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Gabriel Kalil Rocha Pereira

COMPORTAMENTO MECÂNICO E FADIGA DE CERÂMICAS Y-TZP: EFEITO DO DESGASTE E DO ENVELHECIMENTO

Santa Maria, RS
2016

Gabriel Kalil Rocha Pereira

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Tese apresentada ao Curso de Doutorado do Programa de Pós-Graduação em Ciências Odontológicas, Área de Concentração em Odontologia, ênfase em Prótese Dentária, da Universidade Federal de Santa Maria (UFSM, RS), como requisito parcial para obtenção do título de **Doutor em Ciências Odontológicas**.

Orientador: Prof. Dr. Luiz Felipe Valandro

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“A menos que modifiquemos a nossa maneira de pensar,
não seremos capazes de resolver os problemas causados
pela forma como nos acostumamos a ver o mundo”.

(Albert Einstein)

RESUMO

COMPORTAMENTO MECÂNICO E FADIGA DE CERÂMICAS Y-TZP: EFEITO DO DESGASTE E DO ENVELHECIMENTO

AUTOR: GABRIEL KALIL ROCHA PEREIRA
ORIENTADOR: LUIZ FELIPE VALANDRO

Este estudo objetivou a avaliar (1) as alterações superficiais (topografia e rugosidade); (2) o comportamento mecânico (estabilidade estrutural – percentual de fase monoclínica, resistência a flexão biaxial, confiabilidade estrutural – análise de Weibull); e (3) o comportamento a fadiga (limite de fadiga) de cerâmicas Y-TZP em relação a dois fatores: "desgaste" e " envelhecimento". Primeiramente foi avaliado o comportamento mecânico de uma nova cerâmica Y-TZP para confecção de restaurações monolíticas através da confecção de discos (N=180) segundo as instruções da ISO-6872:2008 para ensaios de flexão avaliando os dois fatores em estudo. Em um segundo momento, baseado na falta de consenso na literatura a cerca do real efeito (positivo ou negativo) da degradação hidrotérmica em autoclave sobre o comportamento mecânico de cerâmicas Y-TZP foi realizada uma revisão sistemática com meta-análise de estudos in vitro avaliando este tema. Em um terceiro momento, foi feita uma comparação entre os diferentes protocolos de envelhecimento mais utilizados na literatura, em discos cerâmicos, segundo a ISO-6872:2008, avaliando uma condição adicional de associação de estímulos aos quais este material é corriqueiramente submetido em um cenário clínico. Em um quarto momento, foi avaliado o comportamento sob fadiga de duas cerâmicas Y-TZP (uma para confecção de infraestruturas de próteses dentárias parciais fixas – N=80 discos, e outra para restaurações monolíticas – N=80 discos) levando em consideração ambos fatores em estudo. Em um quinto momento, foi executada uma revisão sistemática com metanálise buscando elucidar o efeito do desgaste sobre o comportamento mecânico, avaliando o efeito dos diferentes parâmetros envolvidos nesse procedimento. Baseado nos estudos laboratóriais há indícios de que tanto o desgaste quanto o envelhecimento utilizado não promoveram um efeito deletério nas propriedades mecânicas da Y-TZP, já que foi observado aumento de resistência característica e de limite de fadiga estatisticamente significantes em resposta ao mecanismo de tenacificação promovido pelo aumento de fase monoclínica na superfície deste material. Baseado nas revisões sistemáticas e meta-análises ficou claro o efeito dos parâmetros utilizados para o envelhecimento em autoclave nas propriedades mecânicas da Y-TZP, onde observa-se que o autoclave é uma ferramenta efetiva em promover a LTD, se utilizados parâmetros como: pelo menos 2 bar de pressão, tempo maior que 20 horas e temperaturas de pelo menos 134°; quanto aos efeitos do desgaste observou-se que é possível desgastar sem comprometer a resistência do material, sendo que baixas velocidades, instrumentos de menor granulação e irrigação abundante são fundamentais para diminuir o risco de introdução de defeitos críticos que acarretariam efeitos deletérios sobre as propriedades mecânicas da cerâmica.

Palavras-chave: Envelhecimento. Tratamentos de superfície. Materiais odontológicos. Prótese dentária. Zircônia parcialmente estabilizada por óxido de ítrio.

ABSTRACT

MECHANICAL AND FATIGUE BEHAVIOUR OF Y-TZP CERAMICS: EFFECT OF GRINDING AND AGING

AUTHOR: GABRIEL KALIL ROCHA PEREIRA
ADVISER: LUIZ FELIPE VALANDRO

This study aimed to evaluate the, (1) surface changes (topography and roughness); (2) mechanical behaviour (structural stability – monoclinic phase content, biaxial flexural strength and structural reliability – Weibull analysis); and (3) fatigue behaviour (fatigue limit) of Y-TZP ceramics taking into consideration two main factors: "grinding" and "aging". First, it was evaluated the mechanical behaviour of a new Y-TZP material for monolithic restorations using discs (N=180) in accordance to ISO-6872:2008 guidelines for ceramic flexural strength testing. In a second moment, based on the contradictory existing literature regarding the real effect (positive or negative) of hydrothermal degradation in autoclave on the mechanical behaviour of Y-TZP ceramics, it was performed a systematic review and meta-analysis of in vitro studies aiming to clarify this topic. In a third moment the effects of the most used aging methodologies at the mechanical behaviour of Y-TZP discs were compared, considering additionally one condition associating stimuli commonly observed in clinical scenarios. In a fourth step, it was evaluated the fatigue behaviour of two Y-TZP ceramics (one for frameworks of fixed partial dental prosthesis – N=80 discs, and one for monolithic restorations – N=80 discs) according to ISO-6872:2008 taking into consideration both factors previously descripted. In a fifth step, it was executed a systematic review and metanalysis for the effect of grinding, considering each parameter involved on grinding protocol. Our findings indicate that grinding and aging do not impact deleteriously on the material (Y-TZP) mechanical properties. In fact, it was observed a statistical increase for characteristic strength and fatigue limit in response to the toughening mechanism promoted by tetragonal to monoclinic phase transformation at the superficial grains (increase on monoclinic phase content). Based on the systematic reviews and metanalysis it was clear that the aging parameters used in the autoclave, define the final effect on the material mechanical properties, where it was noticed that at least 2 bar pressure for periods longer than 20 hours, with temperature above 134°C should be employed; regarding grinding it could be noticed that it is possible to grind the ceramic surface without compromise it`s mechanical properties. For that slow-speed motor, low-grit size instruments and abundant coolant are mandatory to decrease the risk of critical defect introduction that could be deleterious to the material mechanical properties.

Key Words: Aging. Surface treatments. Dental prosthesis. Dental materials. Zirconium oxide partially stabilized by yttrium.

SUMÁRIO

1. INTRODUÇÃO GERAL

A alta demanda por materiais que propiciem estética, biosegurança e propriedades mecânicas superiores, têm instigado o desenvolvimento de novos materiais dentários para Odontologia Restauradora. Dentre estes, vêm se destacando a aplicação de restaurações monolíticas *full-contour* de zircônia (Y-TZP, Yttrium-stabilized Tetragonal Zirconia Polycristal) (DENRY; KELLY, 2014).

A zircônia é um material policristalino metaestável (PICCONI; MACCAURO, 1999) que quando submetido a estímulo físico e/ou químico responde através de uma transformação de fase (tetragonal para monoclínica) que resulta em uma expansão volumétrica localizada levando ao fechamento de defeitos/trincas pré-existentes, dificultando a propagação (falha catastrófica) destas (CHEVALIER; GREMILLARD; DEVILLE, 2007; GARVIE; NICHOLSON, 1972; HANNINK, 2000; PEREIRA et a;., 2015^{a}; PEREIRA et al., 2015^{b}).

Chevalier, Gremillard e Deville, 2007, demonstraram que alguns fatores são determinantes para as propriedades ópticas, mecânicas e de susceptibilidade a degradação dessa cerâmica, como: tamanho do grão, densidade, conteúdo de estabilizante utilizado, homogeneidade de distribuição (harmonização dos componentes), ciclo de sinterização, e quantidade de tensão residual interna (introduzida em diferentes momentos durante o processamento).

Desde o evento Prozyr em 2001, onde milhares de próteses de quadril de zircônia fraturaram precocemente, grandes avanços no processamento da zircônia foram alcançados, o que resultou em cerâmicas Y-TZP com adequadas propriedades óticas, mecânicas e de resistência a degradação disponíveis para o uso em Odontologia (CHEVALIER; GREMILLARD; DEVILLE, 2007). Entre estes avanços, destaca-se o advento da zircônia translúcida (por exemplo, Zirlux FC *full-contour* Zirconia, Ardent; Zenostar T, Wieland Dental; Katana^{TM} Zirconia, Kuraray Noritake Dental; In-Ceram YZ HT, VITA).

Clinicamente, diversos cenários podem levar a necessidade da confecção de próteses parciais fixas dentárias para restabelecimento estético e funcional. Inicialmente, a alternativa proposta era a confecção de uma infraestrutura de zircônia que posteriormente seria recoberta por uma porcelana feldspática. Esta combinação resulta em excelente estética, e acreditava-se que pela existência de uma infraestrutura altamente resistente de zircônia o conjunto seria resistente, entretanto, estudos clínicos observaram altas taxas de falha por delaminação (*chipping*) da cerâmica de cobertura (BEUER et al., 2010; CHAAR; KERN, 2015; PIHLAJA; NAPANKANGAS; RAUSTIA, 2016).

Desta forma, restaurações monolíticas surgem como uma alternativa viável onde dispensa-se a aplicação de uma porcelana de cobertura e assim, elimina-se o problema de *chipping* (BEUER et al., 2012; NAKAMURA et al., 2015; SABRAH et al., 2013). Adicionalmente, essa configuração permite a redução da espessura de material restaurador o que resulta em um preparo ainda mais conservador (DENRY; KELLY, 2014). Estas características são altamente atrativas para Odontologia Restauradora, porque amplia-se a aplicabilidade do material e permite a solução de situação complexas, como por exemplo onde há pouco espaço interoclusal.

É importante destacar que apesar da alta precisão alcançada pelos sistemas de usinagem CAD/CAM (Computer Aided Design/ Computer Aided Machining), ajustes (usualmente executados com brocas diamantadas) são comumente necessários objetivando um perfeito contato oclusal, proximal e um adequado perfil emergencial da peça protética (ABOUSHELIB; FEILZER; KLEVERLAAN, 2009; JING et al., 2014; PEREIRA et al., 2014; PEREIRA et al., 2015[a]; PREIS et al., 2015), entretanto até o momento pouco se sabe sobre as consequências a longo prazo desses ajustes, desta forma os fabricantes têm recomendado que este procedimento de ajuste seja evitado, mas quando necessário deve ser executado com muita cautela para evitar introdução de defeitos.

Nitidamente uma caracterização do comportamento da zircônia após tratamento de superfície (desgaste), assim como da susceptibilidade a degradação à baixas temperaturas (*low-temperature degradation* – LTD) se torna necessária, já que os desfechos causados por procedimentos de ajuste corriqueiramente necessários na clínica não são claros; e não existe consenso na literatura a cerca da susceptibilidade a degradação das propriedades mecânicas que este material pode sofrer quando submetido a um ambiente hostil (como o ambiente oral), especialmente se considerado condições de fatores associados (em exemplo: fadiga + degradação à baixas temperaturas; ajustes + envelhecimento).

Por tanto, essa tese se objetiva a avaliar/caracterizar os efeitos do desgaste com pontas diamantadas e do envelhecimento de cerâmicas Y-TZP indicadas para confecção de infraestruturas de próteses parciais fixas e restaurações monolíticas, tendo em vista os desfechos: (1) alterações superficiais (análises topográficas em MEV e AFM; assim como rugosidade parâmetros Ra e Rz); (2) comportamento mecânico (estabilidade estrutural – percentual de fase monoclínica, resistência a flexão biaxial, confiabilidade estrutural – análise de Weibull); (3) comportamento a fadiga (limite de fadiga).

Para efeitos de apresentação esta Tese intitulada **"Comportamento Mecânico e fadiga de cerâmicas Y-TZP: Efeito do desgaste e do envelhecimento"** foi formatada em cinco estudos:

ARTIGO 1 – Mechanical behaviour of a Y-TZP ceramic for monolithic restorations: Effect of grinding and low-temperature aging.
Publicado em "*Materials Science and Engineering C: Materials for Biological Applications*" - *Fator de impacto = 3.420; Qualis A2.*

ARTIGO 2 – Low-temperature degradation of Y-TZP ceramics: a systematic review and meta-analysis of in vitro studies.
Publicado em "*Journal of the Mechanical Behavior of Biomedical Materials*" - *Fator de impacto = 2.876; Qualis A2*

ARTIGO 3 – Comparison of different low-temperature aging protocols: its effects on the mechanical behavior of Y-TZP ceramics.
Publicado em "*Journal of the Mechanical Behavior of Biomedical Materials*" - *Fator de impacto = 2.876; Qualis A2*

ARTIGO 4 – Fatigue limit of polycrystalline zirconium oxide ceramics: Effect of grinding and low-temperature aging.
Publicado em "*Journal of the Mechanical Behavior of Biomedical Materials*" - *Fator de impacto = 2.876; Qualis A2*

ARTIGO 5 – The effect of grinding on the mechanical behavior of Y-TZP ceramics: a systematic review and meta-analyses.
Submetido para "*Journal of the Mechanical Behavior of Biomedical Materials*" - *Fator de impacto = 2.876; Qualis A2*

2. ARTIGO 1 - Mechanical behavior of a Y-TZP ceramic for monolithic restorations: effect of grinding and low-temperature aging

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Running title: Effect of grinding and LTD on Y-TZP.

Abstract

This study aimed to investigate the effects of grinding with diamond burs and low-temperature aging on the mechanical behavior (biaxial flexural strength and structural reliability), surface topography, and phase transformation of a Y-TZP ceramic for monolithic restorations. Disc-shaped specimens (Zirlux FC, Ivoclar Vivadent) were manufactured according to ISO:6872-2008 and divided in accordance with two factors: "grinding – 3 levels" and "LTD – 2 levels". Grinding was performed using a contra-angle handpiece under constant water-cooling with different grit-sizes (extra-fine and coarse diamond burs). LTD was simulated in an autoclave at 134ºC, under a pressure of 2 bar, over a period of 20 h. Surface topography analysis showed an increase in roughness based on surface treatment grit-size (Coarse>Xfine>Ctrl), LTD did not influence roughness values. Both grinding and LTD promoted an increase in the amount of m-phase, although different susceptibilities to degradation were observed. According to existing literature the increase of m-phase content is a direct indicative of Y-TZP degradation. Weibull analysis showed an increase in characteristic strength after grinding (Coarse=Xfine>Ctrl), while for LTD, distinct effects were observed (Ctrl<Ctrl LTD; Xfine=Xfine LTD and Coarse=Coarse LTD). Weibull moduli were statistically similar between all tested groups. Within the limits of this current study, it was feasible to notice that both aging in autoclave for 20 h (LTD) and grinding showed not to be detrimental to the mechanical properties of Zirlux FC Y-TZP ceramic.

Key Words: Low-temperature Degradation. Dental prosthesis. Dental materials. Surface treatments. Mechanical Properties. Flexural strength. Zirconium oxide partially stabilized by yttrium.

1. Introduction

Currently, there is a large number of dental materials and ceramic systems available for clinical use (Denry & Kelly, 2014). Among these options, the scientific community has been demonstrating great interest in Y-TZP ceramic (Yttrium-stabilized Tetragonal Zirconia Polycristal), mainly motivated by the high strength that such materials present (Piconi & Maccauro, 1999; Lazar et al., 2008) it has been applied in a wide range of applications for dental restorations (unit or multi-unit fixed dental prostheses) (Denry & Kelly, 2014).

Initially, Y-TZP was used to manufacture the infrastructure of fixed partial dentures that is covered by feldspathic porcelain, associating good strength and esthetics (Denry & Kelly, 2008). This alternative, although promising, when assessed in clinical trials (Monaco et al., 2015; Christensen & Ploeger 2010; Raigrodski et al., 2006; Sailer et al., 2007, Beuer et al., 2010) presented the chipping or fracture of the veneering porcelain as the main reason for failure. One obvious solution recently proposed for this problem is the monolithic full-contour restorations of zirconia (Beuer et al., 2012; Sabrah et al. 2013; Nakamura et al. 2015), which, in addition to extinguishing chipping and fracturing of the veneering porcelain, allows a more conservative tooth preparation as it requires a thinner thickness, making the application of a veneering porcelain dispensable.

Zirconia is a polymorphic metastable material (Piconi & Maccauro, 1999) that when used as monolithic restoration will be daily exposed directly to different stimuli such as oral mastication forces, exposure to water and different temperatures, pH changes, and oral microorganisms (Chevalier et al., 2007; Inokoshi et al., 2015; Lucas et al., 2015[a]; Cotes et al., 2014; Egilmez et al., 2014; Turp et al., 2012, Bordin et al., 2015). In addition to the fact that after the restoration machining at CAD/CAM systems (computer aided design/ computer aided machining), adjustments (with diamond grinding instruments) are usually needed in order to achieve a better adaptation and an adequate emergency profile (Aboushelib et al., 2009; Iseri et al., 2012; Amaral et al., 2013; Pereira GKR et al., 2014; 2015a).

Literature shows that these distinct stimuli may trigger a tetragonal (*t*) to monoclinic (*m*) phase transformation; in addition to superficial alterations (Chevalier et al., 2007; Denry & Kelly, 2014). Literature states that the increase of *m*-phase content is directly related with the degradation of the zirconia material (low-temperature degradation - LTD) (Chevalier et al., 2007; Muñoz-Tabares et al., 2012; Kim et al., 2009; Ban et al., 2008) and as this degradation mechanism develops, it might promote superficial alterations and a consequent deleterious impact on the zirconia's mechanical properties, which compromises the predictability of longevity of the prosthetic rehabilitation (Kobayashi et al., 1981; Kim et al., 2009; Lughi & Sergo, 2010; Chevalier, 2007; Pereira et al., 2015b).

Chevalier et al. (2007) states that the material's susceptibility to *t-m* phase transformation will depend on: density, stabilizer content, grain size, processing characteristics (i.e. homogeneity, manufacturing, preparation) and presence of residual stress. Being so, it appears that Y-TZP's response when submitted to stimuli will be material dependent (any change on materials characteristics could lead to a distinct response). Zhang (2014) show that one alternative that has been used to enhance optical properties (translucency) of Y-TZP for monolithic restorations is the reduction of grain size. Thus it is expected that those new materials will present to be less sensitive to t-m phase transformation (Lucas et al., 2015[b]), which theoretically will make the material more resistant to LTD, although simultaneously it would decrease the potential of the transformation toughening mechanism.

The recommendation of Y-TZP full-contour monolithic restorations could bring clear advantages but, there is little information on literature regarding the susceptibility to LTD of these new Y-TZP materials recently introduced in the Dental Market, especially regarding the interaction between the effect of grinding and the different stimuli present at oral environment (previously described). Thus, before the recommendation of Y-TZP monolithic restoration, scientific community needs to extensively explore this topic. For that, *in vitro* laboratorial tests, although present inherent difficulties to simulate all these conditions, may generate important insights, disregard this important step may bring irreversible consequences like the Prozir episode in 2001, where thousands of Y-TZP femoral heads failed because they presented an increased susceptibility to LTD effects (Chevalier et al., 2007).

Therefore, the following research aimed to evaluate the effect of adjustments (grinding with diamond burs, as it is a procedure commonly executed clinically, having literature showed that it could impact on the material's susceptibility to degradation) and low-temperature aging in a steam autoclave (most used aging methodology that combines water and temperature stimuli) on the mechanical behavior of a ceramic for Y-TZP monolithic restorations. The hypothesis tested is that both (1) grinding with extra-fine/coarse diamond burs and (2) low-temperature aging will be deleterious to zirconia's mechanical properties.

2. Materials and Methods

2.1 Sample preparation

Disc-shaped specimens (N=180) were manufactured according to ISO:6872-2008. As *full-contour* zirconia (LOT 637328 Rev.2, Zirlux FC, Ivoclar Vivadent, Amherst, EUA) is provided by the manufacturer only in a disc shape format (100 mm diameter), it was necessary to manually slice this block, with diamond disc (Diamond Disc #7045 - Macro total double faced with big roles, KG Sorensen, Cotia, Brazil) coupled to an electric motor (perfecta 300, W&H Dentalwerk Burmoos GmbH, Burmoos, Austria) under 12000 rpm, into smaller rectangular blocks (20 mm long x 20 mm wide), afterwards one metal cylinder was bonded at each side of the ceramic block in order to transform the rectangular blocks into cylinders (18 mm diameter) using a 600–1200 grit SiC paper (3M, St. Paul, MN, USA) under water-cooling. Thereby, slices were obtained with 1.6 mm thickness using a precision saw (ISOMET 1000, Buehler, Lake Bluff, IL, USA).

In order to remove irregularities inherent to the specimens' preparation, the surfaces were fine ground with 1200 grit SiC paper and cleaned in an ultrasonic bath (1440 D – Odontrobras, Ind. E Com. Equip. Méd. Odonto. LTDA, Ribeirao Preto, Brazil) using 78%

isopropyl alcohol for 10 min. Conclusively, the specimens were sintered (Zyrcomat T, Vita Zahnfabrik, Bad Sackingen, Germany) according to the manufacturer's instructions (heat rate 1: 10°C/min until 600°C, dwell time: 0:00 min; heat rate 2: 5°C/min until 1500°C; dwell time: 120 min; followed by slow cooling with furnace opening at temperatures below 500°C), resulting in discs with final dimensions of approximately 15 mm (diameter) and 1.2 mm (thickness). Samples presenting discrepancies in length above the standard variation preconized by ISO:6872-2008 (1.2 ± 0.2mm) were discarded, and the remaining samples (n=30) were divided according to grinding conditions (three levels) and aging (two levels), as shown in Table 1.

2.2 Surface treatment

Samples from the control group (Ctrl) remained untouched after the sintering process – "as-sintered" samples.

2.2.1. Grinding

Grinding was performed by a single trained operator using diamond burs (#3101G – grit size 181 µm, and #3101FF – grit size 25 µm; both cylindrical burs with flat tips from KG Sorensen, Cotia, Brazil) in a slow-speed motor (Kavo Dental, Biberach, Germany) associated with a contra-angle handpiece (T2 REVO R170 contra-angle handpiece up to 170,000rpm, Sirona, Bensheim, Germany) under constant water-cooling (≈30mL/min). The diamond bur was replaced after each specimen.

For standardization of the wear thickness and to guarantee that the entire surface was submitted to grinding, the specimens were marked with a permanent marking pen (Pilot, São Paulo, Brazil) and affixed to a device to assure parallelism between the specimen and the diamond bur, allowing movement only horizontally (of the base where the specimen was attached). Then, the grinding procedure was performed manually up to the point that the marking was completely eliminated. This procedure standardized the wear thickness and improved the reproducibility of the grinding treatment, although this strong movement control is not available in a typical clinical setting (Pereira et al., 2015a).

2.3. Low-temperature aging

Low-Temperature Degradation (LTD) was simulated in an autoclave (Sercon HS1-0300 n11560389/1) at 134°C, under a 2 bar pressure, over a period of 20 h (Chevalier, 2007; Pereira et al., 2015a). For that, all specimens were placed simultaneously on an autoclave tray disposed carefully where each specimen remained sided to each other without any direct contact among then.

2.4. Phase analysis

Quantitative analysis of phase transformation was conducted (n=2) to determine the relative amount of *m*-phase and depth of the transformed layer under each condition. The analysis was performed using an x-ray diffractometer (Bruker AXS, D8 Advance, Karlsruhe, Germany). Spectra were collected in the 2θ range of 25–35° at a step interval of 1 s and step size of 0.03°. The amount of m-phase (X_M) was calculated applying the method developed by Garvie & Nicholson (1972):

$$Xm = \frac{(\bar{1}11)M + (111)M}{(\bar{1}11)M + (111)M + (111)T} \qquad \text{Eq. (1)}$$

where: $(\bar{1}11)_M$and $(111)_M$ represent the monoclinic peaks (2θ=28° and 2θ=31.2°, respectively) and $(111)_T$ indicates the intensity of the respective tetragonal peak (2θ=30°). The volumetric fraction (F_m) of the m-phase was calculated according to Toraya et al. (1984):

$$Fm = \frac{1.311 \cdot Xm}{1+0.311 \cdot Xm} \qquad \text{Eq. (2)}$$

The depth of the transformed layer (TZD) was calculated on the basis of the amount of the *m*-phase, considering that a constant fraction of grains had symmetrically transformed to m-phase along the surface, as described by Kosmac et al. (1981):

$$TZD = \left(\frac{sen\theta}{2\mu}\right)\left[\ln\left(\frac{1}{1-Fm}\right)\right] \qquad \text{Eq. (3)}$$

where θ=15° (the angle of reflection), μ=0.0642 is the absorption coefficient, and F_M is the amount of m-phase obtained using Eqs. (1) and (2).

2.5. Surface topography and roughness analysis

For the qualitative and quantitative determination of the surface topography pattern generated by grinding, the specimens were analyzed in a surface roughness tester (n=30, Mitutoyo SJ-410, Mitutoyo Corporation, Takatsu-ku, Kawasaki, Kanagawa, Japan), scanning electron microscope (SEM) (n=2, JSM-6360, JEOL, Tokyo, Japan), and atomic force microscope (AFM) (n=2, Agilent Technologies 5500 equipment, Chandler, Arizona, USA).

For surface roughness analysis, six measurements (measured range until 80μm it might be expected an accuracy of 0.001μm) were conducted for each specimen (3 along the grinding direction, 3 in the opposite direction), according to the ISO:1997 parameters (Ra – arithmetical mean of the absolute values of peaks and valleys measured from a medium plane (μm) and Rz – average distance between the five highest peaks and five major valleys found in the standard (μm)) with a cut-off (n=5), λC 0.8 mm and λS 2.5 μm. Arithmetic mean values of all measurements from each specimen were obtained.

For scanning electron microscopy, two specimens from each group were submitted to sputter-coating with a gold-palladium alloy and images were obtained with a 1000x magnification.

For atomic force microscopy, two specimens from each group were submitted to the analysis and images were obtained by non-contact methodology and specific probes from an area of 20x20 µm (PPP-NCL probes, Nanosensors, Force constant = 48 N/m) and manipulation at specific computer software (Gwyddion™ version 2.33, GNU, Free Software Foundation, Boston, MA, USA).

Prior to the surface topography analysis, all specimens were submitted to the cleaning protocol in an ultrasonic bath as described previously.

2.6. Biaxial flexure test

Samples (n=30) were subjected to a biaxial flexure strength test according to ISO:6872-2008. Disc-shaped specimens were positioned with the treated surface facing down (tensile stress) on three support balls (Ø=3.2 mm), which were placed 10 mm apart from each other in a triangular position. The assembly was immersed in water and a flat circular tungsten piston (Ø=1.6 mm) was used to apply an increasing load (1 mm/min) until catastrophic failure using a universal testing machine (EMIC DL 2000, São José dos Pinhais, Brazil). Before testing, adhesive tape was fixed on the compression side of the discs to avoid spreading the fragments (Quinn, 2007) and also to provide better contact between the piston and the sample (Wachtman et al., 1972). Flexural strength was calculated according to ISO:6872-2008:

$$\sigma = -0.2387 \cdot \frac{p(X-Y)}{b^2} \qquad \text{Eq. (4)}$$

where σ is the maximum tensile stress (MPa), P is the total load to fracture (N), b is the thickness at fracture origin (mm), and X and Y are calculated according to:

$$X = (1+v)\ln\left(\frac{r_2}{r_3}\right)^2 + \left[\frac{(1-v)}{2}\right]\left(\frac{r_2}{r_3}\right)^2 \qquad \text{Eq. (5)}$$

$$Y = (1+v)\left[1+\ln\left(\frac{r_1}{r_3}\right)^2\right] + (1-v)\left(\frac{r_1}{r_3}\right)^2 \qquad \text{Eq. (6)}$$

where ν is Poisson's ratio ($\nu = 0.25$), $r_1$is the radius of the support circle (5 mm), $r_2$is the radius of the loaded area (0.8 mm), and $r_3$is the radius of the specimen (7.5 mm).

2.7. Data analyses

Mean and standard deviations of the roughness data (Ra and Rz) were calculated. As roughness data assumed a nonparametric distribution (tested by Shapiro-Wilk normality test), Kruskal-Wallis and the post-hoc Dunn‘s test were performed, in addition to Pearson Correlation test between the Ra roughness data and biaxial flexural data.

The statistic used to describe reliability of the ceramic material was based on the

Weibull statistical analysis (Weibull, 1951), which is a way to describe the variation of resistance obtaining the Weibull modulus (m) and the characteristic strength (σ_C) with a confidence interval of 95%, as determined in a diagram according to DIN ENV 843-5, 2007:

$$\ln \ln \left(\frac{1}{1-F}\right) = m \ln \sigma_c - m \ln \sigma_0 \qquad \text{Eq. (7)}$$

where F is the failure probability, $\sigma_0$the initial strength, $\sigma_c$the characteristic strength, and m is the Weibull modulus. The characteristic strength is considered to be the strength at a failure probability of approximately 63%, being the Weibull modulus used as a measure of the distribution of strengths, expressing the reliability of the material.

2.8. Failure analysis

A fractography examination was performed using a light microscope (Stereo Discovery V20; Carl Zeiss, Gottingen, Germany) on a representative part of the specimens to determine the origin of the fracture.

3. Results

SEM and AFM analysis show that grinding with diamond burs (Xfine and Coarse) created the same surface pattern, regardless of the grit-size, with the presence of parallel scratches following the direction of bur movement, while aging did not cause a relevant alteration of this pattern (Fig. 1 and 2).

Kruskal-Wallis and Dunn's post-hoc tests for roughness data showed that low-temperature aging did not promote any statistically significant alteration from none of the evaluated conditions (Ctrl = Ctrl Ltd; Xfine = Xfine Ltd; Coarse = Coarse Ltd), and that grinding with diamond burs promotes an increase in roughness values with magnitude directly related to the instrument's grit-size (Ctrl < Xfine < Coarse) (Table 2).

The calculated Pearson linear correlation coefficient (Table 2) between the respective strength and roughness data indicated that a very weak correlation exists for Ctrl, Ctrl Ltd, Xfine Ltd, Coarse, Coarse Ltd groups (0 < (r) < 0.3); being a weak correlation noticed for the Xfine group (0.3 < (r) < 0.6) (Crespo, 1997).

The Weibull statistical analysis shows that concerning reliability (*m* value), neither grinding nor aging was able to reduce the Weibull modulus of the Y-TZP tested (Table 2; Weibull plots are shown in Fig. 3). Regarding characteristic strength, grinding promoted a statistically significant increase regardless of the grit-size (Ctrl < Xfine = Coarse). Low-temperature aging did not promote any deleterious impact on material's mechanical properties, in fact for Ctrl group it was observed a statistically significant increase (Ctrl < Ctrl Ltd = Xfine = Xfine Ltd = Coarse = Coarse Ltd).

X-ray diffraction (Table 2; spectra shown in Fig. 4) showed that grinding and low-temperature aging promoted a noticeable increase in *m*-phase content, apparently without any relation with the grit-size of the grinding tool, as Xfine group presented similar *m*-phase content values to the Coarse group both before and after aging (*m*-phase ≈ 9% before, ≈ 40% after). Grinding affected the material's susceptibility to *t-m* phase transformation during low-temperature aging, since it is possible to notice lower *m*-phase content for ground groups after aging (38.74 % and 42.76 %) when compared with the Ctrl group with aging (67.97%), even that the ground groups presented higher *m*-phase content values before aging (9.49 % and 9.66 %), compared with ctrl group (0 %) (Table 2).

Failure analysis, on light microscope, of representative specimens of all evaluated condition showed that all fractures started at the side of the specimen submitted to tensile stress (treated surface) at the center region (Fig. 5).

4. Discussion

Grinding with diamond burs with different grit-sizes increased zirconia's characteristic strength, leading to the rejection of the first hypothesis. The increase in characteristic strength promoted by grinding can be explained by the higher *m*-phase content on the materials surface, thus demonstrating the toughening mechanism, already extensively reported in the literature (Hannink, 2000; Amaral et al., 2013; Pereira et al., 2015a).

In this concern, the literature shows conflicting results of the effects of grinding with diamond instruments on material's mechanical properties. Some studies (Amaral et al., 2013; Pereira et al., 2015a) show a positive effect (transformation toughening mechanism), where grinding promotes a *t-m* phase transformation. It consequently brings a volumetric expansion ≈4% at a localized area around superficial defects resulting in a compression stress concentration around such defects, arresting crack propagation (Garvie & Nicholson, 1972). Other studies (Kosmac et al., 1999; Iseri et al., 2012) observed that grinding introduces important superficial defects and there upon the impact is feasibly deleterious.

Kim et al. (2010) explained that several factors could influence the mechanical behavior of Y-TZP ceramic after grinding, such as: size of crystalline grains (Preis et al., 2015; Li & Watanabe 1998), sintering conditions (Inokoshi et al., 2014; 2015), the pressure applied during grinding, speed of grinding tool, presence or absence of cooling (Kosmac et al., 1999); which means, the materials characteristics and the methodology used for grinding.

The results showed that the grit-size from the grinding tool did not affect the intensity of *t-m* phase transformation mechanism; at the same time, it was observed that the higher values of roughness (Ra and Rz parameters) did not increase the susceptibility of the material to LTD, contrary to what was demonstrated by Pereira et al. (2015a). This difference may be explained by the differences in materials and sintering conditions, in this current study, a Y-TZP ceramic proper for monolithic restoration manufacturing was applied (Zirlux, Ivoclar Vivadent) and the sintering recommended by the manufacturer was longer than the one preconized by Lava (3M Espe, Seefeld, Germany), used by Pereira et al. (2015a). In fact, Lava ceramic is known to present a larger grain, being more susceptible to LTD effects (Chevalier, 2007).

It may be observed at XRD spectra (Fig. 4), a hump at the left shoulder of the $(111)_T$ peak for ground and aged (LTD) specimens, this hump has been related to the formation of orthorhombic (*o*) or rhombohedral (*r*) phase (Kitano et al., 1988; Ruiz & Ready, 1996) or lattice distortion (Kondoh, 2004). The formation of orthorhombic or rhombohedral phase is induced by external stress, while, lattice distortion is resulted from the presence of residual stress. Therefore, the presence of this hump is a direct evidence for the presence of residual stress (Ho et al., 2009). Additionally it may be observed in Ctrl Ltd XRD spectra the increase of $(111)_M$ peak, while in ground and ground Ltd specimens we mainly observe the presence of $(\bar{1}11)_M$, according to Christensen & Carter (1998) the $(\bar{1}11)_M$ is the most stable *m* configuration.

In summary, it appears that grinding stimuli triggers t-m phase transformation favoring $(\bar{1}11)_M$ (more stable configuration) while at same time lead to *t-r/o* phase transformation and that aging in autoclave promoted an extensive alteration leading to also appearance of $(111)_M$ phase (more instable in comparison to $(\bar{1}11)_M$), which is not observed even in ground Ltd specimens. Thus it appears that both mechanism lead to the presence (increase) of residual stress (Ho et al., 2009).

Grinding promoted an increase in roughness values (Ra and Rz parameters) directly related to the diamond bur grit-size, likewise demonstrated by Pereira et al. (2015a) and Preis et al. (2015). However, aging did not promote an alteration of such values, which demonstrates that the Y-TZP ceramic evaluated presents a low susceptibility to low-temperature degradation (as aging did not affect roughness, neither mechanical properties, although it caused great increase in m-phase content).

The absence of linear correlation between flexural strength and roughness (parameter Ra) observed in this study may be explained by Quinn (2007), who states that the presence of correlation is observed only in some specific cases, defined by the balance between the depth of the defects introduced by grinding compared to the existing surface flaws. In some cases, the depth of the introduced cracks is similar to that of the existing surface flaws and, therefore, a correlation would not be expected. However, when the introduced cracks are deeper than the existing surface flaws, a stronger correlation is noticed.

Regarding structural reliability (Weibull modulus), neither grinding nor aging promoted a statistically significant alteration. Higher *m*-values correspond to materials with a uniform distribution of highly homogeneous flaws with a narrower strength distribution, whereas lower *m*-values indicate non-uniform distribution of highly variable crack lengths (broad strength distribution) (Quinn and Morrell, 1991; Quinn and Quinn, 2010). Thus, if one treatment promotes higher *m*-values, it could be considered as an option for clinical use, even if it has a lower characteristic strength.

Additionally literature states Weibull modulus, for Y-TZP ceramic, ranging from 4.31 to 21.59 for current dental ceramics (Ramos et al., 2016; Pereira et al., 2015a; Pereira et al., 2014; Karakoca et al., 2009). We may note that this means in an increased variability (increased range), which may be explained by the difference in materials, processing and conditions evaluated in each study. On the other hand, in this present study, m values ranged from 6.9 to 18.0, but no statistical difference was observed, demonstrating that none of the surface treatments caused degradation of the structural reliability of the material, as may be noted by the close distribution of the Weibull plots presented in fig 3.

Our findings show that, for the studied Y-TZP ceramic for monolithic restorations (Zirlux FC), the act of grinding seemed to be more important than the grit-size from the grinding tool itself, as differences were not observed in m-phase content, surface topography pattern (although it promoted differences in roughness), and, more importantly, at biaxial flexural strength and structural reliability, both before and after aging in autoclave. This behavior was not noticed in previous studies (Pereira et al., 2014; 2015a; Kim et al., 2010) with other ceramic materials (Lava Frame, 3M ESPE and IPS e.max ZirCAD, Ivoclar-Vivadent), in which m-phase content increased when changing the grit-size. Thus, it is important to consider that it seems that even small differences (composition, manufacturing, sintering) between this distinct Y-TZP ceramic brands found on Dental Market will change the response when submitted to these stimuli (susceptibility to transformation and low-temperature degradation).

In relation to LTD, previous studies (Chevalier et al., 2007, Kim et al., 2010, Arata et al. 2014; Inokoshi et al., 2015) showed that the protocol of 134°C, 2 bar for 20 hours, promotes an extensive *t-m* phase transformation (approximately 55 – 80% *m*-phase content). Additionally Kim et al. (2009) and Ban et al. (2008) stated that flexural strength was affected negatively only when at least 50% of *m*-phase was detected. Therefore, this protocol was chosen because it would guarantee enough time to observe any difference on susceptibility to degradation promoted by grinding, as also observed in a previous study (Pereira et al. 2015a).

In the present research, aging in autoclave statistically increased the characteristic strength values for Ctrl group, while it did not promote any alteration for the ground groups, thus our second hypothesis was also rejected. The increase in characteristic strength observed for Ctrl group can be explained by the notable increase in *m*-phase content (0% to 67.97%), which results in the toughening mechanism previously mentioned. The fact that aging did not alter for ground groups might also been explained by the *t-m* phase transformation, and consequently the toughening mechanism, that were already unleashed by the grinding procedure before the exposure to aging, and aging for 20 h in autoclave was not sufficient to promote low-temperature degradation (LTD) effects.

Another important observation is that although grinding promoted *t-m* phase transformation before aging, this procedure also altered the susceptibility of Y-TZP ceramic to *t-m* phase transformation in response to the aging procedure, and by that, we observed lower *m*-phase content for ground aged groups in comparison to Ctrl-LTD (Table 2). The remaining question is how this ground Y-TZP ceramic would behave at a clinical environment being constantly exposed to mechanical cycling and hydrothermal degradation (probably a hostile condition).

Although the present study shows that grinding did not promote any deleterious impact on the mechanical behavior of YZ ceramic, it is important to highlight that this was an *in-vitro* study. Directly extrapolation of these results to a clinical condition should be done with caution, in addition to the fact that in this study we only submitted the material to hydrothermal stimuli in addition to surface treatment (clinical adjustments), and in a clinical environment it will be exposed to an association of different stimuli as mentioned before. Additionally, this study only assessed the influence of these factors on mechanical behavior and at a clinical condition grinding and LTD might also affect other factors such as optical properties and oral microorganism adhesion.

Thus, more studies evaluating this association of stimuli should be done to better understand this condition. In addition, the longevity of YZ monolithic restorations will depend on the material's resistance to low-temperature degradation caused by the different stimuli that it will be imposed to. It is also important to highlight that as literature shows the response of Y-TZP ceramics (i.e. mechanical behavior, susceptibility to LTD, among others) is material dependent, as described previously here, thus extrapolation of the current findings, for different Y-TZP ceramic materials, should be done carefully.

5. Conclusions

- Grinding showed not to be detrimental to the mechanical properties of the studied Y-TZP ceramic, resulting in an increase in characteristic strength and *m*-phase content, without compromising the structural reliability and decreasing the susceptibility of *t-m* phase transformation of the material during aging.
- Low-temperature aging in autoclave for 20 hours did not promote any deleterious impact on the mechanical properties of Zirlux FC Y-TZP ceramic, although it promoted an important increase in *m*-phase content on the material.

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Figures and Tables

Figures

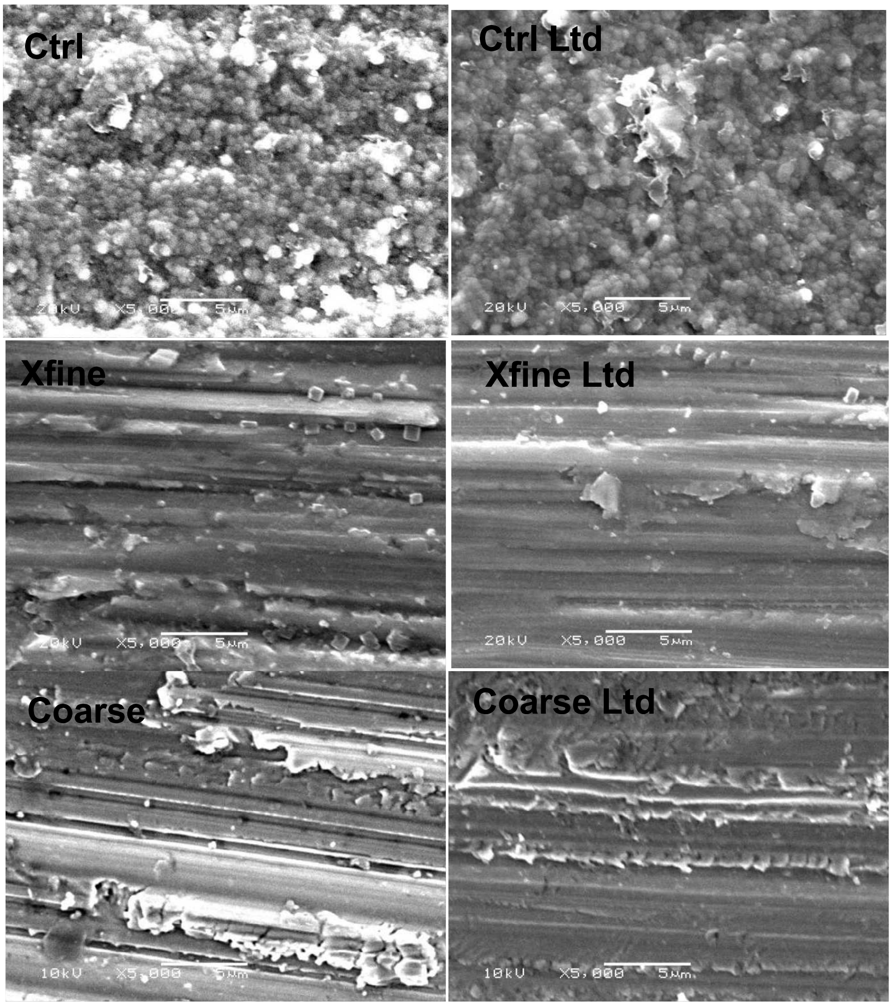
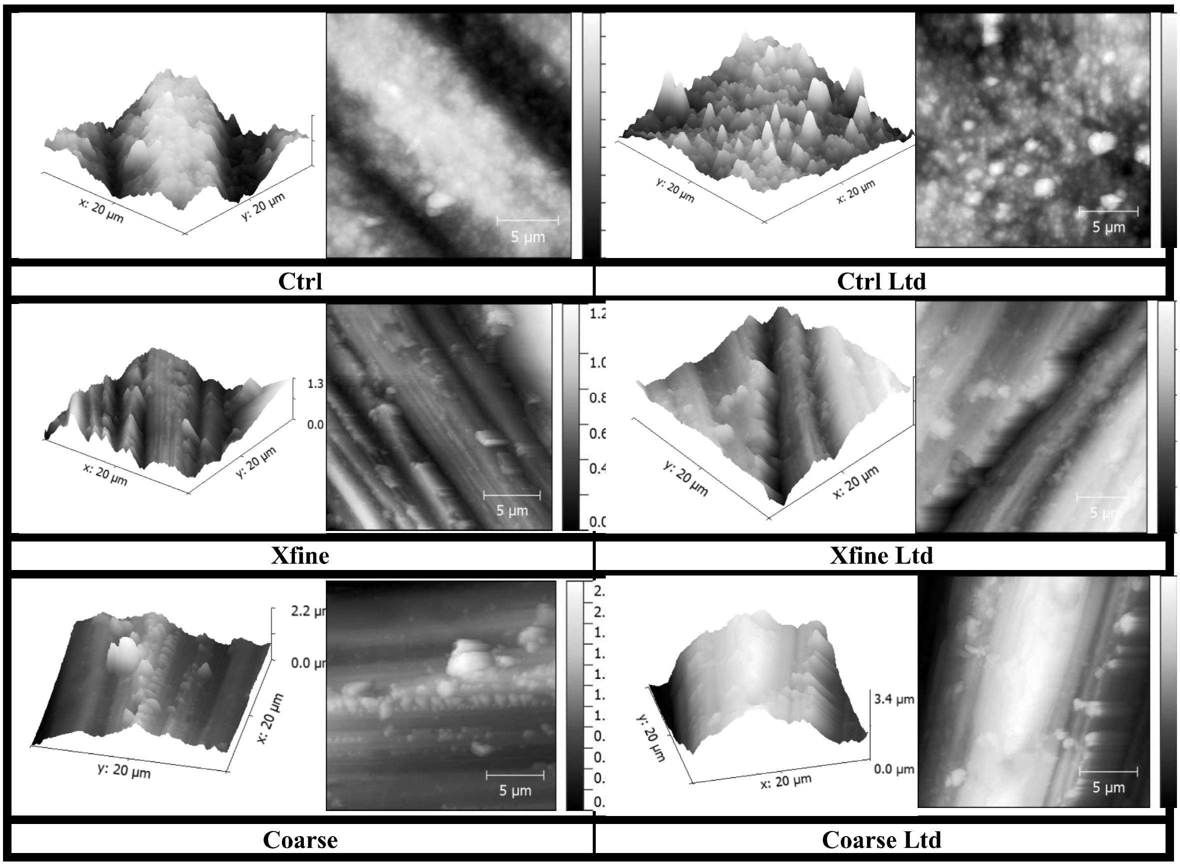


Fig 1. Scanning Electron Microscopy micrographics (×5000 magnification) of the different evaluated conditions elucidating the topography pattern alteration generated by grinding procedure and the absence of modifications promoted by aging.



Ctrl

Ctrl Ltd

Xfine

Xfine Ltd

Coarse

Coarse Ltd

Fig 2. Atomic Force micrographics of the different evaluated conditions elucidating the topography pattern alteration generated by grinding procedure and the absence of modifications promoted by aging.

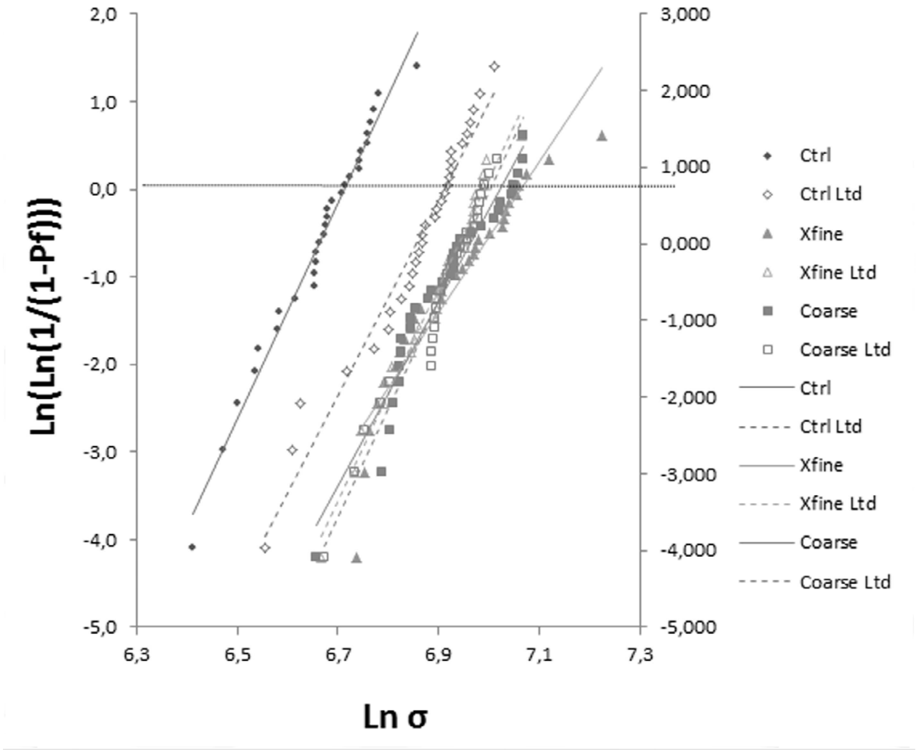


Fig 3. Weibull Analysis plot for testing groups data.

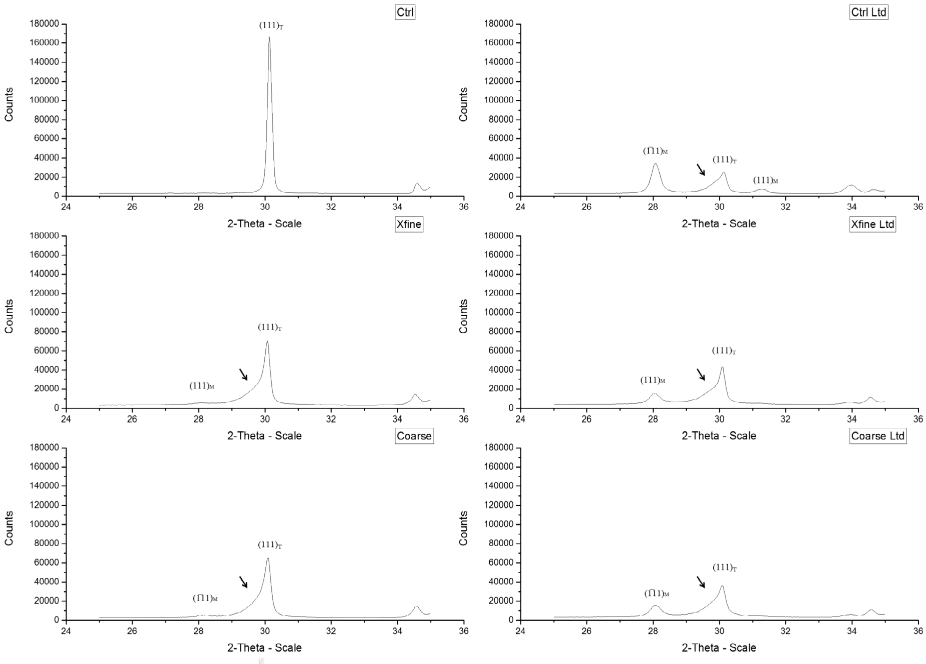


Fig 4. XRD spectra collected from all evaluated conditions (top left – Ctrl; middle left – Xfine; bottom left – Coarse, in addition to respective conditions after Ltd on the right). According to Kitano et al., (1988) and Ruiz & Ready, (1996), this hump (marked by the arrow) is related to the presence of orthorhombic or rhombohedral phase.

Fig 5. Representative micrographs (a – Ctrl; b – Ctrl Ltd; c – Coarse; d – Coarse Ltd) of fractured surfaces (fractography examination) using a Light Microscope. The region under the half-circle indicates that the fracture origins initiated at a superficial/subsuperficial defect where concentrated tension stress. The arrows (➔) indicate the crack propagation direction into the opposite side where concentrated compression stress (Compression Curl region). Xfine and Xfine Ltd groups presented similar fractographic patterns that those observed on Coarse and Coarse Ltd.

Tables

Table 1- Experimental Design

Groups	**Study Factors**	
	Surface treatment	**LTD**
Ctrl	Control, *as-sintered* (without any additional treatment)	Without
Ctrl Ltd		With
Xfine	Grinding with extra-fine diamond bur (#3101FF, grit size 25 µm, KG Sorensen, Cotia, Brazil)	Without
Xfine Ltd		With
Coarse	Grinding with coarse diamond bur (3101G – grit size 181 µm, KG Sorensen, Cotia, Brazil)	Without
Coarse Ltd		With

Table 2 – Weibull analysis data (characteristic strength σ_c with 95% confidence interval and weibull moduli – m with 95% confidence interval); roughness analysis data (Ra and Rz parameters) with standard deviation (SD) and Pearson correlation between biaxial flexural strength and roughness Ra value; in addition to, X-ray Difractometry analysis (*m*-phase content and depth of the transformed layer - TZD).

Groups	**σ_c (CI 95%)**	**m (CI 95%)**	**Roughness Ra ± SD (µm)**	**Roughness Rz ± SD (µm)**	**Pearson linear coefficient (σ x Ra)**	***m*-phase content (%)**	**TZD (µm)**
Ctrl	823.4 (794.8-852.2)^{B}	12.3 (8.6-15.8)^{A}	0.31 ± 0.16^{A}	2.59 (± 1.27)^{A}	-0.22 (p= 0.23)	0.00	0.00
Ctrl Ltd	1002.8 (964.4-1041.6)^{A}	11.1 (7.8-14.3)^{A}	0.27 (± 0.05)^{A}	2.15 (± 0.41)^{A}	-0.07 (p= 0.67)	67.97	6.76
Xfine	1087.3 (1040.2-1135.1)^{A}	9.8 (6.9-12.6)^{A}	0.64 (± 0.16)^{B}	4.29 (± 1.00)^{B}	-0.38 (p= 0.03)	9.49	0.50
Xfine Ltd	1033.7 (1002.0-1065.6)^{A}	13.9 (9.8-17.9)^{A}	0.67 (± 0.13)^{B}	4.41 (± 0.73)^{B}	-0.00 (p= 0.96)	38.74	2.48
Coarse	1057.4 (1019.6-1095.5)^{A}	11.9 (8.4-15.4)^{A}	1.32 (± 0.24)^{C}	6.74 (± 1.20)^{C}	0.11 (p= 0.55)	9.66	0.50
Coarse Ltd	1045.6 (1013.7-1077.6)^{A}	14.0 (9.9-18.0)^{A}	1.10 (± 0.20)^{C}	6.77 (± 1.13)^{C}	-0.07 (p= 0.67)	42.76	2.82

3. ARTIGO 2 - Low-temperature degradation of Y-TZP ceramics: a systematic review and meta-analysis

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Running title: LTD of YTZP ceramics – a systematic review

Abstract

The aim of this study was to systematically review the literature to assess if low-temperature degradation (LTD) simulation in autoclave promotes deleterious impact on the mechanical properties and superficial characteristics of Y-TZP ceramics compared to the non-aged protocol. The MEDLINE via PubMed electronic database was searched with included peer-reviewed publications in English language and with no publication year limit. From 413 potentially eligible studies, 49 were selected for full-text analysis, 19 were included in the systematic review with 12 considered in the meta-analysis. Two reviewers independently selected the studies, extracted the data, and assessed the risk of bias. Statistical analysis were performed using RevMan 5.1, with random effects model, at a significance level of $p<0.05$. Descriptive analysis of monoclinic phase content data showed that aging in autoclave promotes an increase in m-phase content (ranging from 0 up to 13.4% before and 2.13 up to 81.4% after aging) with intensity associated to the material susceptibility and to the aging parameters (time, pressure and temperature). Risk of bias analysis showed that only 1 study presented high risk, while the majority showed medium risk. Five meta-analyses (factor: aging x control) were performed considering global and subgroups analyses (pressure, time, temperature and m-phase % content) for flexural strength data. In the global analysis a significant difference ($p<0.05$) was observed between conditions, favoring non-aging group. Subgroup analysys revealed statistical difference ($p<0.05$) favoring non-aging, for aging time > 20 hours. However, for shorter aging times (≤ 20 hours), there was no difference between groups. Pressure subgroup analysis presented a statistical difference ($p<0.05$) only when a pressure ≥ 2 bar was employed, favoring non-aging group. Temperature subgroup analysis showed a statistical difference ($p<0.05$) only when temperature = 134°C was used, favoring the non-aging group. M-phase % content analysis presented statistical difference ($p<0.05$) when more than 50% of m-phase content was observed, favoring non-aging group. High heterogeneity was found in some comparisons. Aging in autoclave promoted low-temperature degradation, impacting deleteriously on mechanical properties of Y-TZP ceramics. However, the effect of LTD depends on some methodological parameters indicating that aging time higher than 20 hours; pressure ≥ 2 bar and temperature of 134 °C are ideal parameters to promote LTD effects, and that those effect are only observed when more than 50% m-phase content is observed.

Key Words: Aging in autoclave. Hydrothermal degradation. Dental prosthesis. Dental materials. Zirconium oxide partially stabilized by yttrium.

1. Introduction

Nowadays, several studies have been performed on metal-free ceramic restorations due to the high aesthetic requirements by patients and to the continuous search for materials with suitable mechanical properties. Restorations that combine both aesthetic properties of veneering porcelain and the high strength of an Yttrium-stabilized Tetragonal Zirconia Polycrystal (Y-TZP) infrastructure (Conrad H., et al. 2007) has been suggested as an excellent restorative option. However, such rehabilitation systems present chipping of the veneering porcelain as the main failure factor (Beuer F., et al., 2009; 2012). In this sense, Y-TZP monolithic restorations have been proposed as an alternative treatment once it removes the presence of the veneering porcelain (Beuer., F et al., 2009; 2012).

Y-TZP stands out among other restorative materials due to its elevated chemical and dimensional stability besides the superior mechanical properties (Piconi & Maccauro, 1999). Owing to the poor meta-stability of zirconia crystals, yttria (3% mol) was added to pure zirconia to stabilize the tetragonal phase at room temperature (Piconi & Maccauro, 1999). Therefore, the volume expansion (≈3%) that occurs when crystals transform from tetragonal to monoclinic phases is prevented (Piconi & Maccauro, 1999; Garvie & Nicholson, 1972). The $t \rightarrow m$ phase transformation will eventually occur when local stress is generated (Kosmac T., et al. 1999; Zhang Y., et al. 2006; Amaral M., et al. 2013; Kim J., et al. 2010; Pereira G., et al. 2015) and in the presence of water (Amaral M., et al., 2013; Kim J., et al. 2010; Pereira G., et al. 2015; Ban S., et al. 2008; Kim H., et al. 2009), which is known as hydrothermal degradation or low-temperature degradation (LTD) (Kobayashi K., et al. 1981).

It was observed that, when Y-TZP is submitted to a humidity environment with temperatures between 150-400ºC, it spontaneously suffers a low-temperature degradation process (Kobayashi K., et al. 1981). LTD initially occurs at superficial grains, where water is incorporated into zirconia grains by filling oxygen vacancies, and later spreads to the surface increasing its roughness (Sato & Shimada, 1985; Yoshimura M., et al. 1987). Afterwards, LTD proceeds into the bulk material (Yoshimura M., et al. 1987) and jeopardizes the strength, fracture toughness, and density of Y-TZP structures (Ban S., et al. 2008; Hirano M, 1992; Lughi & Sergo, 2010). Steam autoclave treatments at increased temperatures (120–140ºC) have been used to effectively induce LTD, since phase transformation of Y-TZP crystals occurs in the presence of water or steam (Amaral M., et al. 2013; Kim J., et al. 2010; Ban S., et al. 2008; Chevalier J, 1999; Borchers L., et al. 2010; Lee T. et al., 2012). According to Kim H. and collaborators (2009), a LTD simulation method using steam autoclave displays a strain-induced transformation (*t→m*) depending on the applied temperature and the amount of resulting *m*-phase (Kim H. et al. 2009).

The current literature shows that aging zirconia in autoclave (Kosmac T. et al. 1999; Kim H. et al. 2009; Cattani-Lorente M., et al. 2011) may positively or negatively influences the mechanical strength of Y-TZP ceramics, however its real effect remains unclear. First, the aging stimuli triggers a toughening mechanism, in response to a t-m phase transformation, leading to an improvement of the mechanical properties (Pereira G., et al. 2015; Amaral M., et al. 2013; Garvie & Nicholson et al. 1972), than it progress and result in a deleterious effect (Kobayashi K., et al. 1981). Further, Y-TZP has been recommended for monolithic restoration, which exposes the material directly to the oral environment, consisting in a more hazardous condition (association between mechanical stimuli, water and temperatures).

Since the real effect of aging in autoclave on the mechanical properties and superficial characteristics of the Y-TZP ceramic is not clear yet, it becomes interesting to perform a systematic review that takes it into account and guides future studies. Thus, the aim of this study was to systematically review the literature for *in vitro* studies to assess if low-temperature degradation simulation promotes deleterious impact on the mechanical properties, structural stability and superficial characteristics of Y-TZP ceramics compared to the non-aged protocol.

2. Materials and Methods

2.1 Search Strategy

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher D., et al. 2009). The MEDLINE electronic database via PubMed was searched to identify studies that could be considered. The following search strategies were performed: computer search of database, review of reference lists of all included articles, and contact with authors and experts on the issue. The search included peer-reviewed publications only in English language and with no publication year limit. The last search was made in 14 august 2015.

2.2 Focused Question

"Does the LTD have any effect on the mechanical properties, superficial characteristics and structural stability of Y-TZP ceramics?

2.3 PICOs

The population, intervention, comparison and outcomes, i.e. the "PICOs" for this systematic review were defined as follows:

Population: Y-TZP ceramic specimens;

Intervention: low temperature degradation (LTD);

Comparison: Y-TZP ceramic without LTD (control);

Outcomes: phase transformation, mechanical properties, strength, hardness, toughness, stiffness, roughness, density and porosity;

Study design: *in vitro* studies.

The MeSH and free-text terms, also described in table 1, were used and the search strategy was as follows: (((((((zirconium[MeSH Terms]) OR zirconi*) OR zirconium oxide) OR Y-TZP) OR yttria stabilized polycrystalline tetragonal zirconia) OR yttria stabilized tetragonal zirconia)) AND ((((((((Low temperature degradation) OR Low-temperature degradation) OR hydrothermal degradation) OR hydrothermal ag*) OR thermal degradation) OR thermal ag*) OR aging) OR ageing) OR water storage)) AND ((((((((((((((((structural stability) OR phase stability) OR phase transformation) OR surface topography) OR surface morphology) OR surface characteristic*) OR mechanical properties) OR mechanical behaviour) OR strength) OR resistance) OR hardness) OR toughness) OR stiffness) OR roughness) OR density) OR porosity) OR fracture) OR flexural).

2.4 Inclusion Criteria

The inclusion criteria for study selection were: (i) *in vitro* studies, (ii) English language, (iii) yttrium-stabilized tetragonal zirconia polycrystal (Y-TZP) ceramic, (iv) low-temperature degradation (LTD) in autoclave, (v) mechanical properties, structural stability (phase transformation) and/or superficial characteristics.

2.5 Exclusion Criteria

Studies that did not have a proper control group, did not use Y-TZP ceramic (with addition of dopants), did not evaluate the effects of hydrothermal degradation in autoclave (temperature, pressure and time stimulus), did not evaluate mechanical properties or surface characteristics and that evaluated the behavior of Y-TZP implants and femoral heads were excluded from evaluation.

2.6 Search steps: screening and selection

A flow diagram elucidating all the search steps execution is presented in Figure 1.

Step 1: Titles and abstracts were reviewed by two independent authors (G.K.R.P. and A.B.V.) and selected per their consensus according to the inclusion criteria. If consensus was not reached, the abstract was set aside for further evaluation.

Step 2: Full-text articles of abstracts selected in step 1 were retrieved and reviewed by 2 independent authors (G.K.R.P. and A.B.V.). Inclusion was based on consensus between these 2 investigators. Disagreements were discussed with a third author (L.F.V.).

Step 3: Two authors (G.K.R.P. and A.B.V.) evaluated together the reference lists of all articles selected in step 2, and full texts of potentially interesting studies were examined.

For each step independently executed, it was calculated the coefficient of inter-rater agreement (Kappa) between evaluators (G.K.R.P. and A.B.V). It was observed a 0.92 kappa coefficient for step 1 and a 0.87 kappa coefficient for step 2.

2.7 Data Extraction

A protocol for data extraction was defined and evaluated by 2 authors (G.K.R.P. and A.B.V.). Any disagreement was discussed with a third author (A.F.M.). Data were extracted from full-text of included articles using a standardized form. The authors categorized similar information into groups according to the main outcomes of interest. If data were not presented or the mean and standard deviations values could not be extracted, the authors were contacted three times via e-mail and the study was excluded if any missing important information was not supported.

2.8 Risk of Bias Assessment

The risk of bias evaluation was based on and adapted from previous studies (Sarkis-Onofre R., et al. 2014; Montagner A., et al. 2014) and evaluated the description of the following parameters for the study's quality assessment: sample size calculation, randomization of ceramic specimen, specimen preparation clearly stated and executed in a standardized and reproducible way, sintering cycle used according to the manufacturer's instructions, aging parameter clearly specified, test executed by a single blinded operator and specimen dimension and flexural test executed following International Standard Rules (i.e. ISO, ASTM, and others). For each parameter values from 0 to 2 were attributed: 0 - if the authors clearly reported the parameter; 1 – if the author reported the execution/respect of the parameter but accuracy of the execution is unclear; 2 – if the author not specified the parameter or the information is not present. If the total sum of the attributed values ranged between 0 up to 4 it was considered a low risk, between 5 up to 9 a medium risk and 10 up to 14 a high risk of bias.

For the studies that only evaluated phase transformation stability, flexural strength parameters had no attributed value, so the total sum ranged from: 0 up to 3 low risk, 4 to 8 medium risk and 9 to 12 high risk.

2.9 Data Analyses

For the meta-analysis, only the data from flexural strength were considered, once few studies evaluated the other properties. Phase transformation data were not included in the meta-analysis as insufficient data were provided by the studies and required information was missing. Thus, phase transformation data was included only in the systematic review and the data were presented as a descriptive analysis.

For the meta-analysis, flexural strength data (means and standard-deviations) for LTD aging vs. control (non-aging) were global and subgroup analyzed. Global analyses took into account all included studies, and subgroup analyses assessed the different aging parameters (pressure, time and temperature) where two strata were created for each parameter. Additionally, a subgroup analysis on m-phase % content observed after aging was executed, considering three strata.

All analyses were conducted in Review Manager Software 5.1 (Copenhagen, Nordic Cochrane Centre, Cochrane Collaboration) using a random effect model. Pooled effect estimates were obtained by comparing the means of flexural strength value and were expressed as the raw mean difference among the groups. A p value ≤ 0.05 was considered statistically significant (Z test). Statistical heterogeneity of the treatment effect among studies was assessed via the Cochran Q test, with a threshold p value of 0.1, and the inconsistency I^2 test, in which values > 50% were considered indicative of high heterogeneity.

For studies that evaluated more than one Y-TZP material, each material was considered independently, for each evaluated parameter (time, temperature and pressure). Additionally, for studies that evaluated at the same Y-TZP material under different conditions taking into consideration the same parameter, an equation proposed by the Cochrane Handbook was used to calculate single sample size, mean and standard deviation values for each experimental and/or control groups. (Higgins J., et al. 2011).

3. Results

3.1 Search and selection

From 413 potentially eligible studies, 49 were selected for full-text analysis, 19 were included in the systematic review with 12 considered in the meta-analysis (Figure 1). The characteristics of the included studies are presented in Table 2.

3.2 Risk of bias

Of the 19 studies included in the systematic review, only 1 (5.3%) presented high risk of bias, while the majority (18 studies - 94.7%) showed medium risk of bias. The results are described in Table 3.

3.3 Descriptive analysis

The descriptive analysis of phase transformation data is presented in Table 4. It can be noted that aging in autoclave promotes an increase in m-phase content (ranging from 0 up to 13.4% before aging and 2.1 up to 81.4% after) with intensity of phase transformation directly related to the material susceptibility and to the parameters used for aging (time, pressure and temperature), independently of the methodology used for m-phase quantification. Data from X-ray Diffractometry (XRD) analysis showed that it is not common to perform a statistical evaluation of the monoclinic phase content data. Further, most studies did not present mean and standard deviation values of those data.

3.4 Meta-analysis

A total of 5 meta-analyses were performed for flexural strength data, considering 12 studies. The meta-analysis results are presented in Figure 2. Studies that evaluated more than one Y-TZP material were inserted more than one time in each meta-analysis, considering the data of each material (Borchers L., et al. 2010; Flinn B., et al. 2012; 2014; Siarampi E., et al. 2014).

For the first analysis (global analysis), LTD aging vs. control (no aging), 18 data sets were considered, although 12 studies were included (Figure 2A). It was observed a statistical difference ($p<0.05$) between conditions (aging x non-aging), favoring non-aging group, which presents the higher flexural strength values. The heterogeneity parameter I^2 was 94%.

For the second meta-analysis, a subgroup analysis considering aging time (≤ 20 hours or >20 hours) was performed, using 21 data sets, although 12 studies were included (Figure 2B). The results showed a statistical difference ($p<0.05$) between evaluated conditions (aging x non-aging), favoring non-aging. For aging time > 20 hours, the same trend was found, with non-aged group showing higher flexural strength than the aged one. However, for shorter aging times (≤ 20 hours), there was no significant difference between groups. The I^2 was 96.4%.

For the third meta-analysis, a subgroup analysis for pressure (< 2 bar pressure or ≥ 2 bar pressure) was performed and considered 17 data sets, although 11 studies were included (Figure 2C). One study was excluded from this analysis as there is no specification of the pressure parameter employed (Kosmac T., et al. 2008). It was noted a statistical difference ($p<0.05$) between evaluated conditions (aging x non-aging) only when a pressure ≥ 2 bar was employed, with non-aged group showing higher flexural strength than the aged one, while there was no statistical difference between groups when a pressure < 2 bar was used. The heterogeneity parameter I^2 was 0%.

For the fourth meta-analysis, a subgroup analysis for temperature (< 134 ^{o}C temperature or = 134 ^{o}C temperature) was performed and considered 18 data sets, although 12 studies were included (Figure 2D). The results favored the non-aging group only when temperature equal to 134 ^{o}C was used ($p<0.05$), however when the temperature was lower than 134^{o}C, no statistical difference was found between groups (aging x non-aging). The heterogeneity parameter I^2 was 0%.

For the fifth meta-analysis, a subgroup analysis considering the m-phase % content observed after aging (≤ 25% m-phase content ≤ 50% m-phase content) was performed and considered 20 data sets, although 12 studies were included (Figure 2E). The results favored the non-aging group only when m-phase % content was higher than 50% ($p<0.05$). While, when the m-phase % content was lower than 50%, no statistical difference was found between groups (aging x non-aging). The heterogeneity parameter I^2 was 62.3%.

4. Discussion

The present study was able to show the linearity of different parameters used on low-temperature degradation methods and summarizes the *in vitro* data of the effect of low-temperature degradation in autoclave on the mechanical properties and structural stability (phase transformation) of Y-TZP ceramics when compared to non-aging protocols. The LTD presented a negative influence on flexural strength of Y-TZP ceramics; however it was dependent on some methodological parameters as: pressure, temperature and time of aging.

After more than 30-year of research (Kobayashi et al. 1981), the exact mechanism of LTD is still under discussion. The most accepted theory is that the increase of internal stresses associated with the penetration of water (H_2O) inside the lattice (Schubert & Frey, 2005), triggers the initiation of the *t→m* phase transformation (Yoshimura et al. 1987; Schubert & Frey, 2005). Thus, a cascade of events occurs, with the transformation propagating first inside one grain (Deville & Chevalier, 2003, Schmauder & Schubert, 1986), and progressively invading the surface by a nucleation-and-growth (N-G) mechanism (Chevalier et al., 1999, Chevalier, 2007; Muñoz-Tabares et al., 2011). The number of nuclei increases continuously with the stresses, owing to the penetration of water (time dependent) (Lucas et al. 2014). At the same time, growth occurs because of the transformation of one-grain puts its neighbors under tensile stresses, favoring their transformation under the effect of water (Chevalier, 2007).

The *t→m* phase transformation in zirconia is martensitic in nature (Chevalier, 2007). A martensitic transformation is a "change in crystal structure that is athermal, diffusionless and involves the simultaneously, cooperative movement of atoms over distances less than an atomic diameter, so as to result in a macroscopic change of shape of transformed regions" (Kelly & Rose 2002).

Several studies on aging and behavior of zirconia were performed (Chevalier, 2007, Cales et al., 1994, Kobayashi et al. 1981, Chevalier et al. 1999, 2007; Deville et al., 2005), which lead to the formulation of new International Standard Rules for zirconia processing (i.e. ISO:6872-2008; ISO:13356-2008) regulating material's microstructure, testing and required aging sensitivity. According to ISO:13356-2008, the monoclinic phase content should not exceed the maximum of 25% for Y-TZP implants to be considered suitable for biomedical purposes after aging in autoclave at 134°C, 2 bar for 5 hours (Siarampi et al., 2014).

Among the studies that performed aging at 5 hours, only Egilmez et al. (2014) observed a greater amount of monoclinic phase (25.4%) in Lava Frame zirconia (3M ESPE). In order to understand this data, some factors should be taken into account: (1) high m-phase content before aging (13.4%) is reported, and further, (2) no polishing procedure was performed to regularize specimens' topography, as usually described in most of papers. Thus, this surface probably presented an increased roughness and a higher concentration of superficial defects, which may have increased this material susceptibility to *t→m* transformation during aging. Xiao et al., 2012 and Flinn et al., 2014 also observed a higher m-phase content before aging in all evaluated materials (5% - 10.8% and 2% - 12,4%; respectively), although the sample preparation protocol is unclear, likewise at which moment the polishing was performed, before or after sintering. Among all the remaining studies, X-ray diffraction showed only 0% to 3% of m-phase before aging.

According to Chevalier (2007) aging can be controlled for a given zirconia ceramic, and the most important parameter that will limit aging effects is density. Lower density (especially in the presence of open porosity) offers water molecules an easy access to the bulk of the material, resulting in aging not only on the surface but also on the internal surfaces (pores and crack surfaces) (Yoshimura et al. 1987; Chevalier, 2007). The inquiring fact is that this systematic review aimed to evaluate the effect of density on Y-TZP ceramic, characterized as the most important factor in aging sensitivity, and observed a lack of studies regarding its influence on mechanical properties. Thus more studies are desirable to better understand its influence.

Because *t→m* phase transformation is a crystallographic change, aging can be easily characterized by techniques sensitive to crystallography or chemical environment. Among then, XRD (X-ray Diffractometry) is the most used one (Deville et al. 2005), however, this analysis presents some limitations: (1) it is restricted a superficial or near surface analysis (typically no more than the top few microns is analysed) (Deville, 2005; Chevalier, 2007); (2) is also not a very precise tool for monoclinic content lower than 5% making it unsuitable for monitoring the beginning of the transformation (Cotes et al., 2014; Chevalier, 2007). In addition, there are two alternatives to quantify m-phase content of Y-TZP: (1) the Garvie and

Nicholson modified by Toraya equation (Toraya et al., 1984); and (2) Rietveld method, that takes into consideration the presence of c-phase and because of that it is believed to be more precise (Arata et al. 2014).

Other alternative to quantify m-phase content is Raman spectroscopy (Chevalier, 2007), that appears to be more sensitive than XRD to detect small traces of m-phase (Kim et al. 1997) and also permits the mensuration of the internal stress in the material (Clarke & Adar, 1982; Teixeira et al. 1999). Although far less used than XRD (only Inokoshi et al 2015 and Siarampi et al. 2014) among the studies included in this study, Raman spectroscopy is one of the most powerful tools for characterizing zirconia LTD (Pezzotti & Porporatti, 2004).

Regarding mechanical properties effects after aging in autoclave, it was observed different effects on Y-TZP ceramics, depending on the applied temperature and on the amount of resulting m-phase (Kim et al. 2009). In the present study, LTD had a weakening effect on flexural strength of Y-TZP ceramics, both in general and in all subgroups analysis. M-phase % content subgroup analysis showed that the flexural strength only decreased when at least 50% of m-phase was detected on the material's surface. This fact was previously stated by Kim et al., 2009, and Ban et al., 2008 and is confirmed by the present study results. Only one study was the exception (Pereira et al. 2015) in the m-phase % content subgroup analysis, where an increasing on flexural strength was observed, although 53.5% of m-phase was noted.

In temperature subgroup analysis, it was observed a difference between the evaluated conditions (aging x non-aging) only when a temperature equal to 134°C was employed, while there was no difference for lower temperatures. As Nucleation and growth curves are temperature dependent, less time is needed for transformation to occur at higher temperatures, while more time is needed at lower temperatures (Lucas et al., 2014).

Based upon the proper behavior observed in *in vitro* and *in vivo* studies on biomedical area, the diversity of zirconia-based ceramic materials is increasing in Dentistry. Lately, the use of Y-TZP as full-contour monolithic restorations has been proposed, which brings the advantage of more conservative tooth preparation, as it requires a thinner thickness and the application of veneering porcelain is dispensable (Beuer et al., 2012; Sabrah et al. 2013; Nakamura et al. 2015). Thus, the zirconia will be directly exposed to the oral environment (plenty moisture, temperature, and mechanical stimuli), by that constituting an ideal scenario for LTD to take place and consequently increasing the possibility of deleterious impact on the longevity of those restorations. Therefore, before the recommendation of such monolithic restorations, it needs to be submitted to laboratorial tests, evaluating the materials sensitivity and susceptibility to aging, disregard this step could lead to catastrophic effects as those observed in Prozir episode in 2001 (Chevalier, 2007).

Low-temperature degradation simulation of zirconia is usually conducted in autoclave or steam chambers, where the pressure of water vapor, temperature and elapsed time are the controlled experimental variables (Lughi & Sergo, 2010). The choice of the best autoclave protocol to simulate LTD is controversial, as *in-vitro* correlation of the required time for the acceleration test and its correspondence with longevity of Y-TZP ceramic at environmental clinical condition is challenging. It is important to state that this systematic review evaluated *in vitro* studies and presents some limitations, thus it should have caution to extrapolate the results in clinical conditions.

Researchers may follow the instructions of ISO:13356-2008 when evaluating the behavior of the material and its requirements to be used in a clinical environment, which it should not present more than 25% of m-phase content when submitted to autoclave aging for 134°C, 2 bar for 5 hours; or follow the parameters suggested in this meta-analysis for evaluate and characterize the aging behavior and its effects on mechanical properties, which at least 2 bar pressure, for more than 20 hours at temperatures equal than 134°C seems to be the most adequate.

The high heterogeneity observed in some analysis could be explained by 3 main reasons: (1) the high variability of tested materials, as small deviations in materials composition and/or grain structure may lead to a large change in aging behavior; (2) high variability of the methodologies employed for sample preparation, aging treatment and flexural strength testing; (3) the included studies presented, in their majority, medium and high risk of bias, a small number of samples and (consequently) high standard deviations, and a high number of covariables, favoring the heterogeneity.

In addition, flexural strength data were investigated under static loading instead of dynamic loading, ceramic restorations are susceptible to fatigue failure, mainly due the presence of moisture and cyclic masticatory forces. Fatigue failure may be defined as the fracture of the material due to progressive brittle cracking and slow crack propagation under repeated cyclic stresses of an intensity below of the material normal strength (Zhang et al., 2013; Wiskott et al., 1995), thus dynamic loading better simulates failure pattern observed by intraoral occlusal loading. Furthermore, specimens evaluated have a simplified format instead of a crown-shape, and by that constitute another limitation of our findings.

5. Conclusion

Aging in autoclave effectively promotes low-temperature degradation effects on Y-

TZP ceramics, where a decrease at the mechanical properties (flexural strength) was observed, in addition to an important increase in m-phase content.

Some aging parameters as time (longer than 20 hours), pressure (at least 2 bar) and temperature (equal to 134°C) significantly affected the flexural strength evidencing a possible protocol for LTD simulation. Flexural strength decreasing was only present when more than 50% of m-phase content was observed.

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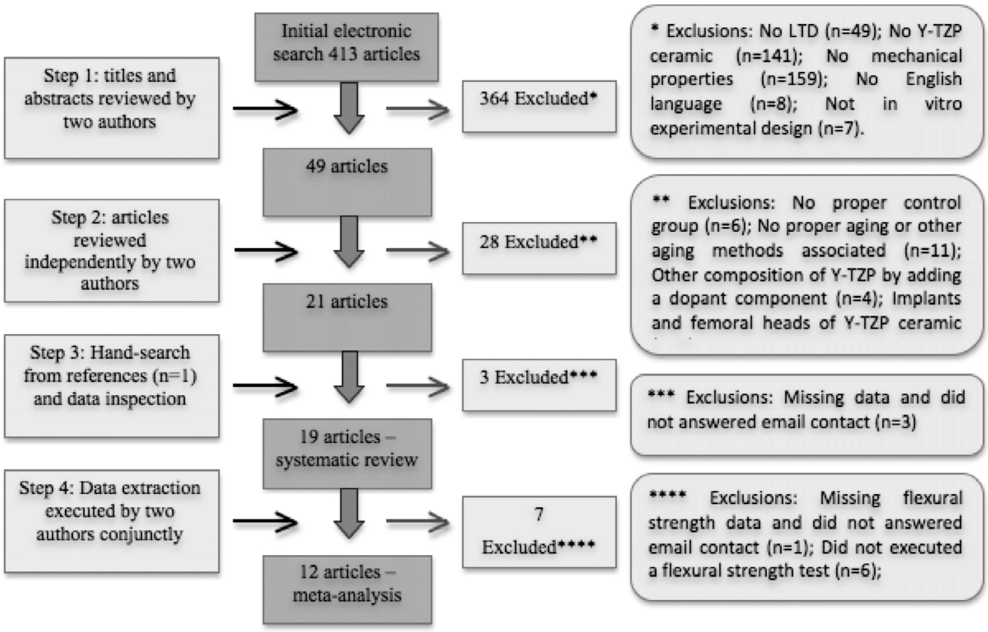
Figures and Tables

Figures



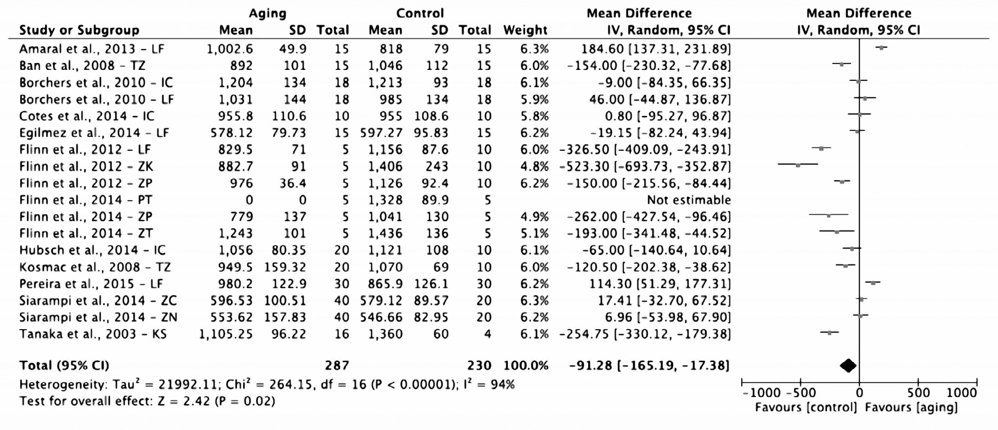
* Exclusions: No LTD (n=49); No Y-TZP ceramic (n=141); No mechanical properties (n=159); No English language (n=8); Not in vitro experimental design (n=7).

** Exclusions: No proper control group (n=6); No proper aging or other aging methods associated (n=11); Other composition of Y-TZP by adding a dopant component (n=4); Implants and femoral heads of Y-TZP ceramic

*** Exclusions: Missing data and did not answered email contact (n=3)

**** Exclusions: Missing flexural strength data and did not answered email contact (n=1); Did not executed a flexural strength test (n=6);

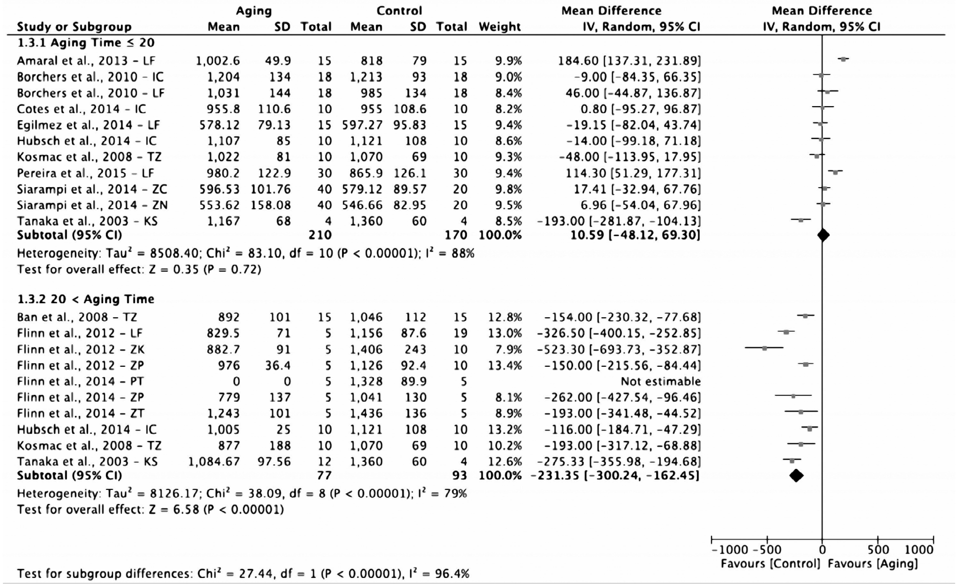
Figure 1. Flow diagram of study selection according to PRISMA statement



	Aging			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Amaral et al., 2013 - LF	1,002.6	49.9	15	818	79	15	6.3%	184.60 [137.31, 231.89]
Ban et al., 2008 - TZ	892	101	15	1,046	112	15	6.0%	-154.00 [-230.32, -77.68]
Borchers et al., 2010 - IC	1,204	134	18	1,213	93	18	6.1%	-9.00 [-84.35, 66.35]
Borchers et al., 2010 - LF	1,031	144	18	985	134	18	5.9%	46.00 [-44.87, 136.87]
Cotes et al., 2014 - IC	955.8	110.6	10	955	108.6	10	5.8%	0.80 [-95.27, 96.87]
Egilmez et al., 2014 - LF	578.12	79.73	15	597.27	95.83	15	6.2%	-19.15 [-82.24, 43.94]
Flinn et al., 2012 - LF	829.5	71	5	1,156	87.6	10	6.0%	-326.50 [-409.09, -243.91]
Flinn et al., 2012 - ZK	882.7	91	5	1,406	243	10	4.8%	-523.30 [-693.73, -352.87]
Flinn et al., 2012 - ZP	976	36.4	5	1,126	92.4	10	6.2%	-150.00 [-215.56, -84.44]
Flinn et al., 2014 - PT	0	0	5	1,328	89.9	5		Not estimable
Flinn et al., 2014 - ZP	779	137	5	1,041	130	5	4.9%	-262.00 [-427.54, -96.46]
Flinn et al., 2014 - ZT	1,243	101	5	1,436	136	5	5.1%	-193.00 [-341.48, -44.52]
Hubsch et al., 2014 - IC	1,056	80.35	20	1,121	108	10	6.1%	-65.00 [-140.64, 10.64]
Kosmac et al., 2008 - TZ	949.5	159.32	20	1,070	69	10	6.0%	-120.50 [-202.38, -38.62]
Pereira et al., 2015 - LF	980.2	122.9	30	865.9	126.1	30	6.2%	114.30 [51.29, 177.31]
Siarampi et al., 2014 - ZC	596.53	100.51	40	579.12	89.57	20	6.3%	17.41 [-32.70, 67.52]
Siarampi et al., 2014 - ZN	553.62	157.83	40	546.66	82.95	20	6.2%	6.96 [-53.98, 67.90]
Tanaka et al., 2003 - KS	1,105.25	96.22	16	1,360	60	4	6.1%	-254.75 [-330.12, -179.38]
Total (95% CI)			**287**			**230**	**100.0%**	**-91.28 [-165.19, -17.38]**

Heterogeneity: $Tau^2 = 21992.11$; $Chi^2 = 264.15$, df = 16 ($P < 0.00001$); $I^2 = 94\%$
Test for overall effect: Z = 2.42 (P = 0.02)

A



	Aging			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.3.1 Aging Time ≤ 20								
Amaral et al., 2013 - LF	1,002.6	49.9	15	818	79	15	9.9%	184.60 [137.31, 231.89]
Borchers et al., 2010 - IC	1,204	134	18	1,213	93	18	9.0%	-9.00 [-84.35, 66.35]
Borchers et al., 2010 - LF	1,031	144	18	985	134	18	8.4%	46.00 [-44.87, 136.87]
Cotes et al., 2014 - IC	955.8	110.6	10	955	108.6	10	8.2%	0.80 [-95.27, 96.87]
Egilmez et al., 2014 - LF	578.12	79.13	15	597.27	95.83	15	9.4%	-19.15 [-82.04, 43.74]
Hubsch et al., 2014 - IC	1,107	85	10	1,121	108	10	8.6%	-14.00 [-99.18, 71.18]
Kosmac et al., 2008 - TZ	1,022	81	10	1,070	69	10	9.3%	-48.00 [-113.95, 17.95]
Pereira et al., 2015 - LF	980.2	122.9	30	865.9	126.1	30	9.4%	114.30 [51.29, 177.31]
Siarampi et al., 2014 - ZC	596.53	101.76	40	579.12	89.57	20	9.8%	17.41 [-32.94, 67.76]
Siarampi et al., 2014 - ZN	553.62	158.08	40	546.66	82.95	20	9.5%	6.96 [-54.04, 67.96]
Tanaka et al., 2003 - KS	1,167	68	4	1,360	60	4	8.5%	-193.00 [-281.87, -104.13]
Subtotal (95% CI)			**210**			**170**	**100.0%**	**10.59 [-48.12, 69.30]**
Heterogeneity: $Tau^2 = 8508.40$; $Chi^2 = 83.10$, df = 10 ($P < 0.00001$); $I^2 = 88\%$								
Test for overall effect: Z = 0.35 (P = 0.72)								
1.3.2 20 < Aging Time								
Ban et al., 2008 - TZ	892	101	15	1,046	112	15	12.8%	-154.00 [-230.32, -77.68]
Flinn et al., 2012 - LF	829.5	71	5	1,156	87.6	19	13.0%	-326.50 [-400.15, -252.85]
Flinn et al., 2012 - ZK	882.7	91	5	1,406	243	10	7.9%	-523.30 [-693.73, -352.87]
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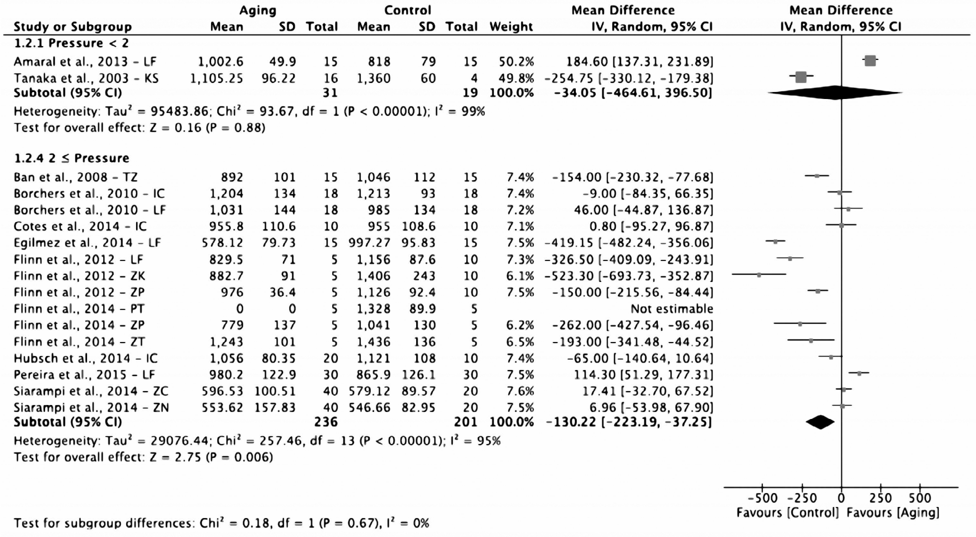
Flinn et al., 2014 - PT	0	0	5	1,328	89.9	5		Not estimable
Flinn et al., 2014 - ZP	779	137	5	1,041	130	5	8.1%	-262.00 [-427.54, -96.46]
Flinn et al., 2014 - ZT	1,243	101	5	1,436	136	5	8.9%	-193.00 [-341.48, -44.52]
Hubsch et al., 2014 - IC	1,005	25	10	1,121	108	10	13.2%	-116.00 [-184.71, -47.29]
Kosmac et al., 2008 - TZ	877	188	10	1,070	69	10	10.2%	-193.00 [-317.12, -68.88]
Tanaka et al., 2003 - KS	1,084.67	97.56	12	1,360	60	4	12.6%	-275.33 [-355.98, -194.68]
Subtotal (95% CI)			**77**			**93**	**100.0%**	**-231.35 [-300.24, -162.45]**
Heterogeneity: $Tau^2 = 8126.17$; $Chi^2 = 38.09$, df = 8 ($P < 0.00001$); $I^2 = 79\%$								
Test for overall effect: Z = 6.58 (P < 0.00001)								

Test for subgroup differences: $Chi^2 = 27.44$, df = 1 ($P < 0.00001$), $I^2 = 96.4\%$

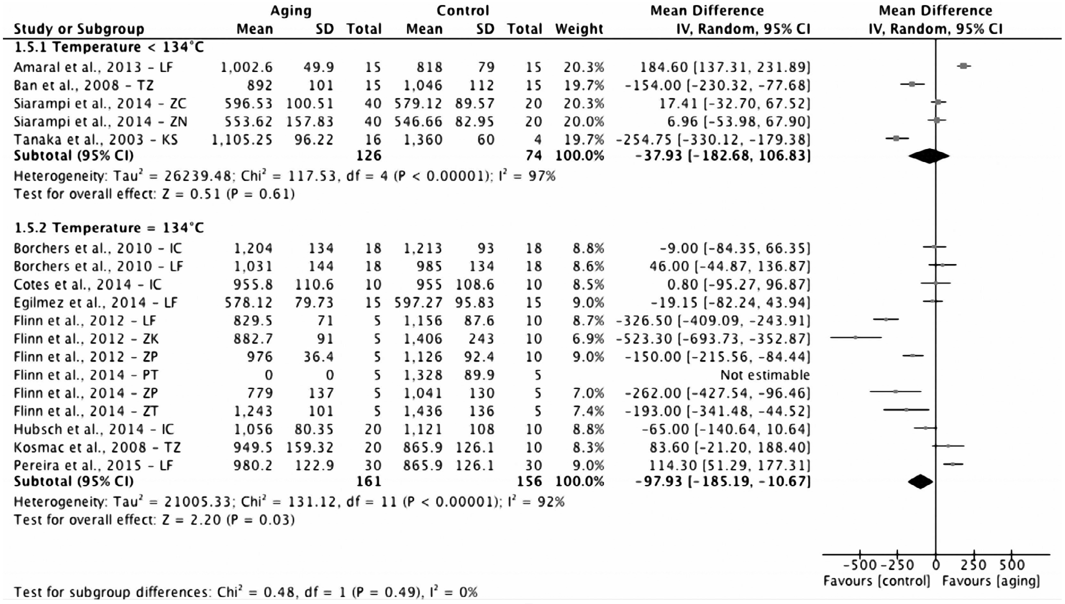
B



	Aging			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.2.1 Pressure < 2								
Amaral et al., 2013 - LF	1,002.6	49.9	15	818	79	15	50.2%	184.60 [137.31, 231.89]
Tanaka et al., 2003 - KS	1,105.25	96.22	16	1,360	60	4	49.8%	-254.75 [-330.12, -179.38]
Subtotal (95% CI)			**31**			**19**	**100.0%**	**-34.05 [-464.61, 396.50]**
Heterogeneity: $Tau^2 = 95483.86$; $Chi^2 = 93.67$, df = 1 ($P < 0.00001$); $I^2 = 99\%$								
Test for overall effect: Z = 0.16 (P = 0.88)								
1.2.4 2 ≤ Pressure								
Ban et al., 2008 - TZ	892	101	15	1,046	112	15	7.4%	-154.00 [-230.32, -77.68]
Borchers et al., 2010 - IC	1,204	134	18	1,213	93	18	7.4%	-9.00 [-84.35, 66.35]
Borchers et al., 2010 - LF	1,031	144	18	985	134	18	7.2%	46.00 [-44.87, 136.87]
Cotes et al., 2014 - IC	955.8	110.6	10	955	108.6	10	7.1%	0.80 [-95.27, 96.87]
Egilmez et al., 2014 - LF	578.12	79.73	15	997.27	95.83	15	7.5%	-419.15 [-482.24, -356.06]
Flinn et al., 2012 - LF	829.5	71	5	1,156	87.6	10	7.3%	-326.50 [-409.09, -243.91]
Flinn et al., 2012 - ZK	882.7	91	5	1,406	243	10	6.1%	-523.30 [-693.73, -352.87]
Flinn et al., 2012 - ZP	976	36.4	5	1,126	92.4	10	7.5%	-150.00 [-215.56, -84.44]
Flinn et al., 2014 - PT	0	0	5	1,328	89.9	5		Not estimable
Flinn et al., 2014 - ZP	779	137	5	1,041	130	5	6.2%	-262.00 [-427.54, -96.46]
Flinn et al., 2014 - ZT	1,243	101	5	1,436	136	5	6.5%	-193.00 [-341.48, -44.52]
Hubsch et al., 2014 - IC	1,056	80.35	20	1,121	108	10	7.4%	-65.00 [-140.64, 10.64]
Pereira et al., 2015 - LF	980.2	122.9	30	865.9	126.1	30	7.5%	114.30 [51.29, 177.31]
Siarampi et al., 2014 - ZC	596.53	100.51	40	579.12	89.57	20	7.6%	17.41 [-32.70, 67.52]
Siarampi et al., 2014 - ZN	553.62	157.83	40	546.66	82.95	20	7.5%	6.96 [-53.98, 67.90]
Subtotal (95% CI)			**236**			**201**	**100.0%**	**-130.22 [-223.19, -37.25]**
Heterogeneity: $Tau^2 = 29076.44$; $Chi^2 = 257.46$, df = 13 ($P < 0.00001$); $I^2 = 95\%$								
Test for overall effect: Z = 2.75 (P = 0.006)								

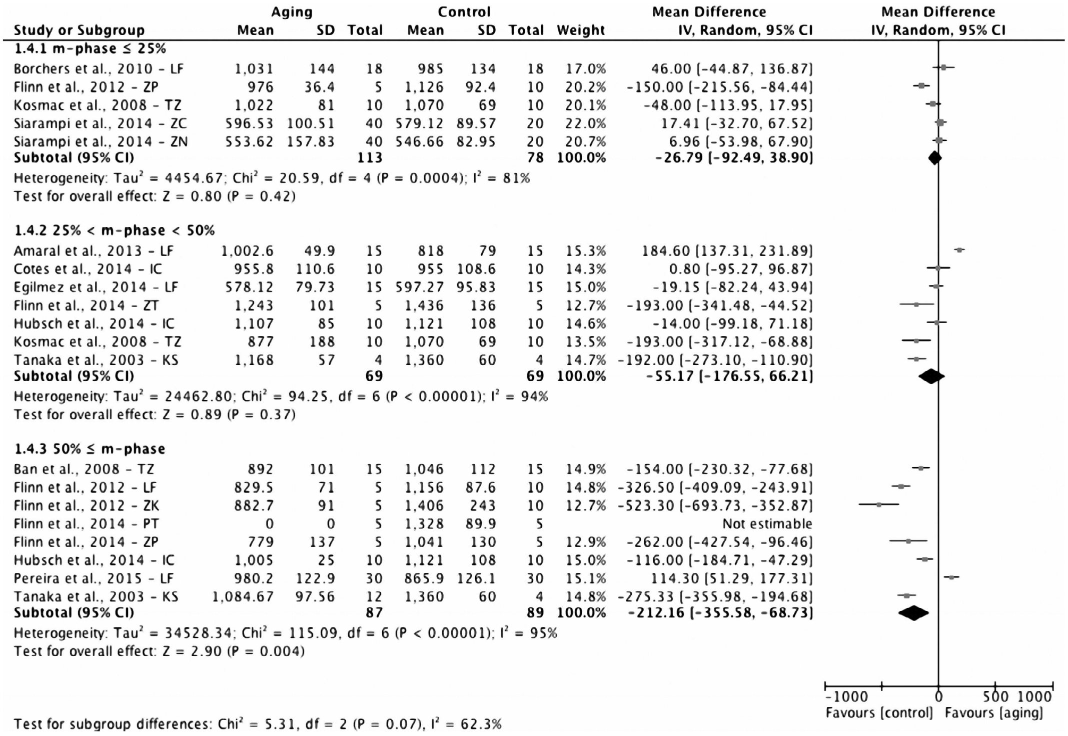
Test for subgroup differences: $Chi^2 = 0.18$, df = 1 ($P = 0.67$), $I^2 = 0\%$

C



	Aging			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.5.1 Temperature < 134°C								
Amaral et al., 2013 - LF	1,002.6	49.9	15	818	79	15	20.3%	184.60 [137.31, 231.89]
Ban et al., 2008 - TZ	892	101	15	1,046	112	15	19.7%	-154.00 [-230.32, -77.68]
Siarampi et al., 2014 - ZC	596.53	100.51	40	579.12	89.57	20	20.3%	17.41 [-32.70, 67.52]
Siarampi et al., 2014 - ZN	553.62	157.83	40	546.66	82.95	20	20.0%	6.96 [-53.98, 67.90]
Tanaka et al., 2003 - KS	1,105.25	96.22	16	1,360	60	4	19.7%	-254.75 [-330.12, -179.38]
Subtotal (95% CI)			**126**			**74**	**100.0%**	**-37.93 [-182.68, 106.83]**
Heterogeneity: Tau² = 26239.48; Chi² = 117.53, df = 4 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 0.51 (P = 0.61)								
1.5.2 Temperature = 134°C								
Borchers et al., 2010 - IC	1,204	134	18	1,213	93	18	8.8%	-9.00 [-84.35, 66.35]
Borchers et al., 2010 - LF	1,031	144	18	985	134	18	8.6%	46.00 [-44.87, 136.87]
Cotes et al., 2014 - IC	955.8	110.6	10	955	108.6	10	8.5%	0.80 [-95.27, 96.87]
Egilmez et al., 2014 - LF	578.12	79.73	15	597.27	95.83	15	9.0%	-19.15 [-82.24, 43.94]
Flinn et al., 2012 - LF	829.5	71	5	1,156	87.6	10	8.7%	-326.50 [-409.09, -243.91]
Flinn et al., 2012 - ZK	882.7	91	5	1,406	243	10	6.9%	-523.30 [-693.73, -352.87]
Flinn et al., 2012 - ZP	976	36.4	5	1,126	92.4	10	9.0%	-150.00 [-215.56, -84.44]
Flinn et al., 2014 - PT	0	0	5	1,328	89.9	5		Not estimable
Flinn et al., 2014 - ZP	779	137	5	1,041	130	5	7.0%	-262.00 [-427.54, -96.46]
Flinn et al., 2014 - ZT	1,243	101	5	1,436	136	5	7.4%	-193.00 [-341.48, -44.52]
Hubsch et al., 2014 - IC	1,056	80.35	20	1,121	108	10	8.8%	-65.00 [-140.64, 10.64]
Kosmac et al., 2008 - TZ	949.5	159.32	20	865.9	126.1	10	8.3%	83.60 [-21.20, 188.40]
Pereira et al., 2015 - LF	980.2	122.9	30	865.9	126.1	30	9.0%	114.30 [51.29, 177.31]
Subtotal (95% CI)			**161**			**156**	**100.0%**	**-97.93 [-185.19, -10.67]**
Heterogeneity: Tau² = 21005.33; Chi² = 131.12, df = 11 (P < 0.00001); I² = 92%								
Test for overall effect: Z = 2.20 (P = 0.03)								
Test for subgroup differences: Chi² = 0.48, df = 1 (P = 0.49), I² = 0%								

D



	Aging			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.4.1 m-phase ≤ 25%								
Borchers et al., 2010 - LF	1,031	144	18	985	134	18	17.0%	46.00 [-44.87, 136.87]
Flinn et al., 2012 - ZP	976	36.4	5	1,126	92.4	10	20.2%	-150.00 [-215.56, -84.44]
Kosmac et al., 2008 - TZ	1,022	81	10	1,070	69	10	20.1%	-48.00 [-113.95, 17.95]
Siarampi et al., 2014 - ZC	596.53	100.51	40	579.12	89.57	20	22.0%	17.41 [-32.70, 67.52]
Siarampi et al., 2014 - ZN	553.62	157.83	40	546.66	82.95	20	20.7%	6.96 [-53.98, 67.90]
Subtotal (95% CI)			**113**			**78**	**100.0%**	**-26.79 [-92.49, 38.90]**
Heterogeneity: Tau² = 4454.67; Chi² = 20.59, df = 4 (P = 0.0004); I² = 81%								
Test for overall effect: Z = 0.80 (P = 0.42)								
1.4.2 25% < m-phase < 50%								
Amaral et al., 2013 - LF	1,002.6	49.9	15	818	79	15	15.3%	184.60 [137.31, 231.89]
Cotes et al., 2014 - IC	955.8	110.6	10	955	108.6	10	14.3%	0.80 [-95.27, 96.87]
Egilmez et al., 2014 - LF	578.12	79.73	15	597.27	95.83	15	15.0%	-19.15 [-82.24, 43.94]
Flinn et al., 2014 - ZT	1,243	101	5	1,436	136	5	12.7%	-193.00 [-341.48, -44.52]
Hubsch et al., 2014 - IC	1,107	85	10	1,121	108	10	14.6%	-14.00 [-99.18, 71.18]
Kosmac et al., 2008 - TZ	877	188	10	1,070	69	10	13.5%	-193.00 [-317.12, -68.88]
Tanaka et al., 2003 - KS	1,168	57	4	1,360	60	4	14.7%	-192.00 [-273.10, -110.90]
Subtotal (95% CI)			**69**			**69**	**100.0%**	**-55.17 [-176.55, 66.21]**
Heterogeneity: Tau² = 24462.80; Chi² = 94.25, df = 6 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 0.89 (P = 0.37)								
1.4.3 50% ≤ m-phase								
Ban et al., 2008 - TZ	892	101	15	1,046	112	15	14.9%	-154.00 [-230.32, -77.68]
Flinn et al., 2012 - LF	829.5	71	5	1,156	87.6	10	14.8%	-326.50 [-409.09, -243.91]
Flinn et al., 2012 - ZK	882.7	91	5	1,406	243	10	12.7%	-523.30 [-693.73, -352.87]
Flinn et al., 2014 - PT	0	0	5	1,328	89.9	5		Not estimable
Flinn et al., 2014 - ZP	779	137	5	1,041	130	5	12.9%	-262.00 [-427.54, -96.46]
Hubsch et al., 2014 - IC	1,005	25	10	1,121	108	10	15.0%	-116.00 [-184.71, -47.29]
Pereira et al., 2015 - LF	980.2	122.9	30	865.9	126.1	30	15.1%	114.30 [51.29, 177.31]
Tanaka et al., 2003 - KS	1,084.67	97.56	12	1,360	60	4	14.8%	-275.33 [-355.98, -194.68]
Subtotal (95% CI)			**87**			**89**	**100.0%**	**-212.16 [-355.58, -68.73]**
Heterogeneity: Tau² = 34528.34; Chi² = 115.09, df = 6 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 2.90 (P = 0.004)								
Test for subgroup differences: Chi² = 5.31, df = 2 (P = 0.07), I² = 62.3%								

E

Figure 2. Forest plots according to the meta-analyses. *Global* (**A**) *Aging subgroup analysis*: (**B**) Aging time; (**C**) Pressure; (**D**) Temperature; (**E**) m-phase % content.

Tables

Terms used	Y-TZP	LTD	Outcomes
MESH	zirconium	-	-
free-text	zirconi*; zirconium oxide; Y-TZP; yttria stabilized polycrystalline tetragonal zirconia; yttria stabilized tetragonal zirconia.	Low temperature degradation; Low-temperature degradation; hydrothermal degradation; hydrothermal ag*; thermal degradation; thermal ag*; aging; ageing; water storage.	structural stability; phase stability; phase transformation; surface topography; surface morphology; surface characteristic*; mechanical properties; mechanical behaviour; strength; resistance; hardness; toughness; stiffness; roughness; density; porosity; fracture; flexural;

Table 1. Research strategy (with MESH and free-text terms).

Author/year	Country	YTZP name	Brand	Low Temperature Aging Protocol	XRD Parameters	Flexural Strength
Amaral et al., 2013	Brazil	Lava Frame (LF)	3M ESPE	127°± 1°C and 1.5 bar for 12 h	20° to 65°, step size of 0.03°, 0,5s per step	Biaxial strength (piston on three balls)
Arata et al., 2014	Brazil	VITA In Ceram YZ (IC)	VITA	103°C and 2.07 bar for 138 h	20° to 80°, step size of 0.02°, 10 s per step	---
Ban et al., 2008	Japan	TZ-3YB-E (TZ)	Tosoh	121°C under 2 bar for 10 days	2θ angles between 27° and 32° at 1°/min	Biaxial strength (piston on three balls)
Borchers et al., 2010	Germany	Lava Frame (LF)	3M ESPE	134°C and 3 bar for 8 h	15° to 110°, step size of 0.03°, 4 s per step	Biaxial strength (piston on three balls)
		VITA In Ceram YZ (IC)	VITA			
Cattani-Lorente et al., 2011	Switzerland	Lava Frame (LF)	3M ESPE	140°C and 1 bar for 1, 4, 7 days	26° to 64°, step size of 0.01°, 2 s per step	---
Cotes et al., 2014	Brazil	VITA In Ceram YZ (IC)	VITA	134°C and 2 bar for 12 h	20° to 80°, step size of 0.02°, 10 s per step	Biaxial strength (piston on three balls)
Egilmez et al., 2014	Turkey	Lava Frame (LF)	3M ESPE	134°C and 2 bar for 5 h	20° to 40°, step size of 0.02°, 1 s per step	Uniaxial strength (three point bend test)
Flinn et al., 2012	USA	Lava Frame (LF)	3M ESPE	134°C and 2 bar for 50, 100, 150 and 200 h	27° to 36°, step size of 0.02°	Uniaxial strength (four point bend test)
		Zirkonzahn (ZK)	Zirkonzahn			
		Zirprime (ZP)	Kuraray Noritake			
Flinn et al., 2014	USA	Prettau (PT)	Zirkonzahn	134°C and 2 bar for 5, 50, 100, 150 and 200 h	27° to 36°, step size of 0.02°	Uniaxial strength (four point bend test)
		Zirprime (ZP)	Kuraray Noritake			
		Zirtough (ZT)	Kuraray Noritake			
Hubsch et al., 2014	Germany	VITA In Ceram YZ (IC)	VITA	134°C and 3 bar for 4, 8, 16, 32, 64 and 128 h	25° to 35°, step size of 0.2°, 4 s per step	Biaxial strength (piston on three balls)
Inokoshi et al., 2014	Belgium	Aadva (AD)	GC	134°C and 2 bar for 6 h	27° to 33°, step size of 0.02°, 2 s per step	---
		IPS e.max ZirCAD (ZC)	Ivoclar			
		Vita In Ceram YZ (IC)	VITA			
Inokoshi et al., 2015	Belgium	Aadva (AD)	GC	134°C and 2 bar for 40 h	20° to 90°, step size of 0.01°, 3 s per step	---
		VITA In Ceram YZ (IC)	VITA			
		IPS emax ZirCAD (ZC)	Ivoclar			
		Lava Frame (LF)	3M ESPE			
		Lava Plus (LP)	3M ESPE			

Kim et al., 2010	USA	IPS emax ZirCAD (ZC)	Ivoclar	122°C and 2 bar for 0 to 20 h	27° to 33°, step size of 0.02°, 1.2 s per step	---
Kosmac et al., 2008	Slovenia	TZ-3YB-E (TZ)	Tosoh	134°C and 1 bar for 2 to 24 h	Not specified	Biaxial strength (piston on three balls)
Lucas et al., 2014	USA	Not specified	3M ESPE	121°C and 1 bar for 1, 3, and 5 h / 134°C and 2 bar for 1, 3 and 5 h	25° to 33°, step size of 0.02°, 12 s per step	---
Pereira et al., 2015	Brazil	Lava Frame (LF)	3M ESPE	134°C and 2 bar for 20 h	25° to 35°, step size of 0.03°, 1 s per step	Biaxial strength (piston on three balls)
Siarampi et al., 2014	Greece	IPS emax ZirCAD (ZC)	Ivoclar	121°C and 2 bar for 5 and 10 h	5° to 75°, step size of 0.02°, 2s per step	Uniaxial strength (three point bend test)
		ZENO Zir (ZN)	Wieland Dental			
Tanaka et al., 2003	Japan	Kobe Steel Co. (KS)	Kobe	121°C and 1.5 bar for 6, 12, 18, 36, 72, 108, and 190 h	25° to 37°, all other parameters are not specified	Uniaxial strength (three point bend test)
Xiao et al., 2012	China	Lava Frame (LF)	3M ESPE	134°C and 2 bar for 5, 10, 15 and 20 h	26° to 33°, step size of 0.02°, 1 s per step	Uniaxial strength (three point bend test)
		Upcera (UP)	Shenzhen			
		Cercon (CC)	Dentsply			

Table 2. Characteristics from the studies included in the systematic review.

Author/Year	Random	Sintering	Sample Preparation	International Standard for Strength Testing	Aging Parameters	Sample Size	Operator	Total	Risk of Bias
Amaral et al., 2013	2	1	0	0	0	2	2	7	Medium
Arata et al., 2014	2	1	0	NA	0	2	NA	5	Medium
Ban et al., 2008	2	1	1	0	0	2	2	8	Medium
Borchers et al., 2010	0	1	1	0	0	2	2	6	Medium
Cattani-Lorente et al., 2011	2	0	1	NA	0	2	NA	5	Medium
Cotes et al., 2014	0	1	0	0	0	2	2	5	Medium
Egilmez et al., 2014	0	0	0	1	0	2	2	5	Medium
Flinn et al., 2012	2	0	1	1	0	1	2	7	Medium
Flinn et al., 2014	2	0	1	1	0	1	2	7	Medium
Hubsch et al., 2014	0	2	1	0	0	2	2	7	Medium
Inokoshi et al., 2014	2	2	1	NA	0	2	NA	7	Medium
Inokoshi et al., 2015	2	0	0	NA	0	2	NA	4	Medium
Kosmac et al., 2008	0	1	0	0	1	2	2	6	Medium
Kim et al., 2010	0	1	1	NA	0	2	NA	4	Medium
Lucas et al., 2014	0	2	0	NA	0	2	NA	4	Medium
Pereira et al., 2015	2	0	0	0	0	2	2	6	Medium
Siarampi et al., 2014	2	0	0	0	0	2	2	6	Medium
Tanaka et al., 2003	2	2	1	2	0	2	2	11	High
Xiao et al., 2012	2	0	1	0	0	2	2	7	Medium

Table 3. Risk of Bias of the Studies Considering Aspects Reported in the Materials & Methods Section

Author/Year	Yz Material	Methodology for m-phase quantification	Sample Size	Before Aging M-phase (SD)	Aging Protocol	After Aging M-phase (SD)
Amaral et al., 2013	Lava Frame 3M ESPE	from peaks height by Garvie and Nicholson equation modified by Toraya	2	1,37%	127°C, 1.5 bar for 12 hours	23,4% 12h;
Arata et al., 2014	In Ceram YZ VITA	from peaks height by Garvie and Nicholson equation modified by Toraya	4	0%	103°C, 2.07 bar for 138 hours	23,2% 6h; 42,9% 20h; 72,0% 40h; 80,6% 60h; 81,8% 138h;
		from the area under the peaks by Garvie and Nicholson equation modified by Toraya	4	0%		36,1% 6h; 53,9% 20h; 66,1% 40h; 71,0% 60h; 73,3% 138h;
		Rietveld method	4	0%		30,5% 6h; 49,9% 20h; 57,3% 40h; 59,9% 60h; 63,2% 138h;
Ban et al., 2008	TZ-3YB-E Tosoh	from peaks height by Garvie and Nicholson equation modified by Toraya	3	0,3%	121°C, 2 bar for 10 days	49,9% 10 days;
Borchers et al., 2010	Lava Frame 3M ESPE	Rietveld method	4	2%	134°C, 3 bar for 8 hours	7% 8h;
	In Ceram YZ VITA		Not executed			-
Cattani-Lorente et al., 2011	Lava Frame 3M ESPE	Rietveld method	5	0,4% (±0,9)	134°C, 1 bar for 1, 4 and 7 days	31% (±12) 24h; 64% (±7) 96h; 68% (±6) 168h;
Cotes et al., 2014	In Ceram YZ VITA	from peaks height by Garvie and Nicholson equation modified by Toraya	10	0%	134°C, 2 bar for 12 hours	30% 12h;
Egilmez et al., 2014	Lava Frame 3M ESPE	from peaks height by Garvie and Nicholson equation modified by Toraya	0	13,35%	134°C, 2 bar for 5 hours	25,4% 5h;
Flinn et al., 2012	Lava Frame 3M ESPE	from peaks height by Garvie and Nicholson equation	3	0%	134°C, 2 bar for 50, 100, 150 and 200 hours	not presented
	Zirconzahn Zirconzahn		3	0%		80% for 200h;
	Zirprime		3	0%		25% for 200h;

	Kuraray Noritake					
Flinn et al., 2014	Prettau Zirconzahn	from peaks height by Garvie and Nicholson equation	3	3,08% (±0,28)	134°C, 2 bar for 5, 50, 100, 150 and 200 hours	79% (±2) 200h;
	Zirprime Kuraray Noritake		3	1,95% (±0,48)		75% (±0,52) 200h;
	Zirtough Kuraray Noritake		3	12,4% (±0,6)		31,4% (±4,4) 200h;
Hubsch et al., 2014	In Ceram YZ VITA	from peaks height by Garvie and Nicholson equation modified by Toraya	4	0%	134°C, 3 bar for 4, 8, 16, 32, 64 and 128 hours	23% (±1,7) 4h 46% (±2,2) 16h 69% (±0,9) 32h 75% (±0,2) 64h 76% (±0,1) 128h
Inokoshi et al., 2014	Aadva GC	Garvie and Nicholson equation modified by Toraya	3	1,02% (±0,2)	134C and 2 bar for 6h	14,5% (±0.9)
	IPS e.max ZirCAD Ivoclar			1,11% (±0,3)		15,5% (±1.1)
	In Ceram Yz VITA			1,09% (±0,3)		15,5% (±1.3)
Inokoshi et al., 2015	Aadva GC	Garvie and Nicholson equation modified by Toraya	3	0%	134°C, 2 bar for 40 hours	13,5% 4h 41,0% 20h 54,7% 30h 64,5% 40h
	In Ceram YZ VITA			0%		13,5% 4h 45,9% 20h 59,1% 30h 67,5% 40h
	IPS e.max ZirCAD Ivoclar			0%		8,6% 4h 56,2% 20h 71,3% 30h 78,4% 40h
	Lava Frame 3M ESPE			0%		17,1% 4h 55,5% 20h 68,9% 30h 75,9% 40h
	Lava Plus 3M ESPE			0%		3,3% 4h 52,9% 20h 71,4% 30h

						77,8% 40h
Kosmac et al., 2008	TZ-3YB-E Tosoh	Garvie and Nicholson equation	10	m<1%	134°C, 1 bar for 2 to 24 hours (artificial saliva as solution)	5,1% (±0,4) 2h 25,6% (±4,1) 24h
Kim et al., 2010	IPS e.max ZirCAD Ivoclar	Garvie and Nicholson equation	3	0%	122°C, 2 bar 0 to 20 hours	55% 20h
Lucas et al., 2014	Not specificate 3M ESPE	from the area under the peaks by Garvie and Nicholson equation	5	0,73% (±0,1)	121°C, 1 bar for 1, 3 and 5 hours	2,1% (±1,1) 1h 6,3% (±1,1) 3h 9,3% (±1,1) 5h
					134°C, 2 bar for 1, 3 and 5 hours	2,9% (±0,5) 1h 12,6% (±1,9) 3h 18,1% (±1,6) 5h
Pereira et al., 2015	Lava Frame 3M ESPE	from peaks height by Garvie and Nicholson equation modified by Toraya	2	0%	134°C, 2 bar for 20 hours	53,3% 20h
Siarampi et al., 2014	IPS e.max ZirCAD Ivoclar	from the area under the peaks by Garvie and Nicholson equation	10	0%	121°C, 2 bar for 5 and 10 hours	5% 5h 11% 10h
	Zeno Zir Wieland			0%		4% 5h 14% 10h
Tanaka et al., 2003	Kobe Steel Co. Kobe	Garvie and Nicholson equation modified by Toraya	4	0,4%	121°C, 1,5bar for 6, 12, 18, 36, 72, 108, or 190 h	81% 190h
Xiao et al., 2012	Lava Frame 3M ESPE	Garvie and Nicholson equation	3	7,7% (±1,32)	134°C, 2 bar for 5,10, 15 and 20 hours (eletric stove)	9,5% (±1,0) 5h 11,6% (±1,9) 10h 12,2%(±2,3) 15h 13,0%(±1,4) 20h
	Upcera Shenzen			10,84% (±1,29)		14,8% (±2,0) 5h 24,6% (±2,2) 10h 29,6%(±3,3) 15h 35,2%(±2,5) 20h
	Cercon Smart Dentsply			4,95% (±0,65)		5,9% (±0,7) 5h 6,6% (±0,8) 10h 7,2%(±0,9) 15h 8,5%(±0,9) 20h

Table 4. **Phase transformation descriptive analysis from included studies**

4. ARTIGO 3 - Comparison of different low-temperature aging protocols: its effects on the mechanical behavior of Y-TZP ceramics

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Running title: Comparison of low-temperature aging protocols effect on YTZP.

Abstract

This study evaluated the effect of different protocols of low-temperature degradation simulation on the mechanical behavior (structural reliability and flexural resistance), the surface topography (roughness), and phase transformation of a Y-TZP ceramic. Disc-shaped specimens (1.2mm x 12mm, Lava Frame, 3M ESPE, Seefeld, Germany) were manufactured according to ISO:6872-2008 and divided (n=30) according to the aging protocol executed: "Ctrl" – *as-sintered* – without any treatment; "Dist Water" – stored at distilled water at 37°C for 365 days; "MC" mechanical cycling into two steps: First – 200N, 2.2Hz for 2.000.000 cycles, Second – 450N, 10Hz for 1.000.000 cycles; "Aut" – steam autoclave at 134°C, 2 bar (200Kpa) for 20 h; "Aut+MC"– Aut and MC methods. Roughness analysis (µm) showed, for Ra parameter, higher statistically significant values for Ctrl 0.68 (0.27), while for Rz parameter, the highest values were observed for Ctrl 4.43(1.53) and Aut 2.24 (0.62). Surface topography analysis showed that none aging method promoted surface alterations when compared to control group. Phase transformation analysis showed that all aging methods promoted an increase in m-phase content (Ctrl: 0.94%, Dist Water: 20.73%, MC: 9.47%, Aut: 53.33% and Aut+MC: 61.91%). Weibull Analysis showed higher statistical characteristic strength values for Aut (1033.36 MPa) and Dist Water (1053.76 MPa). No aging method promoted deleterious impact either on the biaxial flexural strengths or on the structural reliabilities (Weibull moduli). Also, none of the aging methods promoted reduction of Y-TZP mechanical properties; thus the development of new methodologies and the association between mechanical stimuli and hydrothermal degradation should be considered to better understand the mechanism of low-temperature degradation.

Key words: low-temperature degradation, aging methods, biaxial flexural strength, Y-TZP, dental ceramics.

1. Introduction

For a long time, the metal-ceramic restorations were the only option for making unit or multiple fixed dental prostheses (FDPs). Currently, the aesthetic requirement allied to the advancement of CAD / CAM (*computer assisted design / computer assisted machining*) procedures in the 80s, made zirconia-based prostheses occupy considerable space devoted by metal-ceramic prostheses (Denry & Kelly, 2014).

Zirconia is a high-strength ceramic material (Piconi & Maccauro, 1999) that is able to respond with a transformation toughening mechanism when it is submitted to localized stimuli, such as stress and presence of water associated with temperature changes. These stimuli promote a crystallographic alteration (tetragonal *(t)* to monoclinic *(m)* phase transformation), which results in a localized volume increase and a compression stress concentration around superficial defects that difficult fracture propagation (Garvie & Nicholson, 1972; Piconi & Maccauro, 1999; Egilmez, et al. 2014; Pereira, et al. 2015).

Nonetheless the clinical and scientific community has become cautious regarding the clinical use of zirconia-based ceramics, given Prozir episode (2001), in which thousands of implanted femoral heads prematurely failed in consequence of a high susceptibility of this material to degradation (Chevalier, 2007). Kobayashi and collaborators (1981) observed that when zirconia is exposed to an environment with high humidity and low temperatures (150-400°C), a spontaneous deleterious phenomenon associated with the transformation from tetragonal to monoclinic phase ($t \rightarrow m$) occurs. This phenomenon is known as low temperature degradation (LTD) or hydrothermal degradation.

Lately, the use of Y-TZP as full-contour monolithic restorations has been proposed, which brings the advantages of: (1) a more conservative tooth preparation, since it requires a thinner thickness, which is a highly attractive characteristic for situations when strength, function, and aesthetics are required (Denry & Kelly, 2014), and (2) dispenses the application of veneering porcelain (Beuer, et al. 2012; Sabrah, et al. 2013; Nakamura, et al. 2015).

It is important to note that clinically these restorations will be submitted to different associated stimuli (mechanical stimulus, action of water and temperatures, biofilm, ph) and by that constituting an ideal plausible scenario for LTD to take place. Therefore it is relevant to evaluate and understand the behavior of such restorations when submitted to in vitro scenarios with aging approaches that simulate these conditions.

However, the literature has only been evaluating LTD mechanism with regards to isolated factors: storage in distilled water, storage in acidic solutions (i.e.: acetic acid), autoclave cycles, steam chambers – boiling storage, mechanical cycling (Chevalier et al., 2007; Inokoshi et al., 2015; Lucas et al., 2015; Cotes et al., 2014; Egilmez et al., 2014; Turp et al., 2012). To the authors' knowledge, there is only one study (Cotes et al., 2014) that has evaluated aging with association of different stimuli (autoclave + mechanical cycling).

Thus, before the recommendation of such monolithic restorations, an evaluation of the material's sensitivity and susceptibility to aging needs to be further investigated in laboratorial tests. The present *in vitro* study aims to investigate and compare the effects of different aging protocols (among the most described ones in the literature) on the biaxial flexural strength, surface topography, structural stability, and phase transformation of a Y-TZP ceramic.

2. Materials and Methods

2.1 Sample Preparation

Disc shaped specimens (N=150) of Y-TZP ceramic (Lot no. 1125100522 – Lava Frame, 3M ESPE, Seefeld, Germany) were manufactured according to ISO:6872-2008. Zirconia pre sintered blocks were ground into cylinders using 600–1200 grit Sic paper (3M, St Paul, MN, USA) under water-cooling; they were then sectioned applying a precision saw machine (ISOMET 1000, Buehler, IL) into the discs. Aiming to remove any irregularity introduced by the cutting procedure, the specimens were polished with 1200-grit SiC paper and then they were cleaned in an ultrasonic bath (1440 D – Odontrobras, Ind. & Com. Equip. Méd. Odonto. LTDA, Ribeirao Preto, Brazil) with 78% isopropyl alcohol for 10min and sintered in a Zyrcomat T furnace (Vita Zahnfabrik, Germany), at 1530 °C for 120 min.

The disc final dimensions were 15 mm diameter X 1.2 mm thickness. After sintering, the specimens were carefully selected. Specimens presenting discrepancies in length above the standard variation (1.2 +/- 0.2 mm) recommended by ISO:6872-2008 were discarded.

2.2 Aging procedures

The specimens were randomly assigned into 5 groups (n=30) according to the aging treatment to be executed:

Ctrl: Control - "*as-sintered*" – no aging treatment.

Dist Wat: storage - immersion in distilled water in a steam (Laboratory Thermo incubator - FANEM, Sao Paulo, Brazil) at 37◦C for 365 days.

Aut: submitted to a thermal cycle of 20 hours in a steam autoclave (Sercon HS1-0300 nº1560389/1) at 134◦C and 2 bars (200Kpa) (Pereira, et al. 2015). This protocol has been chosen because previous literature (Chevalier, 2007; Kim, et al. 2010; Arata, et al. 2014; Inokoshi, et al. 2015) showed that the protocol of 134°C, 2 bar (200Kpa) for 20 hours, promotes an extensive *t-m* phase transformation (approximately 55 - 80% *m*-phase content). Additionally, Kim, et al. (2009) and Ban, et al. (2008) stated that flexural strength was affected negatively only when at least 50% of *m*-phase was detected on the material's surface. Therefore, this protocol has been chosen because it would allow enough time to observe any difference on susceptibility to degradation promoted by grinding, as it also observed in a previous study (Pereira, et al. 2015).

MC: Mechanical cycling – divided into two steps and executed in biaxial flexural test according to ISO:6872-2008:

First step – axial load of 200N, frequency of 2.2 Hz, 2 x 10^6 cycles in distilled water at 37°C at a pneumatic mechanical fatigue simulator (Erios ER 1 force of 11000, Erios, São Paulo, SP, Brazil).

Second step – axial load of 450N, frequency of 10 Hz and 10^6 cycles at room temperature in a servo-hydraulic mechanical fatigue simulator (Instron ElectroPuls E3000, Instron Corporation, United States).

This protocol, 2 steps of mechanical cycling, has been chosen because literature shows that from the clinical point of view, maximum masticatory forces may easily achieve 300–400 N and far reduced average chewing forces of approximately 220 N in the molar region (Proschel & Morneburg, 2002; Hidaka et al., 1999). Thus, the aim was to first submit the material to a condition that simulates the average strength applied in a clinical environment and then in the second step to a hazardous condition that simulates the worst clinical scenario.

Aut + MC: Steam autoclave + Mechanical cycling – association of both methodologies previously described.

2.3 Phase analysis by x-ray diffraction

A quantitative analysis of phase transformation has been conducted (n=3) to determine the relative amount of *m*-phase and depth of the transformed layer under each aging condition evaluated. Specimens submitted to mechanical cycling had their surface submitted to tensile stress evaluated. The analysis was performed using an X-ray diffractometer (Bruker AXS, D8 Advance, Karlsruhe, Germany). Spectra were collected in the 2θ range of 25–35° at a step interval of 1 s and step size of 0.03°. The amount of *m*-phase (X_M) was calculated using the method developed by Garvie & Nicholson (1972):

$$Xm = \frac{(-111)M+(+111)M}{(-111)M+(+111)M+(101)T} \qquad \text{Eq. (1)}$$

Where: $(-111)_M$ and $(111)_M$ represent the intensity of the monoclinic peaks (2θ=28° and 2θ=31.2°, respectively) and $(101)_T$ indicates the intensity of the respective tetragonal peak (2θ=30°). The volumetric fraction (F_m) of the m-phase was calculated according to Toraya, et al. (1984):

$$Fm = \frac{1.311 \cdot Xm}{1+0.311 \cdot Xm} \qquad \text{Eq. (2)}$$

The depth of the transformed layer (TZD) was calculated on the basis of the amount of the *m*-phase, considering that a constant fraction of grains had symmetrically transformed to *m*-phase along the surface, as described by Kosmac, et al. (1981):

$$TZD = \left(\frac{sen\theta}{2\mu}\right)\left[\ln\left(\frac{1}{1-Fm}\right)\right] \qquad \text{Eq. (3)}$$

where θ=15° (the angle of reflection), μ=0.0642 is the absorption coefficient, and FM is the amount of m-phase obtained using Eqs. (1) and (2).

2.4 Surface roughness analysis and SEM

For the quantitative and qualitative determination of surface topography pattern alteration by aging mechanism, the specimens were analyzed in a surface roughness tester (n = 30, Mitutoyo SJ-410, Japan) and Scanning Electron Microscope (SEM) (n = 3, JSM-6360, JEOL, Japan), respectively.

For surface roughness analysis, 6 measurements (measured range until 80 μm where it might be expected an accuracy of 0.001 μm) were conducted for each specimen (3 on x-axis, 3 on y-axis) according to ISO 1997 parameters (Ra – arithmetical mean of the absolute values of peaks and valleys measured from a medium plane (μm); and Rz – average distance between the five highest peaks and 5 major valleys found in the standard (μm)) with a cut-off (n = 5), λC 0.8 mm and λS 2.5 μm. After that, arithmetic mean values of all measurements from each specimen were obtained.

Prior to the surface topography analysis, all specimens were submitted to the cleaning protocol in an ultrasonic bath as described previously.

2.5 Biaxial flexure test

Specimens were subjected to a biaxial flexure strength test according to ISO:6872-2008. Disc-shaped specimens were positioned on three support balls (Ø = 3.2 mm), which were positioned 10 mm apart from each other in a triangular position. The assembly was immersed in water and a flat circular tungsten piston (Ø = 1.6 mm) was used to apply an increasing load (1 mm/min) until catastrophic failure using a universal testing machine (EMIC DL 2000, Sao Jose dos Pinhais, Brazil). Before testing, adhesive tape was fixed on the compression side of the discs to avoid spreading the fragments (Quinn, 2007) and to provide better contact between the piston and the sample (Wachtman, et al. 1972). Flexural strength was calculated according to:

$$\sigma = -0.2387 \cdot \frac{p(X-Y)}{b^2} \qquad \text{Eq. (4)}$$

where σ is the maximum tensile stress (MPa), P is the total load to fracture (N), b is the thickness at fracture origin (mm), and X and Y are calculated according to:

$$X = (1+v)\ln\left(\frac{r_2}{r_3}\right)^2 + \left[\frac{(1-v)}{2}\right]\left(\frac{r_2}{r_3}\right)^2 \qquad \text{Eq. (5)}$$

$$Y = (1 + v)\left[1 + \ln\left(\frac{r_1}{r_3}\right)^2\right] + (1 - v)\left(\frac{r_1}{r_3}\right)^2 \qquad \text{Eq. (6)}$$

where ν is Poisson’s ratio (according to ISO:6872-2008 = 0.25), r_1 is the radius of the support circle (5 mm), r_2 is the radius of the loaded area (0.8 mm), and r_3 is the radius of the specimen (7.5 mm).

2.6 Statistical analysis

Statistical analysis was performed with Statistix for Windows (Analytical Software Inc., version 8.0, 2003, Tallahassee, FL, USA). Data were tabulated and subjected to descriptive analysis, normality and homoscedasticity test. Since roughness data presented a non-parametric distribution, Kruskal-Wallis All-Pairwise Comparisons Test was performed.

Considering that the failure on ceramic materials originates from the most severe defect, the size and spatial distribution of defects justify the need for a statistical approach (Weibull, 1951). Thus, the statistic used to describe the reliability of the ceramic material was based on the Weibull statistical analysis, which is a way to describe the variation of the resistance obtaining the Weibull modulus (*m*) and the characteristic strength (σ_c) with a confidence interval of 95%, determined in a diagram (according to DIN ENV 843-5):

$$\ln\ln\left(\frac{1}{1-F}\right) = m \ln \sigma_c - m \ln \sigma_0 \qquad \text{Eq. (7)}$$

where F is the failure probability, σ_0 the initial strength, σ_c the characteristic strength, and *m* is the Weibull modulus. The characteristic strength is considered to be the strength at a failure probability of approximately 63% and the Weibull modulus is used as a measure of the distribution of strengths, expressing the reliability of the material.

3. Results

3.1 Phase transformation analysis

XRD analysis (Table II) demonstrated that aging in autoclave (AUT and AUT+MC) promoted the highest percentages of monoclinic phase, followed by storage in distilled water and then by mechanical cycling, Ctrl group presented almost 0% of m-phase. Transformed zirconia depth (TZD) data demonstrates the same pattern observed in m-phase content analysis, autoclave aging promoted higher TZD values compared to other aging methods (AUT+MC > AUT > DIST WAT > MC > CTRL).

3.2 Roughness and Scanning Electron Microscopy (SEM)

Table II shows that Ctrl group presented the highest statistically values observed for Ra roughness ($P < 0.05$), while for Rz roughness ($P < 0.05$) the highest statistical values were observed for Ctrl and AUT groups.

Micrographics from SEM (Figure 1) demonstrated that all aging methods were unable to promote any topographical change on the pattern observed from *as sintered* surface (Ctrl).

3.3 Biaxial flexural strength

Regarding characteristic strength (Table I), it is noticed that AUT and DIST WAT groups were higher statistically than other groups (Ctrl = MC = AUT + MC). In terms of reliability (Weibull`s moduli) no aging protocol promoted a deleterious impact in comparison to control group.

4. Discussion

Several studies have been developed aiming to predict the behavior of dental materials in the oral cavity, especially regarding longevity. The purpose of this study was to investigate and compare the effects of different *in vitro* aging methods (most described in literature) on a zirconia ceramic. The Y-TZP ceramic is a relatively new material used in dentistry, so properties related to longevity and susceptibility to degradation are still uncertain, therefore little information on the behavior of zirconia subjected to cyclic loads for a long time in a hostile environment (as the oral) is known. The attempts of simulating: changes of temperature occurring in mouth; chewing and moisture, although difficult, they are essential to understanding the clinical performance of Y-TZP (Wiskott, et al. 1995; Itinoche, et al. 2006; Papanagiotou, et al. 2006; Pittayachawan, et al. 2009; Nemli, et al. 2012).

Literature has been taking into consideration the amount of m-phase detected on zirconia surface as a predictor to the presence of LTD. Our data show that the groups submitted to autoclave stimuli (AUT, AUT+MC) presented higher *m*-phase content in association to higher depth of transformed layer, in accordance to the literature (Amaral, et al. 2013, Cotes, et al. 2014), but they did not result in decrease of mechanical properties. It is interesting to note that although AUT group presented a great amount of m-phase content, it was observed an increase in biaxial flexural strength compared to CTRL, this may be explained by the toughening mechanism that zirconia has, where *t-m* phase transformation leads to a volumetric expansion ≈4% at a localized area around superficial defects resulting in a compression stress concentration around these defects and consequently arresting crack propagation (Garvie & Nicholson, 1972, Amaral, et al. 2013; Pereira, et al. 2015).

The most accepted theory to describe LTD mechanism is that the increase of internal stresses associated with the penetration of water (H_2O) inside the lattice (Schubert & Frey, 2005), triggers the initiation of the t-m phase transformation (Yoshimura, et al. 1987; Schubert & Frey, 2005). Thus, a cascade of events occurs with the transformation propagating first inside one grain (Deville & Chevalier, 2003, Schmauder & Schubert, 1986), and progressively invading the surface by a nucleation-and-growth (N-G) mechanism (Chevalier, et al. 1999, Chevalier, 2007; Muñoz-Tabares, et al. 2011). The number of nuclei increases continuously with the stresses, owing to the penetration of water (time dependent) (Lucas, et al. 2015). At the same time, growth occurs due to the fact that the transformation of one-grain puts its neighbors under tensile stress, favoring their transformation under the effect of water (Chevalier, 2007).

Being so, LTD initially occurs at superficial grains where water is incorporated into zirconia grains by filling oxygen vacancies, later spreading to the surface increasing its roughness (Sato & Shimada, 1985; Yoshimura, et al. 1987). Afterwards, LTD proceeds into the bulk material (Yoshimura, et al. 1987) and jeopardizes the strength, fracture toughness, and density of Y-TZP structures (Ban, et al. 2008; Hirano, 1992; Lughi & Sergo, 2010).

In addition, our data support that it is important to associate different aging methods (mechanical stimuli with temperature and humidity), when evaluating zirconia's susceptibility to LTD. The AUT + MC group presented the highest m-phase content and lower biaxial flexural strength when compared to AUT aging method alone. This probably could be explained by mechanical stimuli triggering stress concentration around defects resulting in subcritical crack growth. Subcritical crack growth leads to mechanical properties decrease over time (Ritter, 1995), which results in an increased risk of catastrophic fracture in reduced stress application, in other words, results in acceleration of the fracture process (Zhang, et al. 2004).

According to Chevalier (2007), aging can be controlled for a given zirconia ceramic (material dependence), for that, density, stabilizer content, grain size, homogeneity of phase distribution, and residual stress state on the surface play a main role in terms of t-m transformability. Hence, it can highlight the grain size factor (Li & Watanabe, 1998): larger tetragonal grain size typically provides for lower phase stability (Lee, et al. 2012; Nakamura, et al. 2011). LavaTM ceramic presented a large grain size, as already reported (Lee et al., 2012); thus, there is a greater possibility of phase transformation for that material (Chevalier, et al. 2004; Basu, et al. 2004).

We have noticed that each aging treatment promoted distinct effects on material's surface. Although all of them promoted an increase in m-phase content (with different intensities), the most important aspect is that none of the aging methods promoted a decrease on biaxial flexural strength (in comparison to as-sintered group), but the hazardous condition was observed when autoclave stimuli was associated with mechanical cycling (AUT + MC group), as it promotes lower resistance values statistically and presented the highest m-phase content in comparison to only AUT group. Exposing zirconia ceramics to this association of stimuli provides important insights since it better reproduces clinical conditions (in comparison to all other methodologies) (Itinoche, et al. 2006).

Regarding Weibull Moduli, it is feasible to notice that none of the evaluated aging methods promoted a deleterious impact on this parameter, indicating that there was no decrease on the material's structural reliability. In fact, some aging methodologies promoted an increase on Weibull moduli in comparison to Ctrl (*as sintered* condition) probably in response to the already described toughening mechanism that zirconia has, which difficults crack propagation (Garvie & Nicholson, 1972).

Considering the fact that this is an *in vitro* study, extrapolation of these findings to a clinically relevant scenario should be conducted with caution. One important limitation is the difficulty to define which *in vitro* aging protocol would produce relevant clinical data, although it becomes clear the importance of associating mechanical stress with water and temperature stimuli, allowing fatigue and low temperature degradation to take place. More studies are necessary to better characterize LTD mechanism and to fully understand this subject.

5. Conclusions

- None of the evaluated aging methods (most described in literature) promoted any deleterious impact on biaxial flexural strength of zirconia ceramics, although intense t-m phase transformation was observed.
- Association between autoclave aging and mechanical cycling promoted the highest t-m phase transformation and resulted in decrease of biaxial flexural strength in comparison to autoclave aging alone.

Thus, the development of new methodologies and the association of mechanical stimuli and hydrothermal degradation should be considered to better understand the mechanism of long-term low-temperature degradation.

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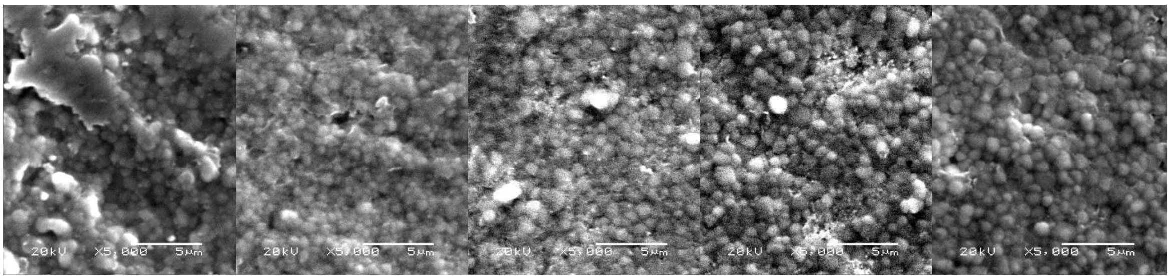
Figures and Tables

Figures

Figure 1 – SEM images of Y-TZP surface after aging treatment, 5000x of magnification.



Ctrl **Aut** **MC** **Aut + MC** **Dist Wat**

Tables

Table I – Characteristic strength (σc), Weibull's moduli (m), and respective Confidence Intervals.

Groups	σ_c	CI (95%)	*m*	CI (95%)
Ctrl	917.58 A	870.87 – 965.41	8.3253 a	5.83 – 10.7
MC	985 AB	957.64 – 1012.35	15.444 bc	10.81 – 19.85
AUT	1033.36 BC	986.9 – 1080.63	9.457 ab	6.62 – 12.16
AUT + MC	959.41 A	939.14 – 979.54	20.369 c	14.25 – 26.18
DIST WAT	1053.76 C	1020.38 – 1087.27	13.514 abc	9.46 – 17.37

* Capital letters indicate statistical difference between the characteristic resistance (σ_c) and lower letters indicate statistical difference between Weibull modulus (*m*).

Table II – Roughness analysis – Mean of Ra and Rz Values (Standard Deviation) and the Statistical significances and DRX analysis – m-phase content and depth of transformed layer (μm)

Group	Ra Mean (μm)	Rz Mean (μm)	m-phase (%)	Depth of transformed layer (μm)
Ctrl	0.68 (0.27) A	4.43 (1.53) a	0,94%	0,05
MC	0.19 (0.04) C	1.57 (0.22) b	9,47%	0,50
AUT	0.28 (0.13) B	2.24 (0.62) a	53,33%	3,86
AUT + MC	0.18 (0.03) BC	1.61 (0.22) bc	61,91%	4,89
DIST WAT	0.16 (0.06) C	1.34 (0.20) c	20,73%	1,18

* Capital letters indicate statistical difference between the roughness Ra parameter and lower letters indicate statistical difference between roughness Rz parameter.

5. ARTIGO 4 - Fatigue limit of polycrystalline zirconium oxide ceramics: effect of grinding and low-temperature aging

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Running title: Grinding and LTD on fatigue limit of Y-TZP ceramics.

Abstract

The following study aimed to evaluate the effect of grinding and low-temperature aging on the fatigue limit of Y-TZP ceramics for frameworks and monolithic restorations. Disc specimens from each ceramic material, Lava Frame (3M ESPE) and Zirlux FC (Amherst) were manufactured according to ISO:6872-2008 and assigned in accordance with two factors: (1) "surface treatment" - without treatment (as-sintered, Ctrl), grinding with coarse diamond bur (181µm; Grinding); and (2) "low-temperature aging (LTD)" – presence and absence. Grinding was performed using a contra-angle handpiece under constant water-cooling. LTD was simulated in an autoclave at 134ºC under 2-bar pressure for 20 h. Mean flexural fatigue limits (20,000 cycles) were determined under sinusoidal loading using stair case approach. For Lava ceramic, it was observed a statistical increase after grinding procedure and different behavior after LTD stimuli (Ctrl < Grinding; Ctrl < Ctrl Ltd; Grinding = Grinding Ltd); while for Zirlux, grinding and low-temperature aging promoted a statistical increase in the fatigue limit (Ctrl < Grinding; Ctrl < Ctrl Ltd; Grinding < Grinding Ltd). An important increase was observed in m-phase content after both stimuli (grinding and LTD), although with different intensities. Additionally, fatigue test did not promote increase of m-phase content. Thus, tested grinding and low temperature aging did not damage the fatigue limit values significantly for both materials evaluated, even though those conditions promoted increase in m-phase.

Keywords: Fatigue. Mechanical cycling. Grinding. Low-temperature degradation. Zirconium oxide partially stabilized by yttrium.

1. Introduction

Nowadays, Y-TZP ceramics (Yttrium-stabilized Tetragonal Zirconia Polycristal) are being considered one of the best options to produce all-ceramic FDPs (fixed dental prosthesis - single or multi-unit), as they associate superior strength (provided by a Y-TZP framework) with good esthetics (provided by a feldspathic porcelain veneering) (Denry & Kelly, 2014). In fact, zirconia is a polymorphic metastable material (Piconi & Maccauro, 1999) that when required (submitted to stimuli – mechanical, physical, and/or chemical) may respond through a phase transformation mechanism (tetragonal (*t*) to monoclinic (*m*)) (Garvie & Nicholson, 1972; Hannink, 2000; Lazar et al., 2008; Amaral et al., 2013; Pereira et al., 2015a).

Literature states distinct effects of this phase transformation mechanism: first, it was noted an increase on mechanical properties, which is known as transformation toughening mechanism (Hannink, 2000; Amaral et al., 2013; Pereira et al., 2015a); then as this transformation spreads through ceramics surface and subsurface (promoting grains detachment/pullout and introduction of micro cracks on the grains neighbor areas), it promotes roughness increase, reduction in strength, fracture toughness, and density (Chevalier 2007; Ban et al., 2008; Kim et al., 2009; Flinn 2012, 2014; Egilmez 2014; Pereira et al., 2015b). This spontaneous degradation mechanism is known as low-temperature degradation (LTD) (Kobayashi et al. 1981).

Currently, besides FDPs application, Y-TZP ceramics has being proposed for manufacturing monolithic *full-contour* restorations (Beuer et al., 2012; Sabrah et al. 2013; Nakamura et al. 2015). One of the advantages of this application is the possibility of an even more conservative tooth preparation, once it requires a thinner thickness and the application of veneering porcelain is dispensable. This could mean in an obvious solution for one of the most reported (clinical trials) reasons of failures of Y-TZP FDPs (chipping or fracture of the veneering porcelain) (Raigrodski et al., 2006; Sailer et al., 2007; Beuer et al., 2010; Christensen & Ploeger 2010; Monaco et al., 2015).

Although the indication of monolithic full-contour restoration has clear advantages, it also means that Y-TZP ceramic will be daily exposed directly to the oral environment (presence of different stimuli, such as: oral mastication forces, exposure to water, temperature (low-temperature degradation), pH changes, oral microorganisms (Chevalier et al., 2007; Inokoshi et al., 2015; Lucas et al., 2015[a]; Cotes et al., 2014; Egilmez et al., 2014; Turp et al., 2012, Bordin et al., 2015), which means an environment that could accelerate the LTD mechanism development.

In addition, another important aspect is that after machining at CAD/CAM (computer aided design / computer aided machining) systems, clinical adjustments (with diamond grinding instruments) are usually needed to achieve a better adaptation and an adequate emergency/occlusion profile (Aboushelib et al., 2009; Amaral et al., 2013; Pereira et al., 2014; 2015a). Literature has already shown that grinding might introduce different types of damage (defects), such as scratches and cracks of various depths, which penetrate toward the bulk of the material (Ban et al., 2008; Quinn et al., 2005; Papanagiotou et al., 2006). Besides the introduction of defects, it may also trigger the t – m phase transformation mechanism (Muñoz-Tabares & Anglada 2012; Pereira et al., 2014; 2015a), but there is few data regarding the effect of this procedure on the Y-TZP ceramic susceptibility to LTD (Kosmac et al., 2008, Amaral et al., 2013, Pereira et al., 2015a).

Clinically, ceramic restorations are susceptible to fatigue failure, mainly due to the presence of moisture and cyclic chewing forces (Gonzaga et al., 2011). Fatigue failure may be defined as the fracture of the material due to progressive brittle cracking under repeated cyclic stresses of intensity below the material normal strength (Zhang et al., 2013; Wiskott et al., 1995). Although this fact is already extensively known, there are few studies so far assessing the fatigue life behavior of Y-TZP ceramics (Kosmac et al., 2008, Nakamura et al. 2015), and to the authors knowledge none took into account surface treatments (grinding) and susceptibility to LTD. It is feasible to notice that these stimuli directly result on introduction of defects onto the materials surface and subsurface, probably increasing the risk of a premature failure in a fatigue life scenario (Hondrum, 1992; Kelly, 2004; Mitov et al., 2011), which might affect the predictability and longevity of the prosthetic rehabilitation.

Thus, before we may recommend the application of Y-TZP monolithic restorations (hazardous condition – directly exposed to oral environment) and aiming to better understand the behavior of Y-TZP as a framework material in FDPs, well delineated in-vitro studies to evaluate the effects of grinding and LTD mechanism in addition to the susceptibility of degradation of this ceramic on the fatigue limit are required. Hence, this study aimed to evaluate the effect of grinding with diamond burs and low-temperature aging in a steam autoclave at the fatigue limit (staircase method) of Y-TZP ceramics for frameworks and monolithic restorations.

2. Material and Methods

2.1. Specimen preparation

Pre-sintered zirconia blocks (LOT 637328 Rev.2, Zirlux FC, Ivoclar Vivadent, Amherst, USA; and LOT 70201131797 Lava Frame, 3M ESPE, Seefeld, Germany) were ground into cylinders in a polishing machine (EcoMet/AutoMet 250, Buehler, United States) using a 600 grit silicon carbide paper and then cut under water irrigation with a diamond saw (ISOMET 1000, Buehler, Lake Bluff, IL, USA), resulting in eighty (N=80) zirconia specimens, from each ceramic material, with initial dimensions of 18 mm diameter and 1.65 mm thickness. The discs were then polished with a 1200 grit silicon carbide paper, cleaned in 78% isopropyl alcohol ultrasonic bath for 10 min and sintered according to each manufacturer's recommendation.

After sintering, the specimens were carefully inspected, being discarded those presenting discrepancies in dimensions above the standard variation (1.2±0.2 mm in length, 14±2 mm in diameter), indicated by ISO:6872-2008. Then the specimens (after approved by the inspection) from each ceramic material were randomly allocated into four groups (n=20) according to the surface treatment executed (grinding with Coarse diamond bur x as-sintered – without treatment) and aging (presence x absence) (Table 1).

2.1.1. Surface treatments

Samples from the control group (Ctrl) remained untouched after the sintering process – "as-sintered" samples.

2.1.2. Grinding

Grinding was performed by a single trained operator using diamond burs (#3101G – grit size 181 µm; KG Sorensen, Cotia, Brazil) in a slow-speed motor (Kavo Dental, Biberach, Germany) associated with a contra-angle handpiece (T2 REVO R170 contra-angle handpiece up to 170,000 rpm, Sirona, Bensheim, Germany) under constant water-cooling (≈30 mL/min). The diamond bur was replaced after each specimen.

For standardization of the wear thickness and to guarantee that the entire specimen surface was submitted to grinding, the specimens were marked with a permanent marking pen (Pilot, São Paulo, Brazil) and affixed to a device to assure parallelism between the specimen and diamond bur, which allowed for movement only in the horizontal direction. Then, the grinding procedure was performed until the marking was completely eliminated. This procedure standardized the wear thickness and improved the reproducibility of the grinding treatment, although this strong movement control is not available in a typical clinical setting (Pereira et al., 2015a).

2.1.3. Low-temperature aging

Low-Temperature Degradation (LTD) was simulated in an autoclave (Sercon HS1-0300 n11560389/1) at 134°C, under 2 bar pressure, over a period of 20 h (Chevalier 2007; Pereira et al., 2015a).

2.2. Surface topography and roughness analysis

To determine the surface topography pattern presented in each evaluated condition, the specimens (n=20) were analyzed in a surface roughness tester (Mitutoyo SJ-410, Mitutoyo Corporation, Kawasaki, Japan) and Atomic Force Microscope (AFM) (n=2, Agilent Technologies 5500 equipment, Chandler, Arizona, USA).

Surface roughness analysis (in a measured range until 80µm it would be expected an accuracy of 0.001µm) has been conducted considering six measurements for each specimen (3 along the grinding direction, 3 in the opposite direction), according to the ISO:1997 parameters (Ra – arithmetical mean of the absolute values of peaks and valleys measured from a medium plane (μm) and Rz – average distance between the five highest peaks and five major valleys found in the standard (μm)) with a cut-off (n=5), λC 0.8 mm and λS 2.5 μm. Arithmetic mean values of all measurements from each specimen were obtained.

For Atomic Force Microscopy, two specimens from each group were submitted to the analysis, being images obtained by non-contact methodology and specific probes from an area of 20x20 μm (PPP-NCL probes, Nanosensors, Force constant = 48 N/m) and manipulation at specific computer software (Gwyddion™ version 2.33, GNU, Free Software Foundation, Boston, MA, USA).

Prior to the surface topography analysis, all specimens were submitted to the cleaning protocol in an ultrasonic bath as previously described.

2.3. Flexural fatigue strength testing

Samples (n=20) were subjected to a biaxial flexural fatigue limit test (Instron ElectroPuls E3000, Instron Corporation, Norwood, MA, United States; maximum estimated error 0.5% from the maximum load cell capacity, as we used a 5KN load cell, it would be expected a maximum error of 25N) according to ISO:6872-2008. The specimens were positioned with the treated surface facing down (tensile stress) on three support balls (Ø=3.2 mm), which were positioned 10 mm apart from each other in a triangular position. The assembly was immersed into water and a flat circular tungsten piston (Ø=1.6 mm) was used to apply the force at the center of the disc. Before testing, adhesive tape was fixed on the compression side of the discs in order to avoid the fragments to be spread (Quinn, 2007) and to provide better contact between the piston and the sample (Wachtman et al., 1972).

The biaxial flexure fatigue limit was determined for each group with a lifetime of 20,000 cycles using the staircase approach method described by Collins (1992). Sinusoidal loading was applied, with amplitude ranging from a minimum of 10 MPa, just to avoid the movement of the specimen, to the maximum tensile applied with a frequency of 6 Hz (6 cycles per second).

The initial stress and the step size were determined, for each condition, based on the results of the monotonic biaxial tests (Table 2). Then the first specimen of each group was tested and depending on the survival or failure of this specimen, the next disc was tested with a tensile increment higher or lower than the initial stress, respectively. Thus, stress controlled all fatigue tests, and the load (N) required to achieve the desired stress (MPa) was calculated according to ISO:6872-2008, for each tested sample:

$$\sigma = -0.2387 \cdot \frac{p(X-Y)}{b^2} \qquad \text{Eq. (1)}$$

Where: σ is the maximum tensile stress (MPa), P is the total load to fracture (N), b is the thickness at fracture origin (mm), and X and Y are calculated as follows:

$$X = (1 + v)\ln\left(\frac{r_2}{r_3}\right)^2 + \left[\frac{(1 - v)}{2}\right]\left(\frac{r_2}{r_3}\right)^2 \qquad \text{Eq. (2)}$$

$$Y = (1 + v)\left[1 + \ln\left(\frac{r_1}{r_3}\right)^2\right] + (1 - v)\left(\frac{r_1}{r_3}\right)^2 \qquad \text{Eq. (3)}$$

Where ν is Poisson's ratio (ν = 0.25, according to ISO:6872-2008), r_1 is the radius of the support circle (5 mm), r_2 is the radius of the loaded area (0.8 mm), and r_3 is the radius of the specimen (7.5 mm).

After testing, the mean biaxial flexure fatigue limit (σ_f) was calculated, according to Collins (1992), based on the data of the less frequent event (survival or failure), using the Eq. (4):

$$\sigma_f = \sigma_{f0} + d[{}^{\sum in_i}\!/_{\sum n_i} \pm {}^1\!/_2] \qquad \text{Eq. (4)}$$

Where: σ_{f0} is the lowest stress level considered in the analysis and d is the step size. The negative sign is used if the less frequent event is a failure; otherwise the positive sign is used (less frequent event survival). The lowest stress level considered is designated i=0, the next i=1, and so on, and n_i is the number of failures or survivals at the given stress level.

To obtain the CI (95%, α = 0.05) of the mean biaxial flexure fatigue limit, the following equations were used (Collins, 1992):

$$\sigma\mathrm{f} - 1.96(\sigma\mathrm{m}) \leq \mathrm{CI} \leq \sigma\mathrm{f} + 1.96(\sigma\mathrm{m}) \qquad \text{Eq. (5)}$$

Where: σ_f is the mean biaxial flexure fatigue strength (previously obtained, sample value), and σ_m is the standard deviation (SD) of the estimate mean fatigue limit (population value), obtained as follows:

$$\sigma_\mathrm{m} = \frac{G}{\sqrt{N}}\sigma \qquad \text{Eq. (6)}$$

Where: G is a nonlinear function d/σ (takes into consideration the step size (d) assumed for fatigue test and the standard deviation of the population (σ)), as σ is not known it has to be estimated σ (sample data), as follows (Collins, 1992):

$$\hat{\sigma} = 1.62(d)\left[\frac{\sum n_i \sum i^2 n_i - (\sum i n_i)^2)}{(\sum n_i)^2} + 0.029\right] \text{ if } \frac{\sum n_i \sum i^2 n_i - (\sum i n_i)^2)}{(\sum n_i)^2} \geq 0.3 \qquad \text{Eq. (7)}$$

$$\hat{\sigma} = o.53(d) \quad \text{if } \frac{\sum n_i \sum i^2 n_i - (\sum i n_i)^2)}{(\sum n_i)^2} < 0.3 \qquad \text{Eq. (8)}$$

2.4. Fractographic analysis

After the mechanical tests, a fractography examination was performed using a light microscope (Stereo Discovery V20; Carl Zeiss, Gottingen, Germany) on a representative part of the specimens to determine the region of fracture origin.

2.5. Phase analysis by X-Ray Diffraction (XRD Analysis)

Quantitative analysis of phase transformation was conducted to determine the relative amount of monoclinic phase present in the ceramic surface, for each condition evaluated both before (n=2) and after (all specimens that survived) fatigue test, using a x-ray diffractometer (D8 Advanced XRD, Bruker AXS GmbH, Germany) with a length wave of 1.5416 Å (CuK_α) from 25-35° 2θ, at a step interval of 1s and step size of 0.03°. The amount of m-phase (X_M) and the volumetric fraction (F_m) was calculated using the method developed by Garvie & Nicholson (1972) modified by Toraya et al. (1984):

$$Xm = \frac{(-111)M+(+111)M}{(-111)M+(+111)M+(101)T} \qquad \text{Eq. (9)}$$

$$Fm = \frac{1.311 \cdot Xm}{1+0.311 \cdot Xm} \qquad \text{Eq. (10)}$$

Where: $(-111)_M$ and $(+111)_M$ represent the monoclinic peaks (2θ=28° and 2θ=31.2°, respectively) and $(111)_T$ indicates the intensity of the respective tetragonal peak (2θ=30°).

2.6. Data analysis

Statistical analysis was executed using Minitab 16 and Statistix 8.0. Roughness data (Ra and Rz) were analyzed by Kruskal-Wallis and post-hoc Dunn's test, while One-way ANOVA and post-hoc Tukey' test were used for flexure fatigue limit data.

3. Results

AFM analysis shows that grinding with diamond burs (grinding) altered the surface pattern, compared to *as sintered* condition (no grinding – Ctrl), in which it is noticed parallel scratches following the direction of bur movement, while aging did not cause any relevant alteration in surface pattern (Figure 1).

Kruskal-Wallis and Dunn's post-hoc tests from roughness data show that aging did not alter the roughness values (Ra and Rz parameters) for as-sintered condition (Ctrl = Ctrl Ltd) but on grinding conditions, aging statistically increased Ra and Rz mean values (Grinding < Grinding Ltd) for both materials. Grinding statistically increased mean Ra and Rz values for both materials as well (Table 2).

The pattern of run outs (survivals) and failures for each group is described in Fig. 2. For Lava, aging statistically increased mean fatigue strength for the as-sintered condition (Ctrl

< Ctrl Ltd), while aging did not alter the fatigue limit statistically, for ground groups (Grinding = Grinding Ltd); grinding promoted an increase in fatigue limit, compared to as-sintered (Table 2). For Zirlux, aging statistically increased the mean fatigue strength (Ctrl < Ctrl Ltd; and Coarse < Coarse Ltd); grinding also statistically increased the mean fatigue strength values (Ctrl < Grinding) (Table 2).

Failure analysis on a light microscope of representative specimens of all evaluated condition showed that all fractures started at the side of the specimen submitted to tensile stress (treated surface) at the center region (Fig. 3).

XRD analysis from specimens before fatigue testing shows an important increase in *m*-phase content caused by both evaluated factors (aging in autoclave and grinding): grinding promoted an increase in *m*-phase and altered the susceptibility of the material to further transformation when aged, and by that Grinding Ltd presented less *m*-phase content than Ctrl Ltd. This behavior was observed in both tested materials (Lava and Zirlux). XRD analysis from specimens that survived fatigue testing shows that the *m*-phase content values were similar to those before the test (Table 2).

4. Discussion

Grinding and aging conditions did not damage the fatigue limit of the studied zirconia materials, although those different materials behave distinctly. In fact, it was observed an increase in fatigue limit, when comparing grinding Vs as sintered, for both materials, which may be explained by the transformation toughening mechanism already described on literature (Hannink, 2000).

When Y-TZP ceramics are submitted to stimuli (mechanical, physical, and/or chemical) it responds through a *t-m* phase transformation mechanism (Garvie & Nicholson, 1972; Hannink, 2000). This t-m phase transformation results in a volumetric expansion ≈4% at a localized area around superficial defects resulting in compression stress concentration around these defects and consequently arresting crack propagation (Garvie & Nicholson, 1972; Hannink, 2000). Thus, this is the reason why both Y-TZP ceramics evaluated presented higher fatigue limit values after stimuli (grinding and aging in autoclave).

Literature has been showing that the prolonged exposure to stimuli (especially action of water and temperature) will lead to the saturation of *t-m* phase transformation on ceramic surface and then it will start to spread into the material's core. This progression may result in deleterious consequences, such as: grains detachment/pullout and introduction of microcracks, resulting in roughness increase, reduction of strength, fracture toughness, and density

(Chevalier 2007; Ban et al., 2008; Lazar et al. 2008; Kim et al., 2009; Flinn 2012, 2014; Egilmez 2014).

The absence of deleterious impact of grinding and low-temperature degradation on the zirconium oxide ceramics brings to attention two important aspects: (1) the evaluated Y-TZP ceramics demonstrated a good resistance to aging (LTD effects) and to grinding (with coarse diamond bur), as the fatigue limit was not damaged by the aforementioned conditions; (2) *in vitro* test simulation of the oral environment is difficult (Kelly et al. 1999, 2010), although we associate grinding (coarse diamond bur), aging in autoclave (134°C at 2 bar for 20 h), and an accelerated fatigue test (stair case approach), which could provide important insights regarding the aging mechanism of zirconia ceramic, it may not fully represent the oral environment. Additionally, there is no information on literature about the relation between time of clinical exposure and *in-vitro* laboratorial stimuli (aging in autoclave and accelerated fatigue test).

Basically, grinding could cause a positive or a negative impact on mechanical properties; when the depth of the defects introduced by grinding is greater than the one of the compressive layer created by *t-m* phase transformation it may result in higher levels of tensile stresses concentration, which could increase the incidence of catastrophic failures (Kosmac et al., 1999, 2008; Guazzato et al., 2005). Nevertheless, when the depth of these defects is smaller than the one of the compressive stress layer (created by transformation toughening mechanism), crack propagation is hindered and catastrophic failures are avoided by the surrounding compressive stresses (Papanagiotou et al., 2006; Chevalier et al., 2007).

Apparently, what defines whether grinding will impact positively or negatively is: (1) Y-TZP ceramic characteristics, i.e. size of crystalline grains (Preis et al., 2015; Li & Watanabe 1998), composition and sintering conditions (Inokoshi et al., 2014; 2015) which will dictate the susceptibility to *t-m* phase transformation of this material; (2) the methodology used for grinding, i.e. the pressure applied during grinding, speed and grit size of grinding tool, presence or absence of cooling (Kosmac et al., 1999).

According to Lucas et al. 2015[b], a significant correlation was noticed between the grain size and the amount of monoclinic transformation, where smaller grains experienced less transformation. Lava ceramic is known to present a larger grain size and by that, it is more prone to t-m phase transformation (Lucas et al. 2015[b], Chevalier 2007), while there is no information about Zirlux grain size. Thus, it is important to highlight that any alteration in ceramics characteristics will be important and impact on the material's response to stimuli.

Since Prozir episode in 2001, where thousands of Y-TZP femoral heads failed because they presented an increased susceptibility to LTD effects (Chevalier, 2007), scientific community has intensively evaluated LTD of Y-TZP ceramics. When Y-TZP is submitted to a humidity environment with temperatures between 150-400ºC, it spontaneously suffers a low-temperature degradation process (Kobayashi K., et al. 1981). The aging method that has been used to evaluate LTD effects on Y-TZP ceramics is the storage in autoclave (associating temperature and water stimuli) (Chevalier, 2007), although it is not clear yet the "gold standard" parameter (which would speed and successfully promote the LTD effects) that has to be used.

At first, LTD occurs at superficial grains (*t-m* phase transformation), where water is incorporated into zirconia grains by filling oxygen vacancies, and later spreads to the surface resulting in roughness increase, reduction of strength, fracture toughness, and density (Sato & Shimada, 1985; Yoshimura M., et al. 1987). Hence, this mechanism is time dependent; accelerated in the presence of water and temperature, but up to now, literature has not taken into consideration the influence of different stimuli, such as interaction of oral mastication forces, exposure to water (moisture), temperature and pH changes, and presence of oral microorganisms (Chevalier, 2007; Inokoshi et al., 2015; Lucas et al., 2015[a]; Cotes et al., 2014; Egilmez et al., 2014; Turp et al., 2012, Bordin et al., 2015), which such material will be submitted daily in a clinical environment. Our study evaluated the interaction between grinding and autoclave aging and we did not depict deleterious impact on biaxial flexural fatigue limit.

Regarding roughness findings, aging in autoclave did not become a rougher surface when considering the *as sintered* condition for both materials. This suggests that even 20 h in autoclave was not enough for promoting the expected LTD effects (increase in roughness and decrease in mechanical properties), although approximately 60% of m-phase was observed on ceramic. For ground condition, aging in autoclave promoted an increase in roughness for both materials, although this surface presented lower m-phase content (approximately 40%).

These differences might be explained by the differences of superficial topography. *As sintered* condition presented an initial smoother surface, which could restrict the effects of water to a more superficial area. While for grinding condition, as it presented an initial rougher surface (in addition to the the possibility of the introduction of superficial micro cracks during grinding), which might have allowed water more accessibility to deeper crystallographic grains and as a result probably it could have enhanced the mechanism of grains detachment, which leaded to an increase in roughness after aging in autoclave.

Regarding mechanical behavior of dental ceramics (i.e. Y-TZP), it has already been known that these materials present a brittle nature, and by that, supporting little or no plastic deformation (Kelly, 2004; Hondrum, 1992). Additionally, they undergo a process named slow crack growth (SCG) when subjected to repetitive loading (fatigue – mechanical cycling) of low level in humid environment, as the oral environment (Gonzaga et al., 2011).

Failure of these restorations happens when the stress intensity factor (K_I) at the crack tip reaches a critical level (K_{Ic}); this factor is based on the crack length, being the applied stress and a shape factor “Y” based on the type of stress, material’s dimensions, and crack geometry (Gonzaga et al., 2011, Quinn 2007). Thus, throughout repetitive loading (fatigue), the stress will concentrate around internal defects and as it concentrates it promotes increase on the energy at the crack tip, which causes crack’s propagation (Mitov et al., 2011), and consequently increases the probability of catastrophic failure. So, their strength is sensitive to the presence of defects (Kelly, 2004; Hondrum, 1992), as we have noted grinding procedure and an increased susceptibility to LTD may result in introduction of defects on the ceramic surface, which could be harmful.

It is important to notice that although a deleterious impact on fatigue limit was not observed in comparison to Ctrl, between all evaluated conditions, if we compare the presented values with the monotonic strength value previously described on literature, for the same materials, we notice an important decrease (for Lava Frame ranging between approximately 20 to 40%; for Zirlux ranging between 30 to 40%), being in agreement with the literature (Kelly et al. 1999, 2010). This fact emphasizes the importance to use a fatigue life scenario to evaluate the mechanical behavior of Y-TZP ceramics.

Although the present study showed that grinding and low-temperature aging did not promote any deleterious impact on the mechanical behavior (fatigue limit) of Y-TZP ceramics, it is important to highlight that more studies evaluating the association of different aging stimuli under fatigue scenario are needed, in order to better understand and elucidate LTD mechanism and the effects of grinding on Y-TZP ceramics, besides the influence of the oral environment stimuli on the longevity of such restorations.

5. Conclusions

The tested grinding and low temperature aging procedures did not damage the fatigue limits (stair case approach) significantly for both materials evaluated, even though those conditions promoted increase in m-phase.

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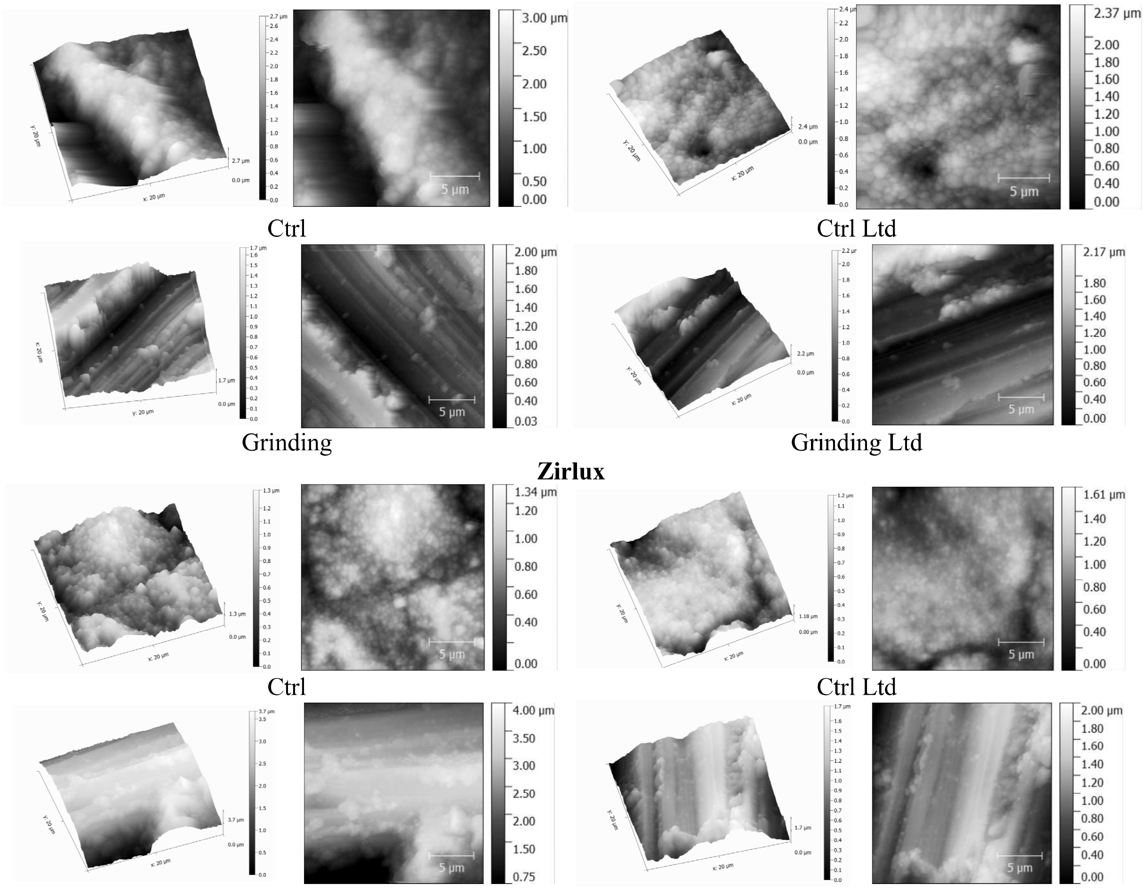
Figures and Tables

Figures

Figure 1 – Atomic Force micrographics


Lava

Ctrl

Ctrl Ltd

Grinding

Grinding Ltd

Zirlux

Ctrl

Ctrl Ltd

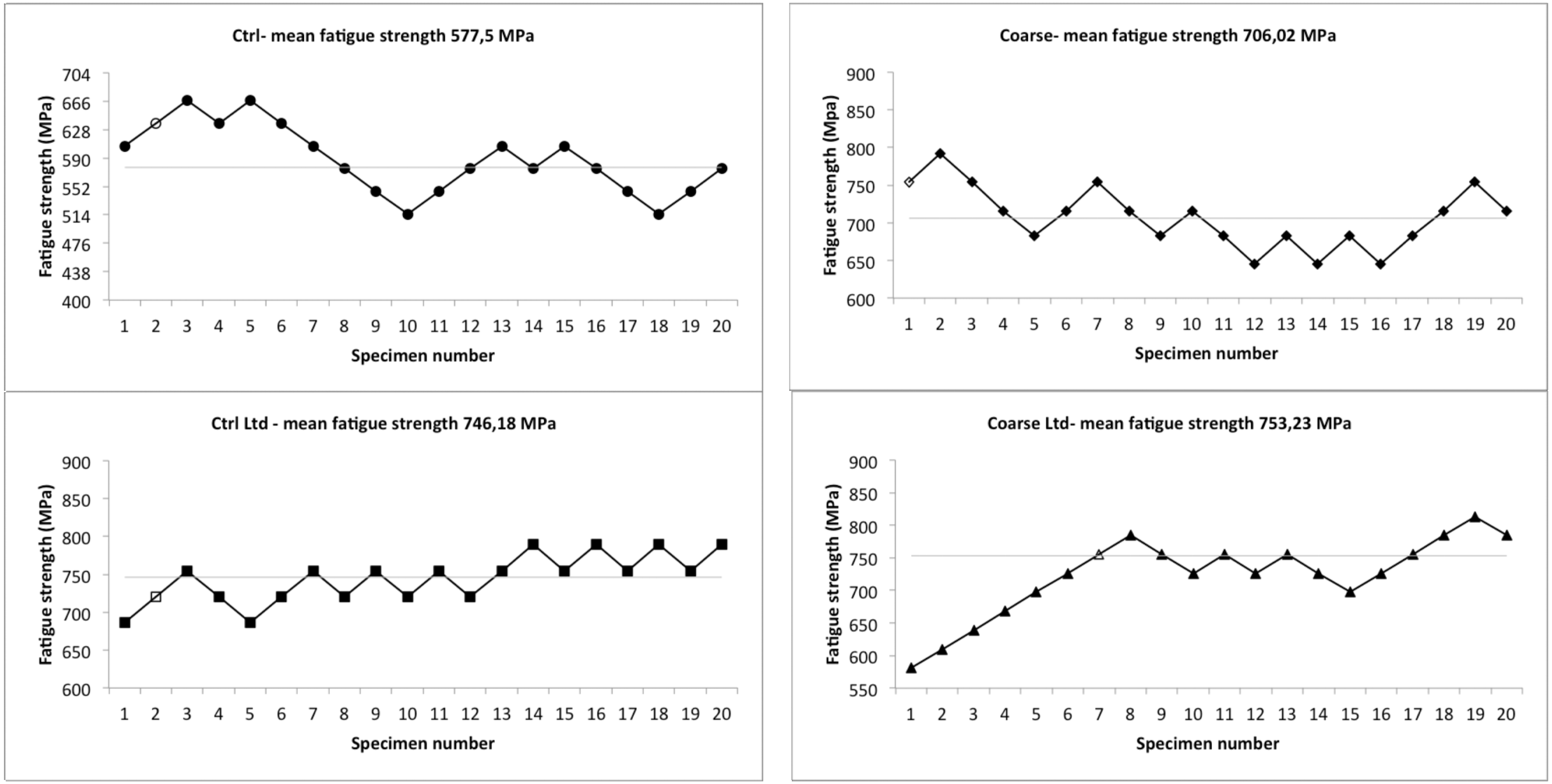
Grinding

Grinding Ltd

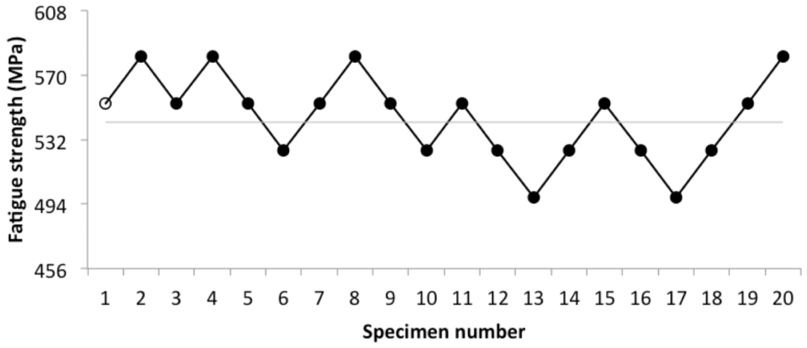
Fig 1. Atomic Force micrographics (area of 20x20 µm) of the different evaluated conditions elucidating the topography pattern alteration generated by grinding procedure and no modifications promoted by aging.

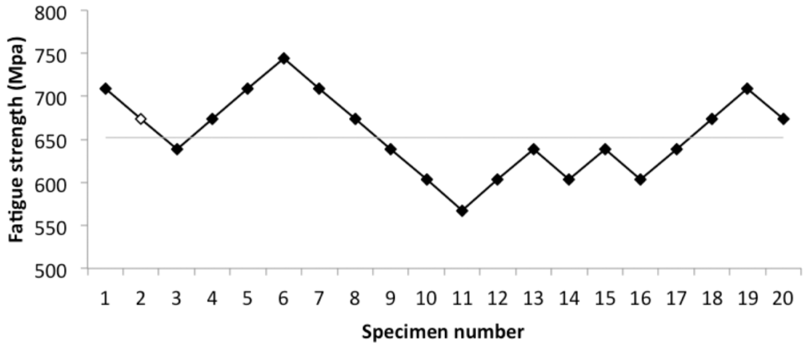
Figure 2 – Pattern of runouts (survival) and failures for each group observed during fatigue testing.

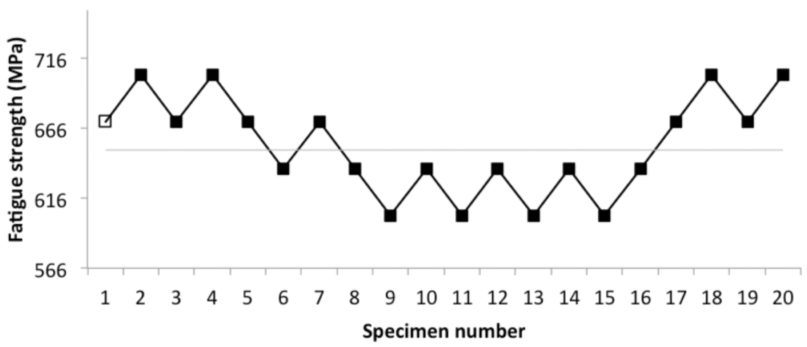
LAVA



ZIRLUX FC


Ctrl - mean fatigue strength 542,24 MPa


Coarse - mean fatigue strength 652,07 MPa


Ctrl Ltd - mean fatigue strength 650,17 MPa

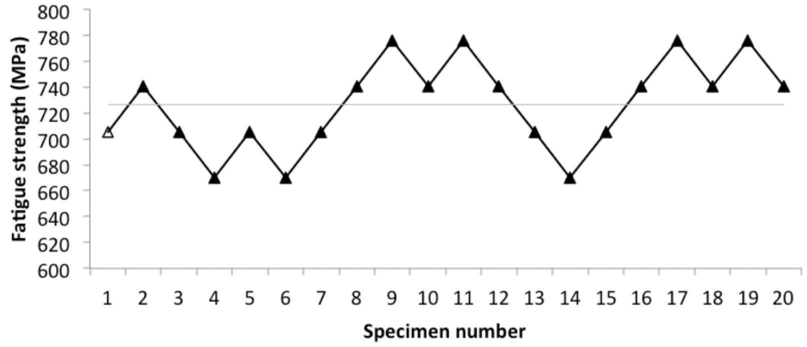

Coarse Ltd- mean fatigue strength 753,23 MPa

Fig 3. Representative micrographics (a – Ctrl; b – Ctrl Ltd; c – Grinding; d – Grinding Ltd) of fractured surfaces (fractography examination) using a Light Microscope. The region under the half-circle indicates the fracture origins initiated at a superficial/subsuperficial defect where concentrated tension stress. The arrows (➔) indicate the crack propagation direction into the opposite side where concentrated compression stress (Compression Curl region). Specimens from both Y-TZP ceramics (Zirlux and Lava) presented the same fractographic pattern for each evaluated condition.

Tables

Table 1- Experimental Design

Material brand	**Groups**	**Study factors**		**N = 160**
		Surface Treatment	**LTD**	
Lava Frame, 3M ESPE	Ctrl	Control, *as-sintered* (without any additional treatment)	Without	20
	Ctrl Ltd		With	20
	Grinding	Grinding with coarse diamond bur (3101G – grit size 181 µm, KG Sorensen, Cotia, Brazil)	Without	20
	Grinding Ltd		With	20
Zirlux FC, Ivoclar-Vivadent	Ctrl	Control, *as-sintered* (without any additional treatment)	Without	20
	Ctrl Ltd		With	20
	Grinding	Grinding with coarse diamond bur (3101G – grit size 181 µm, KG Sorensen, Cotia, Brazil)	Without	20
	Grinding Ltd		With	20

Table 2. Monotonic biaxial mean strength, initial fatigue test strength (70% of monotonic biaxial mean strength) and the step size (5% of Initial strength) for fatigue testing (staircase); Mean fatigue limit (σ_f), standard deviation (SD) and 95% confidence interval (CI) from staircase tests, in addition to roughness statistical (α=0.05) analysis (Mean value ± Standard Deviation of parameter Ra and Rz - µm) and percentage (%) of m-phase content before and after fatigue testing.

Material brand	**Groups**	**Monotonic mean strength (MPa)**	**Initial fatigue test strength (MPa)**	**Step (MPa)**	**Fatigue limit in MPa**		**Roughness (µm)**		**m-phase content (%)**	
					σ_f (± SD)	**95% CI**	**Ra ± (SD)**	**Rz ± (SD)**	**Before fatigue testing**	**After fatigue testing**
LAVA FRAME	**Ctrl**	865.9	606.1	30.3	577.5 (±57.2)^{A}	(557.70 – 597.31)	0.29 (±0.18)^{a}	2.54 (±1.36)^{a}	0	0
	Ctrl Ltd	980.1	686.1	34.3	746.2 (±25.9)^{B}	(722.46 -769.90)	0.31 (±0.15)^{a}	2.58 (±1.04)^{a}	58.85	57.83
	Grinding	1076.9	753.8	37.7	706 (±62.1)^{B}	(681.28 – 730.76)	1.11 (±0.22)^{b}	6.70 (±1.09)^{b}	11.25	13.81
	Grinding Ltd	830.0	581	29.1	753.2 (±39.8)^{B}	(731.71 – 774.74)	1.28 (±0.24)^{c}	7.44 (±1.13)^{c}	37.48	36.84
ZIRLUX FC	**Ctrl**	790.0	553.0	27.7	542.2 (±25.6)^{a}	(525.49 – 558.98)	0.27 (±0.08)^{a}	2.16 (±0.57)^{a}	0	3.83
	Ctrl Ltd	958.1	670.7	33.5	653.9 (±45)^{b}	(627.10 – 680.69)	0.32 (±0.14)^{a}	2.47 (±1.02)^{a}	67.97	66.71
	Grinding	1013.1	709.2	35.5	652.1 (±83.9)^{b}	(601.07 – 703.07)	1.04 (±0.27)^{b}	6.51 (±1.49)^{b}	9.66	12.87
	Grinding Ltd	1007.7	705.4	35.3	726.5 (±41.1)^{c}	(701.85 – 751.25)	1.10 (±0.28)^{c}	6.74 (±1.43)^{c}	42.76	42.21

**Different letters indicate statistically significant differences: For fatigue limit it was used One-Way ANOVA and post-hoc Tukey; for Roughness data (Ra and Rz) Kruskall-Wallis and post-hoc Dunn`s test*

6. ARTIGO 5 - The effect of grinding on the mechanical behavior of Y-TZP ceramics: a systematic review and meta-analyses

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Running title: Grinding of YTZP ceramics – a systematic review.

Abstract

The aim of this study was to systematically review the literature to assess the effect of grinding on the mechanical properties, structural stability and superficial characteristics of Y-TZP ceramics. The MEDLINE via PubMed and Web of Science (ISI - Web of Knowledge) electronic databases were searched with included peer-reviewed publications in English language and with no publication year limit. From 342 potentially eligible studies, 73 were selected for full-text analysis, 30 were included in the systematic review with 20 considered in the meta-analysis. Two reviewers independently selected the studies, extracted the data, and assessed the risk of bias. Statistical analyses were performed using RevMan 5.1, with random effects model, at a significance level of 0.05. A descriptive analysis considering phase transformation, Y-TZP grain size, Vickers hardness, residual stress and aging of all included studies were executed. Four outcomes were considered in the meta-analyses (factor: grinding x as-sintered) in global and subgroups analyses (grinding tool, grit-size and cooling) for flexural strength and roughness (Ra) data. A significant difference ($p<0.05$) was observed in the global analysis for strength, favoring as-sintered; subgroup analyses revealed that different parameters lead to different effects on strength. In the global analysis for roughness, a significant difference ($p<0.05$) was observed between conditions, favoring grinding; subgroup analyses revealed that different parameters also lead to different effects on roughness. High heterogeneity was found in some comparisons. Generally grinding promotes decrease in strength and increase in roughness of Y-TZP ceramics. However, the use of a grinding tool that allows greater accuracy of the movement (i.e. contra angle hand-pieces coupled to slow speed turbines), small grit size (< 50μm) and the use of plenty coolant seem to be the main factors to decrease the defect introduction and allow the occurrence of the toughening transformation mechanism, decreasing the risk of deleterious impact on Y-TZP mechanical properties.

Key Words: Grinding. Strength. Roughness. Hardness. Residual stress. Grain size. Aging. Dental prosthesis. Dental Ceramics.

1. Introduction

Over the last years scientific community has been demonstrating great interest in Y-TZP ceramic (Yttrium-stabilized Tetragonal Zirconia Polycrystalline ceramic), mainly motivated by its high fracture strength, improved optical and biocompatibility properties (Piconi & Maccauro, 1999). Basically, zirconia is a polymorphic metastable material that when required (submitted to a stimuli – mechanical, physical and/or chemical) may respond through a phase transformation mechanism (tetragonal (*t*) to monoclinic (*m*)) (Garvie & Nicholson, 1972; Hannink, 2000; Amaral et al., 2013; Pereira et al., 2015).

Nowadays, Y-TZP has been used in Prosthetic Dentistry for the manufacturing of infrastructure of fixed partial dentures (FDPs) that would be covered by feldspathic porcelain (Denry & Kelly, 2014); and as full-contour monolithic restorations dispensing the application of a feldspathic porcelain (Beuer et al., 2012; Sabrah et al. 2013; Nakamura et al. 2015), which eliminates the problem of chipping and fracture of the veneering porcelain (the most common reason for failure of veneered zirconia FDPs - Beuer et al., 2010; Chaar & Kern, 2015; Pihlaja et al., 2016). Moreover, it allows a more conservative tooth preparation as requires thinner thickness (Denry & Kelly, 2014).

It is important to consider that with both applications (infrastructure of FDPs or full-contour monolithic restorations) after the restoration manufacturing by CAD/CAM (Computer Aided Design / Computer Aided Machining) systems, adjustments (with diamond grinding instruments) are usually needed to achieve a better fit, an adequate emergency profile and to enhance the occlusal relation (Aboushelib et al., 2009; Preis 2015[b]; Jing 2014; Pereira et al., 2014; 2015[a]).

In this concern, the literature shows conflicting results on the effects of grinding with diamond instruments on Y-TZP's mechanical properties. Some studies (Amaral et al., 2013; Pereira et al., 2015[a]; Ramos et al., 2016) show a positive effect due to the phase transformation toughening mechanism, where grinding triggers a *t-m* phase transformation, which results in a volumetric expansion of ~4% around the superficial defects, inducing compressive stress concentration and consequently arresting crack propagation (Garvie & Nicholson, 1972). However, other studies (Kosmac et al., 1999; Kosmac et al., 2000; Curtis et al., 2006; Kosmac et al., 2007; Kosmac et al., 2008; Iseri et al., 2012) observed that grinding introduces important superficial defects that could be deleterious, decreasing the mechanical properties and resulting in higher risk of catastrophic failures.

Thus, the balance between the introduction of superficial defects and the phase transformation toughening mechanism seems to determine the final effect of grinding on the mechanical properties of Y-TZP. Considering this, the protocol of grinding (i.e. grinding tool, grit-size of grinding instrument, presence/absence of cooling, pressure during grinding) may play an important role on this outcome. Therefore, a systematic review may be a helpful tool to clarify the effects of this mechanism and to guide future studies on this topic.

Another important factor that have to be considered regarding Y-TZP ceramics is the susceptibility to aging. LTD (Low-Temperature Degradation) is a spontaneous time dependent degradation mechanism, also related to the t-m phase transformation mechanism (Kobayashi et al., 1981). As it progresses through ceramic surface and subsurface, it may promote grain detachment/pullout and the introduction of micro cracks on the grain neighboring areas, increasing the surface roughness, which impacts on some mechanical and physical properties, as strength, fracture toughness, and density (Chevalier, 2007; Pereira et al., 2015^b).

Literature has been demonstrating that when grinding is executed, a thin layer of compressive residual stress may be formed (Sato et al., 1996; Ho et al., 2009; Jing et al., 2014). Additionally Deville and collaborators (2006) noticed that the formation of this layer protects the surface against new phase transformation; thus, the formation of this compressive residual stress layer may decrease the susceptibility of Y-TZP to LTD. Instead, if grinding introduces extensive critical defects, in addition to increased roughness, without triggering and adequate transformation toughening mechanism, it may enhance water penetration to deeper areas and lead to a higher susceptibility to LTD effects (Chevalier, 2006; Kim et al., 2010).

Thus, this study aimed to systematically review *in vitro* studies to: (1) assess the effect of grinding on the mechanical properties, structural stability and superficial characteristics of the Y-TZP ceramic; (2) determine the influence of the protocol used for grinding (grinding tool, grit-size of grinding tool and presence/absence of coolant) on these outcomes.

2. Materials and Methods

2.1 Search Strategy

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009). Two electronic databases were searched to identify studies that could be considered: 1- MEDLINE electronic database via PubMed; 2- Web of Science (ISI - Web of Knowledge). The following search strategies were performed: computer search of database, review of reference lists of all included articles, and contact with authors and experts on the issue. The search included peer-reviewed publications only in English language and with no publication year limit. The last search was executed on 21 March 2016.

2.2 Focused question

"Does grinding have any effect on the mechanical properties (flexural strength, toughness, hardness), structural stability (phase stability (*t→m* transformation)) and superficial characteristics (roughness) of Y-TZP ceramics?

2.3 PICOs

The population, intervention, comparison and outcomes, i.e. the "PICOs" for this systematic review were defined as follows:

Population: Y-TZP ceramic specimens;

Intervention: grinding;

Comparison: as-sintered condition (Y-TZP ceramic without grinding). As-sintered samples without any treatment after sintering were used as control (baseline);

Outcomes: structural stability, phase stability, phase transformation, surface topography, surface morphology, surface characteristics, roughness, mechanical properties, mechanical behavior, strength, hardness, toughness, stiffness, fracture, flexural;

Study design: *in vitro* studies.

The MeSH and free-text terms were used to compose the search strategy as follows: ((((((((zirconium[MeSH Terms]) OR zirconi*) OR zirconium oxide) OR Y-TZP) OR yttria stabilized polycrystalline tetragonal zirconia) OR yttria stabilized tetragonal zirconia)) AND ((grinding) OR ground)) AND (((((((((((((((structural stability) OR phase stability) OR phase transformation) OR surface topography) OR surface morphology) OR surface characteristic*) OR roughness) OR mechanical properties) OR mechanical behavior) OR strength) OR resistance) OR hardness) OR toughness) OR stiffness) OR fracture) OR flexural)) NOT ((bond*) OR adhesion).

2.4 Inclusion Criteria

The inclusion criteria for study selection were: (i) *in vitro* studies, (ii) yttrium-stabilized tetragonal zirconia polycrystal (Y-TZP) ceramic, (iii) grinding, (iv) mechanical properties, structural stability (phase transformation) and/or superficial characteristics.

2.5 Exclusion Criteria

It was excluded studies that did not have a proper control group, did not use Y-TZP ceramic (with addition of dopants), did not evaluate the effects of grinding, did not evaluate mechanical properties, structural stability or surface characteristics, not presented in English language.

2.6 Search steps: screening and selection

A flow diagram elucidating all the search steps execution is presented in Figure 1.

Step 1: Titles and abstracts were reviewed by two independent authors (G.K.R.P. and S.F.) and selected per their consensus according to the inclusion criteria. If consensus was not reached, the abstract was set aside for further evaluation.

Step 2: Full-text articles of abstracts selected in step 1 were retrieved and reviewed by 2 independent authors (G.K.R.P. and S.F.). Inclusion was based on consensus between these 2 investigators. Disagreements were discussed with a third author (C.J.K.).

Step 3: Two authors (G.K.R.P. and S.F.) evaluated together the reference lists of all articles selected in step 2, and full texts of potentially interesting studies were examined.

For each step independently executed, it was calculated the coefficient of inter-rater agreement (Kappa) between evaluators (G.K.R.P. and S.F.). It was observed a 0.85 Kappa coefficient for step 1 and a 0.94 Kappa coefficient for step 2.

2.7 Data Extraction

A protocol for data extraction was defined and evaluated by 2 authors (G.K.R.P. and S.F). Any disagreement was discussed with a third author (A.F.M.). Data were extracted from full-text of included articles using a standardized form. The authors categorized similar information into groups according to the main outcomes of interest. If data were not presented or the mean and standard deviations values could not be extracted, the authors were contacted three times via e-mail. The study was excluded if any missing important information was not supported.

2.8 Risk of Bias Assessment

The risk of bias evaluation was based on and adapted from previous studies (Sarkis-Onofre et al., 2014; Montagner et al., 2014; Pereira et al., 2015[b]) and evaluated the description of the following parameters for the study's quality assessment: randomization of ceramic specimen, sintering cycle used according to the manufacturer's instructions, specimen preparation clearly stated and executed in a standardized and reproducible way, outcome evaluated following International Standard rules (i.e. ISO, ASTM, and others), grinding protocol clearly specified, execution of sample size analysis, test executed by a single blinded operator. For each parameter values from 0 to 2 were attributed: 0 - if the authors clearly reported the parameter; 1 – if the author reported the execution/respect of the parameter but accuracy of the execution is unclear; 2 – if the author not specified the parameter or the information is not present. If the total sum of the attributed values ranged between 0 up to 4 it was considered a low risk, between 5 up to 9 a medium risk and 10 up to 14 a high risk of bias.

For studies that did not consider any mechanical properties and only evaluate structural stability and superficial characteristics of the Y-TZP ceramic, International Organization for standardization and single blinded operator parameters were not considered. Thus, in these studies, the total sum ranged from: 0 up to 3 low risk, 4 to 6 medium risk and 7 to 10 high risk.

2.9 Data Analyses

Based on data of included studies, it was possible to execute meta-analysis of flexural strength and roughness (Ra) data, once few studies evaluated the other properties. Thus, descriptive analyses were made for the other properties: grain size, phase transformation, Vickers hardness, residual stress and aging effect on flexural strength.

For both meta-analysis (strength and roughness – Ra parameter) data (means and standard-deviations) for ground vs. control (as-sintered) conditions were globally and subgroup analyzed. Global analyses took into account all included studies, and subgroup analyses assessed the different grinding parameters (grinding tool, grit-size and cooling) where two strata were created for cooling parameter (presence/absence) and three strata were considered for grinding tool (grinding machine/high-speed hand-piece/hand-piece coupled to a slow-speed motor) and grit-size (< 50 µm/50 µm to 120 µm /≥120 µm) parameters.

All analyses were conducted in Review Manager Software 5.1 (Copenhagen, Nordic Cochrane Centre, Cochrane Collaboration) using a random effect model. Pooled effect estimates were obtained by comparing the means of flexural strength values and were expressed as the raw mean difference among the groups. A p value ≤ 0.05 was considered statistically significant (Z test). Statistical heterogeneity of the treatment effect among studies was assessed via the Cochran Q test, with a threshold p value of 0.1, and the inconsistency I2 test, in which values > 50% were considered indicative of high heterogeneity.

For studies that evaluated more than one Y-TZP material or more than one grinding condition, each material/condition was considered independently, for each evaluated parameter (grinding tool, grit-size and presence/absence of cooling). Additionally, one study (Subasi et al., 2014) evaluated the mechanical properties (flexural strength) of Y-TZP ceramic after 2/10 firing cycles (simulation of glaze firing recommended by the manufacturer), but considering the same grinding parameters. Thus, for this specific study (Higgins J., et al. 2011), an equation proposed by the Cochrane Handbook was used to calculate single sample size, mean and standard deviation values for each experimental and/or control groups.

3. Results

3.1 Search and selection

From 342 potentially eligible studies, 73 were selected for full-text analysis, 30 were included in the systematic review with 20 were considered in the meta-analysis (Figure 1). The characteristics of the included studies are presented in Table 1.

3.2 Risk of bias

Of the 30 studies included in this systematic review, 3 (10%) presented low risk of bias, 3 (10%) presented high risk of bias, while the majority (24 studies - 80%) showed medium risk of bias. All studies lack reporting if a single blinded operator executed the mechanical test. The results are described in Table 2.

3.3 Descriptive analysis

3.3.1 Phase transformation

The descriptive analysis of phase transformation data is presented in Table 1. From the 30 studies included in the systematic review, only 25 studies evaluated the phase transformation. In most of the studies (21 of the 25 studies), grinding promoted an increase in *m*-phase content (ranging from 0 up to 4.15% before grinding, in the as-sintered condition, and from 2 up to 20% after grinding) with intensity of phase transformation directly related to the material susceptibility and to the parameters used for grinding (grit-size, grinding tool and presence/absence of cooling), independently of the methodology used for *m*-phase quantification.

Some studies (5 of the 25) did not notice the presence of *m*-phase content after grinding (Kosmac et al., 2004; Denry & Holloway 2006; Curtis et al., 2006; Amaral et al., 2013; Strasberg et al., 2014 only on the higher grit-size).

Data from X-Ray Diffractometry (XRD) analysis showed that statistical evaluation of the monoclinic phase is scarce and that the methodology preconized by Garvie & Nicholson, 1972 (modified or not by Toraya et al., 1984) was the most common tool for phase quantification. Further, most studies did not present mean and standard deviation values of those data.

3.3.2 Grain Size

The descriptive analysis of grain size data is presented in Table 3. From the 30 studies included in the systematic review, only 12 studies measured grain size after sintering (Reed & Lejus, 1977; Sato et al., 1996; Kosmac et al., 1999; Kosmac et al., 2000; Kosmac et al., 2004; Kosmac et al., 2007; Kosmac et al., 2008; Ho et al., 2009; Kim et al., 2010; Jing et al., 2014;

Strasberg et al., 2014; Roa et al., 2016). The values ranged between 0.3 up to 1.0 µm.

3.3.3 Vickers Hardness

The descriptive analysis of Vickers hardness data is presented in Table 4. Among the studies included in this systematic review only 3 (Reed & Lejus, 1977; Denry & Holloway, 2006; Curtis et al., 2006) evaluated Vickers hardness (ground x as-sintered condition) and it was possible to retrieve quantitative data from just one study (Curtis et al., 2006). All the three studies reported that grinding improved the Vickers hardness of Y-TZP ceramic.

3.3.4 Residual Stress

The descriptive analysis of residual stress data is presented in Table 5. Among the studies included in this systematic review only 3 (Sato et al., 1996; Ho et al., 2009; Jing et al., 2014) evaluated residual stress (ground x as-sintered condition) and just 2 of them presented quantitative data. According to these studies, grinding induced compressive residual stress causing a reorientation of the superficial crystallites (phase transformations and lattice distortions). This compressive residual stress layer was confined to a thin superficial layer (approximately 10µm), and, according to Jing et al., 2014, it can be removed during polishing and/or annealing. Annealing appears to promote a relaxation of this residual stress depending on the protocol used.

3.3.5 Aging

The descriptive analysis of studies that evaluated grinding effect after aging is presented in Table 6. Among the studies included in this systematic review only 8 evaluated the effects of aging on the mechanical properties of ground vs. as-sintered Y-TZP ceramic (Sato et al., 1996; Kosmac et al., 2007; Kosmac et al., 2008; Kim et al., 2010; Amaral et al., 2013; Pereira et al., 2015[a]; Pereira et al., 2016[a]; Pereira et al., 2016[b]).

Less *m*-phase content was reported for ground Y-TZP than for as-sintered Y-TZP after aging conditions. Regarding the fatigue behavior, Kosmac et al., 2007 and 2008 reported that the survival was very compromised after grinding and different protocols of aging in comparison to the as-sintered aged condition, while Pereira et al., 2016[b] showed an increase in fatigue limit and survival after grinding.

3.4 Meta-analysis

3.4.1 Flexural Strength

A total of 4 meta-analyses were performed for flexural strength data, considering 18 studies. All the flexural strength meta-analysis results are presented in Figure 2. Studies that evaluated more than one Y-TZP material or more than one condition of grinding were inserted more than one time in each meta-analysis, considering the data of each material/grinding protocol (Kosmac et al., 1999; Kosmac et al., 2000; Curtis et al., 2006; Kosmac et al., 2007; Karakoca & Yilmaz, 2009; Iseri et al., 2010; Iseri et al., 2012; Pereira et al., 2014; Pereira et al., 2015[a]; Ramos et al., 2016; Pereira et al., 2016[a]; Pereira et al., 2016[b]), which resulted in 43 data sets.

At the first meta-analysis (global analysis) between grinding vs. control (as-sintered), it was observed a statistical difference ($p<0.05$) between conditions, favoring control group, which presents the higher flexural strength values. The heterogeneity parameter I^2 was 97% (Figure 2A).

For the second meta-analysis, a subgroup analysis considering different grinding tools (grinding machine; high-speed hand-piece; hand-piece coupled to a slow-speed motor) was performed (Figure 2B). The results showed a statistical difference ($p<0.05$) between the evaluated conditions, showing that different grinding tools have different effects on Y-TZP flexural strength. For grinding machine, a statistical difference was found ($p<0.05$), favoring ground condition. For high-speed hand-piece, it was observed a statistical difference ($p<0.05$) favoring as-sintered condition. For hand-pieces coupled to slow-speed motors it was observed no statistical difference ($p>0.05$). The I^2 was 94%.

For the third meta-analysis, a subgroup analysis for grit-size of grinding tool (grit-size < 50μm; 50μm ≤ grit-size < 120μm; 120μm ≤ grit-size) was performed (Figure 2C). It was noted that different grit-sizes of the grinding tool have different effects on Y-TZP flexural strength ($p<0.05$). In smaller grit-sizes a statistical difference ($p<0.05$) was observed, favoring ground condition; while for medium and higher grit-sizes it was observed a statistical difference ($p<0.05$) favoring as-sintered group. The heterogeneity parameter I^2 was 92.8%.

For the fourth meta-analysis, a subgroup analysis for presence x absence of cooling during grinding was performed (Figure 2D). It was observed a statistical difference ($p<0.05$) between evaluated conditions showing that the presence or absence of colling influences the final effect on flexural strength of Y-TZP ceramic. The results favored the as-sintered group when no cooling was used ($p<0.05$), however when cooling was used during grinding, no statistical difference ($p>0.05$) was found between groups (ground x as-sintered). The heterogeneity parameter I^2 was 96.3%.

3.4.2 Roughness (Ra)

A total of 4 meta-analyses were performed for roughness (Ra parameter) data, considering 12 studies. All the roughness Ra meta-analysis results are presented in Figure 3.

Studies that evaluated more than one Y-TZP material or more than one condition of grinding were inserted more than one time in each meta-analysis, considering the data of each material/grinding protocol (Curtis et al., 2006; Karakoca & Yilmaz al., 2009; Pereira et al., 2014; Pereira et al., 2015[a]; Gungor et al., 2015; Ramos et al., 2016; Pereira et al., 2016[a]; Pereira et al., 2016[b]), which resulted in 23 data sets.

At the first meta-analysis (global analysis) between grinding vs. control (as-sintered), it was observed a statistical difference ($p<0.05$) between conditions (grinding x as-sintered), favoring ground group, which presents the higher roughness values. The heterogeneity parameter I^2 was 100% (Figure 3A).

For the second meta-analysis, a subgroup analysis considering different grinding tools (grinding machine; high-speed hand-piece; hand-piece coupled to a slow-speed motor) was performed (Figure 3B). The results showed a statistical difference ($p<0.05$) between evaluated conditions, where different grinding tool lead to different effects on roughness Ra parameter. For grinding machine, a statistical difference was found ($p<0.05$), favoring as-sintered condition (which presented the higher roughness Ra values). While for high-speed hand-piece and for hand-pieces coupled to slow-speed motors, it was observed a statistical difference ($p<0.05$) favoring ground condition. The I^2 was 98.8%.

For the third meta-analysis, a subgroup analysis for grit-size of grinding tool (grit-size $< 50\mu m$; $50\mu m \leq$ grit-size $< 120\mu m$; $120\mu m \leq$ grit-size) was performed (Figure 3C). In general, it was not noted a statistical difference ($p>0.05$) between evaluated conditions. When the sub-groups were considered individually, medium and coarse grit-size ($50\mu m \leq$ grit-size) presented a statistical difference ($p<0.05$) favoring ground conditions. The heterogeneity parameter I^2 was 0%.

For the fourth meta-analysis, a subgroup analysis for presence x absence of cooling during grinding was performed (Figure 3D). In general, it was not noted a statistical difference ($p>0.05$) between evaluated conditions, but, when the sub-groups were considered individually it was noted that ground condition always presented higher values of Ra compared to as-sintered ($p<0.05$). The heterogeneity parameter I^2 was 65.5%.

4. Discussion

This systematic review accessed the effect of grinding on the mechanical properties, structural stability and superficial characteristics of the Y-TZP ceramic. Based on existing data it was possible to execute meta-analyses only for the strength and roughness outcomes. In general, grinding promoted a decrease on Y-TZP strength (Figure 2A) and led to higher roughness values (fig 3A). However, this systematic review showed that the protocol used for grinding seems to affect these outcomes as distinct effects could be observed depending on the grinding tool (Figure 2B and 3B), grit size (Figure 2C and 3C) and presence/absence of coolant (Figure 2D and 3D).

Nevertheless, it is important to highlight that our data support that is possible to promote grinding without decrease Y-TZP strength if a specific protocol is respected. The use of a grinding tool that permits a great control of the movement (i.e. handpieces coupled to slow-speed motors – contra angle attachment), a small grit size (< 50µm) and the use of coolant seems to be the main factors to decrease defect introduction and allow the occurrence of the transformation toughening mechanism.

Basically, literature shows that any adjustment procedure on zirconia surfaces, such as grinding, may induce: 1- superficial modifications, damage, and 2- phase transformation from the tetragonal (t) to monoclinic (m) phase (Karakoca & Yilmaz, 2009; Mochales et al., 2011; Maerten et al., 2013), as also demonstrated by the present systematic review.

Regarding superficial modifications, it has been shown that usually grinding results in rougher surface (Curtis et al., 2006; Karakoca & Yilmaz, 2009; Subasi et al., 2014; Gungor et al., 2015; Pereira et al., 2014; Pereira et al., 2015[a]; Pereira et al., 2016[a]; Pereira et al., 2016[b]). Flury and collaborators (2012) stated that surface roughness might play a crucial role in the resistance of ceramics, usually showing a significant negative correlation with flexural strength (higher roughness with lower flexural strength). On the other hand, Quinn (2007) stated that the presence of correlation is observed only in some specific cases, defined by the balance between the depths of the defects introduced by grinding compared to the existing surface flaws. When the depth of the introduced cracks is similar to that of the existing surface flaws a correlation would not be expected, however, when the introduced cracks are deeper than the existing surface flaws, a stronger correlation is noticed.

Jing and collaborators (2014) stated that micro-defects and residual stresses are introduced during zirconia restoration production from industrial production, lab preparations, and to clinical adjustment. These micro-defects and residual stresses are cumulative and determine the microstructure evolution and the final mechanical properties of Y-TZP restorations. Consequently, the authors stated that caution should be taken (1) to decrease packing voids during the initial pressing of starter powders; (2) to minimize micro-defects from milling; and (3) to eliminate or reduce micro-defects from grinding.

It is already well established that deep surface flaws can act as stress concentrators, reducing the strength values on ceramics (Green, 1983). Literature (Yin et al, 2003; 2006; Quinn et al., 2005) shows that grinding could introduce damage that varies from deep scratches (in addition to chipping) associated with penetrating median cracks, to subsurface lateral cracks and shallow scratches, depending on the grit-size, applied load, and grinding speed. It is believed that those defects are formed due to high and inhomogeneous forces applied by hand to remove the dense material, in other words, a harmful protocol of grinding by lack of control of the movement associated to increased grit-size, load and speed (Yin et al., 2003; Iseri et al., 2010; Jing et al., 2014).

Additionally, grinding may also trigger a martensitic *t-m* phase transformation. A martensitic transformation is a "change in crystal structure that is athermal, diffusionless and involves the simultaneously, cooperative movement of atoms over distances less than an atomic diameter, so as to result in a macroscopic change of shape of transformed regions" (Kelly & Rose, 2002). The energy needed for the transformation is influenced by grain size, with smaller-grained zirconia showing a greater resistance to transformation (Kelly & Denry, 2008).

This phase transformation mechanism is the basis of the high toughness of Y-TZP. Toughening occurs as a result of the stress-induced phase transformation from the tetragonal to monoclinic phase during crack propagation (Gupta et al., 1978). As a crack begins to propagate, tensile stress concentration at the crack tip destabilizes the process zone into the monoclinic phase (which results in a volumetric expansion ~4%). With further propagation, the crack becomes surrounded by transformed zirconia, which produces a compressive stress acting to close the crack (Garvie et al., 1975; Gupta et al., 1978; Hannink et al., 2000; Chevalier et al., 2009).

Literature (Chevalier et al., 2007; Pereira et al., 2015^{b}) has been demonstrating that the Y-TZP susceptibility to *t-m* phase transformation seems to be material dependent (composition, stabilizer, grain size and protocol of processing). Based on that, two descriptive analyses considering these factors were performed (one descriptive analysis of all studies – Table 1; and another one taking into consideration grain size, sintering condition, and stabilizer content – Table 3). It can be noticed some variability in composition, sintering conditions and final grain size of the evaluated materials. Although these factors could influence the materials' susceptibility to phase transformation, the protocol of grinding seems to be the major factor to dictate the final mechanical properties of the material.

Based on the descriptive analysis of the grinding protocol (Table 1), it can be noticed that basically *in vitro* studies has been using 3 main grinding tools to evaluate the effect of grinding: (1) grinding/polishing machines which allow a more standardized and reproducible grinding procedure (Denry & Holloway, 2006; Ho et al., 2009; Amaral et al., 2013; Pereira et al., 2014; Ramos et al., 2016), which are important characteristics for the quality of *in vitro* laboratorial research; (2) slow speed motors (with normal contra-angles or high torque handpieces, which allows high speed by multiplying the speed of the contra-angle, maintaining the high torque proportioned by the slow-speed motor) (Curtis et al., 2006; Karakoca & Yilmaz, 2009; Iseri et al., 2010; Iseri et al., 2012; Subasi et al., 2014; Pereira et al., 2015[a]; Pereira et al., 2016[a]; Pereira et al., 2016[b]); and (3) regular high-speed handpieces (dental turbines) (Iseri et al., 2010; Iseri et al., 2012; Kosmac et al., 1999; Kosmac et al., 2000; Kosmac et al., 2007; Kosmac et al., 2008; Michida et al., 2015).

It may be noticed that when studies use grinding/polishing machines, although the advantages of enhancing standardization and reproducibility, it basically promotes a polishing effect, instead of grinding, irrespective of grit-size, resulting in a surface with less roughness than as-sintered condition (Figure 2B). Based on this fact, two features need to be addressed: (1) the defects introduced by grinding with grinding/polishing machines are different from those introduced by diamond bur, which results in totally distinct surfaces, as demonstrated by Pereira and collaborators (2014); (2) considering that different tools result in different surfaces (with different defects introduced), it is important to evaluate a condition that simulates a clinical scenario, employing a clinically relevant protocol.

Based on these assumptions, grinding/polishing machines seem to not be an adequate tool to simulate the clinical adjustment executed on common clinical practice. In contrast, high-speed handpieces (dental turbines) led to an extensive defect introduction and did not permit a proper phase transformation mechanism, which resulted in compromising Y-TZP mechanical properties (Iseri et al., 2010; Iseri et al., 2012; Kosmac et al., 1999; Kosmac et al., 2000; Kosmac et al., 2007; Kosmac et al., 2008). Thus, the best option seems to be handpieces coupled to slow-speed motors. Among the variety of handpieces to this use, the high torque handpieces with a contra angle attachment (which multiply the velocity of the speed motor achieving speeds comparable to dental turbines without loosing torque) seems to be a good alternative, being able to promote a better control of the grinding procedure in comparison to normal high speed handpieces, which is a fundamental factor on decreasing defect introduction, and also do not compromise the phase transformation mechanism (Jing et al., 2014; Pereira et al., 2014; Pereira et al., 2015[a]; Pereira et al., 2016[a]; Pereira et al., 2016[b]).

Regarding grit-size of the grinding tool, the best option is to use low grit-sizes (< 50 µm), as it promoted higher strength values compared to as-sintered condition (fact explained by transformation toughening mechanism) and did not lead to higher values of roughness. Moreover, the increase in grit-size leads to an increase of defect introduction (Kosmac et al., 2000; Kosmac et al., 2007; Curtis et al., 2006; Pereira et al., 2014; Pereira et al., 2015[a]; Pereira et al., 2016[a]; Pereira et al., 2016[b]).

Regarding the presence/absence of coolant, it can be noticed that its presence led to no statistical difference on strength between grounded and as-sintered condition. It is believed that in the presence of water, while grinding is introducing defects, it is triggering the transformation toughening mechanism that has a counter-balance effect. When grinding is executed without water it was noted a clear decrease of strength, meaning more defect introduction than transformation toughening mechanism.

During grinding without proper cooling the superficial temperature may raise (Swain & Hannink, 1989; Kosmac et al., 2008; Iseri et al., 2012) achieving temperatures above the critical point where *t-m* phase transformation may occur. In this scenario also a reverse *m-t* transformation may happen (Swain & Hannink, 1989). Consequently defects are introduced without the counter-balance of the transformation toughening mechanism, decreasing Y-TZP strength (Kosmac et al., 1999; Kosmac et al., 2000; Kosmac et al., 2007; Kosmac et al., 2008; Karakoca & Yilmaz, 2009; Iseri et al., 2010; Iseri et al., 2012).

Although the benefits of transformation toughening mechanism are known, scientific community is still concerned about the fact that a high *t-m* transformation rate may decrease the mechanical stability over time. In the oral environment, ceramic restorations are susceptible to fatigue failure, mainly due to the presence of cyclic masticatory forces and moisture (Zhang et al., 2013). Fatigue failure may be defined as the fracture of the material due to progressive brittle cracking under repeated cyclic stresses with intensity below the material nominal strength (Wiskott et al., 1995).

A high *m*-phase content previously to the final cementation of the restoration could mean that zirconia have already lost, to some extent, the ability to counter-balance the progressive brittle cracking (crack propagation) by the transformation toughening mechanism (Vagkopoulou et al., 2009). However, there are few studies (Kosmac et al., 2007; Kosmac et al., 2008; Pereira et al., 2016[b]) that evaluated fatigue life of ground Y-TZP, showing conflicting results. Thus, more studies are necessary to clarify this topic.

As stated previously, during grinding, microcracks surrounding the transformed grains are formed. These micro cracks can act as avenues for water penetration into the material (Kim, 1997; Chevalier et al., 1999; Deville et al., 2006; Chevalier et al., 2007; Chevalier et al., 2009; Pereira et al., 2015[a]; 2015[b]), increasing the susceptibility to LTD and jeopardizing the mechanical properties.

On the other hand, some studies show that the introduction of compressive residual stresses on the surface may decrease the susceptibility to LTD (Chevalier et al., 2007; Chevalier et al., 2009). In this case the high *m*-phase content previous to cementation could not be harmful. However, Whalen and collaborators (Whalen et al., 1989) showed that even if the specimens are annealed (heat treated) after grinding, they do not lose their high resistance to degradation; conversely, they become more resistant than specimens in the as-sintered condition. It opens the question of whether the compressive residual stresses are actually essential to explain the degradation resistance of ground specimens, although according to Muñoz-Tabares & Anglada (2012) the microstructure induced by grinding on the surface should play an important role.

The microstructural changes induced by grinding of Y-TZP consist of three well defined layers which are described as follows, from the surface to the interior: (1) a superficial crystallized zone, where the grains diameter range from 10 to 20 nm approximately; (2) a plastically deformed zone; (3) a zone in which tetragonal to monoclinic phase transformation has taken place, which is mainly responsible for the formation of compressive residual stresses that usually increases the flexure strength and apparent fracture toughness of ground specimens (Muñoz-Tabares et al., 2011). Thus, the resistance of hydrothermal degradation would be possibly related to the existence of this very thin layer of tetragonal recrystallised nano-grains (10-20 nm) whose size are smaller than the critical size for transformation in humid environment (Evans et al., 1981; Lange, 1982; Muñoz-Tabares et al., 2011).

More studies are necessary to better elucidate the effect of aging on ground Y-TZP ceramics (Table 6), considering that there are few studies on this topic and that the protocol of grinding plays an important role in this scenario, as demonstrated in this meta-analyses,

Regarding the presence (introduction) of residual stress on the surface after grinding, studies based on XRD analysis of ground Y-TZP have beeen noticing a hump at the left shoulder of the XRD $(111)_T$ peak. This hump has been related to the formation of orthorhombic or rhombohedral phase (Kitano et al., 1988; Ruiz & Ready, 1996), or lattice distortion (Kondoh 2004). The formation of orthorhombic or rhombohedral phase is induced by external stress, while lattice distortion is resulted from the presence of residual stress.

Therefore, the presence of the hump at the left shoulder of $(111)_T$ peak has been considered a direct evidence for the presence of residual stress. Additionally is also observed a change of $I_{(002)T}$/ $I_{(200)T}$ ratio, which has been used as an indication for domain re-orientation (Virkar & Matsumoto, 1986). Thus it suggests that the residual stress is large enough to induce lattice distortion (Ho et al., 2009). However, few studies (Sato et al., 1996; Ho et al., 2009; Jing et al., 2014) measured the residual stress introduced by grinding on Y-TZP surface (Table 5).

According to Ho and collaborators 2009, grinding introduces a compressive stress of 1GPa into the surface region. Additionally, the authors stated that the magnitude of the residual stresses can be determined by using several techniques (Frank et al., 1967; Bernal & Koepke, 1973; Cook et al., 1981; Marshall et al., 1983; Lange et al., 1983; Johnson et al., 1986), but typically, these techniques reveal only the residual stress at the surface region.

Another important mechanical property influenced by grinding is hardness; there are few studies that measured this property before and after grinding (Table 4). All the studies (Reed & Lejus, 1977; Denry & Holloway, 2006; Curtis et al., 2006) agree that after grinding the hardness tends to increase, in comparison to as-sintered condition, the reason of this increase is credited also to the phase transformation mechanism.

Some studies did not observe the presence of *m*-phase after grinding Y-TZP ceramic. One explanation was already explored previously that is the increase on temperature leading to *m-t* reverse phase transformation. An alternative explanation is based on the changes in the XRD spectra after grinding that could be related to rhombohedral phase and/or lattice distortion. It is not clear if the appearance of rhombohedral phase is related to the presence of cubic phase or tetragonal phase on the Y-TZP constitution (Hasegawa, 1983; Ruiz & Readey, 1996), although the *t-m* transformation would be associated with an increase in the volume of the unit cell (5.5%), while a *c-r* transformation would lead to an increase in volume of 5.2%, whereas the increase would only be 3.9% for a *t-r* transformation. Thus, this transformation would also lead to concentration of residual stress and also trigger the toughening mechanism of zirconia (Denry & Holloway, 2006).

Therefore, the absence of *m*-phase would not directly mean the absence of phase transformation mechanism and the increase of mechanical properties after stimuli. Although this bring to attention another important factor, the presence of cubic phase on Y-TZP composition, that according to Chevalier and collaborators (2004) originates from a poor stabilizer distribution leading to a non homogeneous material, from which a larger yttria content concentrates on specific grains that assume the cubic configuration while the surrounding tetragonal grains becomes less stable, as presents less stabilizer content, resulting in an increased susceptibility to aging.

The high heterogeneity observed in some analysis could be explained by 3 main reasons: (1) the high variability of tested materials, as small deviations in materials composition and/or grain structure may lead to a large change in mechanical behavior; (2) the high variability of the methodologies employed for sample preparation, grinding and flexural strength test; (3) the majority of the included studies presented medium risk of bias, a small number of samples and (consequently) high standard deviations, and a high number of covariables, favoring the heterogeneity.

The limitations of these meta-analyses are that only *in vitro* studies using a simplified specimen geometry instead of crown-shaped specimens were evaluated; the lack of standardization on grinding protocols among the studies; the lack of studies that considered aging (LTD) and fatigue (slow crack growth). It is important that further studies consider the effects of the treatments executed after grinding (as polishing, heat treatment and glazing) on the mechanical properties of Y-TZP.

5. Conclusion

- It seems to be possible to execute grinding of Y-TZP without impact deleteriously on the strength of Y-TZP ceramics, although a tendency of an increase in roughness seems expected.
- The main approach for avoiding jeopardizing Y-TZP is to choose a protocol that introduces the fewer possible defects on the surface. Hence, a grinding tool that permits a great control of the movement (i.e. handpieces coupled to slow speed motors – contra angle attachment), small tool grit size (< 50μm) and the use of plenty coolant seem to be a suitable protocol.

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Figures and Tables

Table 1. Data from all studies included in the systematic review, describing the main characteristics from material, grinding protocol and phase transformation descriptive analyses.

Study	Country	Material	Grinding Protocol	Grit-size	Coolant	Outcome	Phase analysis parameter	*m*-phase quantification methodology	*m*-phase (%)	
									As-sintered	Ground
Roa et al., 2016	Spain	Y-TZP powder from Tosoh	Plane surface grinding was performed using a diamond abrasive disk (MD-Piano 220, Struers) with a load pressure and speed of respectively 0.25 MPa and 300rpm.	220 grit	Water	Characterization of density, grain-size and crystalline phases.	XRD - CuKα, 40kV,30mA, step interval 20-100°, 0.017°/step, 4 s per step	Garvie and Nicholson modified by Toraya	0%	≈7%
Pereira et al., 2016[a]	Brazil	Zirlux FC (Ivoclar Vivadent)	Single trained operator using diamond burs in a slow-speed motor (Kavo Dental) associated with a contra-angle handpiece (T2 REVO R170 - up to 170.000rpm, Sirona) under constant watercooling. The diamond bur was replaced after each specimen. Additional care was taken for standardizing thickness and movement of grinding.	25µm	Water – 30ml/min	Phase analysis, Surface topography by SEM and AFM, Roughness and Biaxial flexure strength (piston on three-balls).	XRD - CuKα, 40kV,40mA, step interval 25-35°, 0.03°/step, 1 s per step	Garvie and Nicholson modified by Toraya	0%	9.49%
				181µm						9.66%
Pereira et al., 2016[b]	Brazil	Lava Frame (3M Espe)	Same described in Pereira et al., 2016[a].	181µm	Water – 30ml/min	Phase analysis, Surface topography by AFM, Roughness and Biaxial flexure fatigue limit (piston on three-balls).	Same described in Pereira et al., 2016[a].	Garvie and Nicholson modified by Toraya	0%	13.81%
		Zirlux FC (Ivoclar Vivadent)								12.87%

Ramos et al., 2016	Brazil	Lava Frame (3M Espe)	Samples attached to a polishing machine (Automet 250, Buehler) and subjected to abrasion with diamond discs (Dia-Grid, Allied High Tech Products)	25µm	Water	Biaxial flexural strength (piston–on-three-balls), Phase transformation analysis (XRD), Roughness (Ra and Rz) and Micromorphological pattern (SEM).	XRD - CuKα, 40kV,40mA, step interval 20-65°, 0.03°/step and 0.5s per step.	Garvie and Nicholson	4.15%	8.4%
				160µm						15.6%
				200µm						15.6%
Michida et al., 2015	Switzerland	InCeram 2000 Yz Cubes (VITA)	The bars were initially wet ground and finished using a fin-grit diamond rotary cutting instrument in a high-speed handpiece under water irrigation for 10s.	30µm	Water	Flexural strength (4-point bending test), Phase transformation analysis (XRD), Micromorphological pattern (3D optical profilometer and SEM).	XRD - CuKα, 40kV,40mA, step interval 20-60°, 0.02°/step and 1s per step.	Garvie and Nicholson modified by Toraya	0%	12.96%
Gungor et al., 2015	Turkey	KAVO Everest Zs-blank (Kavo Dental) Noritake Alliance Zirconia (Noritake)	The discs were ground from 1.1mm to 1±0.02mm at a rotational speed of 20.000 rpm. Diamond instruments changed after each group (10 specimens).	100µm	Without – Dry	Only the parameters roughness and *m*-phase were considered on this review. Beside those it was evaluated biaxial flexural strength (in a bilayer setup)	XRD - CuKα, 40kV,40mA, step interval 20-40°, 0.02°/step.	Garvie and Nicholson	0.815% (±0.10)	3.377% (±0.15)
Preis et al., 2015[a]	Germany	Cercon HT (Degudent)	Specimens were ground with a diamond bur using a dental turbine under standardized conditions (forward and reverse movement, 10 seconds, water cooling, 1 N).	27-76µm	Water	Only the parameters of roughness (Ra and Rz) for the condition as-sintered x grinding were considered. Afterwards, the authors evaluated the efficiency of polishing kits	Did not execute phase analysis			

						following the outcomes roughness and SEM images.				
Pereira et al., 2015[a]	Brazil	Lava Frame (3M Espe)	Single trained operator using diamond burs in a slow-speed motor (Kavo Dental) associated with a contra-angle handpiece (T2 REVO R170 - up to 170.000rpm, Sirona) under constant watercooling. The diamond bur was replaced after each specimen. Additional care was taken for standardizing thickness and movement of grinding.	25µm	Water – 30ml/min	Phase analysis, Surface topography by SEM, Roughness, Biaxial flexure strength (piston on three-balls), Fractography analysis by SEM.	XRD - CuKα, 40kV,40mA , step interval 25-35°, 0.03°/step, 1 s per step	Garvie and Nicholson modified by Toraya	0%	9%
				181µm						12.78%
Preis et al., 2015[b]	Germany	Cercon HT (Degudent)	Grinding was done with a diamond bur under standardized conditions (permanent watercooling, 1N, 160.000rpm, 10s).	27-76µm	Water cooling	The authors evaluated surface properties of monolithic zirconia after surface treatment and wear simulation, following the outcomes roughness, micromorphological topography by SEM and Phase analysis (XRD). This studied was excluded from meta-analyses because of missing data (exact values were not exposed) and because authors did not answered email contact, thus, the study findings were considered during review`s discussion.				
		Cercon Base (Degudent)								
Subasi et al., 2014	Turkey	InCeram YZ (VITA)	The ceramic surfaces were ground using a hand-piece at a grinding speed of 20.000rpm for 10 seconds, without water spray. It was used a gentle stroking motion and the diamond bur was changed after every 5 specimens.	110µm	Without – Dry	Surface examination by SEM, roughness (Ra), Phase transformation analysis, 3-point flexural strength.	XRD - CuKα, 20-40°, 0.02°/step, 1.8 s per step	Garvie and Nicholson modified by Toraya	0%	3%

Pereira et al., 2014	Brazil	Lava Frame (3M Espe)	Grinding was executed with diamond discs (Dia-Grid, Allied High Tech Products) under 60N for 10 min, with 300 rpm of the base (clockwise) and 40 rpm of the head-device (anticlockwise) under constant water cooling.	25µm	Water – 500ml/min	Phase analysis, Surface topography by SEM, Roughness, Biaxial flexure strength (piston-on-three-balls).	XRD - CuKα, 40kV,40mA, step interval 25-35°, 0.03°/step, 1 s per step	Garvie and Nicholson modified by Toraya	0%	7%
				160µm						19%
Jing et al., 2014	Sweden	Y-TZP powder from Tosoh	Clinically adjusted (CA) specimens were prepared by grinding the fully dense 3-YTZP crowns using a high-speed handpiece at 300.000 rpm under water cooling.	80µm + SiC bur	Water	The authors evaluate the formation of micro-defects and residual stress in zirconia dental restorations by different processing techniques. The outcomes were Phase analysis (XRD), surface examination by SEM	XRD - CuKα, step interval 20-80°, 0.03°/step, 3° per min	Authors reference Kosmac et al., 1999 which used Garvie and Nicholson	Missing Data	
			Grinding fully sintered bodies were made as reference and a grinding wheel with diamonds was used at a speed of 20m/s.	106-125µm					1%	5.82%
Strasberg et al., 2014	USA	IPS e.max ZirCAD (Ivoclar Vivadent)	Specimens were ground with disks containing diamond particles in a polishing machine (Metaserv 3000, Buehler). Three different particle sizes were employed with two different loads (10 and 40N). Authors stated that the grinding protocol	15µm	Water	Surface examination by AFM and SEM, Phase transformation analysis (XRD, GIXRD and Raman). Evaluated as-sintered, grinding and regenerated conditions.	XRD - CuKα, 45kV,40mA, step interval 20-70°, 0.05°/step, 1 s per step;	Garvie and Nicholson modified by Toraya	Indicated *m*-phase content that vanishes after regeneration thermal treatment (healing), authors did not report this data.	

			could be considered as a fine grinding in dental community and that the typical machining would be more deleterious and executed with higher grit sizes.	45µm			GIXRD - step interval 27-32°, 0.02°/step, 1.5 s per step, in five different incidence angles (α=1,2,5,10 and 15°)		0%	Ranged between 3-20% based on the applied load, grit-size particle and angle of incidence during GIXRD.
				70µm			Raman - helium:neon excitation laser with wavelength of 632.8mm		Did not detected any sign of *m*-phase	
Amaral et al., 2013	Brazil	Lava Frame (3M Espe)	Reference Kim et al., 2010 - Grinding in a polishing machine with diamond disc for 1 min under water cooling.	150µm	Water	Phase transformation (XRD), Roughness and Biaxial flexure test (piston on three-balls)	CuKα, step interval 20-65°, 0.03° and 0.5s per step.	Garvie and Nicholson modified by Toraya	1.37%	1.35%
Iseri et al., 2012	Turkey	Zirkonzahn	The disks from grinding group were produced with a smaller disc in the center region (1mm height and 3 mm diameter), thus grinding was executed in a proper	First – 220µm	Without – Dry	Temperature during grinding and Biaxial flexural strength (piston on three-balls).	Did not execute phase analysis			

			device standardizing this procedure with a high-speed handpiece or micromotor (low-speed) continually or periodically, under 1N pressure until the inner disc was removed.	Final - 150µm						
Iseri et al., 2010	Turkey	Zirkonzahn	Same protocol of Iseri et al., 2012. The difference was that here the authors used a 3-point flexural test in bars.	First – 220µm Final - 150µm	Without – Dry	Only 3-point flexural strength.	Did not execute phase analysis			
Kim et al., 2010	USA	IPS e.max ZirCAD (Ivoclar Vivadent)	Specimens were ground in a polishing machine with diamond discs of 3 grit-sizes, specifically chosen to simulate dental diamond burs (same grit-size)	30µm 162µm 200µm	With	Surface examined by SEM, Phase transformation analysis (XRD)	CuKα, step interval 27-33°, 0.02°/step, 1° per min;	Garvie and Nicholson	≈0%	≈5%
Ho et al., 2009	Taiwan	Y-TZP powder from Tosoh	Specimens were abrasive grounded, until the depth of cut of 200µm) in a surface grinder with resin bonded diamond wheel under constant cooling. The table speed was 0.26m/s, and the wheel speed 36.7m/s.	44µm	Water based oil emulsion grinding fluid	Surface examined by SEM, Phase transformation analysis, Residual stress quantification, Biaxial flexure strength test (ball on three balls)	XRD with incidence angle 15°, 0.03°/step, 2° per min	Relationship proposed by Evans et al., 1984	1%	3%
							XRD sin$^2\Psi$ technique, 144-146°, incidence angle of 5°.		For residual stress	
Karakoca & Yilmaz, 2009	Turkey	Cercon (Dentsply)	Specimens were ground by using a diamond bur under 20.000rpm without cooling. The burs were replaced after every 5 specimens.	100µm	Without – Dry	Roughness, Phase transformation analysis (XRD), Biaxial flexure strength (piston on three ball)	CuKα, 40kV,40mA, step interval 20-34°, 0.01°/step	Garvie and Nicholson	0%	5.16% (±0.38)
		Zirkonzahn							1.75% (±0.38)	4.98% (±0.81)

Kosmac et al., 2008	Slovenia	Y-TZP powder from Tosoh	A coarse-grit diamond burr mounted on a high-speed hand piece was chosen for the dry surface grinding, in order to simulate clinical conditions. Load applied of 100g (finger pressure) and the grinding speed was 150.000 rpm	150µm	Without - Dry	Phase transformation analysis, Biaxial flexure strength before and after aging (fatigue - 10^6 cycles + different storages)	CuKα radiation, was the only available information	Garvie and Nicholson	<1%	4%
Kosmac et al., 2007	Slovenia	4 types of Y-TZP powder from Tosoh	It was used the same protocol described on Kosmac et al., 2008 for both grit-sizes.	50µm	Without – Dry	Surface examination by SEM, Grain size and Indentation toughness measurements, Biaxial flexure test (fatigue - 10^6 cycles + different storages) and mechanical properties of biscuit and root post ceramic specimens	Same of Kosmac et al., 2008		0%	<5%
				150µm						
Kou et al., 2006	Sweden	Denzir	Grinding was executed for 30s (each step) using a Kavo hand piece (26.000 rpm) with diamond rotary cutting instruments. First a medium grit-size, then a fine and after an extra-fine.	107-126µm	Water	Only evaluated roughness (Ra) and surface examination by SEM. Each specimen had its roughness evaluated in the as-sintered, ground (final) and polishing conditions. The data was not exposed in the manuscript, only the statistical differences and images from superficial defects. Thus this study was excluded from meta-analyses but kept on the review for discussion.				
				76µm						
				46µm						

Curtis et al., 2006	Ireland	Lava Frame (3M Espe)	Grinding with a super-torque 630B hand-piece (Kavo) up to 300.000rpm to ensure a consistent grinding speed. It was used a fine grit-size to evaluate a gentle grinding regime and a coarse to promote a more severe one, with and without cooling. Regarding pressure, authors stated that it was used a gentle stroke motion ensuring minimal pressure. The burs were replaced every 5 specimens.	20-40µm	Without – Dry	Biaxial flexure strength test (knife edge support and ball indenter), Surface examination by SEM, Phase transformation analysis (XRD), Roughness and Vickers hardness.	Step interval 26-65°, 0.02°/step, 1.8s/step	Rietveld refinement (TOPAS computer software)	Noticed the presence of tetragonal and cubic phases. Did not noticed *m*-phase.
				125-150µm	Water				
Denry & Holloway, 2006	USA	Cercon Base (Dentsply)	Ground manually under water for 1 min on a diamond disk.	30-40µm	Water	Density (Archimedes' method), Phase transformation (XRD), Surface examination by SEM, Vickers Indentatios, Biaxial flexural strength test (ball-on-ring).	CuKα, step interval 28-65°, 1°/min. Additional XRD scans (28-32°, 0.25°/min) were performed for determine peak position.	Did not quantify. The authors observed as main crystalline phase the tetragonal phase. Grinding promoted the appearance of a rhombohedral phase that was also noted after polishing. The position of the (011) XRD peak was significantly different between as-sintered and ground (polished or not). After annealing (thermal heat treatment) the position was similar to as-sintered. These changes are associated with residual lattice strain introduced by grinding and polishing.	
Kosmac et al., 2004	Slovenia	3 types of Y-TZP powders from Tosoh	Same protocol described on Kosmac et al., 2008 (pressure 100g, 150.000rpm, high-speed)	50µm	Without – Dry	Biaxial flexural strength, Phase transformation	Did not specify	Only phase after storage on as-sintered conditions.	
				150µm					

Kosmac et al., 2000	Slovenia	3 types of Y-TZP powders from Tosoh	Same protocol described on Kosmac et al., 2008 (pressure 100g, 150.000rpm, high-speed) the difference is that the authors evaluated also a condition with coolant.	50µm	Without – Dry	Surface examination by SEM, Phase transformation analysis (XRD), Grain size measurement and Biaxial flexure strength.	CuKα radiation, was the only available information	Garvie and Nicholson	Data missing	≈4% all ground conditions
				150µm	Water					
Kosmac et al., 1999	Slovenia	2 types of Y-TZP powder from Tosoh	Same protocol described on Kosmac et al., 2008 (pressure 100g, 150.000rpm, high-speed) the difference is that the authors evaluated also a condition with coolant.	150µm	Without – Dry	Density (Archimedes' method), Surface examination by SEM, Fracture toughness	CuKα radiation, was the only available information	Garvie and Nicholson	0%	≈4% all ground conditions
					Water					
Sato et al., 1996	Japan	3 types of Y-TZP powders from Tosoh	Grinding with diamond wheels (200,400 and 800-grit) was employed. First, with 200-grit until 10µm removal; and then with each other wheels until 20µm was removed.	-	Water	Optical micrograph examination, Phase transformation analysis (XRD), Residual stress, Influence of aging and Indentation toughness	CuKα, 40kV,30mA , speed of 1°/min	Garvie and Nicholson	It is not clear the values, but authors stated that grinding promoted transformation on different depths (more coarse lead to transformation in deeper layers).	
Kim et al., 1995	Korea	Y-TZP powder from Tosoh	Hand-abrasion of the specimens for 3 to 30 times on a 180grit SiC paper.	-	-	Phase transformation (XRD)	CuKα radiation, was the only available information	Not clear	0%	≈4% only on the severe condition
Reed & Lejus, 1977	USA/ France	2 types of Y-TZP powders	Specimen was diamond surface ground, wet, using a milling machine.	-	Not clear	Phase transformation (XRD), Vickers hardness		Garvie and Nicholson	0%	≈2%

Table 2. Risk of Bias of the studies included on systematic review considering the aspects reported in the Materials & Methods section.

Author/Year	Random	Sintering	Manufacturing	International Organization for Standardization	Grinding Protocol	Sample Size	Operator	Total	Risk of Bias
Roa et al., 2016	2	1	0	-	1	2	-	6	Medium
Pereira et al., 2016[a]	2	0	0	0	0	2	2	6	Medium
Pereira et al., 2016[b]	0	0	0	0	0	2	2	4	Low
Ramos et al., 2016	2	1	1	0	0	2	2	8	Medium
Michida et al., 2015	0	1	0	2	1	2	2	8	Medium
Gungor et al., 2015	2	0	0	0	1	2	2	7	Medium
Preis et al., 2015[a]	0	0	1	0	0	2	2	5	Medium
Pereira et al., 2015[a]	2	1	1	0	0	2	2	8	Medium
Preis et al., 2015[b]	2	1	0	-	0	2	-	5	Medium
Subasi et al., 2014	2	2	1	0	0	2	2	9	Medium
Pereira et al., 2014	2	1	1	0	0	2	2	8	Medium
Jing et al., 2014	2	1	1	-	1	2	-	7	High
Strasberg et al., 2014	2	0	0	-	0	2	-	4	Medium
Amaral et al., 2013	2	1	1	0	0	2	2	8	Medium
Iseri et al., 2012	2	2	1	0	0	0	2	7	Medium
Iseri et al., 2010	0	0	1	0	0	2	2	5	Medium
Kim et al., 2010	0	0	1	-	1	2	-	4	Medium
Ho et al., 2009	2	1	0	2	0	2	2	9	Medium
Karakoca & Yilmaz, 2009	0	0	0	0	0	2	2	4	Low
Kosmac et al., 2008	0	1	0	1	1	2	2	7	Medium
Kosmac et al., 2007	0	1	0	1	1	2	2	7	Medium
Kou et al., 2006	0	0	0	-	0	2	-	2	Low
Curtis et al., 2006	0	0	0	2	0	2	2	6	Medium
Denry & Holloway, 2006	0	0	0	2	1	2	2	7	Medium
Kosmac et al., 2004	2	1	0	1	1	2	2	9	Medium
Kosmac et al., 2000	2	1	0	1	1	2	2	9	Medium
Kosmac et al., 1999	0	1	0	2	1	2	2	8	Medium
Sato et al., 1996	2	1	1	-	0	2	-	6	Medium
Kim et al., 1995	2	1	1	-	1	2	-	7	High
Reed & Lejus, 1977	2	1	1	-	2	2	-	8	High

Table 3 - Descriptive analysis of Y-TZP grain size after sintering, considering only the studies that measured this outcome.

Study	Material	Stabilizer content (Yttrium %)	Sintering conditions	Grain Size
Roa et al., 2016	Tz 3YSBE from Tosoh	3% + 0.25% Al_2O_3	1450°C for 2 hours (first uniaxially pressed at 100 MPa)	0.34 ± 0.02 µm
Strasberg et al., 2014	IPS e.max ZirCAD from Ivoclar Vivadent	4-6% + 0-1%Al_2O_3	1500°C	<1µm
Jing et al., 2014	3Y-TZP (did not specify which kind) from Tosoh	3%	1550°C (first uniaxially pressed at 30MPa followed by CIP-ing at 200 MPa)	0.3 – 1µm
Kim et al., 2010	IPS e.max ZirCAD from Ivoclar Vivadent	4-6% + 0-1%Al_2O_3	1500°C	0.5µm
Ho et al., 2009	Tz 3YB powder from Tosoh	3%	1550°C for 1 hour (first uniaxially pressed at 13 MPa)	0.72µm
Kosmac et al., 2008	Tz 3YBE powder from Tosoh	3% + 0.25% Al_2O_3	1520°C for 2 hours (first uniaxially pressed at 147 MPa)	0.51µm
Kosmac et al., 2007	Tz 3YB powder from Tosoh	3%	1500°C for 2 hours	0.31µm
	Tz 3YSB powder from Tosoh		1550°C for 4 hours	0.44µm
	Tz 3YBE powder from Tosoh	3% + 0.25% Al_2O_3	1450°C for 4 hours	0.51µm
	Tz 3YSBE from Tosoh		1530°C for 4 hours	0.59µm
Kosmac et al., 2004	Tz 3YB powder from Tosoh	3%	1500°C for 2 hours	0.31µm
	Tz 3YSB powder from Tosoh		1550°C for 4 hours	0.44µm
	Tz 3YBE powder from Tosoh	3% + 0.25% Al_2O_3	1450°C for 4 hours	0.51µm
	Tz 3YSBE from Tosoh		1530°C for 4 hours	0.59µm
Kosmac et al., 2000	Tz 3YSBE from Tosoh	3% + 0.25% Al_2O_3	1550°C for 4 hours	0.57µm
Kosmac et al., 1999	Tz 3YB powder from Tosoh	3%	1500°C for 2 hours	0.31µm
	Tz 3YSB powder from Tosoh		1550°C for 4 hours	0.44µm
Sato et al., 1996	2Y-TZP (did not specify which kind) from Tosoh	2%	1500°C for 2 hours (first uniaxially pressed at 30MPa then isostatically pressed at 200MPa - HIPped)	0.3µm
	3Y-TZP (did not specify which kind) from Tosoh	3%		
	4Y-TZP (did not specify which kind) from Tosoh	4%		
Reed & Lejus, 1977	4.5 Y-TZP (did not specify which kind and brand)	4.5%	Do not specify	≈1µm
	7 Y-TZP (did not specify which kind and brand)	7%		

Table 4 - Descriptive data from Vickers hardness, considering only the studies that measured this outcome.

Study	**Material**	**Description**	**Grinding protocol**	**Vickers Hardness (Mean ± SD)**	
				Before grinding	**After grinding**
Curtis et al., 2006	Lava Frame	Specimens randomly selected and submitted to a Vickers hardness test with a diamond pyramid head of a Duramin-1 Vickers hardness tester (Struers) under a predetermined load (9.807N) over 15s to induce a diamond-shaped indent. The size of each diagonal distance was measured and the Vickers hardness was calculated according to the surface area of the indent.	Grinding without coolant with fine diamond bur	1590 ± 91	1729 ± 249
			Grinding without coolant with coarse diamond bur		1674 ± 301
			Grinding with coolant with fine diamond bur		1662 ± 234
			Grinding with coolant with coarse diamond bur		1640 ± 403
Denry & Holloway et al., 2006	Cercon base	Specimens were indented under a 98.1N load with a Vickers hardness tester. Optical digital micrographs were taken immediately after indentation in Nomarski interference contrast.	Ground manually under water for 1 min on a 600-grit diamond disk.	There were observed cracks on polished specimens and ground and polished specimens. The specimens that were only ground did not present any crack. Indicating that this load was not enough to promote crack on ground surface. Authors state that this behavior is in indicative of compressive stress introduced by this procedure.	
Reed & Lejus, 1977	2 Y-TZP with 4,5 and 7 mol% stabilized (did not specify brand)	Vickers hardness of ground and polished material was determined at room temperature for a series of load (100-500 gms) using a Leitz Durimet and at high temperature for a load of 500 gms using a Nikon HT-5 microhardness tester.	Diamond surface ground wet using a milling machine.	Data presented in figures. Authors states that the hardness of ground materials were significantly greater, and that can be concluded that phase transformation produces a harder material.	

Table 5 - Descriptive analysis of the studies that evaluated residual stress concentration after grinding Y-TZP ceramic.

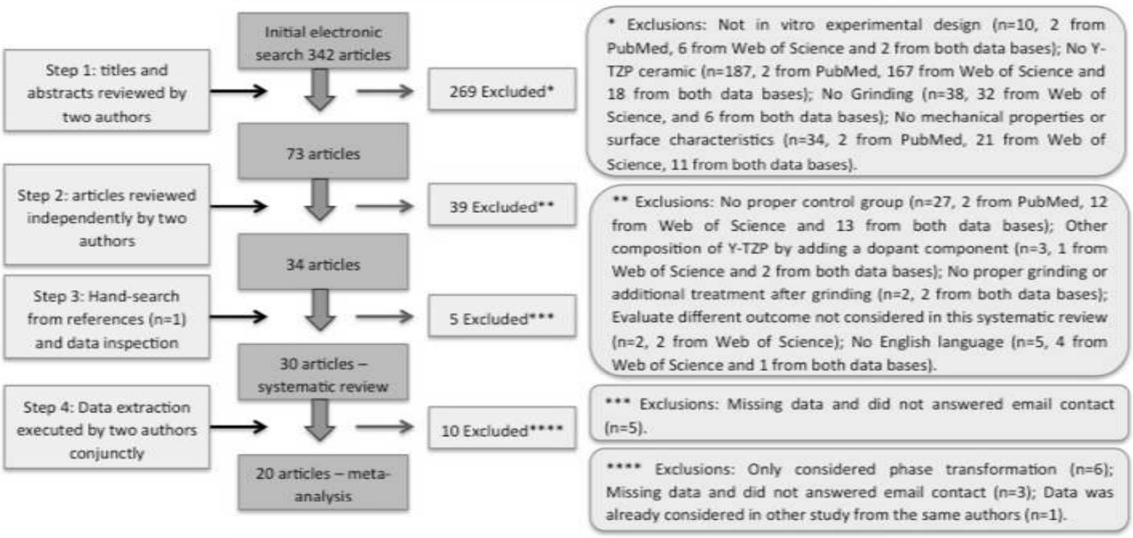
Study	**Material**	**Grinding Protocol**	**Description**	**Stress Residual**	
				Before grinding	**After grinding**
Jing et al., 2014	Authors discuss residual stress and defects introduction taking into consideration the characterizations of surface and phase that they have executed (although they did not quantify this outcome). They state, based on their data and existing literature, that becomes clear that grinding (clinical adjustment) induces residual stress, generally in a layer with 0.12μm thick, although authors state that usually this layer is to shallow to withstand polishing and annealing treatments. Being so, the grinding protocol employed present a main role in this outcome. Finally they conclude that grinding should be minimized as much as possible and the precision on manufacturing 3Y-TZP restorations need to be optimized.				
Ho et al., 2009	Tz-3Y powder from Tosoh	Abrasive grinding was performed using a surface grinder with a resin bonded 325-grit diamond wheel with a water-based oil emulsion fluid as a coolant. The parameters were table speed 0.26m/s and wheel surface speed of 36.7m/s.	The residual stress was measured by using a X-ray $\sin^2 \Psi$ technique (D5000, Siemens Co., Germany). The diffraction angle 2θ/min varied from 144° to 146°, with a incidence angle of 5°.	-32 *	-1075
Sato et al., 1996	Y-TZP powders from Tosoh	Abrasive grinding in a grinding machine with diamond disc with a table speed of $39.3x10^{-2}$ m/s. Authors noted a inversion between the relation of intensities from the peak T(200) and T(002) from as-sintered samples in comparison to ground samples. At discussion they correlate this data with existing literature that states that this inversion is triggered by the existence of residual stress introduced by grinding causing a reorientation of the crystallites. According to the authors, the introduction of this residual stress was the responsible for turning the ceramic surface of ground specimens less susceptible to the effects (new t-m phase transformation) of storage in hot oil. After annealing this residual stress decreases partially or totally, depending on the protocol.		-8.8	-711 along grinding direction/ -1054 perpendicular to grinding direction

* Note: "-" denote compressive stress.

Table 6 - Description of the main findings from studies that executed aging of ground Y-TZP ceramic.

Study	Material	Aging methodology	Description
Pereira et al., 2016[a]	Zirlux FC from Ivoclar Vivadent	Autoclave at 134°C, 2 bar pressure for 20h	Authors observed phase transformation after grinding (≈9% for both grit size, as-sintered presented 0%) but after aging it was observed less susceptibility to phase transformation, as ground groups presented 38-43% of m-phase and as-sintered condition 68%.
Pereira et al., 2016[b]	Lava Frame from 3M ESPE Zirlux FC from Ivoclar Vivadent	Autoclave at 134°C, 2 bar pressure for 20h in association with fatigue testing (staircase approach 20.000 cycles 6hz)	Authors observed phase transformation after grinding (9 - 11% depending on the Y-TZP brand, as-sintered presented 0%) but after aging it was observed less susceptibility to phase transformation, as ground groups presented 36-43% of m-phase and as-sintered condition 57-67%. Aged groups presented higher fatigue limit and survival probability than as-sintered condition.
Pereira et al., 2015[a]	Lava Frame from 3M ESPE	Autoclave at 134°C, 2 bar pressure for 20h	Authors observed phase transformation after grinding (9-12% depending on grit size, as-sintered presented 0%) but after aging it was observed less susceptibility to phase transformation as ground groups presented 15-29% of *m*-phase and as-sintered condition 53%.
Amaral et al., 2013	Lava Frame from 3M ESPE	Autoclave at 127°C, 1.5 bar pressure for 12h	Authors did not observe phase transformation induced by grinding procedure (≈0% for as-sintered and ground conditions) but ground specimens presented less *m*-phase content after aging (15% for ground an 26.4% for as-sintered).
Kim et al., 2010	IPS e.max ZirCAD from Ivoclar Vivadent	Steam autoclave at 122°C, 2 bar pressure for predetermined durations.	Grinding introduce different kinds of superficial defects and induced phase transformation (≈0% on as-sintered to ≈5% for ground), although decreased the susceptibility to new phase transformations after aging for 20h (≈55% on as-sintered to ≈30% for ground).
Kosmac et al., 2008	Tz-3YSB-E from Tosoh	Fatigue test (10^6 cycles 50 to 850N 15hz) in artificial saliva after 2 or 24h aging in autoclave at 134°C. Specimens who survived submitted to biaxial flexure strength test.	The survival rate from the control groups submitted to aging 2h was 60% and 24h was 50%, while the groups submitted to dry grinding (with 150μm grit size) presented 10% after 2h autoclave and 0% after 24h in autoclave. Thus, authors stated that these results imply that stress-assisted corrosion plays an important role in fatigue behavior after aging.
Kosmac et al., 2007	Tz-3YSB-E from Tosoh	Fatigue test (10^6 cycles 50 to 850N 15hz) in air or artificial saliva and specimens who survived submitted to biaxial flexure strength test.	The survival rate from the control groups submitted to fatigue in air (64%) and artificial saliva (50%) was higher then the observed after dry grinding (with 150μm grit size) in air (20%) and in artificial saliva (10%). The strength of the surviving samples tested in air presented a mean flexural strength similar to the particular group before fatigue, while the samples in artificial saliva presented a reduction of 10-15%.
Sato et al., 1996	3 kinds of Y-TZP from Tosoh (2,3 and 4 mol% of stabilizer)	Immersion in white spindle and chlorinated paraffin oils at 473K (200°C) for different setting times.	Grinding promoted phase transformation and decreased the sensitive of this surface to new transformations under interaction with lubricants in increased temperatures. This decreased sensitivity was still observed after annealing of the ground surface. Data exposed in graphics and figures.

Figures



* Exclusions: Not in vitro experimental design (n=10, 2 from PubMed, 6 from Web of Science and 2 from both data bases); No Y-TZP ceramic (n=187, 2 from PubMed, 167 from Web of Science and 18 from both data bases); No Grinding (n=38, 32 from Web of Science, and 6 from both data bases); No mechanical properties or surface characteristics (n=34, 2 from PubMed, 21 from Web of Science, 11 from both data bases).

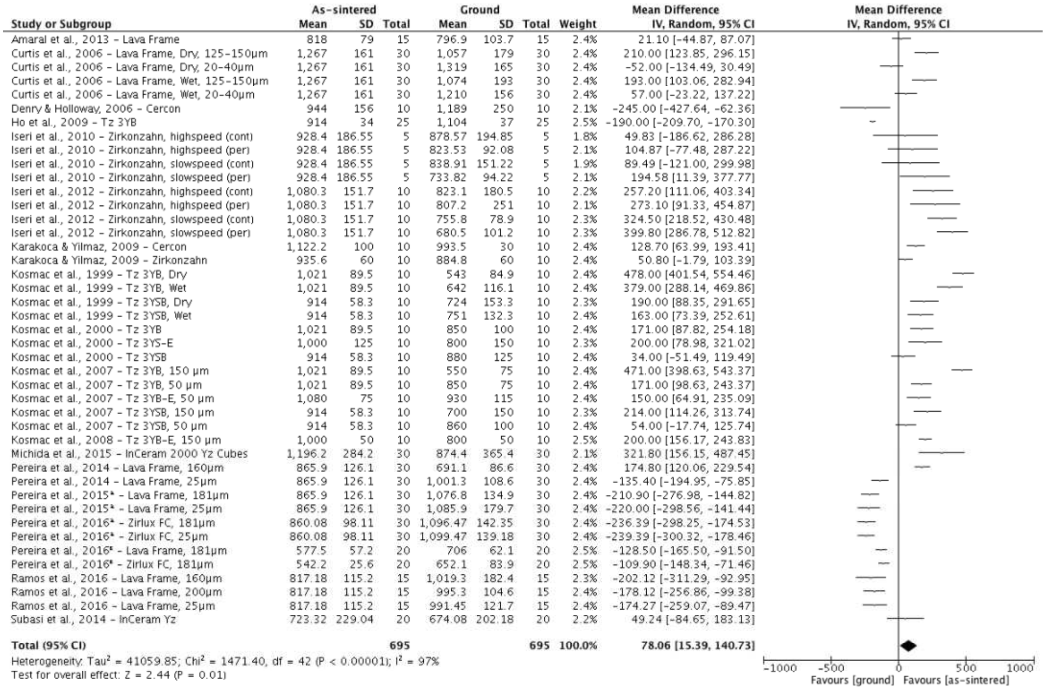
** Exclusions: No proper control group (n=27, 2 from PubMed, 12 from Web of Science and 13 from both data bases); Other composition of Y-TZP by adding a dopant component (n=3, 1 from Web of Science and 2 from both data bases); No proper grinding or additional treatment after grinding (n=2, 2 from both data bases); Evaluate different outcome not considered in this systematic review (n=2, 2 from Web of Science); No English language (n=5, 4 from Web of Science and 1 from both data bases).

*** Exclusions: Missing data and did not answered email contact (n=5).

**** Exclusions: Only considered phase transformation (n=6); Missing data and did not answered email contact (n=3); Data was already considered in other study from the same authors (n=1).

Figure 1. Flow diagram of study selection according to PRISMA statement

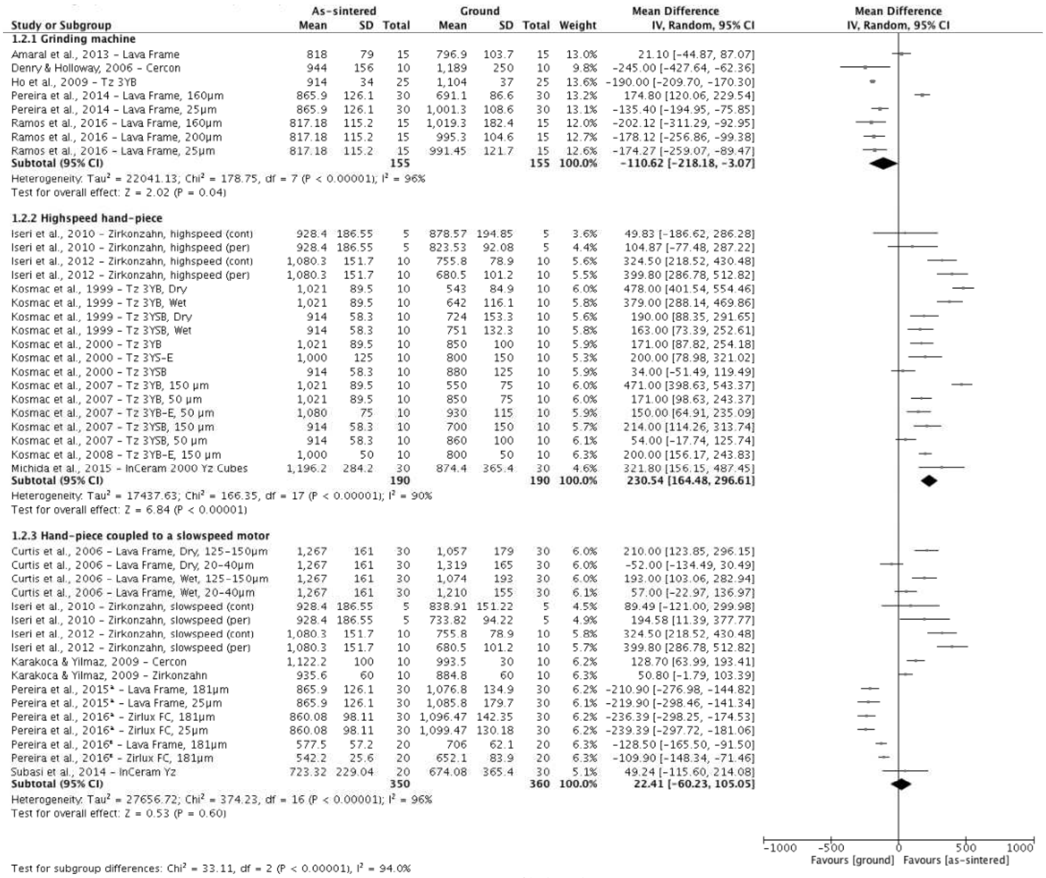
Figure 2. Flexural strength meta-analyses (A- Global; B- Grinding tool subgroup; C- Grit-size subgroups; D- Presence/absence of cooling subgroups).



	As-sintered			Ground				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Amaral et al., 2013 - Lava Frame	818	79	15	796.9	103.7	15	2.4%	21.10 [-44.87, 87.07]
Curtis et al., 2006 - Lava Frame, Dry, 125-150μm	1,267	161	30	1,057	179	30	2.4%	210.00 [123.85, 296.15]
Curtis et al., 2006 - Lava Frame, Dry, 20-40μm	1,267	161	30	1,319	165	30	2.4%	-52.00 [-134.49, 30.49]
Curtis et al., 2006 - Lava Frame, Wet, 125-150μm	1,267	161	30	1,074	193	30	2.4%	193.00 [103.06, 282.94]
Curtis et al., 2006 - Lava Frame, Wet, 20-40μm	1,267	161	30	1,210	156	30	2.4%	57.00 [-23.22, 137.22]
Denry & Holloway, 2006 - Cercon	944	156	10	1,189	250	10	2.1%	-245.00 [-427.64, -62.36]
Ho et al., 2009 - Tz 3YB	914	34	25	1,104	37	25	2.5%	-190.00 [-209.70, -170.30]
Iseri et al., 2010 - Zirkonzahn, highspeed (cont)	928.4	186.55	5	878.57	194.85	5	1.8%	49.83 [-186.62, 286.28]
Iseri et al., 2010 - Zirkonzahn, highspeed (per)	928.4	186.55	5	823.53	92.08	5	2.1%	104.87 [-77.48, 287.22]
Iseri et al., 2010 - Zirkonzahn, slowspeed (cont)	928.4	186.55	5	838.91	151.22	5	1.9%	89.49 [-121.00, 299.98]
Iseri et al., 2010 - Zirkonzahn, slowspeed (per)	928.4	186.55	5	733.82	94.22	5	2.1%	194.58 [11.39, 377.77]
Iseri et al., 2012 - Zirkonzahn, highspeed (cont)	1,080.3	151.7	10	823.1	180.5	10	2.2%	257.20 [111.06, 403.34]
Iseri et al., 2012 - Zirkonzahn, highspeed (per)	1,080.3	151.7	10	807.2	251	10	2.1%	273.10 [91.33, 454.87]
Iseri et al., 2012 - Zirkonzahn, slowspeed (cont)	1,080.3	151.7	10	755.8	78.9	10	2.3%	324.50 [218.52, 430.48]
Iseri et al., 2012 - Zirkonzahn, slowspeed (per)	1,080.3	151.7	10	680.5	101.2	10	2.3%	399.80 [286.78, 512.82]
Karakoca & Yilmaz, 2009 - Cercon	1,122.2	100	10	993.5	30	10	2.4%	128.70 [63.99, 193.41]
Karakoca & Yilmaz, 2009 - Zirkonzahn	935.6	60	10	884.8	60	10	2.4%	50.80 [-1.79, 103.39]
Kosmac et al., 1999 - Tz 3YB, Dry	1,021	89.5	10	543	84.9	10	2.4%	478.00 [401.54, 554.46]
Kosmac et al., 1999 - Tz 3YB, Wet	1,021	89.5	10	642	116.1	10	2.4%	379.00 [288.14, 469.86]
Kosmac et al., 1999 - Tz 3YSB, Dry	914	58.3	10	724	153.3	10	2.3%	190.00 [88.35, 291.65]
Kosmac et al., 1999 - Tz 3YSB, Wet	914	58.3	10	751	132.3	10	2.4%	163.00 [73.39, 252.61]
Kosmac et al., 2000 - Tz 3YB	1,021	89.5	10	850	100	10	2.4%	171.00 [87.82, 254.18]
Kosmac et al., 2000 - Tz 3YS-E	1,000	125	10	800	150	10	2.3%	200.00 [78.98, 321.02]
Kosmac et al., 2000 - Tz 3YSB	914	58.3	10	880	125	10	2.4%	34.00 [-51.49, 119.49]
Kosmac et al., 2007 - Tz 3YB, 150 μm	1,021	89.5	10	550	75	10	2.4%	471.00 [398.63, 543.37]
Kosmac et al., 2007 - Tz 3YB, 50 μm	1,021	89.5	10	850	75	10	2.4%	171.00 [98.63, 243.37]
Kosmac et al., 2007 - Tz 3YB-E, 50 μm	1,080	75	10	930	115	10	2.4%	150.00 [64.91, 235.09]
Kosmac et al., 2007 - Tz 3YSB, 150 μm	914	58.3	10	700	150	10	2.3%	214.00 [114.26, 313.74]
Kosmac et al., 2007 - Tz 3YSB, 50 μm	914	58.3	10	860	100	10	2.4%	54.00 [-17.74, 125.74]
Kosmac et al., 2008 - Tz 3YB-E, 150 μm	1,000	50	10	800	50	10	2.5%	200.00 [156.17, 243.83]
Michida et al., 2015 - InCeram 2000 Yz Cubes	1,196.2	284.2	30	874.4	365.4	30	2.1%	321.80 [156.15, 487.45]
Pereira et al., 2014 - Lava Frame, 160μm	865.9	126.1	30	691.1	86.6	30	2.4%	174.80 [120.06, 229.54]
Pereira et al., 2014 - Lava Frame, 25μm	865.9	126.1	30	1,001.3	108.6	30	2.4%	-135.40 [-194.95, -75.85]
Pereira et al., 2015^{a} - Lava Frame, 181μm	865.9	126.1	30	1,076.8	134.9	30	2.4%	-210.90 [-276.98, -144.82]
Pereira et al., 2015^{a} - Lava Frame, 25μm	865.9	126.1	30	1,085.9	179.7	30	2.4%	-220.00 [-298.56, -141.44]
Pereira et al., 2016^{a} - Zirlux FC, 181μm	860.08	98.11	30	1,096.47	142.35	30	2.4%	-236.39 [-298.25, -174.53]
Pereira et al., 2016^{a} - Zirlux FC, 25μm	860.08	98.11	30	1,099.47	139.18	30	2.4%	-239.39 [-300.32, -178.46]
Pereira et al., 2016^{b} - Lava Frame, 181μm	577.5	57.2	20	706	62.1	20	2.5%	-128.50 [-165.50, -91.50]
Pereira et al., 2016^{b} - Zirlux FC, 181μm	542.2	25.6	20	652.1	83.9	20	2.5%	-109.90 [-148.34, -71.46]
Ramos et al., 2016 - Lava Frame, 160μm	817.18	115.2	15	1,019.3	182.4	15	2.3%	-202.12 [-311.29, -92.95]
Ramos et al., 2016 - Lava Frame, 200μm	817.18	115.2	15	995.3	104.6	15	2.4%	-178.12 [-256.86, -99.38]
Ramos et al., 2016 - Lava Frame, 25μm	817.18	115.2	15	991.45	121.7	15	2.4%	-174.27 [-259.07, -89.47]
Subasi et al., 2014 - InCeram Yz	723.32	229.04	20	674.08	202.18	20	2.2%	49.24 [-84.65, 183.13]
Total (95% CI)			**695**			**695**	**100.0%**	**78.06 [15.39, 140.73]**

Heterogeneity: $Tau^2 = 41059.85$; $Chi^2 = 1471.40$, $df = 42$ ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: $Z = 2.44$ ($P = 0.01$)

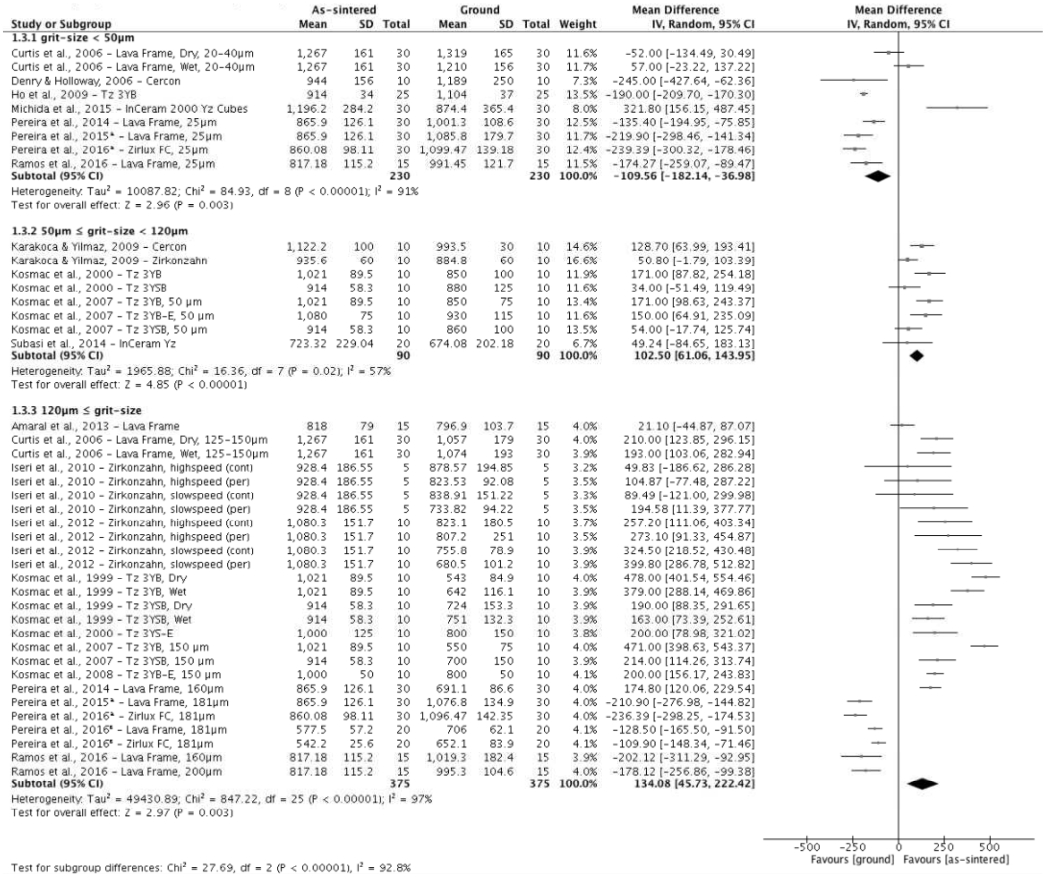
A- Global



	As-sintered			Ground				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
1.2.1 Grinding machine								
Amaral et al., 2013 - Lava Frame	818	79	15	796.9	103.7	15	13.0%	21.10 [-44.87, 87.07]
Denry & Holloway, 2006 - Cercon	944	156	10	1,189	250	10	9.8%	-245.00 [-427.64, -62.36]
Ho et al., 2009 - Tz 3YB	914	34	25	1,104	37	25	13.6%	-190.00 [-209.70, -170.30]
Pereira et al., 2014 - Lava Frame, 160μm	865.9	126.1	30	691.1	86.6	30	13.2%	174.80 [120.06, 229.54]
Pereira et al., 2014 - Lava Frame, 25μm	865.9	126.1	30	1,001.3	108.6	30	13.1%	-135.40 [-194.95, -75.85]
Ramos et al., 2016 - Lava Frame, 160μm	817.18	115.2	15	1,019.3	182.4	15	12.0%	-202.12 [-311.29, -92.95]
Ramos et al., 2016 - Lava Frame, 200μm	817.18	115.2	15	995.3	104.6	15	12.7%	-178.12 [-256.86, -99.38]
Ramos et al., 2016 - Lava Frame, 25μm	817.18	115.2	15	991.45	121.7	15	12.6%	-174.27 [-259.07, -89.47]
Subtotal (95% CI)			**155**			**155**	**100.0%**	**-110.62 [-218.18, -3.07]**
Heterogeneity: $Tau^2 = 22041.13$; $Chi^2 = 178.75$, $df = 7$ ($P < 0.00001$); $I^2 = 96\%$								
Test for overall effect: $Z = 2.02$ ($P = 0.04$)								
1.2.2 Highspeed hand-piece								
Iseri et al., 2010 - Zirkonzahn, highspeed (cont)	928.4	186.55	5	878.57	194.85	5	3.6%	49.83 [-186.62, 286.28]
Iseri et al., 2010 - Zirkonzahn, highspeed (per)	928.4	186.55	5	823.53	92.08	5	4.4%	104.87 [-77.48, 287.22]
Iseri et al., 2012 - Zirkonzahn, highspeed (cont)	1,080.3	151.7	10	755.8	78.9	10	5.6%	324.50 [218.52, 430.48]
Iseri et al., 2012 - Zirkonzahn, highspeed (per)	1,080.3	151.7	10	680.5	101.2	10	5.5%	399.80 [286.78, 512.82]
Kosmac et al., 1999 - Tz 3YB, Dry	1,021	89.5	10	543	84.9	10	6.0%	478.00 [401.54, 554.46]
Kosmac et al., 1999 - Tz 3YB, Wet	1,021	89.5	10	642	116.1	10	5.8%	379.00 [288.14, 469.86]
Kosmac et al., 1999 - Tz 3YSB, Dry	914	58.3	10	724	153.3	10	5.6%	190.00 [88.35, 291.65]
Kosmac et al., 1999 - Tz 3YSB, Wet	914	58.3	10	751	132.3	10	5.8%	163.00 [73.39, 252.61]
Kosmac et al., 2000 - Tz 3YB	1,021	89.5	10	850	100	10	5.9%	171.00 [87.82, 254.18]
Kosmac et al., 2000 - Tz 3YS-E	1,000	125	10	800	150	10	5.3%	200.00 [78.98, 321.02]
Kosmac et al., 2000 - Tz 3YSB	914	58.3	10	880	125	10	5.9%	34.00 [-51.49, 119.49]
Kosmac et al., 2007 - Tz 3YB, 150 μm	1,021	89.5	10	550	75	10	6.0%	471.00 [398.63, 543.37]
Kosmac et al., 2007 - Tz 3YB, 50 μm	1,021	89.5	10	850	75	10	6.0%	171.00 [98.63, 243.37]
Kosmac et al., 2007 - Tz 3YB-E, 50 μm	1,080	75	10	930	115	10	5.9%	150.00 [64.91, 235.09]
Kosmac et al., 2007 - Tz 3YSB, 150 μm	914	58.3	10	700	150	10	5.7%	214.00 [114.26, 313.74]
Kosmac et al., 2007 - Tz 3YSB, 50 μm	914	58.3	10	860	100	10	6.1%	54.00 [-17.74, 125.74]
Kosmac et al., 2008 - Tz 3YB-E, 150 μm	1,000	50	10	800	50	10	6.3%	200.00 [156.17, 243.83]
Michida et al., 2015 - InCeram 2000 Yz Cubes	1,196.2	284.2	30	874.4	365.4	30	4.6%	321.80 [156.15, 487.45]
Subtotal (95% CI)			**190**			**190**	**100.0%**	**230.54 [164.48, 296.61]**
Heterogeneity: $Tau^2 = 17437.63$; $Chi^2 = 166.35$, $df = 17$ ($P < 0.00001$); $I^2 = 90\%$								
Test for overall effect: $Z = 6.84$ ($P < 0.00001$)								
1.2.3 Hand-piece coupled to a slowspeed motor								
Curtis et al., 2006 - Lava Frame, Dry, 125-150μm	1,267	161	30	1,057	179	30	6.0%	210.00 [123.85, 296.15]
Curtis et al., 2006 - Lava Frame, Dry, 20-40μm	1,267	161	30	1,319	165	30	6.0%	-52.00 [-134.49, 30.49]
Curtis et al., 2006 - Lava Frame, Wet, 125-150μm	1,267	161	30	1,074	193	30	6.0%	193.00 [103.06, 282.94]
Curtis et al., 2006 - Lava Frame, Wet, 20-40μm	1,267	161	30	1,210	155	30	6.1%	57.00 [-22.97, 136.97]
Iseri et al., 2010 - Zirkonzahn, slowspeed (cont)	928.4	186.55	5	838.91	151.22	5	4.5%	89.49 [-121.00, 299.98]
Iseri et al., 2010 - Zirkonzahn, slowspeed (per)	928.4	186.55	5	733.82	94.22	5	4.9%	194.58 [11.39, 377.77]
Iseri et al., 2012 - Zirkonzahn, slowspeed (cont)	1,080.3	151.7	10	755.8	78.9	10	5.8%	324.50 [218.52, 430.48]
Iseri et al., 2012 - Zirkonzahn, slowspeed (per)	1,080.3	151.7	10	680.5	101.2	10	5.7%	399.80 [286.78, 512.82]
Karakoca & Yilmaz, 2009 - Cercon	1,122.2	100	10	993.5	30	10	6.2%	128.70 [63.99, 193.41]
Karakoca & Yilmaz, 2009 - Zirkonzahn	935.6	60	10	884.8	60	10	6.3%	50.80 [-1.79, 103.39]
Pereira et al., 2015^{a} - Lava Frame, 181μm	865.9	126.1	30	1,076.8	134.9	30	6.2%	-210.90 [-276.98, -144.82]
Pereira et al., 2015^{a} - Lava Frame, 25μm	865.9	126.1	30	1,085.8	179.7	30	6.1%	-219.90 [-298.46, -141.34]
Pereira et al., 2016^{a} - Zirlux FC, 181μm	860.08	98.11	30	1,096.47	142.35	30	6.2%	-236.39 [-298.25, -174.53]
Pereira et al., 2016^{a} - Zirlux FC, 25μm	860.08	98.11	30	1,099.47	130.18	30	6.2%	-239.39 [-297.72, -181.06]
Pereira et al., 2016^{b} - Lava Frame, 181μm	577.5	57.2	20	706	62.1	20	6.3%	-128.50 [-165.50, -91.50]
Pereira et al., 2016^{b} - Zirlux FC, 181μm	542.2	25.6	20	652.1	83.9	20	6.3%	-109.90 [-148.34, -71.46]
Subasi et al., 2014 - InCeram Yz	723.32	229.04	20	674.08	365.4	30	5.1%	49.24 [-115.60, 214.08]
Subtotal (95% CI)			**350**			**360**	**100.0%**	**22.41 [-60.23, 105.05]**
Heterogeneity: $Tau^2 = 27656.72$; $Chi^2 = 374.23$, $df = 16$ ($P < 0.00001$); $I^2 = 96\%$								
Test for overall effect: $Z = 0.53$ ($P = 0.60$)								

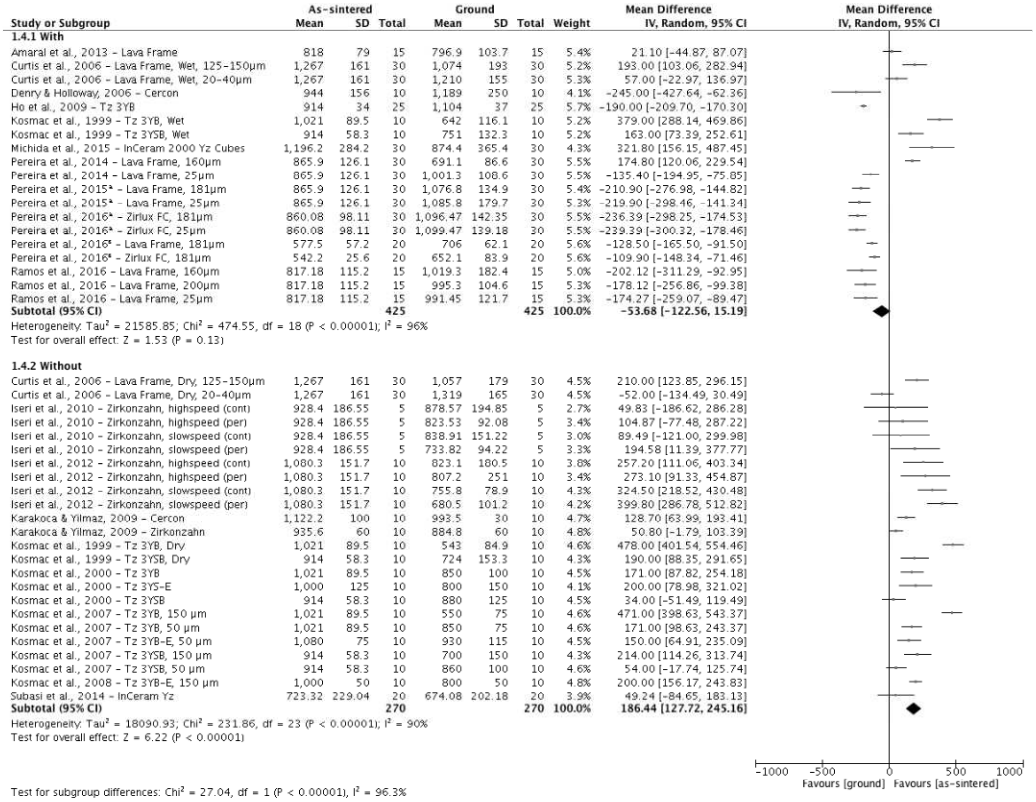
Test for subgroup differences: $Chi^2 = 33.11$, $df = 2$ ($P < 0.00001$), $I^2 = 94.0\%$

B- Grinding tool



Study or Subgroup	As-sintered Mean	As-sintered SD	As-sintered Total	Ground Mean	Ground SD	Ground Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 grit-size < 50µm								
Curtis et al., 2006 - Lava Frame, Dry, 20-40µm	1,267	161	30	1,319	165	30	11.6%	-52.00 [-134.49, 30.49]
Curtis et al., 2006 - Lava Frame, Wet, 20-40µm	1,267	161	30	1,210	156	30	11.7%	57.00 [-23.22, 137.22]
Denry & Holloway, 2006 - Cercon	944	156	10	1,189	250	10	7.3%	-245.00 [-427.64, -62.36]
Ho et al., 2009 - Tz 3YB	914	34	25	1,104	37	25	13.5%	-190.00 [-209.70, -170.30]
Michida et al., 2015 - InCeram 2000 Yz Cubes	1,196.2	284.2	30	874.4	365.4	30	8.0%	321.80 [156.15, 487.45]
Pereira et al., 2014 - Lava Frame, 25µm	865.9	126.1	30	1,001.3	108.6	30	12.5%	-135.40 [-194.95, -75.85]
Pereira et al., 2015^{a} - Lava Frame, 25µm	865.9	126.1	30	1,085.8	179.7	30	11.7%	-219.90 [-298.46, -141.34]
Pereira et al., 2016^{a} - Zirlux FC, 25µm	860.08	98.11	30	1,099.47	139.18	30	12.4%	-239.39 [-300.32, -178.46]
Ramos et al., 2016 - Lava Frame, 25µm	817.18	115.2	15	991.45	121.7	15	11.5%	-174.27 [-259.07, -89.47]
Subtotal (95% CI)			**230**			**230**	**100.0%**	**-109.56 [-182.14, -36.98]**
Heterogeneity: Tau^2 = 10087.82; Chi^2 = 84.93, df = 8 (P < 0.00001); I^2 = 91%								
Test for overall effect: Z = 2.96 (P = 0.003)								
1.3.2 50µm ≤ grit-size < 120µm								
Karakoca & Yilmaz, 2009 - Cercon	1,122.2	100	10	993.5	30	10	14.6%	128.70 [63.99, 193.41]
Karakoca & Yilmaz, 2009 - Zirkonzahn	935.6	60	10	884.8	60	10	16.6%	50.80 [-1.79, 103.39]
Kosmac et al., 2000 - Tz 3YB	1,021	89.5	10	850	100	10	11.9%	171.00 [87.82, 254.18]
Kosmac et al., 2000 - Tz 3YSB	914	58.3	10	880	125	10	11.6%	34.00 [-51.49, 119.49]
Kosmac et al., 2007 - Tz 3YB, 50 µm	1,021	89.5	10	850	75	10	13.4%	171.00 [98.63, 243.37]
Kosmac et al., 2007 - Tz 3YB-E, 50 µm	1,080	75	10	930	115	10	11.6%	150.00 [64.91, 235.09]
Kosmac et al., 2007 - Tz 3YSB, 50 µm	914	58.3	10	860	100	10	13.5%	54.00 [-17.74, 125.74]
Subasi et al., 2014 - InCeram Yz	723.32	229.04	20	674.08	202.18	20	6.7%	49.24 [-84.65, 183.13]
Subtotal (95% CI)			**90**			**90**	**100.0%**	**102.50 [61.06, 143.95]**
Heterogeneity: Tau^2 = 1965.88; Chi^2 = 16.36, df = 7 (P = 0.02); I^2 = 57%								
Test for overall effect: Z = 4.85 (P < 0.00001)								
1.3.3 120µm ≤ grit-size								
Amaral et al., 2013 - Lava Frame	818	79	15	796.9	103.7	15	4.0%	21.10 [-44.87, 87.07]
Curtis et al., 2006 - Lava Frame, Dry, 125-150µm	1,267	161	30	1,057	179	30	4.0%	210.00 [123.85, 296.15]
Curtis et al., 2006 - Lava Frame, Wet, 125-150µm	1,267	161	30	1,074	193	30	3.9%	193.00 [103.06, 282.94]
Iseri et al., 2010 - Zirkonzahn, highspeed (cont)	928.4	186.55	5	878.57	194.85	5	3.2%	49.83 [-186.62, 286.28]
Iseri et al., 2010 - Zirkonzahn, highspeed (per)	928.4	186.55	5	823.53	92.08	5	3.5%	104.87 [-77.48, 287.22]
Iseri et al., 2010 - Zirkonzahn, slowspeed (cont)	928.4	186.55	5	838.91	151.22	5	3.3%	89.49 [-121.00, 299.98]
Iseri et al., 2010 - Zirkonzahn, slowspeed (per)	928.4	186.55	5	733.82	94.22	5	3.5%	194.58 [11.39, 377.77]
Iseri et al., 2012 - Zirkonzahn, highspeed (cont)	1,080.3	151.7	10	823.1	180.5	10	3.7%	257.20 [111.06, 403.34]
Iseri et al., 2012 - Zirkonzahn, highspeed (per)	1,080.3	151.7	10	807.2	251	10	3.5%	273.10 [91.33, 454.87]
Iseri et al., 2012 - Zirkonzahn, slowspeed (cont)	1,080.3	151.7	10	755.8	78.9	10	3.9%	324.50 [218.52, 430.48]
Iseri et al., 2012 - Zirkonzahn, slowspeed (per)	1,080.3	151.7	10	680.5	101.2	10	3.9%	399.80 [286.78, 512.82]
Kosmac et al., 1999 - Tz 3YB, Dry	1,021	89.5	10	543	84.9	10	4.0%	478.00 [401.54, 554.46]
Kosmac et al., 1999 - Tz 3YB, Wet	1,021	89.5	10	642	116.1	10	3.9%	379.00 [288.14, 469.86]
Kosmac et al., 1999 - Tz 3YSB, Dry	914	58.3	10	724	153.3	10	3.9%	190.00 [88.35, 291.65]
Kosmac et al., 1999 - Tz 3YSB, Wet	914	58.3	10	751	132.3	10	3.9%	163.00 [73.39, 252.61]
Kosmac et al., 2000 - Tz 3YS-E	1,000	125	10	800	150	10	3.8%	200.00 [78.98, 321.02]
Kosmac et al., 2007 - Tz 3YB, 150 µm	1,021	89.5	10	550	75	10	4.0%	471.00 [398.63, 543.37]
Kosmac et al., 2007 - Tz 3YSB, 150 µm	914	58.3	10	700	150	10	3.9%	214.00 [114.26, 313.74]
Kosmac et al., 2008 - Tz 3YB-E, 150 µm	1,000	50	10	800	50	10	4.1%	200.00 [156.17, 243.83]
Pereira et al., 2014 - Lava Frame, 160µm	865.9	126.1	30	691.1	86.6	30	4.0%	174.80 [120.06, 229.54]
Pereira et al., 2015^{a} - Lava Frame, 181µm	865.9	126.1	30	1,076.8	134.9	30	4.0%	-210.90 [-276.98, -144.82]
Pereira et al., 2016^{a} - Zirlux FC, 181µm	860.08	98.11	30	1,096.47	142.35	30	4.0%	-236.39 [-298.25, -174.53]
Pereira et al., 2016^{b} - Lava Frame, 181µm	577.5	57.2	20	706	62.1	20	4.1%	-128.50 [-165.50, -91.50]
Pereira et al., 2016^{b} - Zirlux FC, 181µm	542.2	25.6	20	652.1	83.9	20	4.1%	-109.90 [-148.34, -71.46]
Ramos et al., 2016 - Lava Frame, 160µm	817.18	115.2	15	1,019.3	182.4	15	3.9%	-202.12 [-311.29, -92.95]
Ramos et al., 2016 - Lava Frame, 200µm	817.18	115.2	15	995.3	104.6	15	4.0%	-178.12 [-256.86, -99.38]
Subtotal (95% CI)			**375**			**375**	**100.0%**	**134.08 [45.73, 222.42]**
Heterogeneity: Tau^2 = 49430.89; Chi^2 = 847.22, df = 25 (P < 0.00001); I^2 = 97%								
Test for overall effect: Z = 2.97 (P = 0.003)								
Test for subgroup differences: Chi^2 = 27.69, df = 2 (P < 0.00001), I^2 = 92.8%								

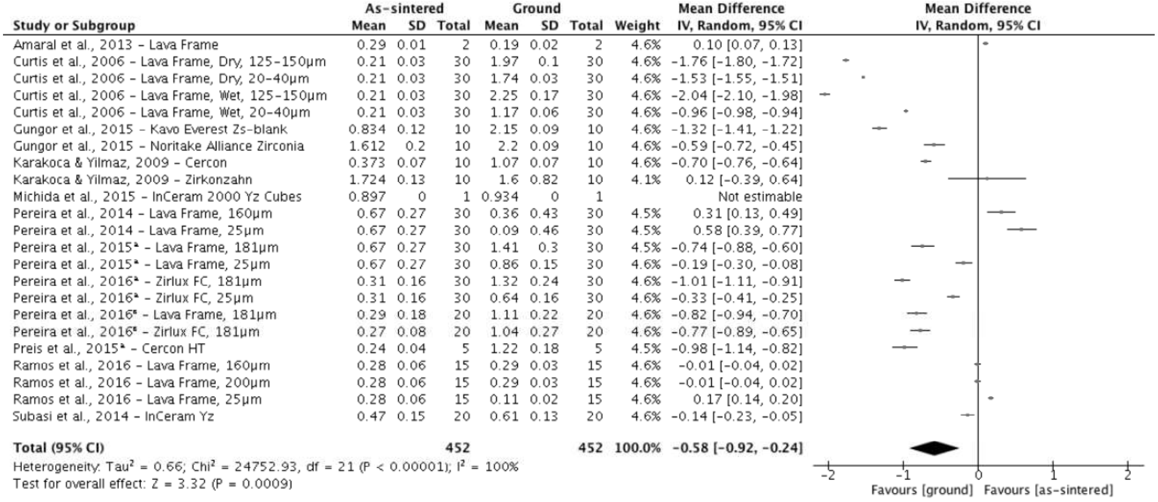
C- Grit-size



Study or Subgroup	As-sintered Mean	As-sintered SD	As-sintered Total	Ground Mean	Ground SD	Ground Total	Weight	Mean Difference IV, Random, 95% CI
1.4.1 With								
Amaral et al., 2013 - Lava Frame	818	79	15	796.9	103.7	15	5.4%	21.10 [-44.87, 87.07]
Curtis et al., 2006 - Lava Frame, Wet, 125-150µm	1,267	161	30	1,074	193	30	5.2%	193.00 [103.06, 282.94]
Curtis et al., 2006 - Lava Frame, Wet, 20-40µm	1,267	161	30	1,210	155	30	5.3%	57.00 [-22.97, 136.97]
Denry & Holloway, 2006 - Cercon	944	156	10	1,189	250	10	4.1%	-245.00 [-427.64, -62.36]
Ho et al., 2009 - Tz 3YB	914	34	25	1,104	37	25	5.7%	-190.00 [-209.70, -170.30]
Kosmac et al., 1999 - Tz 3YB, Wet	1,021	89.5	10	642	116.1	10	5.2%	379.00 [288.14, 469.86]
Kosmac et al., 1999 - Tz 3YSB, Wet	914	58.3	10	751	132.3	10	5.2%	163.00 [73.39, 252.61]
Michida et al., 2015 - InCeram 2000 Yz Cubes	1,196.2	284.2	30	874.4	365.4	30	4.3%	321.80 [156.15, 487.45]
Pereira et al., 2014 - Lava Frame, 160µm	865.9	126.1	30	691.1	86.6	30	5.5%	174.80 [120.06, 229.54]
Pereira et al., 2014 - Lava Frame, 25µm	865.9	126.1	30	1,001.3	108.6	30	5.5%	-135.40 [-194.95, -75.85]
Pereira et al., 2015^{a} - Lava Frame, 181µm	865.9	126.1	30	1,076.8	134.9	30	5.4%	-210.90 [-276.98, -144.82]
Pereira et al., 2015^{a} - Lava Frame, 25µm	865.9	126.1	30	1,085.8	179.7	30	5.3%	-219.90 [-298.46, -141.34]
Pereira et al., 2016^{a} - Zirlux FC, 181µm	860.08	98.11	30	1,096.47	142.35	30	5.5%	-236.39 [-298.25, -174.53]
Pereira et al., 2016^{a} - Zirlux FC, 25µm	860.08	98.11	30	1,099.47	139.18	30	5.5%	-239.39 [-300.32, -178.46]
Pereira et al., 2016^{b} - Lava Frame, 181µm	577.5	57.2	20	706	62.1	20	5.6%	-128.50 [-165.50, -91.50]
Pereira et al., 2016^{b} - Zirlux FC, 181µm	542.2	25.6	20	652.1	83.9	20	5.6%	-109.90 [-148.34, -71.46]
Ramos et al., 2016 - Lava Frame, 160µm	817.18	115.2	15	1,019.3	182.4	15	5.0%	-202.12 [-311.29, -92.95]
Ramos et al., 2016 - Lava Frame, 200µm	817.18	115.2	15	995.3	104.6	15	5.3%	-178.12 [-256.86, -99.38]
Ramos et al., 2016 - Lava Frame, 25µm	817.18	115.2	15	991.45	121.7	15	5.3%	-174.27 [-259.07, -89.47]
Subtotal (95% CI)			**425**			**425**	**100.0%**	**-53.68 [-122.56, 15.19]**
Heterogeneity: Tau^2 = 21585.85; Chi^2 = 474.55, df = 18 (P < 0.00001); I^2 = 96%								
Test for overall effect: Z = 1.53 (P = 0.13)								
1.4.2 Without								
Curtis et al., 2006 - Lava Frame, Dry, 125-150µm	1,267	161	30	1,057	179	30	4.5%	210.00 [123.85, 296.15]
Curtis et al., 2006 - Lava Frame, Dry, 20-40µm	1,267	161	30	1,319	165	30	4.5%	-52.00 [-134.49, 30.49]
Iseri et al., 2010 - Zirkonzahn, highspeed (cont)	928.4	186.55	5	878.57	194.85	5	2.7%	49.83 [-186.62, 286.28]
Iseri et al., 2010 - Zirkonzahn, highspeed (per)	928.4	186.55	5	823.53	92.08	5	3.4%	104.87 [-77.48, 287.22]
Iseri et al., 2010 - Zirkonzahn, slowspeed (cont)	928.4	186.55	5	838.91	151.22	5	3.0%	89.49 [-121.00, 299.98]
Iseri et al., 2010 - Zirkonzahn, slowspeed (per)	928.4	186.55	5	733.82	94.22	5	3.3%	194.58 [11.39, 377.77]
Iseri et al., 2012 - Zirkonzahn, highspeed (cont)	1,080.3	151.7	10	823.1	180.5	10	3.8%	257.20 [111.06, 403.34]
Iseri et al., 2012 - Zirkonzahn, highspeed (per)	1,080.3	151.7	10	807.2	251	10	3.4%	273.10 [91.33, 454.87]
Iseri et al., 2012 - Zirkonzahn, slowspeed (cont)	1,080.3	151.7	10	755.8	78.9	10	4.3%	324.50 [218.52, 430.48]
Iseri et al., 2012 - Zirkonzahn, slowspeed (per)	1,080.3	151.7	10	680.5	101.2	10	4.2%	399.80 [286.78, 512.82]
Karakoca & Yilmaz, 2009 - Cercon	1,122.2	100	10	993.5	30	10	4.7%	128.70 [63.99, 193.41]
Karakoca & Yilmaz, 2009 - Zirkonzahn	935.6	60	10	884.8	60	10	4.8%	50.80 [-1.79, 103.39]
Kosmac et al., 1999 - Tz 3YB, Dry	1,021	89.5	10	543	84.9	10	4.6%	478.00 [401.54, 554.46]
Kosmac et al., 1999 - Tz 3YSB, Dry	914	58.3	10	724	153.3	10	4.3%	190.00 [88.35, 291.65]
Kosmac et al., 2000 - Tz 3YB	1,021	89.5	10	850	100	10	4.5%	171.00 [87.82, 254.18]
Kosmac et al., 2000 - Tz 3YS-E	1,000	125	10	800	150	10	4.1%	200.00 [78.98, 321.02]
Kosmac et al., 2000 - Tz 3YSB	914	58.3	10	880	125	10	4.5%	34.00 [-51.49, 119.49]
Kosmac et al., 2007 - Tz 3YB, 150 µm	1,021	89.5	10	550	75	10	4.6%	471.00 [398.63, 543.37]
Kosmac et al., 2007 - Tz 3YB, 50 µm	1,021	89.5	10	850	75	10	4.6%	171.00 [98.63, 243.37]
Kosmac et al., 2007 - Tz 3YB-E, 50 µm	1,080	75	10	930	115	10	4.5%	150.00 [64.91, 235.09]
Kosmac et al., 2007 - Tz 3YSB, 150 µm	914	58.3	10	700	150	10	4.3%	214.00 [114.26, 313.74]
Kosmac et al., 2007 - Tz 3YSB, 50 µm	914	58.3	10	860	100	10	4.6%	54.00 [-17.74, 125.74]
Kosmac et al., 2008 - Tz 3YB-E, 150 µm	1,000	50	10	800	50	10	4.8%	200.00 [156.17, 243.83]
Subasi et al., 2014 - InCeram Yz	723.32	229.04	20	674.08	202.18	20	3.9%	49.24 [-84.65, 183.13]
Subtotal (95% CI)			**270**			**270**	**100.0%**	**186.44 [127.72, 245.16]**
Heterogeneity: Tau^2 = 18090.93; Chi^2 = 231.86, df = 23 (P < 0.00001); I^2 = 90%								
Test for overall effect: Z = 6.22 (P < 0.00001)								
Test for subgroup differences: Chi^2 = 27.04, df = 1 (P < 0.00001), I^2 = 96.3%								

D- Cooling

Figure 3. Roughness Ra meta-analyses (A- Global; B- Grinding tool subgroups; C- Grit-size subgroups; D- Presence/absence of cooling subgroups).

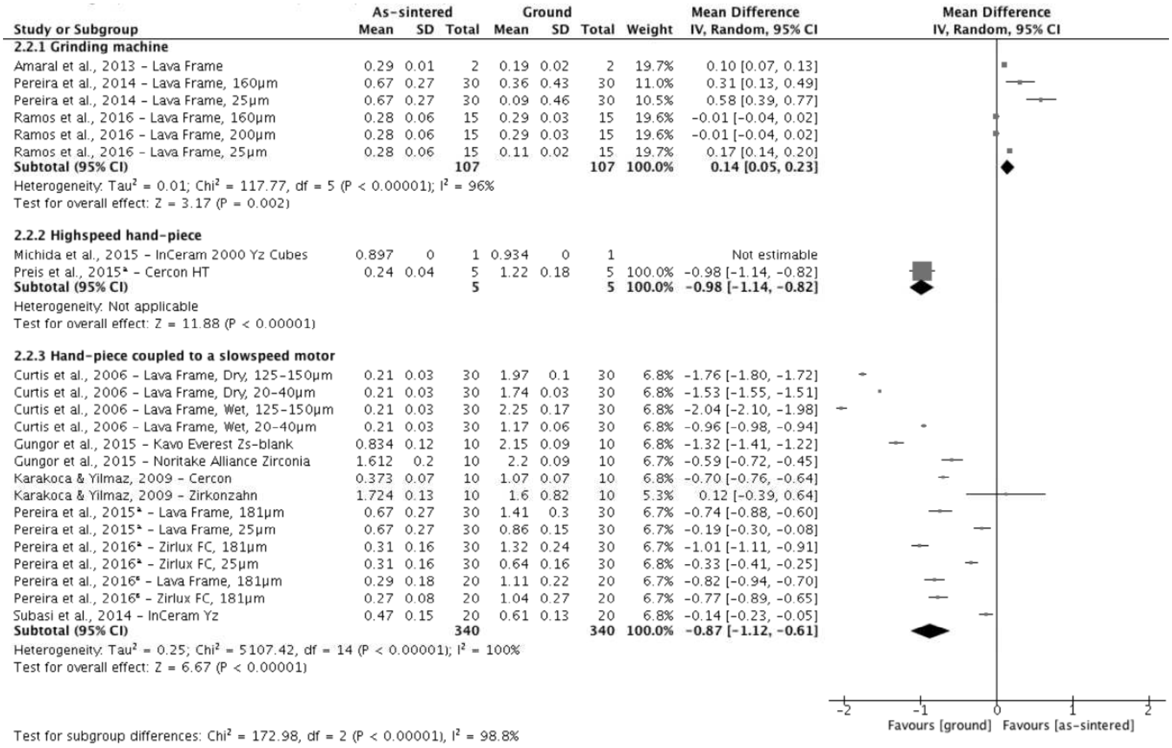


	As-sintered			Ground				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Amaral et al., 2013 – Lava Frame	0.29	0.01	2	0.19	0.02	2	4.6%	0.10 [0.07, 0.13]
Curtis et al., 2006 – Lava Frame, Dry, 125-150µm	0.21	0.03	30	1.97	0.1	30	4.6%	-1.76 [-1.80, -1.72]
Curtis et al., 2006 – Lava Frame, Dry, 20-40µm	0.21	0.03	30	1.74	0.03	30	4.6%	-1.53 [-1.55, -1.51]
Curtis et al., 2006 – Lava Frame, Wet, 125-150µm	0.21	0.03	30	2.25	0.17	30	4.6%	-2.04 [-2.10, -1.98]
Curtis et al., 2006 – Lava Frame, Wet, 20-40µm	0.21	0.03	30	1.17	0.06	30	4.6%	-0.96 [-0.98, -0.94]
Gungor et al., 2015 – Kavo Everest Zs-blank	0.834	0.12	10	2.15	0.09	10	4.6%	-1.32 [-1.41, -1.22]
Gungor et al., 2015 – Noritake Alliance Zirconia	1.612	0.2	10	2.2	0.09	10	4.6%	-0.59 [-0.72, -0.45]
Karakoca & Yilmaz, 2009 – Cercon	0.373	0.07	10	1.07	0.07	10	4.6%	-0.70 [-0.76, -0.64]
Karakoca & Yilmaz, 2009 – Zirkonzahn	1.724	0.13	10	1.6	0.82	10	4.1%	0.12 [-0.39, 0.64]
Michida et al., 2015 – InCeram 2000 Yz Cubes	0.897	0	1	0.934	0	1		Not estimable
Pereira et al., 2014 – Lava Frame, 160µm	0.67	0.27	30	0.36	0.43	30	4.5%	0.31 [0.13, 0.49]
Pereira et al., 2014 – Lava Frame, 25µm	0.67	0.27	30	0.09	0.46	30	4.5%	0.58 [0.39, 0.77]
Pereira et al., 2015^{a} – Lava Frame, 181µm	0.67	0.27	30	1.41	0.3	30	4.5%	-0.74 [-0.88, -0.60]
Pereira et al., 2015^{a} – Lava Frame, 25µm	0.67	0.27	30	0.86	0.15	30	4.6%	-0.19 [-0.30, -0.08]
Pereira et al., 2016^{a} – Zirlux FC, 181µm	0.31	0.16	30	1.32	0.24	30	4.6%	-1.01 [-1.11, -0.91]
Pereira et al., 2016^{a} – Zirlux FC, 25µm	0.31	0.16	30	0.64	0.16	30	4.6%	-0.33 [-0.41, -0.25]
Pereira et al., 2016^{b} – Lava Frame, 181µm	0.29	0.18	20	1.11	0.22	20	4.6%	-0.82 [-0.94, -0.70]
Pereira et al., 2016^{b} – Zirlux FC, 181µm	0.27	0.08	20	1.04	0.27	20	4.6%	-0.77 [-0.89, -0.65]
Preis et al., 2015^{a} – Cercon HT	0.24	0.04	5	1.22	0.18	5	4.5%	-0.98 [-1.14, -0.82]
Ramos et al., 2016 – Lava Frame, 160µm	0.28	0.06	15	0.29	0.03	15	4.6%	-0.01 [-0.04, 0.02]
Ramos et al., 2016 – Lava Frame, 200µm	0.28	0.06	15	0.29	0.03	15	4.6%	-0.01 [-0.04, 0.02]
Ramos et al., 2016 – Lava Frame, 25µm	0.28	0.06	15	0.11	0.02	15	4.6%	0.17 [0.14, 0.20]
Subasi et al., 2014 – InCeram Yz	0.47	0.15	20	0.61	0.13	20	4.6%	-0.14 [-0.23, -0.05]
Total (95% CI)			**452**			**452**	**100.0%**	**-0.58 [-0.92, -0.24]**

Heterogeneity: Tau² = 0.66; Chi² = 24752.93, df = 21 (P < 0.00001); I² = 100%

Test for overall effect: Z = 3.32 (P = 0.0009)

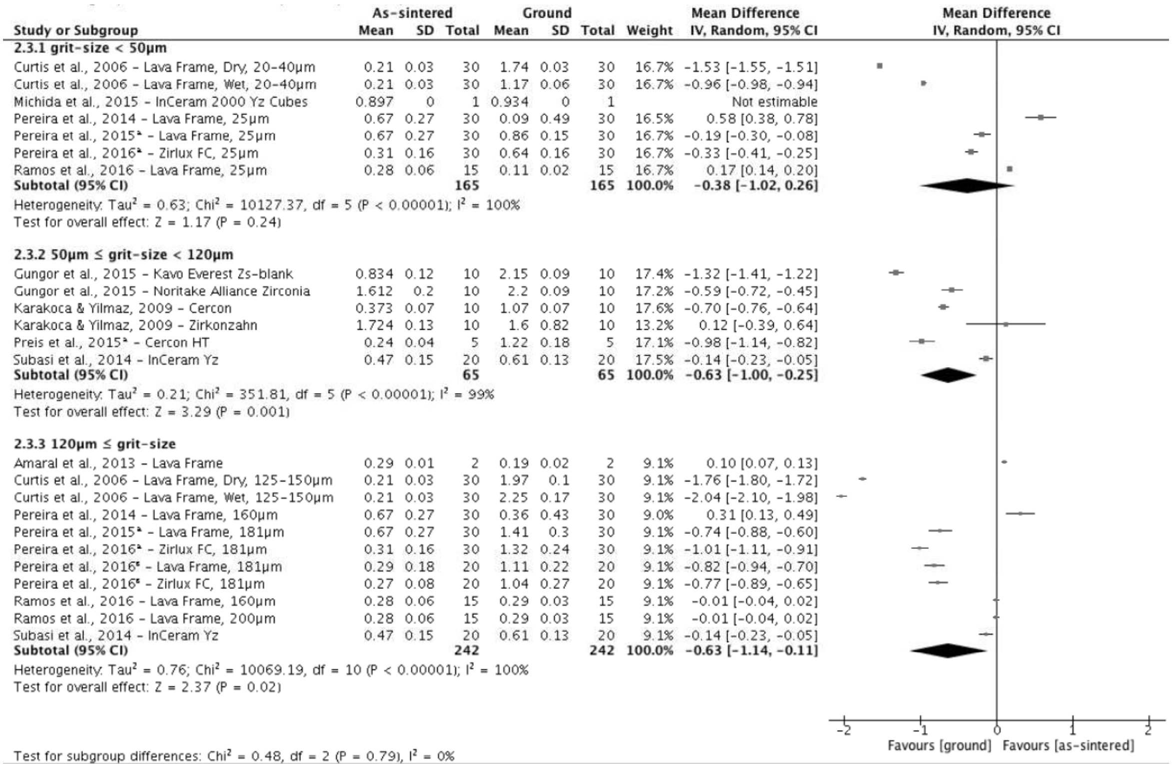
A- Global



	As-sintered			Ground				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
2.2.1 Grinding machine								
Amaral et al., 2013 – Lava Frame	0.29	0.01	2	0.19	0.02	2	19.7%	0.10 [0.07, 0.13]
Pereira et al., 2014 – Lava Frame, 160µm	0.67	0.27	30	0.36	0.43	30	11.0%	0.31 [0.13, 0.49]
Pereira et al., 2014 – Lava Frame, 25µm	0.67	0.27	30	0.09	0.46	30	10.5%	0.58 [0.39, 0.77]
Ramos et al., 2016 – Lava Frame, 160µm	0.28	0.06	15	0.29	0.03	15	19.6%	-0.01 [-0.04, 0.02]
Ramos et al., 2016 – Lava Frame, 200µm	0.28	0.06	15	0.29	0.03	15	19.6%	-0.01 [-0.04, 0.02]
Ramos et al., 2016 – Lava Frame, 25µm	0.28	0.06	15	0.11	0.02	15	19.7%	0.17 [0.14, 0.20]
Subtotal (95% CI)			**107**			**107**	**100.0%**	**0.14 [0.05, 0.23]**
Heterogeneity: Tau² = 0.01; Chi² = 117.77, df = 5 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 3.17 (P = 0.002)								
2.2.2 Highspeed hand-piece								
Michida et al., 2015 – InCeram 2000 Yz Cubes	0.897	0	1	0.934	0	1		Not estimable
Preis et al., 2015^{a} – Cercon HT	0.24	0.04	5	1.22	0.18	5	100.0%	-0.98 [-1.14, -0.82]
Subtotal (95% CI)			**5**			**5**	**100.0%**	**-0.98 [-1.14, -0.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 11.88 (P < 0.00001)								
2.2.3 Hand-piece coupled to a slowspeed motor								
Curtis et al., 2006 – Lava Frame, Dry, 125-150µm	0.21	0.03	30	1.97	0.1	30	6.8%	-1.76 [-1.80, -1.72]
Curtis et al., 2006 – Lava Frame, Dry, 20-40µm	0.21	0.03	30	1.74	0.03	30	6.8%	-1.53 [-1.55, -1.51]
Curtis et al., 2006 – Lava Frame, Wet, 125-150µm	0.21	0.03	30	2.25	0.17	30	6.8%	-2.04 [-2.10, -1.98]
Curtis et al., 2006 – Lava Frame, Wet, 20-40µm	0.21	0.03	30	1.17	0.06	30	6.8%	-0.96 [-0.98, -0.94]
Gungor et al., 2015 – Kavo Everest Zs-blank	0.834	0.12	10	2.15	0.09	10	6.8%	-1.32 [-1.41, -1.22]
Gungor et al., 2015 – Noritake Alliance Zirconia	1.612	0.2	10	2.2	0.09	10	6.7%	-0.59 [-0.72, -0.45]
Karakoca & Yilmaz, 2009 – Cercon	0.373	0.07	10	1.07	0.07	10	6.8%	-0.70 [-0.76, -0.64]
Karakoca & Yilmaz, 2009 – Zirkonzahn	1.724	0.13	10	1.6	0.82	10	5.3%	0.12 [-0.39, 0.64]
Pereira et al., 2015^{a} – Lava Frame, 181µm	0.67	0.27	30	1.41	0.3	30	6.7%	-0.74 [-0.88, -0.60]
Pereira et al., 2015^{a} – Lava Frame, 25µm	0.67	0.27	30	0.86	0.15	30	6.7%	-0.19 [-0.30, -0.08]
Pereira et al., 2016^{a} – Zirlux FC, 181µm	0.31	0.16	30	1.32	0.24	30	6.7%	-1.01 [-1.11, -0.91]
Pereira et al., 2016^{a} – Zirlux FC, 25µm	0.31	0.16	30	0.64	0.16	30	6.8%	-0.33 [-0.41, -0.25]
Pereira et al., 2016^{b} – Lava Frame, 181µm	0.29	0.18	20	1.11	0.22	20	6.7%	-0.82 [-0.94, -0.70]
Pereira et al., 2016^{b} – Zirlux FC, 181µm	0.27	0.08	20	1.04	0.27	20	6.7%	-0.77 [-0.89, -0.65]
Subasi et al., 2014 – InCeram Yz	0.47	0.15	20	0.61	0.13	20	6.8%	-0.14 [-0.23, -0.05]
Subtotal (95% CI)			**340**			**340**	**100.0%**	**-0.87 [-1.12, -0.61]**
Heterogeneity: Tau² = 0.25; Chi² = 5107.42, df = 14 (P < 0.00001); I² = 100%								
Test for overall effect: Z = 6.67 (P < 0.00001)								

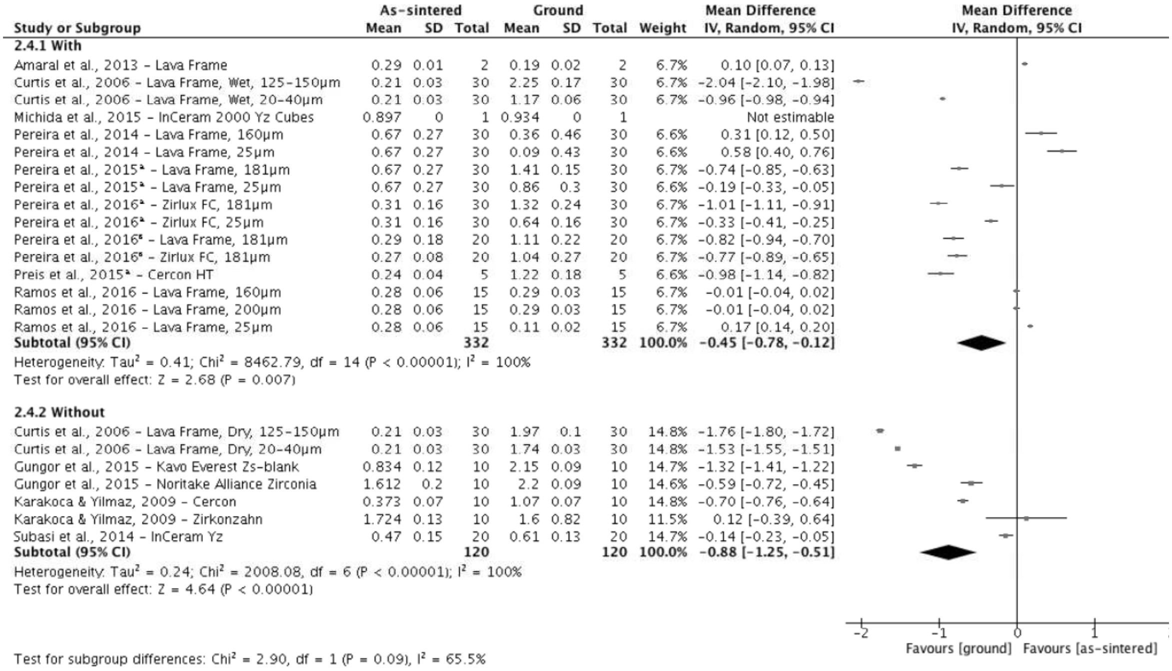
Test for subgroup differences: Chi² = 172.98, df = 2 (P < 0.00001), I² = 98.8%

B- Grinding tool



	As-sintered			Ground				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
2.3.1 grit-size < 50µm								
Curtis et al., 2006 - Lava Frame, Dry, 20-40µm	0.21	0.03	30	1.74	0.03	30	16.7%	-1.53 [-1.55, -1.51]
Curtis et al., 2006 - Lava Frame, Wet, 20-40µm	0.21	0.03	30	1.17	0.06	30	16.7%	-0.96 [-0.98, -0.94]
Michida et al., 2015 - InCeram 2000 Yz Cubes	0.897	0	1	0.934	0	1		Not estimable
Pereira et al., 2014 - Lava Frame, 25µm	0.67	0.27	30	0.09	0.49	30	16.5%	0.58 [0.38, 0.78]
Pereira et al., 2015[a] - Lava Frame, 25µm	0.67	0.27	30	0.86	0.15	30	16.7%	-0.19 [-0.30, -0.08]
Pereira et al., 2016[a] - Zirlux FC, 25µm	0.31	0.16	30	0.64	0.16	30	16.7%	-0.33 [-0.41, -0.25]
Ramos et al., 2016 - Lava Frame, 25µm	0.28	0.06	15	0.11	0.02	15	16.7%	0.17 [0.14, 0.20]
Subtotal (95% CI)			**165**			**165**	**100.0%**	**-0.38 [-1.02, 0.26]**
Heterogeneity: $Tau^2 = 0.63$; $Chi^2 = 10127.37$, df = 5 ($P < 0.00001$); $I^2 = 100\%$								
Test for overall effect: Z = 1.17 (P = 0.24)								
2.3.2 50µm ≤ grit-size < 120µm								
Gungor et al., 2015 - Kavo Everest Zs-blank	0.834	0.12	10	2.15	0.09	10	17.4%	-1.32 [-1.41, -1.22]
Gungor et al., 2015 - Noritake Alliance Zirconia	1.612	0.2	10	2.2	0.09	10	17.2%	-0.59 [-0.72, -0.45]
Karakoca & Yilmaz, 2009 - Cercon	0.373	0.07	10	1.07	0.07	10	17.6%	-0.70 [-0.76, -0.64]
Karakoca & Yilmaz, 2009 - Zirkonzahn	1.724	0.13	10	1.6	0.82	10	13.2%	0.12 [-0.39, 0.64]
Preis et al., 2015[a] - Cercon HT	0.24	0.04	5	1.22	0.18	5	17.1%	-0.98 [-1.14, -0.82]
Subasi et al., 2014 - InCeram Yz	0.47	0.15	20	0.61	0.13	20	17.5%	-0.14 [-0.23, -0.05]
Subtotal (95% CI)			**65**			**65**	**100.0%**	**-0.63 [-1.00, -0.25]**
Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 351.81$, df = 5 ($P < 0.00001$); $I^2 = 99\%$								
Test for overall effect: Z = 3.29 (P = 0.001)								
2.3.3 120µm ≤ grit-size								
Amaral et al., 2013 - Lava Frame	0.29	0.01	2	0.19	0.02	2	9.1%	0.10 [0.07, 0.13]
Curtis et al., 2006 - Lava Frame, Dry, 125-150µm	0.21	0.03	30	1.97	0.1	30	9.1%	-1.76 [-1.80, -1.72]
Curtis et al., 2006 - Lava Frame, Wet, 125-150µm	0.21	0.03	30	2.25	0.17	30	9.1%	-2.04 [-2.10, -1.98]
Pereira et al., 2014 - Lava Frame, 160µm	0.67	0.27	30	0.36	0.43	30	9.0%	0.31 [0.13, 0.49]
Pereira et al., 2015[a] - Lava Frame, 181µm	0.67	0.27	30	1.41	0.3	30	9.1%	-0.74 [-0.88, -0.60]
Pereira et al., 2016[a] - Zirlux FC, 181µm	0.31	0.16	30	1.32	0.24	30	9.1%	-1.01 [-1.11, -0.91]
Pereira et al., 2016[b] - Lava Frame, 181µm	0.29	0.18	20	1.11	0.22	20	9.1%	-0.82 [-0.94, -0.70]
Pereira et al., 2016[b] - Zirlux FC, 181µm	0.27	0.08	20	1.04	0.27	20	9.1%	-0.77 [-0.89, -0.65]
Ramos et al., 2016 - Lava Frame, 160µm	0.28	0.06	15	0.29	0.03	15	9.1%	-0.01 [-0.04, 0.02]
Ramos et al., 2016 - Lava Frame, 200µm	0.28	0.06	15	0.29	0.03	15	9.1%	-0.01 [-0.04, 0.02]
Subasi et al., 2014 - InCeram Yz	0.47	0.15	20	0.61	0.13	20	9.1%	-0.14 [-0.23, -0.05]
Subtotal (95% CI)			**242**			**242**	**100.0%**	**-0.63 [-1.14, -0.11]**
Heterogeneity: $Tau^2 = 0.76$; $Chi^2 = 10069.19$, df = 10 ($P < 0.00001$); $I^2 = 100\%$								
Test for overall effect: Z = 2.37 (P = 0.02)								
Test for subgroup differences: $Chi^2 = 0.48$, df = 2 (P = 0.79), $I^2 = 0\%$								

C- Grit-size



	As-sintered			Ground				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
2.4.1 With								
Amaral et al., 2013 - Lava Frame	0.29	0.01	2	0.19	0.02	2	6.7%	0.10 [0.07, 0.13]
Curtis et al., 2006 - Lava Frame, Wet, 125-150µm	0.21	0.03	30	2.25	0.17	30	6.7%	-2.04 [-2.10, -1.98]
Curtis et al., 2006 - Lava Frame, Wet, 20-40µm	0.21	0.03	30	1.17	0.06	30	6.7%	-0.96 [-0.98, -0.94]
Michida et al., 2015 - InCeram 2000 Yz Cubes	0.897	0	1	0.934	0	1		Not estimable
Pereira et al., 2014 - Lava Frame, 160µm	0.67	0.27	30	0.36	0.46	30	6.6%	0.31 [0.12, 0.50]
Pereira et al., 2014 - Lava Frame, 25µm	0.67	0.27	30	0.09	0.43	30	6.6%	0.58 [0.40, 0.76]
Pereira et al., 2015[a] - Lava Frame, 181µm	0.67	0.27	30	1.41	0.15	30	6.7%	-0.74 [-0.85, -0.63]
Pereira et al., 2015[a] - Lava Frame, 25µm	0.67	0.27	30	0.86	0.3	30	6.6%	-0.19 [-0.33, -0.05]
Pereira et al., 2016[a] - Zirlux FC, 181µm	0.31	0.16	30	1.32	0.24	30	6.7%	-1.01 [-1.11, -0.91]
Pereira et al., 2016[a] - Zirlux FC, 25µm	0.31	0.16	30	0.64	0.16	30	6.7%	-0.33 [-0.41, -0.25]
Pereira et al., 2016[b] - Lava Frame, 181µm	0.29	0.18	20	1.11	0.22	20	6.7%	-0.82 [-0.94, -0.70]
Pereira et al., 2016[b] - Zirlux FC, 181µm	0.27	0.08	20	1.04	0.27	20	6.7%	-0.77 [-0.89, -0.65]
Preis et al., 2015[a] - Cercon HT	0.24	0.04	5	1.22	0.18	5	6.6%	-0.98 [-1.14, -0.82]
Ramos et al., 2016 - Lava Frame, 160µm	0.28	0.06	15	0.29	0.03	15	6.7%	-0.01 [-0.04, 0.02]
Ramos et al., 2016 - Lava Frame, 200µm	0.28	0.06	15	0.29	0.03	15	6.7%	-0.01 [-0.04, 0.02]
Ramos et al., 2016 - Lava Frame, 25µm	0.28	0.06	15	0.11	0.02	15	6.7%	0.17 [0.14, 0.20]
Subtotal (95% CI)			**332**			**332**	**100.0%**	**-0.45 [-0.78, -0.12]**
Heterogeneity: $Tau^2 = 0.41$; $Chi^2 = 8462.79$, df = 14 ($P < 0.00001$); $I^2 = 100\%$								
Test for overall effect: Z = 2.68 (P = 0.007)								
2.4.2 Without								
Curtis et al., 2006 - Lava Frame, Dry, 125-150µm	0.21	0.03	30	1.97	0.1	30	14.8%	-1.76 [-1.80, -1.72]
Curtis et al., 2006 - Lava Frame, Dry, 20-40µm	0.21	0.03	30	1.74	0.03	30	14.8%	-1.53 [-1.55, -1.51]
Gungor et al., 2015 - Kavo Everest Zs-blank	0.834	0.12	10	2.15	0.09	10	14.7%	-1.32 [-1.41, -1.22]
Gungor et al., 2015 - Noritake Alliance Zirconia	1.612	0.2	10	2.2	0.09	10	14.6%	-0.59 [-0.72, -0.45]
Karakoca & Yilmaz, 2009 - Cercon	0.373	0.07	10	1.07	0.07	10	14.8%	-0.70 [-0.76, -0.64]
Karakoca & Yilmaz, 2009 - Zirkonzahn	1.724	0.13	10	1.6	0.82	10	11.5%	0.12 [-0.39, 0.64]
Subasi et al., 2014 - InCeram Yz	0.47	0.15	20	0.61	0.13	20	14.7%	-0.14 [-0.23, -0.05]
Subtotal (95% CI)			**120**			**120**	**100.0%**	**-0.88 [-1.25, -0.51]**
Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 2008.08$, df = 6 ($P < 0.00001$); $I^2 = 100\%$								
Test for overall effect: Z = 4.64 ($P < 0.00001$)								
Test for subgroup differences: $Chi^2 = 2.90$, df = 1 (P = 0.09), $I^2 = 65.5\%$								

D- Cooling

7. DISCUSSÃO GERAL

Nos últimos anos, o uso de restaurações metal-free têm se intensificado exponencialmente em odontologia (DENRY; KELLY, 2014). Dentre as diversas alternativas de materiais cerâmicos, o uso da zircônia (Y-TZP, Yttrium-stabilized Tetragonal Zirconia Polycristal); primeiramente, no formato de infraestrutura com posterior cobertura por cerâmica feldspática em próteses parciais fixas, e mais recentemente, no formato de restaurações monolíticas *full-contour;* surgiram como excelentes alternativas clínicas, apesar da alta complexidade técnica de confecção (BEUER et al., 2010; CHAAR; KERN, 2015; PIJLAJA; NAPANKANGAS; RAUSTIA, 2016).

Entretanto, uma avaliação crítica da literatura existente demonstra que não existe uma completa análise/caracterização comportamental deste material frente aos estímulos aos quais este será corriqueiramente submetido na cavidade oral (tratamentos de superfície para ajuste de formato e relação com os tecidos orais, assim como envelhecimento e fadiga). Desta forma a indicação não se encontra completamente respaldada em literatura existente.

Atualmente existe um consenso sobre a importância da odontologia ser executada baseada em evidências ciêntificas (ISMAIL; BADER, 2004). Esta é a maneira eticamente correta de restabelecer função e estética, garantindo longevidade, sem submeter o paciente a sobre tratamentos ou danos iatrogênicos. Quando considerados os estudos de acompanhamento clínico sobre próteses parciais fixas com infraestrutura de zircônia observa-se uma alta taxa de lascamento da cerâmica de cobertura (*chipping*) parcial ou total, que corriqueiramente desencadeia a necessidade de substituição da restauração em um curto espaço de tempo após confecção (BEUER et al., 2010; CHAAR; KERN, 2015; PIJLAJA; NAPANKANGAS; RAUSTIA, 2016).

Neste sentido, estudos laboratoriais surgem como uma importante ferramenta na caracterização e avaliação comportamental do material cerâmico, assim como da indicação clínica em um cenário extremamente controlado e padronizado. Neste ambiente pode-se avaliar em curto espaço de tempo a resposta do material frente aos estímulos aos quais esse será submetido na clínica odontológica, entretanto, essa análise será tão relevante quanto o poder do protocolo laboratorial em mimetizar/simular a condição clínica vigente.

Baseado neste cenário esta tese foi constituída de 3 partes laboratoriais e 2 revisões sistemáticas com meta-análises com o objetivo de avaliar/caracterizar os efeitos do desgaste com pontas diamantadas e do envelhecimento de cerâmicas Y-TZP indicadas para confecção de infraestruturas de próteses parciais fixas e restaurações monolíticas, tendo em vista buscar contribuir na elucidação deste tema e coletar dados cientificamente embasados para a indicação/aplicabilidade desta cerâmica na odontologia.

Sob as condições apresentadas nessa tese, podemos observar que o envelhecimento em autoclave é uma excelente ferramenta para promover os efeitos da degradação hidrotérmica na cerâmica Y-TZP, e que os parâmetros utilizados influenciam (diferença estatística) no resultado alcançado, apresentando indícios de que um tempo de pelo menos 20 horas, pressão maior ou igual a 2 bar com temperaturas iguais ou acima de 134°C seja o protocolo ideal para avaliar os seus efeitos (PEREIRA et al., 2015[b]).

Podemos observar também que o desgaste e o envelhecimento promoveram um aumento significativo de fase monoclínica na superfície do material o que impactou em um aumento significativo da resistência a flexão biaxial e média de resistência a fadiga, demonstrando que mesmo 20 horas de envelhecimento em autoclave sob 2 bar a 134°C não foram suficientes para promover degradação das propriedades mecânicas dos materiais avaliados (PEREIRA et al., 2015[a]; PEREIRA et al., 2016[a]; PEREIRA et al., 2016[b]).

Logo, os achados desta tese corroboram o mecanismo de tenacificação que esta cerâmica apresenta, elucidando que quando este material é estimulado (estímulos mecânicos, presença de água e/ou temperatura) desencadeia-se uma transformação de fase dos grãos superficiais, levando a um aumento de fase monoclínica na superfície, o que resulta no acúmulo de tensão compressiva residual que atua sobre os defeitos e micro-trincas superficiais, dificultando a propagação de trincas (GARVIE; NICHOLSON, 1972; HANNINK, 2000).

Entretanto as análises de topografia superficial demonstraram que o desgaste promove alterações importantes no padrão observado, aumentando a rugosidade (parâmetros Ra e Rz) e alterando a micro-morfologia superficial, introduzindo defeitos diretamente relacionados com a intensidade da granulação do instrumento utilizado. Dependendo da agressividade do protocolo de desgaste (maior velocidade, menor refrigeração/irrigação, ou uso de instrumentos de maior granulação) mais defeitos são introduzidos na superfície e com isto um efeito deletério nas propriedades mecânicas pode ser observado, o que está de acordo com a literatura existente (GREEN, 1983; YIN; JAHANMIR; YVES, 2003; YIN, et al., 2006; QUINN; IVES; JAHANMIR, 2005; ISERI et al., 2010; JING et al., 2014) onde foram avaliados outros materiais cerâmicos.

Adicionalmente, sabe-se que em um cenário clínico as restaurações são susceptíveis a fraturas por fadiga, principalmente motivadas por cargas mastigatórias cíclicas repetitivas em um ambiente úmido (ZHANG; SAILER; LAWN, 2013). Falhas por fadiga podem ser definidas como a fratura progressiva de um material friável sob tensões cíclicas de intensidade abaixo da resistência nominal característica do material (WISKOTT; NICHOLLS; BELSER, 1995). Baseado nisto, a introdução de defeitos superficiais deve ser sempre evitada.

Ainda existem poucos estudos que consideram o comportamento em fadiga de cerâmicas a base de Y-TZP (KOSMAC; DAKSKOBLER, 2007; KOSMAC et al., 2008; PEREIRA et al., 2016[b]). Nesta tese foi feita uma avaliação pontual através de um ensaio de fadiga acelerada (20.000 ciclos) submetendo esta cerâmica a uma associação de estímulos deletérios (estímulos mecânicos, água e temperatura) e os resultados foram promissores (PEREIRA et al., 2016[b]), já que não foram observados efeitos deletérios no limite de fadiga cerâmico.

Dessa forma, nota-se que essa tese, em adição com a literatura recente, apresenta dados que suportam uma adequada resposta do material frente a estímulos de envelhecimento e desgaste com pontas diamantadas. Tendo em vista que apesar de ter sido observado um aumento de fase monoclínica e alterações de topografia superficial e que não foram observados efeitos deletérios sobre as propriedades mecânicas do material (resistência à flexão e a fadiga biaxial).

Salienta-se que ainda existe a necessidade de mais estudos clínicos com acompanhamento a longo prazo para a total compreensão dos desfechos e intercorrências gerados nestas aplicações reabilitadoras, Apesar do fato de que até o momento, estudos laboratoriais sobre propriedades mecânicas (ensaios monotônicos e sob fadiga) e susceptibilidade a degradação (diferentes métodos de envelhecimento), assim como estudos *in vivo* vem demonstrando resultados promissores para materiais a base de Y-TZP.

8. CONCLUSÃO

Baseado nos achados desta tese, nota-se uma relação direta entre os parâmetros utilizados, tanto para envelhecimento quanto para tratamento de superfície (desgaste com pontas diamantadas), no desfecho final observado (alterações superficiais, introdução de defeitos, impacto em propriedades mecânicas e fadiga).

O envelhecimento em autoclave se demonstrou uma ferramenta capaz de induzir a degradação a baixas temperaturas (LTD) impactando diretamente sobre as propriedades mecânicas do material. Foram observados indícios de que um protocolo com temperaturas acima de 134°C, pressões acima de 2 bar, por um tempo de ciclo de pelo menos 20 horas, seriam os índices mínimos necessários para observar os efeitos deletérios da LTD. Adicionalmente ressalta-se que o material apenas apresentou degradação de propriedades mecânicas quando percentuais de fase monoclínica atingiram índices acima de 50%.

Ainda sobre envelhecimento, nota-se que a associação de diferentes estímulos (fadiga e autoclave – simulando o ambiente oral) acelera e intensifica o processo de envelhecimento cerâmico e por tanto mais estudos que considerem associações de estímulos necessitam ser executados.

Sobre o desgaste nota-se a direta influência dos parâmetros utilizados (velocidade, presença/ausência de irrigação e granulação do instrumento de desgaste) sobre as propriedades mecânicas da cerâmica Y-TZP. Ressalta-se que quanto mais agressivo o protocolo de desgaste utilizado maior o risco de efeito deletério sobre as propriedades mecânicas, desta forma observou-se que o melhor cenário aparenta ser o uso de canetas multiplicadoras de torque acopladas a micromotores de baixa rotação sob irrigação constante e abundante, utilizando-se instrumentos de menor granulação. A partir deste protocolo, utilizado durante os estudos laboratoriais, observaram-se patamares de resistência à flexão e limite de fadiga sempre iguais e/ou superiores aos observados pela condição controle (ausência de desgaste e envelhecimento).

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ANEXO A - AUTHOR GUIDELINES FOR JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS.

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You are urged to visit this site; some excerpts from the detailed information are given here.

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[1] J. van der Geer, J.A.J. Hanraads, R.A. Lupton, The art of writing a scientific article, J. Sci. Commun. 163 (2010) 51–59.

Reference to a book:

[2] W. Strunk Jr., E.B. White, The Elements of Style, fourth ed., Longman, New York, 2000. Reference to a chapter in an edited book:

[3] G.R. Mettam, L.B. Adams, How to prepare an electronic version of your article, in: B.S. Jones, R.Z. Smith (Eds.), Introduction to the Electronic Age, E-Publishing Inc., New York, 2009, pp. 281–304. Reference to a website:

[4] Cancer Research UK, Cancer statistics reports for the UK. http://www.cancerresearchuk.org/ about cancer/statistics/cancerstatsreport/, 2003 (accessed 13.03.03).

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