 (Johnson, 1983; Guazzato et al., 2005; Qeblawi et al., 2010). The *m* for non-autoclaved 3Y-TZP specimens recorded in the present study was 8.3–10.8, which is similar to those reported in previous studies (Guazzato et al., 2005; Pittayachawan et al., 2007). The value of *m* was expected to decrease with the extent of autoclaving-induced LTD because LTD generates micro-cracks on the material surface. Indeed, Siarampi et al. (2014) demonstrated that a zirconia dental product showed lower *m* accompanied with a reduction of strength after 10 h of autoclaving, which was also observed for NC in the present study. However, prolonged autoclaving time (100 h) increased m to > 30 regardless of the specimen color, though the strength of each material showed a tendency to decrease. Similar results were reported by Flinn et al. (2012), who demonstrated that 200 h of autoclaving significantly decreased the flexural strength of zirconia, and the standard deviation of the strength was smaller than that for non-autoclaved material. The smaller standard deviation can be correlated to an increase in *m*. According to the Weibull plot, 100 h of autoclaving narrowed the strength distribution by not only decreasing the higher values but also by increasing the lower values compared with the non-autoclaved group. LTD may influence the stresses present and introduce

micro-cracks at the surface. When the penetration depth of these micro-cracks reaches sufficiently deep into the material, either locally or as an evenly growing layer, the strength will be reduced. Still, in the case of the materials not subjected to autoclaving, a low strength may suggest the presence of defects. Pre-existing defects in the material will respond to autoclaving with the build-up of a local compressive stress zone. Providing the influence from flaws induced by the phase transformation is inferior to that from the pre-existing defects, the strength will increase. Additionally, remaining non-hitherto transformed tetragonal phase will be exposed to tensile stress from the local monoclinic phase and trigged to undergo further phase transformation, an effect referred to as the "autocatalytic effect" (Lughi and Sergo, 2010). Such an autocatalytic effect might give rise to a more even stress-induced transformation, which may also increase the lowest values. The combination of these effects would then result in an increased Weibull modulus.

Regarding the LTD kinetics, Study V demonstrated that the monoclinic fraction on the surface of the zirconia increased with autoclaving time and reached a plateau below 100% as previously reported (Deville et al., 2005). The depth of the monoclinic phase increased with an autoclaving time of up to 200 h. The depth of the monoclinic phase became > 5 μm after 50 h of autoclaving. The results suggest that the monoclinic phase penetrates the bulk of the material even though monoclinic generation on the surface is saturated. This is possibly an effect of inter-granular trigging.

5.2.2 Fracture resistance of monolithic zirconia crowns

Effect of crown thickness

The effect of crown thickness on fracture resistance of monolithic zirconia crowns was evaluated in Study III. The micro-CT analysis revealed that there were significant differences in the axial and the occlusal thickness between the different groups (*i.e.* C/0.5 vs 0.7 vs 1.0, and O/0.5 vs 1.0 vs 1.5). Since other parameters, such as the crown shape and the height of the axial wall, which is known to influence the fracture resistance of posterior all-ceramic crowns

(Scherrer and de Rijk, 1992), were standardized, it is considered that the difference in fracture load for each type of the monolithic zirconia crowns were related to the crown thickness.

In the load-to-failure test, some of the monolithic zirconia crowns with occlusal thickness of 1.5 mm were not fractured even at 10 kN. This result is consistent with a previous report wherein Beuer et al. (2012) demonstrated that 11 out of 12 monolithic zirconia crowns did not fail at 10.5 kN. Their dies imitating tooth 46 with 1.2 mm chamfer preparation and 1.5 mm occlusal reduction seemed comparable to C1.0/O1.5 dies used in the present study.

Based on the multiple regression analysis, the occlusal thickness significantly affected the fracture resistance. It is known that the occlusal thickness of all-ceramic crowns is one of the primary factors influencing stress and fracture resistance (Rekow et al., 2006; Wolf et al., 2008). For the monolithic zirconia crowns tested in the present study, an increase in occlusal thickness with 1 mm resulted in an augmented fracture load with 3465 N according to the multiple regression analysis. Therefore, even for patients with high loading forces, only a small increase in occlusal thickness of a monolithic zirconia crown will probably contribute to augment the fracture resistance. Contrary to the occlusal thickness, the axial thickness of monolithic zirconia crown did not significantly affect the fracture resistance. This finding is in accordance with previous studies on leucite-reinforced glass-ceramic crowns (Tsitrou et al., 2010; Skouridou et al., 2013). However, when a load is applied at a different angle to the tooth axis, the axial thickness might affect the fracture resistance. It was demonstrated that lithium disilicate crowns with a wall thickness of 0.5 mm showed significantly lower fracture resistance than those with wall thicknesses of 1.0 and 1.5 mm when loaded with a tilt of 30° to the tooth axis (Seydler et al., 2014). Although further studies are needed to reach conclusion, based on the present study it might be recommended that the axial wall should be prepared with slight chamfer (*e.g.* 0.5 mm) when monolithic zirconia is used for crowns.

Comparison with monolithic lithium disilicate crowns

A recent systematic review found high survival rate for lithium disilicate single crowns (the 5-year cumulative survival rate: 97.8%) (Pieger et al., 2014). In addition, since IPS e.max press could be used in a monolithic form as in the case of monolithic zirconia crowns, they were used as a control in Study III. Two types of production technique for lithium disilicate restorations are commercially available, one for press technique and the other for CAD/CAM (*e.g.* IPS e.max press and IPS e.max CAD). Since IPS e.max press possesses higher flexural strength (400 ± 40 MPa) than IPS e.max CAD (360 ± 60 MPa) according to the manufacturer's data, the former was used in the present study. Johansson et al. (2014) compared fracture resistance of monolithic zirconia and monolithic lithium disilicate (IPS e.max press) after thermal and mechanical cycling. They reported higher strength for the zirconia crowns compared to lithium disilicate crowns with the same occlusal thickness (≥ 1.8 mm). Although the crowns tested in Study III were not subjected to thermal and mechanical cycling, the fracture load of the monolithic zirconia crowns with an occlusal thickness of 0.5 mm were significantly higher than that of the lithium disilicate crowns with an occlusal thickness of 1.5 mm. Study V additionally demonstrated that mechanical cycling did not affect the fracture resistance of the monolithic zirconia crowns with an occlusal thickness of 0.5 mm. These findings indicate that monolithic zirconia crowns can withstand the forces in the molar region even with a minimal thickness of 0.5 mm. Limiting the occlusal reduction of the abutment preparation would probably contribute not only to the preservation of sound tooth substance but would also ensure adequate height of the axial walls of the abutment tooth, promoting retention and resistance of the crown. The result displaying that the fracture resistance of C0.5/O0.5f crowns was significantly lower than that of C0.5/O0.5 crowns may suggest that several stress points were generated during load due to the shape of the preparation surface with ridges. This would imply that the facetted design is not the most ideal preparation design for the ceramic crown.

Effect of cement

The micro-CT analysis disclosed that the cement space was approximately twice (about 130 μm) as large as that set in the CAD/CAM software (70 μm). Scherrer et al. (1994) demonstrated that the strength of glass-ceramic plates cemented onto composite resin blocks with zinc phosphate cement decreased when the cement thickness increased from 30 to 130 μm. However, they also suggested that the effect of cement thickness could be negligible as long as the polymer resin-based cement was used with a cement thickness of < 300 μm. Thus, it might be considered that the increased cement space observed would have a stronger influence on the fracture resistance of the crowns cemented with zinc phosphate cement than those cemented with polymer resin-based cements. Furthermore, the zinc phosphate cement and glass-ionomer cement showed significantly lower compressive strength than the polymer resin-based cements tested. Nonetheless, there was no significant difference in the fracture resistance of the monolithic zirconia crowns between the various cement groups.

In the case of monolithic zirconia crowns, cementation with polymer resin-based cement may not necessarily result in higher fracture resistance. Zesewitz et al. (2014) demonstrated that there was no significant difference in the fracture load between monolithic zirconia crowns cemented onto metal dies with polymer resin-based cement and those cemented with glass ionomer cement. In the case of zirconia-based restorations, it is considered that conventional cementation is acceptable though polymer resin-based cement might be a first choice (Manicone et al., 2007). Indeed, clinical studies in which zinc phosphate cement and glass ionomer cement were used for cementation of zirconia-based single crowns reported no increased incidence rate of fracture related to the cementation (Ortorp et al., 2012; Tartaglia et al., 2014). As shown in a finite element analysis (Rekow et al., 2006), contribution of cement thickness and cement elastic modulus to maximum principal stress in crowns would be much lower than that of the crown material. Thus, the high strength of zirconia ceramic might prevail against the effect of certain cement properties such as low compressive strength and increased cement film thickness on the fracture resistance of the monolithic zirconia crowns.

Influence of LTD and mechanical cycling

Durability of monolithic zirconia crowns were tested in Study V. The LTD induced by autoclaving significantly decreased the fracture resistance of the crowns. This finding is in agreement with a previous study where Flinn et al. (2012) demonstrated that the flexural strength of zirconia bar specimens with a thickness of 0.2 mm significantly decreased after being autoclaved for 200 h at 134°C. In the present study, the reduction of the fracture load caused by being autoclaved for 100 h was about 30% (from 5683 to 3975 N). The crowns affected by autoclaving-induced LTD still had a fracture resistance that would be sufficiently higher than the average bite force in the molar regions (400 to 890 N) (Anusavice, 2013a). Also, LTD was induced at both the outer and inner surfaces of the crowns as confirmed by SEM imaging. This may differ from LTD induced under clinical situations since the inner surfaces of the crowns cemented to the abutments will not be exposed to any substantial humidity. Thus, it is reasonable to assume that the crowns in this study were tested under more severe conditions than in the clinical situations.

Cyclic loading neither induced the phase transformation nor affected the crown strength even when performed after autoclaving. In addition, no signs of phase transformation was detected with SEM analysis after cyclic loading. However, it is still possible that cyclic loading may have induced the phase transformation at localized areas around micro-cracks since the observations were limited to one cross-section per crown. Cyclic loading with an increased number of cycles might induce the phase transformation and/or generate micro-cracks, resulting in decreased strength. Indeed, Cotes et al. (Cotes et al., 2014) demonstrated that flexural strength decreased as a result of monoclinic phase generation, which was caused when zirconia discs were subjected to 15,000,000 cycles with a load of 200 N. With respect to dental zirconia prostheses, Kohorst et al. (Kohorst et al., 2008) demonstrated that cyclic loading with 1,000,000 cycles and an upper load limit of 100 N significantly decreased the strength of zirconia-based dental bridges. Thus, monolithic zirconia crowns may also be affected by cyclic loading with an increased

number of cycles though the stress distributions under cyclic loading for bridges and crowns will be different. In addition to the number of cycles, in the present study, a rubber sheet was inserted between the crown and indenter to avoid impact damage. That could be a reason for the discrepancy between the earlier reports and the present study. The rubber sheet may suppress the effect of cyclic loading. Before a generalized use of monolithic crowns can be recommended, the effect of point loading on fracture strength and monoclinic phase build-up ought to be evaluated.

6 CONCLUSION

- The biaxial flexural strength was influenced by large grains caused by higher sintering temperature (1575°C).
- Heat treatment mimicking veneering process did not affect the strength of 3Y-TZP.
- Tooth-colored 3Y-TZP containing Fe_2O_3 and Er_2O_3 at concentrations of 0.15 and 0.5 wt.%, respectively, possessed equivalent biaxial flexural strength to non-colored zirconia, and displayed higher resistance to LTD.
- The generation of the monoclinic phase with a fraction of approximately 70% and with a penetration depth of 10-14 μm after 100 h of autoclaving decreased the strength of 3Y-TZP.
- The monoclinic fraction on the surface of 3Y-TZP increased with autoclaving time, and then reached a plateau after 50 h while the depth of the monoclinic phase increased without reaching a plateau.
- The occlusal thickness significantly affected the fracture load of monolithic zirconia crowns but the axial thickness did not.
- The fracture load of the monolithic zirconia crowns with the occlusal thickness of 0.5 mm was significantly higher than that of lithium disilicate crowns with an occlusal thickness of 1.5 mm.
- The compressive strength of the cements differed significantly but did not significantly affect the fracture resistance of monolithic zirconia crowns.
- The monoclinic phase generated by autoclaving-induce LTD resulted in lower fracture resistance of the monolithic zirconia crowns, whereas cyclic loading did not affect the fracture resistance.
- The monolithic zirconia crowns seem to have sufficient strength even when assuming LTD occurs.

The knowledge obtained by the laboratory studies performed suggests that monolithic zirconia crowns with a minimal thickness of 0.5 mm will have the capability of being applied to the molar region with sufficient durability, providing there is a properly controlled fabrication process to avoid unexpected degradation of the material.

7 FUTURE PERSPECTIVES

Laboratory studies performed in this thesis show that monolithic zirconia crowns will withstand biting force in the molar regions. However, it is still uncertain how the value of the knowledge obtained about monolithic zirconia can be interpreted clinically. Although there are several recommendations for laboratory load-to-failure tests, more clinically relevant methods should be established to replicate the fracture of all-ceramic crowns in clinical service. More comprehensive fractographic analysis may provide important information in that sense. Standardizing the size of indenter, material of sheet interspersed between the indenter and crown, cross head speed of loading, and requirements for die material will make it possible to compare the results between different studies. Furthermore, the testing conditions for mechanical cycling should also be standardized. Number of cycles and load will be the most important variables. In this thesis, mechanical cycling was performed with 240,000 cycles, simulating one year of clinical service. Test with higher number of cycles will provide more clinically relevant information in terms of durability.

Besides the mechanical properties, aesthetic qualities of monolithic zirconia restorations should be improved. At present, it is difficult to match the color of the restorations to natural teeth though several shades are available. Thus, the aesthetic of monolithic zirconia restorations are inferior to that of other all-ceramic restorations, at least from a dentist perspective.

Detailed surface analyses including the implications of LTD on surface energy, bacterial colonization and wear behavior are at present inadequately studied and should be focused in the future.

The results obtained in laboratory studies should then be verified in clinical studies. Particularly needed, are randomized control trials where the survival and success rate of monolithic zirconia crowns, as well as patients' perception of aesthetic aspects are compared with those of other types of standard restorations, such as metal-ceramic crowns and other types of all-ceramic crowns. Specifically, long-term clinical results are necessary before a generalized use of monolithic zirconia crowns can be recommended.

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REFERENCES

1. Afferrante, L., Ciavarella, M., Valenza, E. (2006) Is Weibull's modulus really a material constant? Example case with interacting collinear cracks. *Int J Solids Struct* 43*:*5147-5157.
2. Akagawa, Y., Ichikawa, Y., Nikai, H., Tsuru, H. (1993) Interface histology of unloaded and early loaded partially stabilized zirconia endosseous implant in initial bone healing. *J Prosthet Dent* 69*:*599-604.
3. Akagawa, Y., Hosokawa, R., Sato, Y., Kamayama, K. (1998) Comparison between freestanding and tooth-connected partially stabilized zirconia implants after two years' function in monkeys: A clinical and histologic study. *J Prosthet Dent* 80*:*551-558.
4. Akesson, J., Sundh, A., Sjogren, G. (2009) Fracture resistance of all-ceramic crowns placed on a preparation with a slice-formed finishing line. *J Oral Rehabil* 36*:*516-523.
5. Ambre, M.J., Aschan, F., Vult von Steyern, P. (2013) Fracture strength of yttria-stabilized zirconium-dioxide (Y-TZP) fixed dental prostheses (FDPs) with different abutment core thicknesses and connector dimensions. *J Prosthodont* 22*:*377-382.
6. Andersson, B., Taylor, A., Lang, B.R., Scheller, H., Scharer, P., Sorensen, J.A. *et al.* (2001) Alumina ceramic implant abutments used for single-tooth replacement: A prospective 1- to 3-year multicenter study. *Int J Prosthodont* 14*:*432-438.
7. Andersson, B., Glauser, R., Maglione, M., Taylor, A. (2003) Ceramic implant abutments for short-span fpds: A prospective 5-year multicenter study. *Int J Prosthodont* 16*:*640-646.
8. Andersson, M., Oden, A. (1993) A new all-ceramic crown - A dense-sintered, high-purity alumina coping with porcelain. *Acta Odontol Scand* 51*:*59-64.
9. Anusavice, K.J. (2013a). Dental ceramics. In: Phillips' science of dental materials. K.J. Anusavice, C. Shen and H.R. Rawls editors. St. Louis, MO, USA: Saunders, pp. 418-473.
10. Anusavice, K.J. (2013b). Mechanical properties of dental materials. In: Phillips' science of dental materials. K.J. Anusavice, C. Shen and H.R. Rawls editors. St. Louis, MO, USA: Saunders, pp. 48-68.
11. Att, W., Kurun, S., Gerds, T., Strub, J.R. (2006a) Fracture resistance of single-tooth implant-supported all-ceramic restorations: An in vitro study. *J Prosthet Dent* 95*:*111-116.
12. Att, W., Kurun, S., Gerds, T., Strub, J.R. (2006b) Fracture resistance of single-tooth implant-supported all-ceramic restorations after exposure to the artificial mouth. *J Oral Rehabil* 33*:*380-386.
13. Att, W., Komine, F., Gerds, T., Strub, J.R. (2009) Marginal adaptation of three different zirconium dioxide three-unit fixed dental prostheses. *J Prosthet Dent* 101*:*239-247.

14. Attia, A., Kern, M. (2004) Influence of cyclic loading and luting agents on the fracture load of two all-ceramic crown systems. *J Prosthet Dent* 92*:*551-556.
15. Bachle, M., Butz, F., Hubner, U., Bakalinis, E., Kohal, R.J. (2007) Behavior of cal72 osteoblast-like cells cultured on zirconia ceramics with different surface topographies. *Clin Oral Implants Res* 18*:*53-59.
16. Ban, S., Anusavice, K.J. (1990) Influence of test method on failure stress of brittle dental materials. *J Dent Res* 69*:*1791-1799.
17. Ban, S., Sato, H., Suehiro, Y., Nakanishi, H., Nawa, M. (2008) Biaxial flexure strength and low temperature degradation of Ce-TZP/Al_2O_3 nanocomposite and Y-TZP as dental restoratives. *J Biomed Mater Res B* 87B*:*492-498.
18. Batson, E.R., Cooper, L.F., Duqum, I., Mendonca, G. (2014) Clinical outcomes of three different crown systems with CAD/CAM technology. *J Prosthet Dent* 112*:*770-777.
19. Behr, M., Rosentritt, M., Mangelkramer, M., Handel, G. (2003) The influence of different cements on the fracture resistance and marginal adaptation of all-ceramic and fiber-reinforced crowns. *Int J Prosthodont* 16*:*538-542.
20. Beuer, F., Schweiger, J., Edelhoff, D. (2008) Digital dentistry: An overview of recent developments for CAD/CAM generated restorations. *Br Dent J* 204*:*505-511.
21. Beuer, F., Schweiger, J., Eichberger, M., Kappert, H.F., Gernet, W., Edelhoff, D. (2009) High-strength CAD/CAM-fabricated veneering material sintered to zirconia copings - A new fabrication mode for all-ceramic restorations. *Dent Mater* 25*:*121-128.
22. Beuer, F., Stimmelmayr, M., Gueth, J.F., Edelhoff, D., Naumann, M. (2012) In vitro performance of full-contour zirconia single crowns. *Dent Mater* 28*:*449-456.
23. Bindl, A., Luthy, H., Mormann, W.H. (2006) Strength and fracture pattern of monolithic CAD/CAM-generated posterior crowns. *Dent Mater* 22*:*29-36.
24. Bindl, A., Mormann, W.H. (2007) Fit of all-ceramic posterior fixed partial denture frameworks in vitro. *Int J Periodontics Restorative Dent* 27*:*567-575.
25. Biscaro, L., Bonfiglioli, R., Soattin, M., Vigolo, P. (2013) An in vivo evaluation of fit of zirconium-oxide based ceramic single crowns, generated with two CAD/CAM systems, in comparison to metal ceramic single crowns. *J Prosthodont* 22*:*36-41.
26. Branemark, P.I., Adell, R., Breine, U., Hansson, B.O., Lindstrom, J., Ohlsson, A. (1969) Intra-osseous anchorage of dental prostheses. I. Experimental studies. *Scand J Plast Reconstr Surg* 3*:*81-100.
27. Bremer, F., Grade, S., Kohorst, P., Stiesch, M. (2011) In vivo biofilm formation on different dental ceramics. *Quintessence Int* 42*:*565-574.

28. Butz, F., Heydecke, G., Okutan, M., Strub, J.R. (2005) Survival rate, fracture strength and failure mode of ceramic implant abutments after chewing simulation. *J Oral Rehabil* 32*:*838-843.
29. Cales, B. (1998) Colored zirconia ceramics for dental applications. *Bioceramics* 11*:*591-594.
30. Carrillo de Albornoz, A., Vignoletti, F., Ferrantino, L., Cardenas, E., De Sanctis, M., Sanz, M. (2014) A randomized trial on the aesthetic outcomes of implant-supported restorations with zirconia or titanium abutments. *J Clin Periodontol* 41*:*1161-1169.
31. Catelas, I., Petit, A., Zukor, D.J., Marchand, R., Yahia, L., Huk, O.L. (1999) Induction of macrophage apoptosis by ceramic and polyethylene particles in vitro. *Biomaterials* 20*:*625-630.
32. Chevalier, J., Cales, B., Drouin, J.M. (1999) Low-temperature aging of Y-TZP ceramics. *J Am Ceram Soc* 82*:*2150-2154.
33. Chevalier, J., Deville, S., Munch, E., Jullian, R., Lair, F. (2004) Critical effect of cubic phase on aging in 3mol% yttria-stabilized zirconia ceramics for hip replacement prosthesis. *Biomaterials* 25*:*5539-5545.
34. Chevalier, J. (2006) What future for zirconia as a biomaterial? *Biomaterials* 27*:*535-543.
35. Chevalier, J., Gremillard, L., Deville, S. (2007) Low-temperature degradation of zirconia and implications for biomedical implants. *Ann Rev Mater Res* 37*:*1-32.
36. Chevalier, J., Gremillard, L., Virkar, A.V., Clarke, D.R. (2009) The tetragonal-monoclinic transformation in zirconia: Lessons learned and future trends. *J Am Ceram Soc* 92*:*1901-1920.
37. Christel, P., Meunier, A., Heller, M., Torre, J.P., Peille, C.N. (1989) Mechanical-properties and short-term invivo evaluation of yttrium-oxide-partially-stabilized zirconia. *J Biomed Mater Res* 23*:*45-61.
38. Christensen, G.J. (2011) The all-ceramic restoration dilemma: Where are we? *J Am Dent Assoc* 142*:*668-671.
39. Clarke, I.C., Manaka, M., Green, D.D., Williams, P., Pezzotti, G., Kim, Y.H. *et al.* (2003) Current status of zirconia used in total hip implants. *J Bone Joint Surg Am* 85-A Suppl 4*:*73-84.
40. Cotes, C., Arata, A., Melo, R.M., Bottino, M.A., Machado, J.P., Souza, R.O. (2014) Effects of aging procedures on the topographic surface, structural stability, and mechanical strength of a ZrO-based dental ceramic. *Dent Mater* 30: e396-404
41. Cottom, B., Mayo, M. (1996) Fracture toughness of nanocrystalline ZrO_2 - 3 mol% Y_2O_3 determined by vickers indentation. *Scripta Mater* 34*:*809-814.
42. Covacci, V., Bruzzese, N., Maccauro, G., Andreassi, C., Ricci, G.A., Piconi, C. *et al.* (1999) In vitro evaluation of the mutagenic and carcinogenic power of high purity zirconia ceramic. *Biomaterials* 20*:*371-376.

43. Curtis, A.R., Wright, A.J., Fleming, G.J.P. (2006) The influence of surface modification techniques on the performance of a Y-TZP dental ceramic. *J Dent* 34*:*195-206.
44. Degidi, M., Artese, L., Scarano, A., Perrotti, V., Gehrke, P., Piattelli, A. (2006) Inflammatory infiltrate, microvessel density, nitric oxide synthase expression, vascular endothelial growth factor expression, and proliferative activity in peri-implant soft tissues around titanium and zirconium oxide healing caps. *J Periodontol* 77*:*73-80.
45. Denry, I., Kelly, J.R. (2008) State of the art of zirconia for dental applications. *Dent Mater* 24*:*299-307.
46. Depprich, R., Zipprich, H., Ommerborn, M., Naujoks, C., Wiesmann, H.P., Kiattavorncharoen, S. *et al.* (2008) Osseointegration of zirconia implants compared with titanium: An in vivo study. *Head & face medicine* 4*:*30.
47. Deville, S., Gremillard, L., Chevalier, J., Fantozzi, G. (2005) A critical comparison of methods for the determination of the aging sensitivity in biomedical grade yttria-stabilized zirconia. *Appl Biomater* 72B*:*239-245.
48. Dhima, M., Carr, A.B., Salinas, T.J., Lohse, C., Berglund, L., Nan, K.A. (2014) Evaluation of fracture resistance in aqueous environment under dynamic loading of lithium disilicate restorative systems for posterior applications. Part 2. *J Prosthodont* 23*:*353-357.
49. Dion, I., Bordenave, L., Lefebvre, F., Bareille, R., Baquey, C., Monties, J.R. *et al.* (1994) Physico-chemistry and cytotoxicity of ceramics .2. Cytotoxicity of ceramics. *J Mater Sci-Mater M* 5*:*18-24.
50. Egawa, M., Miura, T., Kato, T., Saito, A., Yoshinari, M. (2013) In vitro adherence of periodontopathic bacteria to zirconia and titanium surfaces. *Dent Mater J* 32*:*101-106.
51. Elshazly, E.S., El-Hout, S.M., Ali, M.E.S. (2011) Yttria tetragonal zirconia biomaterials: Kinetic investigation. *J Mater Sci Technol* 27*:*332-337.
52. Estell, T.H., Flengas, S.N. (1970) The electrical properties of solid oxide electrolytes. *Chem Rev* 70*:*339-376.
53. Fabris, S., Paxton, A.T., Finnis, M.W. (2002) A stabilization mechanism of zirconia based on oxygen vacancies only. *Acta Mater* 50*:*5171-5178.
54. Flinn, B., deGroot, D., Mancl, L., Raigrodski, A.J. (2012) Accelerated aging characteristics of three yttria-stabilized tetragonal zirconia polycrystalline dental materials. *J Prosthet Dent* 108*:*223-230.
55. Garvie, R., Hannink, C., R, H., Pascoe, R., T. (1975) Ceramic steel? *Nature* 258*:*703-704.
56. Garvie, R.C., Nicholson, P.S. (1972) Structure and thermomechanical properties of partially stabilized zirconia in CaO-ZrO_2 system. *J Am Ceram Soc* 55*:*152-157.
57. Garvie, R.C., Urbani, C., Kennedy, D.R., Mcneuer, J.C. (1984) Biocompatibility of magnesia-partially stabilized zirconia (Mg-PSZ) ceramics. *J Mater Sci* 19*:*3224-3228.

58. Gehrke, P., Dhom, G., Brunner, J., Wolf, D., Degidi, M., Piattelli, A. (2006) Zirconium implant abutments: Fracture strength and influence of cyclic loading on retaining-screw loosening. *Quintessence Int* 37*:*19-26.
59. Giordano, R. (2006) Materials for chairside CAD/CAM-produced restorations. *J Am Dent Assoc* 137 Suppl*:*14S-21S.
60. Gremillard, L., Martin, L., Zych, L., Crosnier, E., Chevalier, J., Charbouillot, A. *et al.* (2013) Combining ageing and wear to assess the durability of zirconia-based ceramic heads for total hip arthroplasty. *Acta biomaterialia* 9*:*7545-7555.
61. Gross, M.D., Moser, J.B. (1977) A colorimetric study of coffee and tea staining of four composite resins. *J Oral Rehabil* 4*:*311-322.
62. Guazzato, M., Quach, L., Albakry, M., Swain, M.V. (2005) Influence of surface and heat treatments on the flexural strength of Y-TZP dental ceramic. *J Dent* 33*:*9-18.
63. Guess, P.C., Zavanelli, R.A., Silva, N.R., Bonfante, E.A., Coelho, P.G., Thompson, V.P. (2010) Monolithic CAD/CAM lithium disilicate versus veneered Y-TZP crowns: Comparison of failure modes and reliability after fatigue. *Int J Prosthodont* 23*:*434-442.
64. Guo, F.W., Xiao, P. (2012) Effect of Fe_2O_3 doping on sintering of yttria-stabilized zirconia. *J Eur Ceram Soc* 32*:*4157-4164.
65. Hahnel, S., Wieser, A., Lang, R., Rosentritt, M. (2014) Biofilm formation on the surface of modern implant abutment materials. *Clin Oral Implants Res*. Epub ahead of print
66. Hannink, R.H.J., Kelly, P.M., Muddle, B.C. (2000) Transformation toughening in zirconia-containing ceramics. *J Am Ceram Soc* 83*:*461-487.
67. Haraguchi, K., Sugano, N., Nishii, T., Miki, H., Oka, K., Yoshikawa, H. (2001) Phase transformation of a zirconia ceramic head after total hip arthroplasty. *J Bone Joint Surg Br* 83*:*996-1000.
68. Hensten, A., Gjerdet, N.R. (2013). Adverse reactions to dental materials. In: A textbook of fixed prosthodontics: The scandinavian approach. K. Nilner, S. Karlsson and B.L. Dahl editors. Stockholm, Sweden: Gothia Fortbildning, pp. 172-184.
69. Hisbergues, M., Vendeville, S., Vendeville, P. (2009) Zirconia: Established facts and perspectives for a biomaterial in dental implantology. *J Biomed Mater Res B Appl Biomater* 88B*:*519-529.
70. Hjerppe, J., Narhi, T., Froberg, K., Vallittu, P.K., Lassila, L.V. (2008) Effect of shading the zirconia framework on biaxial strength and surface microhardness. *Acta Odontol Scand* 66*:*262-267.
71. Holand, W., Schweiger, M., Frank, M., Rheinberger, V. (2000) A comparison of the microstructure and properties of the IPS Empress 2 and the IPS Empress glass-ceramics. *J Biomed Mater Res* 53*:*297-303.
72. Ichikawa, Y., Akagawa, Y., Nikai, H., Tsuru, H. (1992) Tissue compatibility and stability of a new zirconia ceramic in vivo. *J Prosthet Dent* 68*:*322-326.

73. Itinoche, K.M., Ozcan, M., Bottino, M.A., Oyafuso, D. (2006) Effect of mechanical cycling on the flexural strength of densely sintered ceramics. *Dent Mater* 22*:*1029-1034.
74. Johansson, C., Kmet, G., Rivera, J., Larsson, C., Vult Von Steyern, P. (2014) Fracture strength of monolithic all-ceramic crowns made of high translucent yttrium oxide-stabilized zirconium dioxide compared to porcelain-veneered crowns and lithium disilicate crowns. *Acta Odontol Scand* 72*:*145-153.
75. Johnson, C. (1983). Fracture statistics of multiple flaw distribution. In: Fracture mechanics of ceramics, vol 5. New York, USA: Plenum Press, pp. 365-386.
76. Kang, S.H., Chang, J., Son, H.H. (2013) Flexural strength and microstructure of two lithium disilicate glass ceramics for CAD/CAM restoration in the dental clinic. *Restor Dent Endod* 38*:*134-140.
77. Kaya, G. (2013) Production and characterization of self-colored dental zirconia blocks. *Ceram Int* 39*:*511-517.
78. Kelly, J.R. (1999) Clinically relevant approach to failure testing of all-ceramic restorations. *J Prosthet Dent* 81*:*652-661.
79. Kelly, J.R., Rungruanganunt, P., Hunter, B., Vailati, F. (2010) Development of a clinically validated bulk failure test for ceramic crowns. *J Prosthet Dent* 104*:*228-238.
80. Kelly, P.M., Ball, C.J. (1986) Crystallography of stress-induced martensitic transformations in partially-stabilized zirconia. *J Am Ceram Soc* 69*:*259-264.
81. Khor, K.A., Yang, J. (1997) Lattice parameters, tetragonality (c/a) and transformability of tetragonal zirconia phase in plasma-sprayed ZrO_2-Er_2O_3 coatings. *Mater Lett* 31*:*23-27.
82. Kim, H.T., Han, J.S., Yang, J.H., Lee, J.B., Kim, S.H. (2009) The effect of low temperature aging on the mechanical property & phase stability of Y-TZP ceramics. *J Adv Prosthodont* 1*:*113-117.
83. Kinney, J.H., Marshall, S.J., Marshall, G.W. (2003) The mechanical properties of human dentin: A critical review and re-evaluation of the dental literature. *Crit Rev Oral Biol Med* 14*:*13-29.
84. Kinney, J.H., Gladden, J.R., Marshall, G.W., Marshall, S.J., So, J.H., Maynard, J.D. (2004) Resonant ultrasound spectroscopy measurements of the elastic constants of human dentin. *J Biomech* 37*:*437-441.
85. Kobayashi, K., Kuwajima, H., Masaki, T. (1981) Phase-change and mechanical-properties of ZrO_2-Y_2O_3 solid electrolyte after aging. *Solid State Ionics* 3-4*:*489-493.
86. Kohal, R.J., Weng, D., Bachle, M., Strub, J.R. (2004) Loaded custom-made zirconia and titanium implants show similar osseointegration: An animal experiment. *J Periodontol* 75*:*1262-1268.
87. Kohorst, P., Herzog, T.J., Borchers, L., Stiesch-Scholz, M. (2007) Load-bearing capacity of all-ceramic posterior four-unit fixed partial dentures with different zirconia frameworks. *Eur J Oral Sci* 115*:*161-166.

88. Kohorst, P., Dittmer, M.P., Borchers, L., Stiesch-Scholz, M. (2008) Influence of cyclic fatigue in water on the load-bearing capacity of dental bridges made of zirconia. *Acta Biomater* 4*:*1440-1447.
89. Kondoh, J., Shiota, H., Kawachi, K., Nakatani, T. (2004) Yttria concentration dependence of tensile strength in yttria-stabilized zirconia. *J Alloy Compd* 365*:*253-258.
90. Kosmac, T., Oblak, C., Jevnikar, P., Funduk, N., Marion, L. (1999) The effect of surface grinding and sandblasting on flexural strength and reliability of Y-TZP zirconia ceramic. *Dent Mater* 15*:*426-433.
91. Kosmac, T., Oblak, C., Jevnikar, P., Funduk, N., Marion, L. (2000) Strength and reliability of surface treated Y-TZP dental ceramics. *J Biomed Mater Res* 53*:*304-313.
92. Lange, F.F. (1982) Transformation toughening. Part 3 Experimental-observations in the ZrO_2-Y_2O_3 system. *J Mater Sci* 17*:*240-246.
93. Larsson, C., Vult von Steyern, P., Nilner, K. (2010) A prospective study of implant-supported full-arch yttria-stabilized tetragonal zirconia polycrystal mandibular fixed dental prostheses: Three-year results. *Int J Prosthodont* 23*:*364-369.
94. Larsson, C., Vult Von Steyern, P. (2013) Implant-supported full-arch zirconia-based mandibular fixed dental prostheses. Eight-year results from a clinical pilot study. *Acta Odontol Scand* 71*:*1118-1122.
95. Larsson, C., Wennerberg, A. (2014) The clinical success of zirconia-based crowns: A systematic review. *Int J Prosthodont* 27*:*33-43.
96. Lawson, S. (1995) Environmental degradation of zirconia ceramics. *J Eur Ceram Soc* 15*:*485-502.
97. Le, M., Papia, E., Larsson, C. (2015) The clinical success of tooth- and implant-supported zirconia-based fixed dental prostheses. A systematic review. *J Oral Rehabil*. Epub ahead of print.
98. Li, P., Chen, I.W., Pennerhahn, J.E. (1994) Effect of dopants on zirconia stabilization - An X-ray-absorption. Study: I, Trivalent dopants. *J Am Ceram Soc* 77*:*118-128.
99. Li, R.W., Chow, T.W., Matinlinna, J.P. (2014) Ceramic dental biomaterials and CAD/CAM technology: State of the art. *J Prosthodont Res* 58*:*208-216.
100. Lindhe, J., Berglundh, T. (1998) The interface between the mucosa and the implant. *Periodontol 2000* 17*:*47-54.
101. Linkevicius, T., Apse, P. (2008) Influence of abutment material on stability of peri-implant tissues: A systematic review. *Int J Oral Maxillofac Implants* 23*:*449-456.
102. Lohmann, C.H., Dean, D.D., Koster, G., Casasola, D., Buchhorn, G.H., Fink, U. *et al.* (2002) Ceramic and PMMA particles differentially affect osteoblast phenotype. *Biomaterials* 23*:*1855-1863.
103. Lughi, V., Sergo, V. (2010) Low temperature degradation -aging- of zirconia: A critical review of the relevant aspects in dentistry. *Dent Mater* 26*:*807-820.

104.Mahmood, D.J., Linderoth, E.H., Von Steyern, P.V., Wennerberg, A. (2013) Fracture strength of all-ceramic (Y-TZP) three- and four-unit fixed dental prostheses with different connector design and production history. *Swed Dent J* 37*:*179-187.
105.Manicone, P.F., Rossi Iommetti, P., Raffaelli, L. (2007) An overview of zirconia ceramics: Basic properties and clinical applications. *J Dent* 35*:*819-826.
106.Masaki, T. (1986) Mechanical properties of Y-PSZ after aging at low temperature. *Int J High Tech Ceram* 2*:*85-98.
107.Milleding, P. (2012). Preparation design for traditional fixed full-crown restorations. In: Preparations for fixed prosthodontics. Denmark: Munksgaard, pp. 155-163.
108.Miyazaki, T., Hotta, Y., Kunii, J., Kuriyama, S., Tamaki, Y. (2009) A review of dental CAD/CAM: Current status and future perspectives from 20 years of experience. *Dent Mater J* 28*:*44-56.
109.Miyazaki, T., Nakamura, T., Matsumura, H., Ban, S., Kobayashi, T. (2013) Current status of zirconia restoration. *J Prosthodont Res* 57*:*236-261.
110.Mormann, W.H., Bindl, A., Luthy, H., Rathke, A. (1998) Effects of preparation and luting system on all-ceramic computer-generated crowns. *Int J Prosthodont* 11*:*333-339.
111.Munoz-Saldana, J., Balmori-Ramirez, H., Jaramillo-Vigueras, D., Iga, T., Schneider, G.A. (2003) Mechanical properties and low-temperature aging of tetragonal zirconia polycrystals processed by hot isostatic pressing. *J Mater Res* 18*:*2415-2426.
112.Nakamura, K., Kanno, T., Milleding, P., Ortengren, U. (2010) Zirconia as a dental implant abutment material: A systematic review. *Int J Prosthodont* 23*:*299-309.
113.Nascimento, C., Pita, M.S., Fernandes, F.H., Pedrazzi, V., de Albuquerque Junior, R.F., Ribeiro, R.F. (2014) Bacterial adhesion on the titanium and zirconia abutment surfaces. *Clin Oral Implants Res* 25*:*337-343.
114.Nimeroff, I. (1968) Colorimetry. *Natl Bureau Stand Monogr* 104*:*4-32.
115.Nkamgueu, E.M., Adnet, J.J., Bernard, J., Zierold, K., Kilian, L., Jallot, E. *et al.* (2000) In vitro effects of zirconia and alumina particles on human blood monocyte-derived macrophages: X-ray microanalysis and flow cytometric studies. *J Biomed Mater Res* 52*:*587-594.
116.Nothdurft, F.P., Pospiech, P.R. (2006) Clinical evaluation of pulpless teeth restored with conventionally cemented zirconia posts: A pilot study. *J Prosthet Dent* 95*:*311-314.
117.Odman, P., Andersson, B. (2001) Procera allceram crowns followed for 5 to 10.5 years: A prospective clinical study. *Int J Prosthodont* 14*:*504-509.
118.Oilo, M., Gjerdet, N.R., Tvinnereim, H.M. (2008) The firing procedure influences properties of a zirconia core ceramic. *Dent Mater* 24*:*471-475.
119.Oilo, M., Gjerdet, N.R. (2013) Fractographic analyses of all-ceramic crowns: A study of 27 clinically fractured crowns. *Dent Mater* 29*:*e78-84.

120. Oilo, M., Kvam, K., Tibballs, J.E., Gjerdet, N.R. (2013) Clinically relevant fracture testing of all-ceramic crowns. *Dent Mater* 29*:*815-823.
121. Oilo, M., Hardang, A.D., Ulsund, A.H., Gjerdet, N.R. (2014a) Fractographic features of glass-ceramic and zirconia-based dental restorations fractured during clinical function. *Eur J Oral Sci* 122*:*238-244.
122. Oilo, M., Kvam, K., Gjerdet, N.R. (2014b) Simulation of clinical fractures for three different all-ceramic crowns. *Eur J Oral Sci* 122*:*245-250.
123. Ortorp, A., Kihl, M.L., Carlsson, G.E. (2012) A 5-year retrospective study of survival of zirconia single crowns fitted in a private clinical setting. *J Dent* 40*:*527-530.
124. Papia, E., Larsson, C., du Toit, M., Vult von Steyern, P. (2014) Bonding between oxide ceramics and adhesive cement systems: A systematic review. *J Biomed Mater Res B Appl Biomater* 102*:*395-413.
125. Piconi, C., Burger, W., Richter, H.G., Cittadini, A., Maccauro, G., Covacci, V. *et al.* (1998) Y-TZP ceramics for artificial joint replacements. *Biomaterials* 19*:*1489-1494.
126. Piconi, C., Maccauro, G. (1999) Zirconia as a ceramic biomaterial. *Biomaterials* 20*:*1-25.
127. Pieger, S., Salman, A., Bidra, A.S. (2014) Clinical outcomes of lithium disilicate single crowns and partial fixed dental prostheses: A systematic review. *J Prosthet Dent* 112*:*22-30.
128. Pittayachawan, P., McDonald, A., Petrie, A., Knowles, J.C. (2007) The biaxial flexural strength and fatigue property of Lava Y-TZP dental ceramic. *Dent Mater* 23*:*1018-1029.
129. Pjetursson, B.E., Sailer, I., Zwahlen, M., Hammerle, C.H. (2007) A systematic review of the survival and complication rates of all-ceramic and metal-ceramic reconstructions after an observation period of at least 3 years. Part I: Single crowns. *Clin Oral Implants Res* 18 Suppl 3*:*73-85.
130. Preis, V., Behr, M., Kolbeck, C., Hahnel, S., Handel, G., Rosentritt, M. (2011) Wear performance of substructure ceramics and veneering porcelains. *Dent Mater* 27*:*796-804.
131. Preis, V., Behr, M., Hahnel, S., Handel, G., Rosentritt, M. (2012) In vitro failure and fracture resistance of veneered and full-contour zirconia restorations. *J Dent* 40*:*921-928.
132. Prestipino, V., Ingber, A. (1993a) Esthetic high-strength implant abutments. Part II. *J Esthet Dent* 5*:*63-68.
133. Prestipino, V., Ingber, A. (1993b) Esthetic high-strength implant abutments. Part I. *J Esthet Dent* 5*:*29-36.
134. Qeblawi, D.M., Munoz, C.A., Brewer, J.D., Monaco, E.A., Jr. (2010) The effect of zirconia surface treatment on flexural strength and shear bond strength to a resin cement. *J Prosthet Dent* 103*:*210-220.
135. Rekow, E.D., Harsono, M., Janal, M., Thompson, V.P., Zhang, G. (2006) Factorial analysis of variables influencing stress in all-ceramic crowns. *Dent Mater* 22*:*125-132.

136.Richerson, D. (2006a). Densification. In: Modern ceramic engineering: Properties, processing, and use in design Boca Raton, FL, USA: CRC Press, pp. 477-527.
137.Richerson, D. (2006b). Design approach. In: Modern ceramic engineering: Properties, processing, and use in design Boca Raton, FL, USA: CRC Press, pp. 581-594.
138.Rimondini, L., Cerroni, L., Carrassi, A., Torricelli, P. (2002) Bacterial colonization of zirconia ceramic surfaces: An in vitro and in vivo study. *Int J Oral Maxillofac Implants* 17*:*793-798.
139.Rosentritt, M., Behr, M., Gebhard, R., Handel, G. (2006) Influence of stress simulation parameters on the fracture strength of all-ceramic fixed-partial dentures. *Dent Mater* 22*:*176-182.
140.Rosentritt, M., Behr, M., Burgers, R., Feilzer, A.J., Hahnel, S. (2009) In vitro adherence of oral Streptococci to zirconia core and veneering glass-ceramics. *J Biomed Mater Res B Appl Biomater* 91*:*257-263.
141.Sailer, I., Feher, A., Filser, F., Gauckler, L.J., Luthy, H., Hammerle, C.H. (2007a) Five-year clinical results of zirconia frameworks for posterior fixed partial dentures. *Int J Prosthodont* 20*:*383-388.
142.Sailer, I., Pjetursson, B.E., Zwahlen, M., Hammerle, C.H. (2007b) A systematic review of the survival and complication rates of all-ceramic and metal-ceramic reconstructions after an observation period of at least 3 years. Part II: Fixed dental prostheses. *Clin Oral Implants Res* 18 Suppl 3*:*86-96.
143.Salihoglu, U., Boynuegri, D., Engin, D., Duman, A.N., Gokalp, P., Balos, K. (2011) Bacterial adhesion and colonization differences between zirconium oxide and titanium alloys: An in vivo human study. *Int J Oral Maxillofac Implants* 26*:*101-107.
144.Scarano, A., Piattelli, M., Caputi, S., Favero, G.A., Piattelli, A. (2004) Bacterial adhesion on commercially pure titanium and zirconium oxide disks: An in vivo human study. *J Periodontol* 75*:*292-296.
145.Scherrer, S.S., de Rijk, W.G. (1992) The effect of crown length on the fracture resistance of posterior porcelain and glass-ceramic crowns. *Int J Prosthodont* 5*:*550-557.
146.Scherrer, S.S., de Rijk, W.G. (1993) The fracture resistance of all-ceramic crowns on supporting structures with different elastic moduli. *Int J Prosthodont* 6*:*462-467.
147.Scherrer, S.S., de Rijk, W.G., Belser, U.C., Meyer, J.M. (1994) Effect of cement film thickness on the fracture resistance of a machinable glass-ceramic. *Dent Mater* 10*:*172-177.
148.Scherrer, S.S., Quinn, G.D., Quinn, J.B. (2008) Fractographic failure analysis of a procera allceram crown using stereo and scanning electron microscopy. *Dent Mater* 24*:*1107-1113.
149.Scherrer, S.S., Cattani-Lorente, M., Yoon, S., Karvonen, L., Pokrant, S., Rothbrust, F. *et al.* (2013) Post-hot isostatic pressing: A healing treatment

for process related defects and laboratory grinding damage of dental zirconia? *Dent Mater* 29*:*e180-190.
150. Schindler, H.J., Stengel, E., Spiess, W.E. (1998) Feedback control during mastication of solid food textures - A clinical-experimental study. *J Prosthet Dent* 80*:*330-336.
151. Scott, H., G. (1975) Phase relationships in the zirconia-yttria system. *J Mater Sci* 10*:*1527-1535.
152. Seydler, B., Rues, S., Muller, D., Schmitter, M. (2014) In vitro fracture load of monolithic lithium disilicate ceramic molar crowns with different wall thicknesses. *Clin Oral Investig* 18*:*1165-1171.
153. Shah, K., Holloway, J.A., Denry, I.L. (2008) Effect of coloring with various metal oxides on the microstructure, color, and flexural strength of 3Y-TZP *J Biomed Mater Res B Appl Biomater* 87*:*329-337.
154. Shannon, R.D. (1976) Revised effective ionic-radii and systematic studies of interatomic distances in halides and chalcogenides. *Acta Crystallographica Section A* 32*:*751-767.
155. Shetty, D.K., Rosenfield, A.R., Bansal, G.K., Duckworth, W.H. (1981) Biaxial fracture studies of a glass-ceramic. *J Am Ceram Soc* 64*:*1-4.
156. Siarampi, E., Kontonasaki, E., Andrikopoulos, K.S., Kantiranis, N., Voyiatzis, G.A., Zorba, T. *et al.* (2014) Effect of in vitro aging on the flexural strength and probability to fracture of Y-TZP zirconia ceramics for all-ceramic restorations. *Dent Mater*. E-pub ahead of print
157. Silva, V.V., Lameiras, F.S., Lobato, Z.I. (2002) Biological reactivity of zirconia-hydroxyapatite composites. *J Biomed Mater Res* 63*:*583-590.
158. Skouridou, N., Pollington, S., Rosentritt, M., Tsitrou, E. (2013) Fracture strength of minimally prepared all-ceramic cerec crowns after simulating 5 years of service. *Dent Mater* 29*:*e70-77.
159. Sornsuwan, T., Ellakwa, A., Swain, M.V. (2011) Occlusal geometrical considerations in all-ceramic pre-molar crown failure testing. *Dent Mater* 27*:*1127-1134.
160. Springate, S.D., Winchester, L.J. (1991) An evaluation of zirconium oxide brackets: A preliminary laboratory and clinical report. *Br J Orthod* 18*:*203-209.
161. Stawarczyk, B., Ozcan, M., Schmutz, F., Trottmann, A., Roos, M., Hammerle, C.H. (2013) Two-body wear of monolithic, veneered and glazed zirconia and their corresponding enamel antagonists. *Acta Odontol Scand* 71*:*102-112.
162. Stober, T., Bermejo, J.L., Rammelsberg, P., Schmitter, M. (2014) Enamel wear caused by monolithic zirconia crowns after 6 months of clinical use. *J Oral Rehabil* 41*:*314-322.
163. Sundh, A., Sjogren, G. (2004) A comparison of fracture strength of yttrium-oxide- partially-stabilized zirconia ceramic crowns with varying core thickness, shapes and veneer ceramics. *J Oral Rehabil* 31*:*682-688.

164. Swain, M.V. (1986) Grain-size depencence of toughness and transformability of 2 mol% Y-TZP ceramics. *J Mater Sci Lett* 5*:*1159-1162.
165. Swain, M.V., Rose, L.R.F. (1986) Strength limitations of transformation-toughened zirconia alloys. *J Am Ceram Soc* 69*:*511-518.
166. Tartaglia, G.M., Sidoti, E., Sforza, C. (2014) Seven-year prospective clinical study on zirconia-based single crowns and fixed dental prostheses. *Clin Oral Investig*. Epub ahead of print
167. Tete, S., Mastrangelo, F., Bianchi, A., Zizzari, V., Scarano, A. (2009) Collagen fiber orientation around machined titanium and zirconia dental implant necks: An animal study. *Int J Oral Maxillofac Implants* 24*:*52-58.
168. Tinschert, J., Natt, G., Mautsch, W., Augthun, M., Spiekermann, H. (2001) Fracture resistance of lithium disilicate-, alumina-, and zirconia-based three-unit fixed partial dentures: A laboratory study. *Int J Prosthodont* 14*:*231-238.
169. Torricelli, P., Verne, E., Brovarone, C.V., Appendino, P., Rustichelli, F., Krajewski, A. *et al.* (2001) Biological glass coating on ceramic materials: In vitro evaluation using primary osteoblast cultures from healthy and osteopenic rat bone. *Biomaterials* 22*:*2535-2543.
170. Tsitrou, E.A., Helvatjoglu-Antoniades, M., van Noort, R. (2010) A preliminary evaluation of the structural integrity and fracture mode of minimally prepared resin bonded CAD/CAM crowns. *J Dent* 38*:*16-22.
171. Tsukuma, K., Kubota, Y., Tsukidate, T. (1984). Thermal and mechanical properties of Y_2O_3-stabilized tetragonal zirconia polycrystals. In: Advances in ceramics vol 12, science and technology of zirconia ii. N. Claussen, M. Ruhle and A. Heuer editors. Columbus, Ohio, USA: The American Ceramic Society, pp. 382-390.
172. Vallittu, P.K., Kononen, M. (2013). Biomechanical aspects and material properties. In: A textbook of fixed prosthodontics: The scandinavian approach. K. Nilner, S. Karlsson and B.L. Dahl editors. Stockholm, Sweden: Gothia Fortbildning, pp. 152-171.
173. Vamnes, J.S., Lygre, G.B., Gronningsaeter, A.G., Gjerdet, N.R. (2004) Four years of clinical experience with an adverse reaction unit for dental biomaterials. *Community Dent Oral Epidemiol* 32*:*150-157.
174. van Noort, R., Gjerdet, N.R., Schedle, A., Bjorkman, L., Berglund, A. (2004) An overview of the current status of national reporting systems for adverse reactions to dental materials. *J Dent* 32*:*351-358.
175. Vigolo, P., Mutinelli, S. (2012) Evaluation of zirconium-oxide-based ceramic single-unit posterior fixed dental prostheses (FDPs) generated with two CAD/CAM systems compared to porcelain-fused-to-metal single-unit posterior FDPs: A 5-year clinical prospective study. *J Prosthodont* 21*:*265-269.
176. Virkar, A.V., Huang, J.L., Cutler, R.A. (1987) Strengthening of oxide ceramics by transformation-induced stresses. *J Am Ceram Soc* 70*:*164-170.

177. Vult von Steyern, P. (2013). Dental ceramics in clinical practice. In: A textbook of fixed prosthodontics: The Scandinavian approach. K. Nilner, S. Karlsson and B.L. Dahl editors. Stockholm, Sweden: Gothia Fortbildning, pp. 205-222.
178. Wagner, W.C., Chu, T.M. (1996) Biaxial flexural strength and indentation fracture toughness of three new dental core ceramics. *J Prosthet Dent* 76*:*140-144.
179. Walter, M.H., Wolf, B.H., Wolf, A.E., Boening, K.W. (2006) Six-year clinical performance of all-ceramic crowns with alumina cores. *Int J Prosthodont* 19*:*162-163.
180. Waltimo, A., Kononen, M. (1994) Bite force on single as opposed to all maxillary front teeth. *Scand J Dent Res* 102*:*372-375.
181. Waltimo, A., Nystrom, M., Kononen, M. (1994) Bite force and dentofacial morphology in men with severe dental attrition. *Scand J Dent Res* 102*:*92-96.
182. Webber, B., McDonald, A., Knowles, J. (2003) An in vitro study of the compressive load at fracture of procera allceram crowns with varying thickness of veneer porcelain. *J Prosthet Dent* 89*:*154-160.
183. Welander, M., Abrahamsson, I., Berglundh, T. (2008) The mucosal barrier at implant abutments of different materials. *Clin Oral Implants Res* 19*:*635-641.
184. Wenz, H.J., Bartsch, J., Wolfart, S., Kern, M. (2008) Osseointegration and clinical success of zirconia dental implants: A systematic review. *Int J Prosthodont* 21*:*27-36.
185. Wiskott, H.W., Nicholls, J.I., Belser, U.C. (1995) Stress fatigue: Basic principles and prosthodontic implications. *Int J Prosthodont* 8*:*105-116.
186. Wolf, D., Bindl, A., Schmidlin, P.R., Luthy, H., Mormann, W.H. (2008) Strength of CAD/CAM-generated esthetic ceramic molar implant crowns. *Int J Oral Maxillofac Implants* 23*:*609-617.
187. Yamamuro, T. (2004). Bioceramics. In: Biomechanics and biomaterials in orthopedics. G. Dominique and M. Poitout editors. London: Springer, pp. 22-33.
188. Yamane, K., Ayukawa, Y., Takeshita, T., Furuhashi, A., Yamashita, Y., Koyano, K. (2013) Bacterial adhesion affinities of various implant abutment materials. *Clin Oral Implants Res* 24*:*1310-1315.
189. Yashima, M., Nagatome, T., Noma, T., Ishizawa, N., Suzuki, Y., Yoshimura, M. (1995) Effect of dopant species on tetragonal (t')-to-monoclinic phase-transformation of arc-melted ZrO_2-$RO_{1.5}$ (R=Sm, Y, Er, and Sc) in water at 200°c and 100 mpa pressure. *J Am Ceram Soc* 78*:*2229-2232.
190. Yildirim, M., Fischer, H., Marx, R., Edelhoff, D. (2003) In vivo fracture resistance of implant-supported all-ceramic restorations. *J Prosthet Dent* 90*:*325-331.
191. Yoshimura, M., Noma, T., Kawabata, K., Somiya, S. (1987) Role of H_2O on the degradation process of Y-TZP. *J Mater Sci Lett* 6*:*465-467.

192. Yoshimura, M. (1988) Phase-stability of zirconia. *Am Ceram Soc Bull* 67*:*1950-1955.
193. Youssef, R.E., Throckmorton, G.S., Ellis, E., 3rd, Sinn, D.P. (1997) Comparison of habitual masticatory patterns in men and women using a custom computer program. *J Prosthet Dent* 78*:*179-186.
194. Yucel, M.T., Yondem, I., Aykent, F., Eraslan, O. (2012) Influence of the supporting die structures on the fracture strength of all-ceramic materials. *Clin Oral Investig* 16*:*1105-1110.
195. Zahran, M., El-Mowafy, O., Tam, L., Watson, P.A., Finer, Y. (2008) Fracture strength and fatigue resistance of all-ceramic molar crowns manufactured with CAD/CAM technology. *J Prosthodont* 17*:*370-377.
196. Zembic, A., Kim, S., Zwahlen, M., Kelly, J.R. (2014a) Systematic review of the survival rate and incidence of biologic, technical, and esthetic complications of single implant abutments supporting fixed prostheses. *Int J Oral Maxillofac Implants* 29 Suppl*:*99-116.
197. Zembic, A., Philipp, A.O., Hammerle, C.H., Wohlwend, A., Sailer, I. (2014b) Eleven-year follow-up of a prospective study of zirconia implant abutments supporting single all-ceramic crowns in anterior and premolar regions. *Clin Implant Dent Relat Res.* Epub ahead of print
198. Zeng, K., Oden, A., Rowcliffe, D. (1996) Flexure tests on dental ceramics. *Int J Prosthodont* 9*:*434-439.
199. Zesewitz, T.F., Knauber, A.W., Northdurft, F.P. (2014) Fracture resistance of a selection of full-contour all-ceramic crowns: An in vitro study. *Int J Prosthodont* 27*:*264-266.
200. Zitzmann, N.U., Galindo, M.L., Hagmann, E., Marinello, C.P. (2007) Clinical evaluation of procera allceram crowns in the anterior and posterior regions. *Int J Prosthodont* 20*:*239-241.