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In vivo ageing of zirconia dental ceramics – Part II: highly-translucent and rapid-sintered 3Y-TZP

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Corresponding Author:	Peter Jevnikar University of Ljubljana Medical Faculty Ljubljana, Slovenia
First Author:	Jasna Cotič
Order of Authors:	Jasna Cotič
	Andraž Kocjan
	Sanja Panchevska
	Tomaz Kosmač
	Peter Jevnikar
Abstract:	Objectives 3Y-TZP ceramics with reduced alumina content have improved translucency and are used in monolithic dental restorations without porcelain-based veneers. The workflow can be further streamlined with rapid sintering. This study was designed to assess how these approaches affect ageing when the materials are exposed to the oral environment in vivo . Methods 43 discs were fabricated from 3Y-TZP powder with 0.05% Al_2O_3 and sintered with conventional or rapid regimens (1450°C 2 h, 1530°C 2 h, or 1530°C 25 min). Their surfaces were polished or airborne-particle abraded with 50 µm Al_2O_3 . The discs were incorporated in complete dentures of 16 volunteers and worn continuously for up to 48 months. Ageing changes on disc surfaces were monitored every 6 months by X-ray diffraction, scanning electron microscopy and atomic force microscopy. Data was statistically analyzed with linear models. Results The amount of monoclinic phase on polished surfaces increased linearly, reaching up to 40% after 48 months in vivo . The ageing process observed for rapid sintering was 1.6 times faster compared to conventional sintering. A nano-scale increase in roughness with microcracking was also detected on polished surfaces. Airborne-particle abraded surfaces did not exhibit clear signs of ageing during the course of the study. Significance Highly-translucent 3Y-TZP ceramics are more susceptible to ageing than classic 3Y-TZP. After 4 years in vivo , the extent of degradation did not yet constitute grounds for clinical concern, but was more pronounced in materials prepared with rapid sintering.

Highlights

- Highly-translucent 3Y-TZP is more susceptible to *in vivo* ageing than classic 3Y-TZP.
- Rapid sintering increases the susceptibility to *in vivo* ageing.
- Airborne-particle abrasion suppresses *in vivo* ageing.
- Surface degradation after 4 years *in vivo* was within clinically acceptable range.

Graphical Abstract

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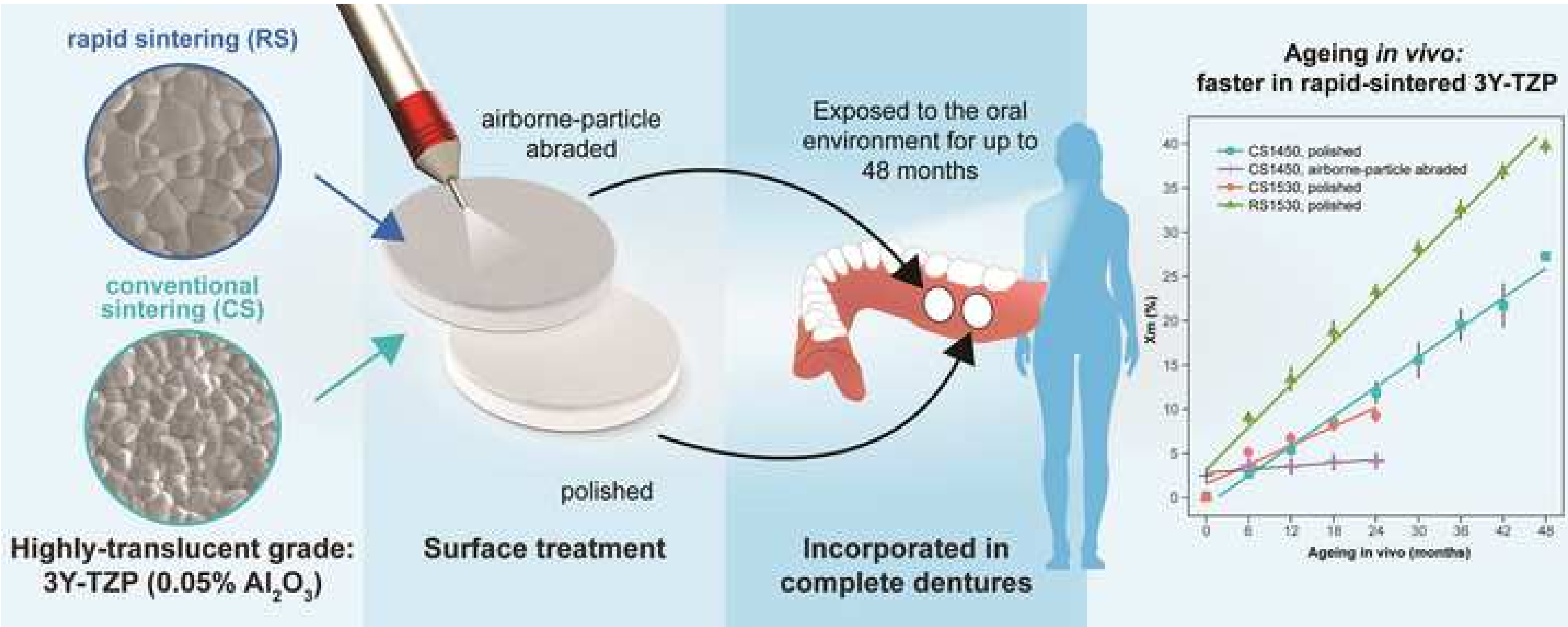


In vivo ageing of zirconia dental ceramics – Part II: highly-translucent and rapid-sintered 3Y-TZP

Jasna Cotič[a], Andraž Kocjan[b], Sanja Panchevska[c], Tomaž Kosmač[b], Peter Jevnikar[a,*],

[a] Department of Prosthodontics, Faculty of Medicine, University of Ljubljana, Hrvatski trg 6, SI-1000 Ljubljana, Slovenia

[b] Department for Nanostructured Materials, Jožef Stefan Institute, Jamova 39, SI-1000 Ljubljana, Slovenia

[c] Faculty of Dentistry, Ss. Cyril and Methodius University, Majka Tereza 43, MK-1000 Skopje, Republic of North Macedonia

* Corresponding author: Peter Jevnikar, Department of Prosthodontics, Faculty of Medicine, University of Ljubljana, Hrvatski trg 6, SI-1000 Ljubljana, Slovenia.

E-mail: peter.jevnikar@mf.uni-lj.si

Keywords: zirconia; high translucency; rapid sintering; *in vivo* ageing; low temperature degradation; airborne-particle abrasion; phase transformation

In vivo ageing of zirconia dental ceramics – Part II: highly-translucent and rapid-sintered 3Y-TZP

Objectives

3Y-TZP ceramics with reduced alumina content have improved translucency and are used in monolithic dental restorations without porcelain-based veneers. The workflow can be further streamlined with rapid sintering. This study was designed to assess how these approaches affect ageing when the materials are exposed to the oral environment *in vivo*.

Methods

43 discs were fabricated from 3Y-TZP powder with 0.05% Al_2O_3 and sintered with conventional or rapid regimens (1450°C 2 h, 1530°C 2 h, or 1530°C 25 min). Their surfaces were polished or airborne-particle abraded with 50 µm Al_2O_3. The discs were incorporated in complete dentures of 16 volunteers and worn continuously for up to 48 months. Ageing changes on disc surfaces were monitored every 6 months by X-ray diffraction, scanning electron microscopy and atomic force microscopy. Data was statistically analyzed with linear models.

Results

The amount of monoclinic phase on polished surfaces increased linearly, reaching up to 40% after 48 months *in vivo*. The ageing process observed for rapid sintering was 1.6 times faster compared to conventional sintering. A nano-scale increase in roughness with microcracking was also detected on polished surfaces. Airborne-particle abraded surfaces did not exhibit clear signs of ageing during the course of the study.

Significance

Highly-translucent 3Y-TZP ceramics are more susceptible to ageing than classic 3Y-TZP. After 4 years *in vivo*, the extent of degradation did not yet constitute grounds for clinical concern, but was more pronounced in materials prepared with rapid sintering.

1. Introduction

This is the second of our two co-published articles about ageing of 3Y-TZP ceramics *in vivo*. The aim was to build on the conclusions of the previous study [ref in vivo paper 1], to move beyond traditional, biomedical grade 3Y-TZP ceramics and investigate ageing properties when modern material variants and processing techniques are applied.

Traditional dental 3Y-TZP ceramics are very opaque and have to be veneered with glass-based porcelain veneers to achieve acceptable aesthetics. As veneers are prone to chipping [1], there is a strong drive to circumvent this problem by using monolithic zirconia instead. The full-contour technique requires specially formulated versions of zirconia ceramics with improved light transmittance. This can be achieved by decreasing the grain size, reducing the porosity [2] and modifying the amount of dopants such as yttria and alumina [3]. Dopants are normally added to aid sintering and control the transformability, and consequently also affect the susceptibility to low temperature degradation (LTD) [4]. Typically, the alumina content in zirconia ceramics is 0.25%, but highly-translucent variants have it reduced to 0.05%. Such concentration of Al^{3+} is not sufficient for the isolated alumina grain formation in the 3Y-TZP matrix during sintering. A decrease in its protective effect against ageing can therefore be expected [5]. Another strategy to improve optical properties is by increasing the yttria content and decreasing the tetragonality of the system. But although cubic Y-TZP ceramic is both translucent and ageing-resistant, it is a very different, mechanically weaker material due to the absence of the *t-m* toughening mechanism [3][5] and was not considered in this study.

As monolithic zirconia restorations do not require veneering, less steps are needed in production, which can be a considerable advantage. A complementary approach to further streamline the workflow is to shorten the sintering times. Sintering typically takes about 12 hours and is the most time-consuming component of working with zirconia ceramics. Modern rapid sintering protocols only take a fraction of this time and are currently gaining traction [6], but knowledge on their effect on the final material's properties is still limited. Increased heating rates and shorter dwell times result in specific material microstructures with larger grain sizes, and the implications for their mechanical performance and translucency are not always beneficial [7][8][9]. Our main goal was to assess the susceptibility of such ceramics to ageing when exposed to the oral environment *in vivo*. The ceramics were prepared with conventional or rapid sintering, and their surfaces were either polished or airborne-particle abraded (sandblasted) to emulate the relevant preparation procedures in a clinical setting. The experimental design used our established methodology with complete dentures as vehicles to hold the ceramic samples in patients' mouths for up to 48 months [ref in vivo paper 1].

2. Materials and methods

2.1 Clinical study background

This clinical study was designed as a collaboration between the Department of Prosthodontics, Faculty of Medicine, University of Ljubljana and Faculty of Dentistry, Ss. Cyril and Methodius University. The study protocol consisted of inserting the ceramic specimens in lower complete dentures worn by patients, as also described in our previous publication [ref in vivo paper 1]. The study was granted approval by the Republic of Slovenia National Medical Ethics Committee (approval no. 61/04/1011). All the procedures were in accordance with the Helsinki Declaration of 1975, as revised in 1983. The following inclusion criteria were used to select the patients:

- good general satisfaction with the existing complete dentures based on the Patient Denture Assessment (PDA) questionnaire [10],
- personal preference and willingness to wear the dentures 24 hours a day,
- no medical history that might interfere with the planned 6-month recall during the course of the study.

The present series consisted of 16 volunteers (5 men and 11 women). They received verbal and written explanation on the study design and the purpose of the research. The participation was confirmed by signing an informed consent form. The participants agreed to take part in a regular 6-month recall program and were free to stop participating at any time. The target time frame was 24 months. Patients were then given the option to continue in the study extension for up to 48 months.

2.2 Preparation of the intraoral ageing devices

The studied ceramic materials to be incorporated into dentures were prepared from commercially available, translucent grade 3Y-TZP granulated powder containing 3 mol% of yttria, 0.05 wt.% of alumina and 3 wt.% of an organic binder (TZ-PX-242A, Tosoh, Tokyo, Japan).

Disc-shaped specimens were dry pressed uniaxially at 150 MPa and sintered to get three distinct ceramic materials, as presented in Table 1 and Fig.1.

Table 1. Overview of sintering regimens, microstructures and surface treatments for materials used in this study. APA = airborne-particle abrasion.

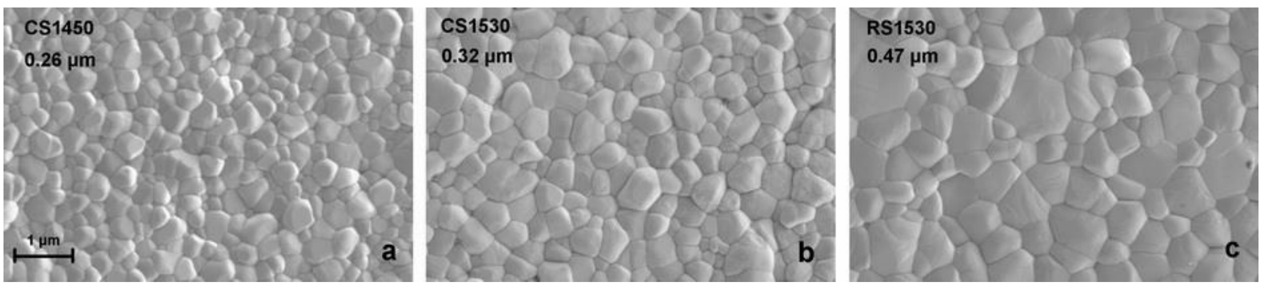
Material	Sintering regimen	Average grain size in µm (SD)	Surface treatment
CS1450	Conventional sintering: heat 5°C/min, dwell 1450°C 2 h, cool 5°C/min until ambient temperature	0.26 (0.02)	Polishing (n=10) APA (n=10)
CS1530	Conventional sintering: heat 5°C/min, dwell 1530°C 2 h, cool 5°C/min until ambient temperature	0.32 (0.03)	Polishing (n=12)
RS1530	Rapid sintering: heat 60°C/min, dwell 700°C 2 min, heat 60 °C/min, dwell 1300°C 2 min, heat 40°C/min, dwell 1530°C 25 min, cool 90°C/min until 700°C, cool 60°C/min until 400°C, cool 40°C/min until ambient temperature	0.47 (0.06)	Polishing (n=11)

After sintering, the final diameter of the discs was 8 mm and their thickness 1 mm. The relative density was determined by the Archimedes' method, using deionized water as the immersion liquid. A theoretical density of ρ_T = 6.08 g/cm^3 for the tetragonal phase was used in the calculations. The relative density exceeded 99% of the theoretical value.

The grain sizes were estimated from FE-SEM images (GeminiSEM, Carl Zeiss AG, Jena, Germany) using the linear-intercept procedure based on the ASTM E112-13 standard without introducing any correction factors. The examined ceramic surfaces were mirror polished, thermally etched (1300°C for 30 min in air) to expose the grain boundaries and examined without any surface coating applied (Fig.1).

Fig. 1

SEM micrographs of the ceramic surfaces prepared with conventional (a, b) or rapid sintering (c). All three materials were produced from the same 3Y-TZP powder with alumina content of 0.05%. The average grain sizes are displayed on the images.



Ten CS1450 specimens were airborne-particle abraded with 50 µm Al_2O_3 particles at a pressure of 2.5 bar, using an air-abrasion unit (Basic IS, Renfert Dental, Hilzingen, Germany). The rest of the specimens were mirror polished. After surface treatments, the specimens were ultrasonically cleaned with acetone and deionized water.

Prior to inserting the ceramic specimens in the dentures, the necessary space was prepared in suitably flat regions of the denture’s sublingual flanges. The patients were instructed to wear their dentures continuously, removing them only for daily cleaning with soapy water and a denture brush. Regular recall visits were scheduled to ensure the patients were in good oral health and could use their dentures without difficulties. If any denture-related lesions were visible on the mucosa, the dentures were adjusted accordingly or relined.

2.3 Ceramic specimen analyses

At every 6-month recall appointment, ceramic specimens were temporarily removed from the dentures and submerged in 2.5% sodium hypochlorite for 10 min to remove the organic debris from the surface. After rinsing, the specimens were cleaned ultrasonically in acetone, ethanol and deionized water for 10 min to prepare them for surface characterizations with XRD, FE-SEM and AFM. XRD patterns were collected using Cu-Kα radiation at 45 kV and 40 mA over the range of 25 to 40 2θ (X'Pert PRO X-Ray diffractometer, PANalytical, Almelo, The Netherlands). The X_m was estimated using the Garvie and Nicholson method [11].

Scanning electron micrographs of ceramic surfaces were taken with FE-SEM (GeminiSEM, Carl Zeiss AG, Jena, Germany) without any surface coating applied. AFM analysis of the polished surfaces was performed in the contact mode with the scan size of 10 μm x 10 μm (Dimension 3100, Veeco Instruments, Plainview, USA). The acquired AFM data was processed with the WSXm 4.0 Beta 8.1 software [12], utilizing three measurements to estimate the mean roughness (Ra).

When the analyses were complete, the specimens were re-inserted in the corresponding patients' dentures using cold-curing acrylic resin. At the end of the study, the discs were permanently removed from the dentures and cross-sections perpendicular to aged surfaces were prepared by FIB machining (Helios Nanolab 650, FEI, Hillsboro, USA). A 0.5 μm layer of platinum film was sputtered on the area of interest, using the ion-beam-assisted gas injection system at 30 kV and 0.43 nA to prevent the extensive curtain effect. FIB trenches were cut at 30 kV and 65 nA and finalized by ion polishing at 30 kV and 21 nA. The transformation depth and changes in the immediate subsurface zone were observed in situ, at an angle of 52°, using the electron probe at 2 kV and 100 pA.

3.4 Statistical analysis

The data on X_m was statistically analysed with linear models using the statistics software package R 3.1.2 [13]. Ageing was treated as a numerical variable expressed as months *in vivo*. Sintering regimen was treated as a descriptive variable with three levels: conventional sintering at 1450°C, conventional sintering at 1530°C and rapid sintering at 1530°C. Surface treatment was treated as a descriptive variable with two levels: polishing or airborne-particle abrasion. Pairwise differences between treatment groups were further examined with Tukey's HSD test. The significance level was set to $\alpha = 0.05$.

3. Results

The retention rate and compliance of study participants was very good. One participant was lost to follow-up after 6 months, one moved abroad after 12 months, and one could not continue wearing their dentures due to suffering a stroke 12 months into the study. After 24 months, 6 participants elected to continue with the study extension for up to 48 months. These participants were wearing polished CS1450 and RS1530 specimens. We were therefore able to obtain 48-month results for these groups, and 24-month results for polished CS1530 and airborne-particle abraded CS1450 specimens.

3.2 Phase composition

XRD analyses revealed changes in phase composition, reflecting the rate and the extent of ageing *in vivo,* as presented in Fig. 2 and Table 2. Before ageing, polished samples were monoclinic phase-free, whereas X_m of the airborne-particle abraded samples was 2.5%. The latter also exhibited low-2θ-angle asymmetric broadening of peak $(111)_{t'}/(101)_t$, the reversed intensity of peaks $(002)_t$ and $(110)_t$, and an increased full width at half maximum (FWHM) value of peak $(002)_t$.

Sintering regimen affected the initial phase composition through sintering-related phase partitioning process. Increasing the sintering temperature increased the amount of untransformable yttria-rich *t'*-ZrO_2 phase. This was evident from the estimated increase in the peak intensity ratio of $I(110)_{t'}/I(110)_t$, which was 0.17 in material CS1450 and 0.21 in material CS1530. In rapid-sintered samples the phase partitioning was even more pronounced and the intensity ratio was 0.37. The increase in sintering temperature or speed also resulted in higher tetragonality of the untransformable, yttria-rich *t'*-ZrO_2 phase. The relevant $(002)_{t'}/(110)_{t`}$ peaks were pushed apart, away from 35° 2θ and closer to peaks $(002)_t$ and $(110)_t$.

After 24 months of ageing *in vivo*, the emergence of monoclinic peak $(1\bar{1}1)_m$ was clearly discernible in polished samples. On the contrary, very little change was observed in the XRD patterns of airborne-particle abraded samples. In material CS1450, the mean X_m has risen to 11.9% in polished samples and to 4.2% in airborne-particle abraded samples. Polished CS1530 samples had the mean X_m of 9.3% after 24 months *in vivo*.

After 48 months *in vivo*, the changes on polished samples developed further, reaching the mean X_m of 39.7% in the rapid-sintered material RS1530 and 27.3% in the conventional-sintered material CS1450.

Fig. 2

XRD patterns obtained from polished (a, b, c) and airborne-particle abraded (d) specimens, before and after ageing *in vivo*. Ceramics prepared with rapid sintering exhibited the most pronounced ageing changes (b). Higher-angle 2θ XRD patterns are presented as close-ups to illustrate how differences in sintering regimens affected phase composition, phase partitioning and the peak intensity ratio $I(110)_{t'}/I(110)_t$.

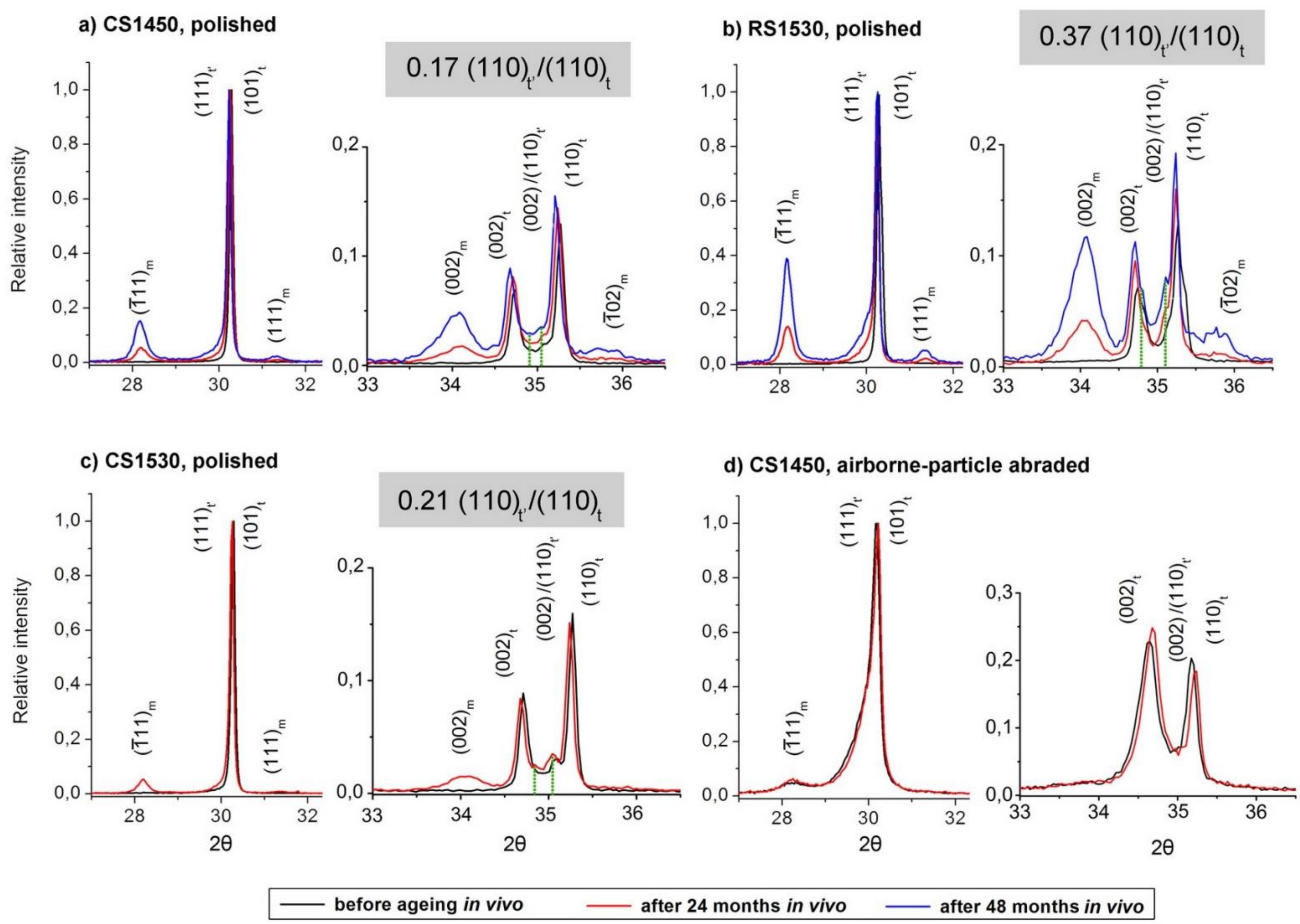


Table 2. Mean values and standard deviations for the monoclinic content (X_m) before and after ageing *in vivo*. Values marked with the same letters are not significantly different from each other (Tukey's HSD test, α= 0.05). APA = airborne-particle abrasion.

Ageing *in vivo* (months)	Material	Surface treatment	X_m in % (SD)
0	CS1450	polished	0.1^{p} (0.14)
0	CS1530	polished	0.0^{p} (0.00)
0	RS1530	polished	0.1^{p} (0.13)
0	CS1450	APA	2.5^{n} (0.31)
6	CS1450	polished	2.7^{n} (0.47)
6	CS1530	polished	5.2^{m} (0.47)
6	RS1530	polished	9.0^{j} (0.66)
6	CS1450	APA	3.6^{n} (0.62)
12	CS1450	polished	5.4^{lm} (0.72)
12	CS1530	polished	6.7^{kl} (0.64)
12	RS1530	polished	13.4^{h} (1.37)
12	CS1450	APA	3.5^{n} (0.68)
18	CS1450	polished	8.4^{j} (0.87)
18	CS1530	polished	8.2^{jk} (0.49)
18	RS1530	polished	18.8^{f} (1.22)
18	CS1450	APA	4.0^{mn} (0.61)
24	CS1450	polished	11.9^{i} (1.22)
24	CS1530	polished	9.3^{j} (0.71)
24	RS1530	polished	23.3^{e} (0.85)
24	CS1450	APA	4.1^{mn} (0.61)
30	CS1450	polished	15.5^{g} (2.02)
30	RS1530	polished	28.2^{d} (0.92)
36	CS1450	polished	19.5^{f} (1.76)
36	RS1530	polished	32.6^{c} (1.10)
42	CS1450	polished	21.7^{e} (2.48)
42	RS1530	polished	36.9^{b} (0.84)
48	CS1450	polished	27.3^{d} (0.49)
48	RS1530	polished	39.7^{a} (0.80)

Statistical analysis with multivariate linear regression determined that ageing, sintering regimen and surface treatment had statistically significant effects on X_m. There were two statistically significant interactions: between ageing and sintering regimen ($p<0.0001$), and between ageing and surface treatment ($p<0.0001$). This indicated that materials prepared with different sintering regimens differed in their ageing behaviour, as did groups that were polished or airborne-particle abraded. To estimate the actual degradation rates, further statistical analysis was conducted separately for each of the four groups and the results are presented in Table 3.

Table 3

Separate linear regression analyses of the X_m progression during ageing *in vivo*. Estimated values are expressed in % change per month.

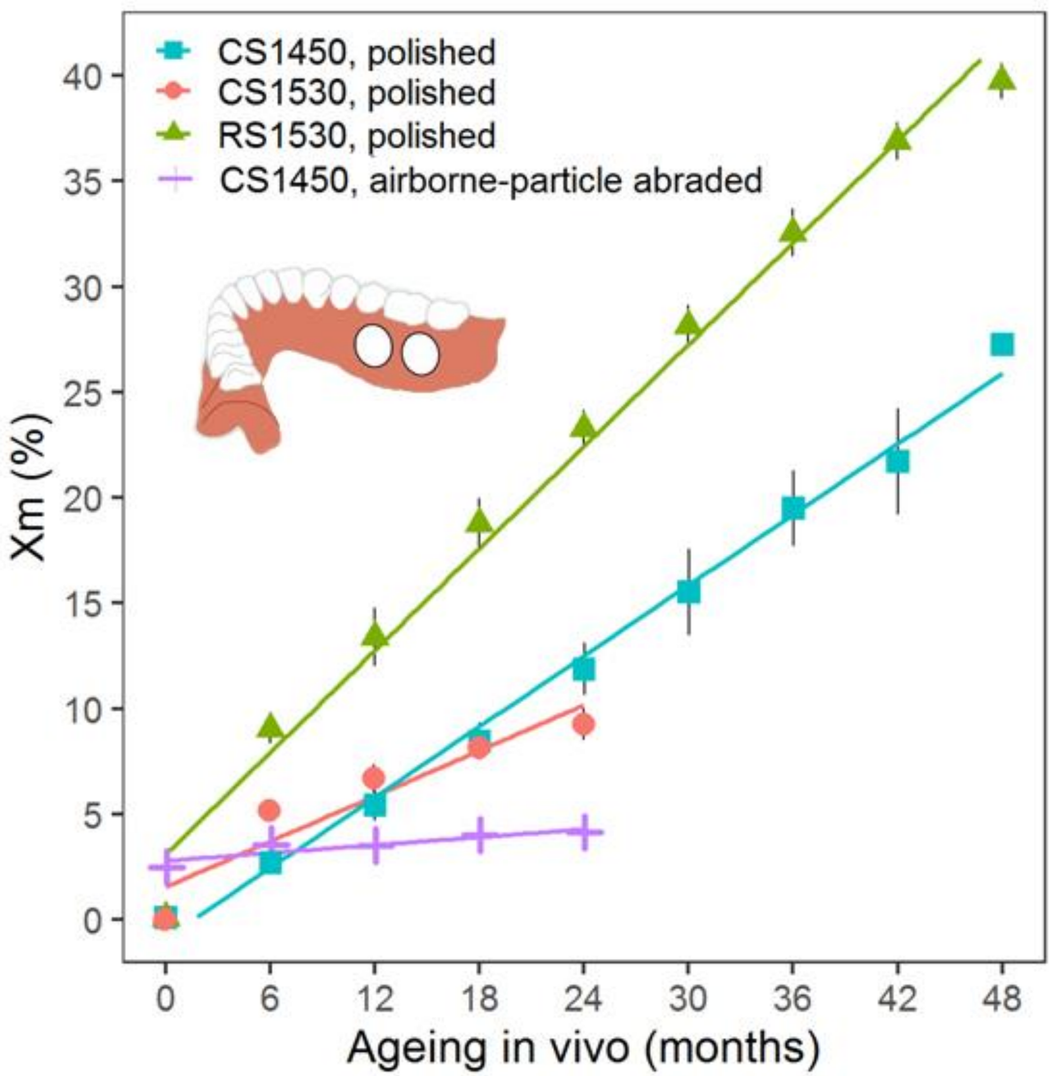
	Estimate	Standard error	*t*-value	*p*-value
CS1450, polished (F=2225 on 1 and 72 degrees of freedom, $p<0.0001$, adjusted $R^2=0.97$)				
Intercept	-0.68	0.28	-2.462	0.0162
Slope	0.54	0.01	47.175	<0.0001
CS1530, polished (F=294.4 on 1 and 49 degrees of freedom, $p<0.0001$, adjusted $R^2=0.85$)				
Intercept	1.47	0.29	5.044	<0.0001
Slope	0.37	0.02	17.175	<0.0001
RS1530, polished (F=3000 on 1 and 65 degrees of freedom, $p<0.0001$, adjusted $R^2=0.98$)				
Intercept	2.74	0.35	7.941	<0.0001
Slope	0.83	0.02	54.773	<0.0001
CS1450, airborne-particle abraded (F=34.47 on 1 and 44 degrees of freedom, $p<0.0001$, adjusted $R^2=0.43$)				
Intercept	2.79	0.15	18.541	<0.0001
Slope	0.07	0.01	5.871	<0.0001

Statistically significant ($p<0.0001$), upward linear trends with exposure time were detected in all groups, but the rate was one order of magnitude faster in polished specimens compared to airborne-particle abraded specimens. Ageing changes were most pronounced in the rapid-sintered material RS1530, where the estimated X_m

increase was 0.83% per month. Polished specimens prepared with conventional sintering aged at a rate of 0.54% per month for material CS1450 and at 0.37% per month for material CS1530. Airborne-particle abraded specimens exhibited an X_m increase of only 0.07% per month. Ageing trends are graphically presented in Fig. 3. While the airborne-particle abraded specimens exhibited a larger initial X_m, the degradation rate of polished specimens was significantly faster.

Fig. 3

Graphical representation of the X_m progression when ceramic specimens in complete dentures were exposed to the oral environment *in vivo*. Data points are shown as mean values ± standard deviations.

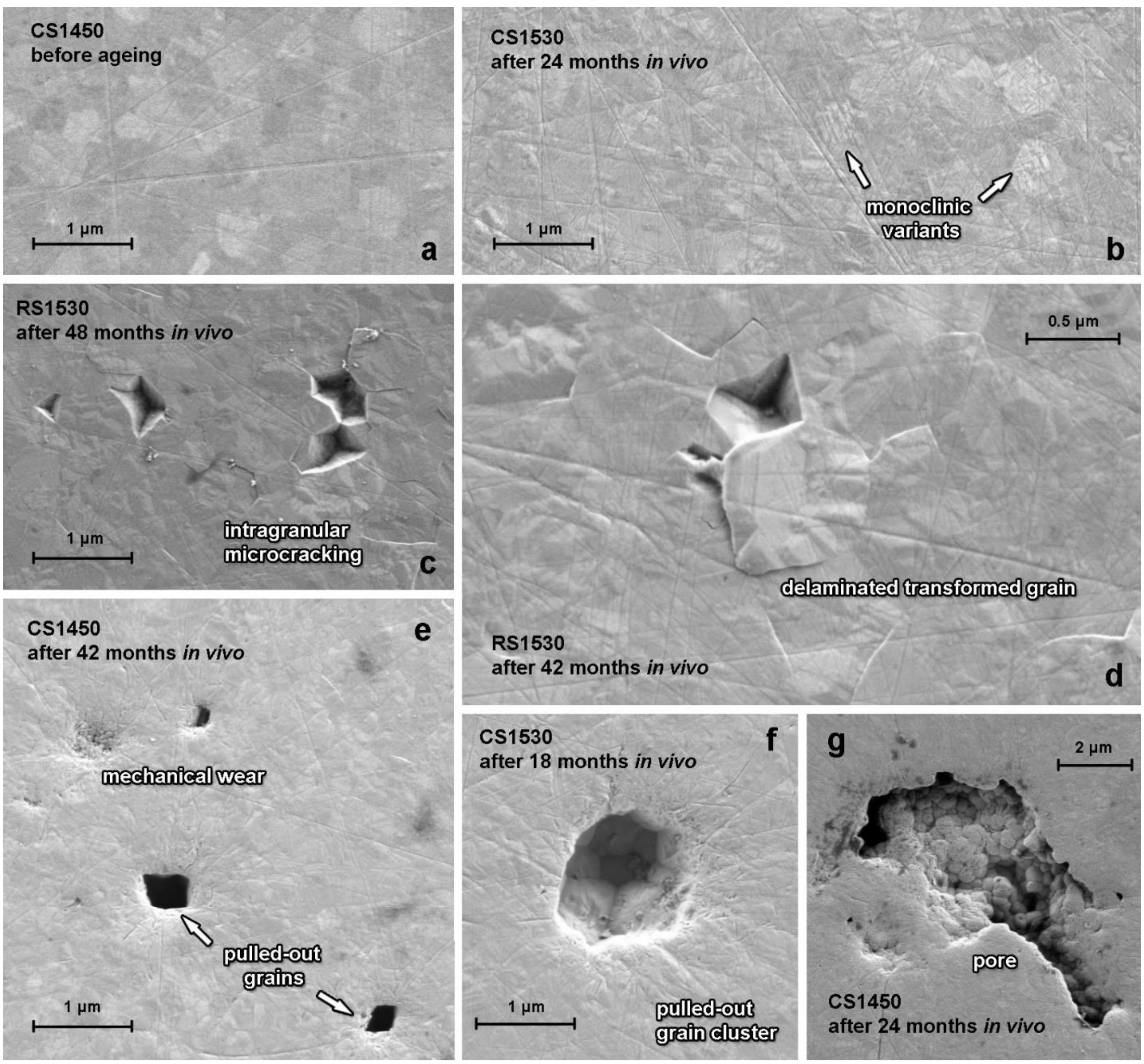


3.3 Surface morphology

During the course of the study, early signs of degradation of the polished surfaces were observed with the microscopy methods. Representative SEM micrographs are displayed in Fig. 4.

Fig. 4

SEM micrographs of polished surfaces before (a) and after ageing *in vivo* (b-g). Initial surface changes consisted of raised regions with transformed monoclinic variants (b). Deterioration progressed with the formation of intergranular microcracks and sloughing of the topmost layer, which was most evident in ceramics following rapid sintering (c, d). Gross mechanical wear, pulled-out grains (e, f) and exposed pores (g) were also discernible on the surfaces.



On non-aged specimens, residual scratches from polishing and the differences in contrast due to random orientations of the underlying grains were the only discernible surface features (Fig. 4a). After *in vivo* exposure, monoclinic variants and intragranular microcracks consistent with ageing-related *t-m* transformation were apparent on the surface (Fig. 4b). More conspicuous changes included individual pulled-out grains and signs of mechanical wear (Fig. 4c-f). The remaining pores, which were either pre-existing on the surface before polishing, or exposed during it, were also discernible (Fig. 4g).

Similar features were also observed with the AFM (Fig. 5). Initially, only scratches associated with polishing were present (Fig. 5a), but after *in vivo* exposure, surface uplifts consistent with monoclinic transformation began to emerge (Fig. 5b-d). After *in vivo* ageing, mean roughness increased from 1.8 nm to up to 5.8 nm, with rapid sintering exhibiting the highest mean values.

Fig. 5

AFM analysis of polished surfaces before (a) and after ageing *in vivo* (b, c, d).

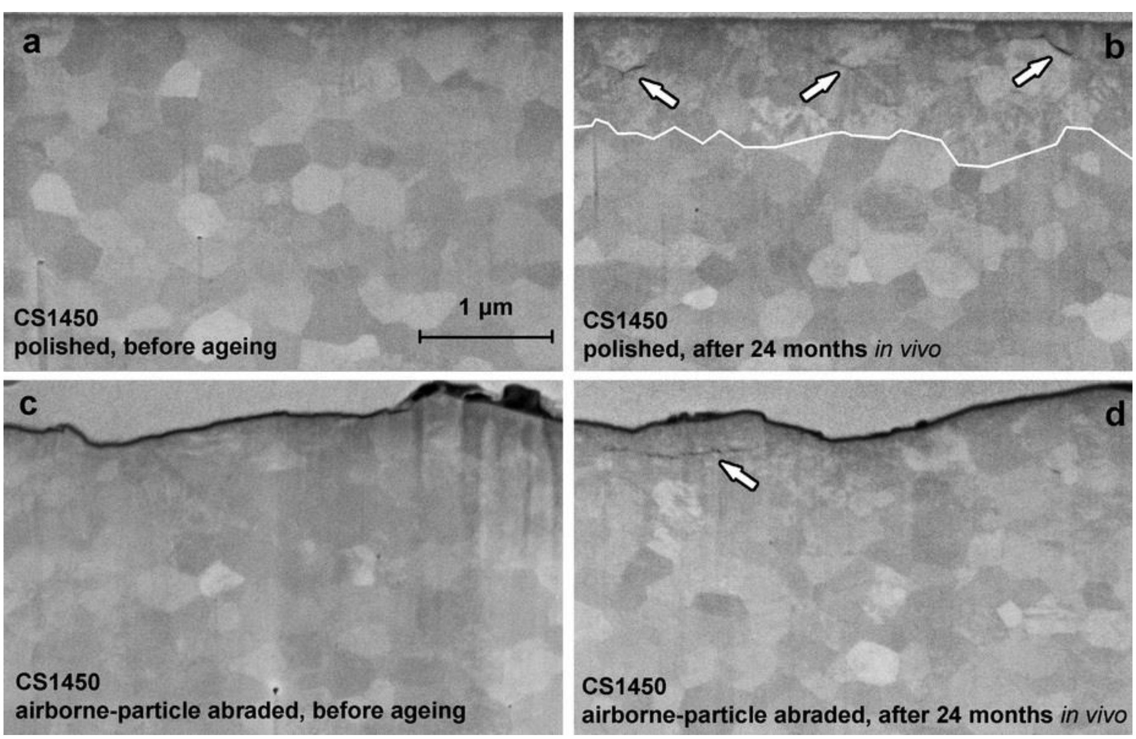
In the case of airborne-particle abraded specimens, ageing-related surface changes were not clearly observable. The SEM examination revealed a varied surface topography with sharp cutting grooves, cracks and broken grains. The surface was heavily plastically deformed to begin with and did not noticeably degrade after 24 months *in vivo*.

3.4 Transformed zone depth

On FIB-prepared cross-sections, direct observation of the immediate subsurface layer not masked with processing artifacts was possible (Fig. 6). Non-aged polished specimens exhibited a uniform microstructure with clearly discernible grains not showing any signs of *t-m* transformation (Fig. 6a). In material CS1450 aged for 24 months *in vivo*, ageing-related *t-m* transformation penetrated approximately 1 μm under the polished surface, as indicated by the white line (Fig. 6b). The transformed layer was about three layers of grains thick with few short intragranular microcracks appearing in the upper part and indicated by black arrows. In contrast, an airborne-particle abraded surface was heavily plastically deformed, but the underlying grains did not exhibit a sharply defined transformation front (Fig. 6c). Instead, they were distinctly altered, with cleavages and shadows resembling multiple domains. No clear signs of ageing-related *t-m* transformation were evident after 24 months *in vivo* (Fig. 6d). A transgranular crack spanning several grains in the immediate subsurface layer is indicated by a black arrow.

Fig. 6

FIB cross-sections representing the immediate subsurface region of polished (a, b) and airborne-particle abraded CS1450 specimens (c, d) before and after 24 months *in vivo*. The white line in (b) indicates the degraded layer under the polished surface after exposure *in vivo*. Microcracks are indicated by white arrows.



4. Discussion

This study has shown that highly-translucent zirconia with reduced alumina content is susceptible to LTD when exposed to the oral cavity. An important finding was that rapid sintering increases polished zirconia ceramics' susceptibility to LTD. The difference was observable even when the same maximum temperature of 1530°C was used in conventional and rapid sintering. This points to an underlying difference in phase composition and microstructure (Fig. 1) that evolves specifically during faster sintering cycles (Table 1). Even though rapid sintering is more time efficient, the obtained microstructure in our study was coarser (Fig. 1b, c) and exhibited more pronounced phase partitioning (Fig. 2b, c). Crystallite-ordered coalescence contributing to grain growth and coarser microstructures was previously shown to occur during rapid sintering in 3Y-TZP [6], as well as in other ceramic systems [14][15][16]. It is assumed that ordered coalescence of intergranular crystallite domains will also shorten the distances needed for lattice diffusion, contributing to enhanced phase partitioning. Consequently, a higher amount of untransformable yttria-rich *t'*-ZrO2 phase is coupled with yttria-lean tetragonal phase which is more susceptible towards LTD [17]. Caution when employing rapid sintering strategies is thus needed.

For materials prepared with conventional sintering, the speed of ageing was comparable to the previously investigated classic, opaque zirconia ceramics, where the X_m rose to 11-13% after 24 months *in vivo* [ref in vivo paper 1]. In the present study, the values for highly-translucent zirconia ceramics ranged between 9% and 12% for the same time period. Considering that the grains in our previous study were coarser (around 0.5 µm compared to around 0.3 µm in this study), this indicates that highly-translucent zirconia ceramics are more susceptible to ageing than the traditional, biomedical 3Y-TZP version. When rapid sintering was employed, the ageing rate was even faster: X_m was 23% after 24 months and almost 40% after 48 months *in vivo.* An important thing to note is the clear linearity observed in this study. In the first 6 months, a somewhat higher increase in X_m occurred in groups sintered at the higher temperature of 1530°C. Later on, the linear growth was uniformly linear and did not appear to decelerate with time. This *in vivo* ageing behaviour differs from non-linearity we previously observed in biomedical zirconia ceramics [ref in vivo paper 1]. A possible underlying reason could be the inherently higher sensitivity of the highly-translucent zirconia ceramics to ageing. Notably, however, the material CS1530 did not exhibit a clearly faster ageing rate compared to CS1450. This was unexpected, but it is likely that the differences in sintering temperatures and grain sizes between these two conventionally-sintered materials were not extensive enough for clear separation. It should also be mentioned that a much shorter *in vivo* study of the same highly-translucent material (TZ-PX-242-A, 1450°C 2h) reported the X_m of 7.8% after just 100 days [18]. This appears several times faster than our results for conventional sintering. The authors used different specimen geometries and a different polishing protocol prior to sintering, but since they only reported one time point, it is impossible to make any deductions about the underlying ageing kinetics [18].

However, and as previously discussed, the material lifetime prediction cannot be made on the basis of the velocity of the transformation alone [19]. One of the crucial aspects of LTD is the deterioration of the surface properties and it is well known that ageing is associated with microcracking, roughening and a decrease in hardness and stiffness [20][21]. This clinical study provides direct evidence that polished surfaces do change during exposure *in vivo*, although the observed changes were minor. Microcracks due to the volumetric expansion associated with the *t-m* phase transformation were present (Fig. 6c, d), but the associated nanoscale roughening was one order in magnitude lower than the clinically relevant 5 µm-gap between primary and secondary crowns used to support removable dentures [22]. Even in rapid sintering, ageing-related topographical changes such as individual pulled-out grains and mechanical wear, were not extensive enough to represent clinical issues. Pores on the surface (Fig. 4g), are, however, of potentially larger clinical concern. While not caused by ageing itself, pores represent both surface flaws and paths for moisture access to the inner parts of the material. The presence of these intragranular pores is likely associated with the 3Y-TZP spray-dried granules which have not completely collapsed during the final stages of powder pressing [23][24]. In addition to that, rapid sintering was previously reported to result in greater porosity due to incomplete grain fusing and growth evolution during the fast sintering cycles [8]. While polishing is commonly seen as a desirable method eliminating surface irregularities, new porous regions can always be uncovered as the pseudo-grain (spray dried grain) structure with weaker boundaries is present throughout the volume of the material. Even though the ageing process is slow, its extent might be importantly influenced by the presence of such flaws.

In contrast to polished surfaces, the surface morphology following airborne-particle abrasion was extensively damaged and did not noticeably degrade during 24 months *in vivo*. The absence of monoclinic variants on the immediate surface might be related to its composition of shattered nano-sized grains, which are thermodynamically more stable due to their small size and therefore not susceptible to transformation. In addition, constraints due to residual stresses hinder the ageing process, as visible in Figs. 6c and d. These *in vivo* results therefore corroborate well with *in vitro* findings, showing that airborne-particle abraded surfaces can be highly ageing-resistant regardless of severe plastic deformation [25]. It needs to be emphasized, however, that residual stresses might be relaxed during thermal treatments which may be applied for finalizing the monolithic 3Y-TZP restorations through colouring and glazing. Annealing is known to affect the microstructure and stress patterns [26][27][28] and might also affect the susceptibility to ageing.

Still, the fact that no major surface degradation was discernible neither in polished nor in airborne-particle abraded surfaces suggests that ageing *in vivo* is not likely to represent a potential clinical threat. Also, however, the time span of only 48 months offers a limited - albeit useful - insight into the ageing process occurring during clinical service, where dental restorations are expected to last a decade or more. Efforts to obtain reliable *in vivo* ageing data for longer time spans with our methodology are restricted by ethical considerations and elderly patient drop-outs due to illness. Similar to our previous *in vivo* study [ref in vivo paper 1], another limitation is that the experimental protocol did not consider any mechanical loading which invariably occurs during clinical service. Wear and ageing were shown to have synergistic effects [29], meaning that cyclic masticatory forces and other mechanical stresses might accelerate micro-crack growth and further increase the wear rate. Previously this was apparent for a number of failed hip prostheses with crater-like surface defects releasing wear debris into the synovial cavity

[30][31]. While it must be emphasized that such degradation is not the norm and was the result of an improper sintering technique [30], improper use of novel sintering protocols could potentially increase such risk. It has been shown that rapid sintering programs affect different brands of zirconia differently, and they should only be used in accordance with the manufacturer's instructions [8].

While ageing renders the surface more sensitive to damage, the actual effects on fracture behaviour and bulk mechanical strength remain the object of future studies. As suggested previously, strength measured by flexure might not be sensitive to a degraded surface layer even with a substantial thickness, possibly because the microcracks are parallel to the surface and not stressed in mode 1 during flexure testing [25]. This resistance to loading is not necessarily comparable to oral conditions, where the geometries, stress patterns and chemical environment are much more complex. While Borges et al. did not detect any decrease in mechanical properties after 100 days *in vivo* [18], Miragaya et al. reported a substantial mechanical weakening after just 60 days of intermittent oral exposure and in the absence of loading [32]. Uniaxial flexural strengths decreased as much as 30% and the corresponding monoclinic phase content was only 7.7%, but the authors suggested that acidic conditions might harm the mechanical properties and aggravate the degradation even in the absence of *t-m* transformation [32]. More research is needed to support this suggestion and it would also be prudent to consider other possible explanations, for example the reliability of uniaxial test results in light of possible edge flaws introduced during the handling of thin, beam-shaped specimens [33]. Edge flaws on thin crown margins were shown to be a common reason for failure of all-ceramic crowns [34][34][35]. These crown margin regions experience considerable hoop stresses during mastication, but ageing may incite spontaneous fracture even in the absence of external loading [23]. Very thin monolithic dental restorations might also be more susceptible to such failure.

5. Conclusion

While this clinical study shows promising results on the *in vivo* ageing stability of highly-translucent 3Y-TZP ceramics, future *in vivo* study designs including occlusal loading would further explore the ageing phenomenon and yield more robust results on the true longevity of 3Y-TZP ceramics in the oral environment. Our findings also support a cautious approach when attempting to streamline the workflows with rapid sintering protocols. The differences between conventional and rapid sintering were clearly observable in this study and even though they did not pose a reason for clinical concern, the possible implications for hydrothermal stability should not be overlooked.

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