

## Bioactive glass coating on zirconia by vacuum sol-dipping method

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In order to the preparation of biodegradable, bioactive and strongly adhered coating layer to the bioinert zirconia substrate, a bioactive glass (BG) was successfully coated on the zirconia plates. To achieve this goal, the zirconia plates dipped into the 45S5 BG sol in the vacuum chamber (vacuum sol-dipping method) followed by sintering to fabricate a strongly adhered BG coating on the zirconia plates. The parameters such as surface morphology and BG coating coverage ability on the zirconia plates have been assessed before and after coating with 45S5 BG. Phase structure of the BG coating based on the X-ray diffraction (XRD) result could be indexed as  $\text{Na}_2\text{Ca}_4(\text{Si}_6\text{O}_{18})$ . The interfacial adhesive strength between the zirconia substrate and BG coating layer was higher than the measured adhesive strength ( $55 \pm 7$  MPa). The viability results approved the satisfying conclusion for the offered coating method on the zirconia substrates.

**Keywords:** Zirconia, Bioactive glass, Sol, Coating

### INTRODUCTION

The introduction of dental implants based on the concept of osseointegration has provided a reliable option for elderly people to replace missing teeth. The emphasis on aesthetics has resulted in a quest for metal-free alternative materials for fabrication of implants, as a result, zirconia has been proposed as an alternative material<sup>1,2</sup>.

Zirconium dioxide,  $\text{ZrO}_2$  (zirconia) especially, yttria doped zirconia, 3Y-TZP, standing for 3 mol% yttria doped zirconia tetragonal polycrystals are often offered as the alternative to titanium<sup>3</sup>. Zirconia is one of the most promising bio-ceramics that used as a dental implant owing its very high mechanical properties for example measured average load-bearing capacities of 755 N for zirconia restorations<sup>4</sup> and comparable osseointegration<sup>5</sup>, translucency<sup>6</sup>, radiopaque<sup>7</sup> bacterial colonization<sup>8</sup> and biocompatibility<sup>9,10</sup> with titanium. Besides because of zirconia tooth-like color its aesthetics improved compared with other metallic dental implants<sup>11</sup>. Therefore, zirconia dental implants gaining more attention in recent years. First vitallium oral endosteal implants coated with zirconia was used on 1975<sup>12</sup>. Akagawa *et al.* used the zirconia for endosseous dental implant *in vivo* on 1993<sup>5</sup>. Animal experiment showed satisfactory osseointegration and good soft and hard tissue biocompatibility of zirconia implants after a 4-week healing period<sup>13</sup>. Interestingly these days it is possible to adjust the zirconia implants color with a different part of applied areas<sup>14</sup> which is an enormous advantage for the zirconia ceramics.

A healing time of 3 to 6 months is recommended for bio-inert implants. To reduce the healing time duration several methods recommended such as coating by a bioactive ceramics<sup>15-17</sup>. However zirconia is considered as a bio-inert ceramic<sup>18</sup> and to have surface with bio-active property, the surface treatments is required<sup>19</sup>. A bioactive glass (BG) is a well-known, degradable bioactive ceramic material<sup>20,21</sup>. Usage of BGs has been enlarged in biomedical applications. The use of BG as coatings on zirconia is proposed in order to combine the mechanical properties of this high-strength material with the biological properties of the bioactive coatings<sup>22</sup>. Ceramic 45S5 BG (45% $\text{SiO}_2$ , 24.5% $\text{Na}_2\text{O}$ , 24.5% $\text{CaO}$ , and 6% $\text{P}_2\text{O}_5$  by weight) have gained researchers attention as a functional biomaterial due to its bioactive surface and osseointegration ability. It has been approved that BG 45S5 can heal and repair bone damages<sup>23,24</sup>. 45S5 BG could be produced by different techniques with different crystallinity such as crystalline melt-cast, amorphous melt-cast and crystalline sol-gel methods<sup>25</sup>. Hench *et al.* reported that partially crystallized glass-ceramic accelerated the ossification process and crystallization of 45S5 BG will not inhibit apatite formation on the coating layer<sup>23</sup>. On the other hand, The BG crystallinity could improve BG mechanical property and that is not playing role in directing protein adsorption<sup>25</sup>.

Zirconia substrate has been coated with melted BG powder produced by conventional or sol-gel derived methods previously<sup>19,22,26,27</sup>. Dip coating of zirconia in the sol-gel solution followed by sintering was reported by Matsuda *et al.*<sup>28</sup> and fabrication of the 45S5 BG coating by dip coating method in the sol-gel solution and its apatite formation ability in the simulated body fluid (SBF) on Mg substrates are reported previously<sup>29,30</sup>.

Color figures can be viewed in the online issue, which is available at J-STAGE.

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In the present study the 45S5 BG coating layer fabricated by vacuum-assisted dipping method<sup>31)</sup> on the zirconia surface which has been named vacuum sol-dipping method. This technique has several advantages such as fast coating procedure, suitable coverage ability, sol impregnation, strong adhesion of BG to the substrate surface and fabrication of BG in low temperature. The important issue is that the coating phase structure after sintering is same with previous studies report. It is also an adoptive method to produce eco-friendly coatings<sup>32)</sup>.

The objective of this study is the assessment of the zirconia surface coated by 45S5 BG vacuum sol-dipping method. Thus in this study, pressed and sintered zirconia substrates BG sol coated on the zirconia substrates by vacuum sol-dipping method and sintered at different temperatures. The morphology, crystal structure of the coated layer and the adhesive strength of the coating layer and *in vitro* cell responses on the zirconia substrate before and after coating were investigated.

## MATERIALS AND METHODS

### Zirconia substrate preparation

Zirconia powder, TZ-3Y-E grade (TOSOH, Tokyo, Japan), with the composition of 97 mol%  $ZrO_2$  stabilized with 3 mol%  $Y_2O_3$  was used to fabricate the substrates. The zirconia tablets were made by biaxial pressing of zirconia powder under  $9.8 \times 10^3$  N force in the stainless steel molds. The pressed tablets were sintered at  $1,400^\circ C$  for 3 h for zirconia substrates fabrication. The zirconia substrates with 1 mm in the thickness and 10 mm in diameter for cell study and 1.2 mm in the thickness and 13 mm in diameter for mechanical property test were used. Prepared zirconia discs' surface morphology was divided into two types; as-sintered and polished by diamond polish paper ( $n=10$ ).

### BG preparation

The 45S5 BG sol made by sol-gel method according to the following procedure. 3.26 mL of 69% nitric acid was added to 47.6 mL of deionized water to create a 1 M nitric acid solution. 0.15 mol (33.5 mL) tetraethylorthosilicate (TEOS, Wako, Tokyo, Japan) was added to the prepared 1 M nitric acid for a final  $H_2O$ :TEOS molar ratio equal to 18. The precursor hydrolysis was performed for 60 min with stirring. The following reagents were allowed to react for 45 min during stirring in the following sequence: 0.017 mol (2.9 mL) triethylphosphate (TEP, Wako), 0.085 mol (20.13 g) calcium nitrate tetrahydrate (Wako), and 0.16 mol (13.52 g) sodium nitrate (Wako)<sup>25)</sup> (shown in Fig. 1).

### Coating method

The polished and as-sintered zirconia discs were vacuum dipped in BG sol 1 to 10 times under the 100 mbar pressure for 60 s and dried at  $60^\circ C$  for 1 h. The dried substrates sintered at  $900^\circ C$  to  $1,200^\circ C$  for 1 h in a programmable furnace with heating rate of  $10^\circ C/min$ , to melt the BG on the surface ( $n=10$ ). Fully coverage ability of the zirconia surface with BG coating and different BG

thicknesses vacuum sol-dipping was investigated by comparing the results using trial and error method.

The coated samples without preparing condition specification were fabricated by one-time BG vacuum sol-dipping of as-sintered zirconia disc followed by sintering at  $1,200^\circ C$  for 1 h.

### Adhesion test

The adhesive strength of the BG coating layer to the zirconia substrate was measured by using an adhesion test apparatus (ROMULUS IV, Epoxy Resin Adhesive, Quad Group, Spokane, WA, USA). The adhesion test schematic and the fractured sample image were shown in Fig. 2. Commercial rivet-shape stud-pin with 2.7 mm diameter and a reinforced epoxy resin (measurable adhesive strength around 70 MPa) layer adhesive with  $50 \mu m$  in thickness on top was attached to the BG coating layer and fixed by a mounting clip. To confirm hardening of the epoxy resin it was heated in an oven at  $150^\circ C$  for 1 h and then cooled in oven to room temperature. The attached stud-pin was pulled with the force rate of 19.61 N/s by the universal testing machine (model 5566S, Instron, Canton, MA, USA). The adhesive strength of the coating layer was determined from the maximum recorded-load. The average adhesive strength and their standard deviation (SD) were measured for ten samples.

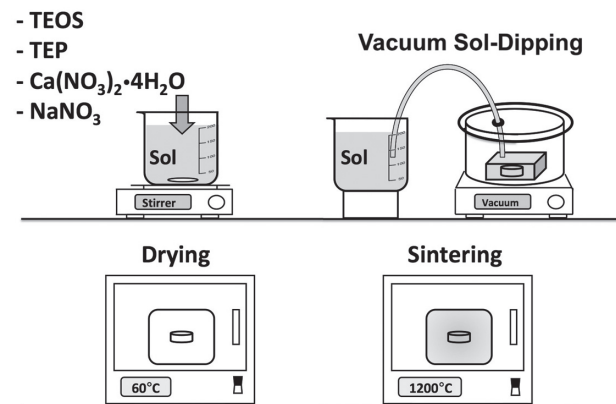


Fig. 1 Schematic image of the procedure for BG coating on the zirconia.

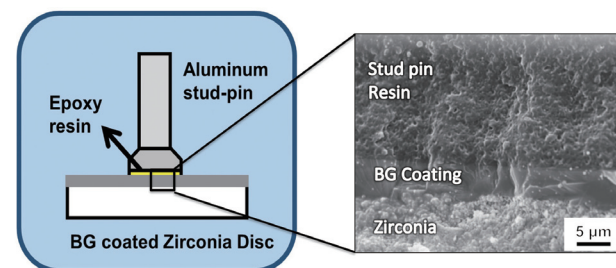


Fig. 2 Schematic image and fractography of the adhesion test zirconia with BG coating.

### Biaxial flexural strength

Flexural properties of the zirconia specimens (1.2 mm in thickness and 13 mm in the diameter) before and after BG coating were examined by biaxial flexural test in accordance with ISO 6872:1995. A universal testing machine (Instron) was used at a crosshead speed 1.0 mm/min. The biaxial flexural test was done at room temperature with a 10.0 mm support circle and a 1.2 mm piston diameter. Ten specimens were examined for each test.

### Characterizations

The coated samples morphological evaluation and fractography were investigated by scanning electron microscopy (SEM: JCM-6000 Plus, JEOL, Tokyo, Japan) and field emission scanning electron microscopy (FE-SEM: JSM-7500 FAM, JEOL) at 15kV of accelerating voltage after the gold sputtering. The crystals image was taken by using a STEM-HAADF (JEM-ARM200F, 200 kV, JEOL). X-ray diffraction (XRD: SmartLab, RIGAKU, Tokyo, Japan) with the Cu-K $\alpha$  ( $\lambda=1.5405 \text{ \AA}$ ) at 40 kV and 40 mA was used to investigate the phase of the untreated and coated specimens with BG coating layer. Chemical composition of the prepared BG in this study was investigated using X-ray fluorescence spectroscopy-energy dispersive X-ray spectrometry (XRF, EDX-800HS, Shimadzu, Kyoto, Japan).

### Cell morphology and viability

The osteoblast cell line MC3T3-E1 (Riken Cell Bank, Tokyo, Japan) was used to perform *in-vitro* study. The cells cultured in MEM Alpha Medium (MEM Alpha; GIBCO, Invitrogen™, Grand Island, NY, USA) containing 10% fetal bovine serum (GIBCO) under a humidified 5% CO<sub>2</sub> air atmosphere at 37°C. The culture medium

was changed every 2 days until the cells confluence. Disc-shaped zirconia specimens, untreated and sol-vacuum BG coated substrates (10 mm diameter and 1 mm thickness) were autoclave-sterilized for 15 min and placed in the 48-well polystyrene plates (Costar, 48 Well Cell Culture Cluster; Corning, Cambridge, MA, USA). The zirconia specimens placed in the 48 well dishes and disseminated 10,000 cells each and cultured.

For the cell morphology the medium for the 3 h cell cultured specimens were aspirated from the wells, then the cells were gently washed by a phosphate buffer solution (PBS) solution. The 2.5% formaldehyde (Wako) in PBS was used to fix the cells on the specimens at 4°C for 2 h. The cells dehydrated in a graded series of ethanol, followed by drying at room temperature. The gold sputtering before SEM observation was next step for photography.

For cell viability the samples with 2, 4 and 6 days cell culture were used. The cells mitochondrial activity was detected using MTS assay kit (CellTiter 96 Aqueous One Solution, Promega, Madison, WI, USA), ( $n=5/\text{group}$ ). After 3 h incubation with MTS assay at 37°C atmosphere of 5% CO<sub>2</sub>, the solution was taken from all wells and 120  $\mu\text{L}$  of the solution was transferred into each well of 96-well plates, and the absorbance was measured using a plate reader (Multiskan FC, Thermo Fisher Scientific) at 490 nm.

Statistical analysis was performed using one-way of variance ANOVA with the Tukey *post hoc*, (SPSS, IBM, Chicago, IL, USA) ( $*p \leq 0.05$ ,  $**p \leq 0.01$ ).

## RESULTS

### BG coating surface coverage

Figure 3 shows the FE-SEM images to evaluate the

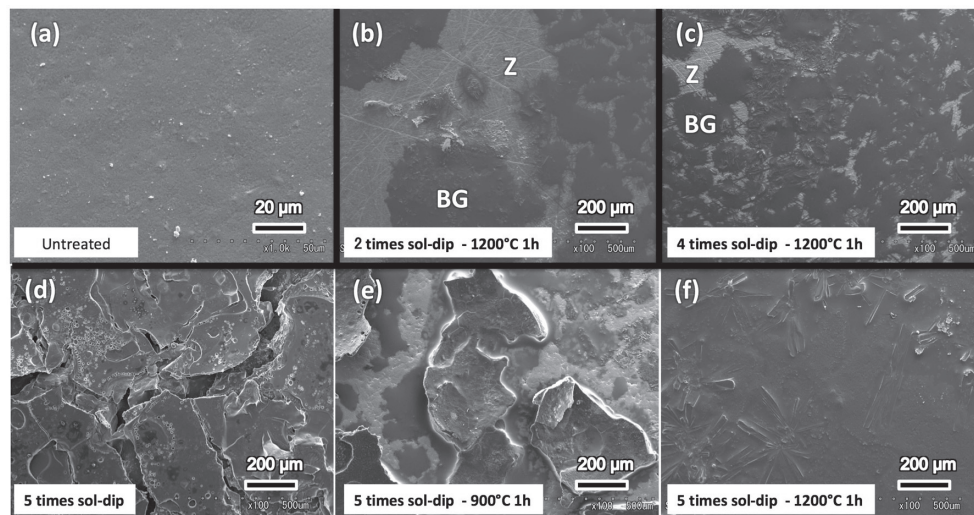


Fig. 3 FE-SEM images of the polished zirconia samples after 0 (a), 2 (b), 4 (c) and 5 times (d) BG coating and also the samples with 5 times BG coating sintered at 900°C (e) 1,200°C (f) for 1 h.



effect of vacuum sol-dipping numbers and sintering temperatures of the BG coating surface coverage on the polished zirconia samples. The polished sample after 2 times (Fig. 3b) and even 4 times (Fig. 3c) BG coatings and sintering at 1,200°C for 1 h zirconia substrates still have some area without BG coating. Figure 3d shows the polished zirconia After 5 times coating and dry before sintering. The zirconia substrates surface after 5 times dipping in sol-vacuum system and sintering at 900°C for 1 h was shown in the Fig. 3e. The BG layer melted partially or softened and could not cover the surface completely. Figure 3f confirmed that after 5 times coating and sintering of coated substrates at 1,200°C for 1 h the surface covered by melted BG completely.

Figure 4 shows the as-sintered zirconia substrates after sintering has rough surface, which BG could cover its surface after only one time coating followed by sintering at 1,200°C for 1 h.

#### BG coating thickness

In the SEM images of the BG coated zirconia fractography, the thickness for the 1 time BG coating at 1,200°C for 1 h was measured around 5  $\mu\text{m}$  (Fig. 5a). By increasing the coating numbers to 5 and 10 times the final sintered coating thickness reach to around 35  $\mu\text{m}$  (Fig. 5b) and 45  $\mu\text{m}$  (Fig. 5c), respectively.

#### BG chemical composition and phase structure

The EDX result for the chemical composition of the

prepared BG in this study by weight was: 43.6%  $\text{SiO}_2$ , 26.0%  $\text{CaO}$ , 25.6%  $\text{Na}_2\text{O}$  and 4.8%  $\text{P}_2\text{O}_5$ . The XRD patterns were used to verify the structure phase of the surface of the specimens before and after BG coating. Regarding the XRD patterns, shown in Fig. 6 the phases before and after BG coating were obviously different. The XRD peaks assigned to zirconia for non-coated substrates and  $\text{Na}_4\text{Ca}_4(\text{Si}_6\text{O}_{18})$  for coated zirconia with BG second crystalline phase  $\text{Na}_2\text{Ca}_4(\text{PO}_4)_2\text{SiO}_4$  also has been found which is reported previously in the other studies<sup>33)</sup>. The zirconia fully covered after coating with BG therefore zirconia peak was disappeared after coating. TEM image of the BG coating also confirms the crystalline structure formation on the zirconia surface after sintering at 1,200°C for 1 h (shown in Fig. 6).

#### Adhesive strength

The measured adhesive strength between the BG coating layer and zirconia specimen, taken from the maximum load, was  $55 \pm 7$  MPa for the zirconia obtained by the BG coating at 1,200°C for 1 h. Figure 7 shows SEM fractography images of the interface after the adhesion test. The results reveal that the fracture was mixture of broken resin and BG coating, which were detected after adhesion test on the substrate surface.

#### Biaxial flexural strength

The mean biaxial flexural strength  $\pm$ SD for untreated and BG coated zirconia were  $718 \pm 98$  and  $680 \pm 56$

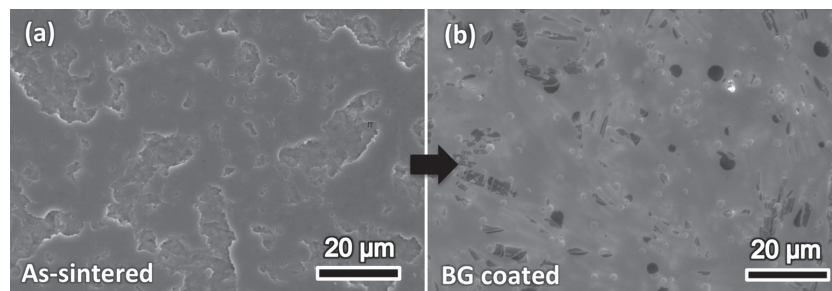


Fig. 4 SEM images of the as-sintered zirconia plates before (a) and after (b) 1 time BG coating and sintering at 1,200°C 1 h.

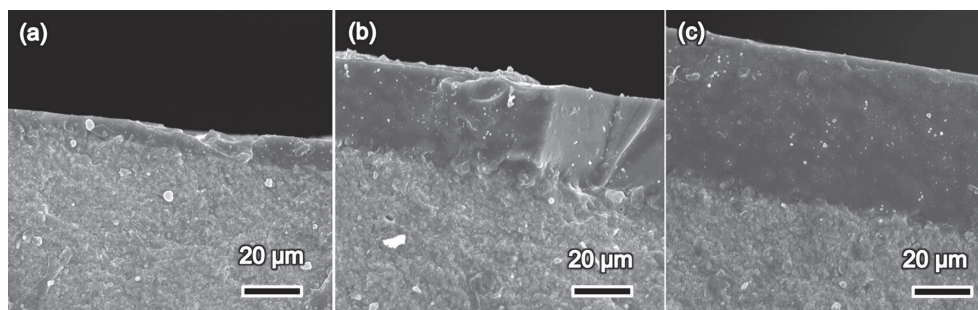


Fig. 5 SEM images of the zirconia sample with BG coating for 1 (a), 5 (b) and 10 times (c) and sintered at 1,200°C for 1 h.

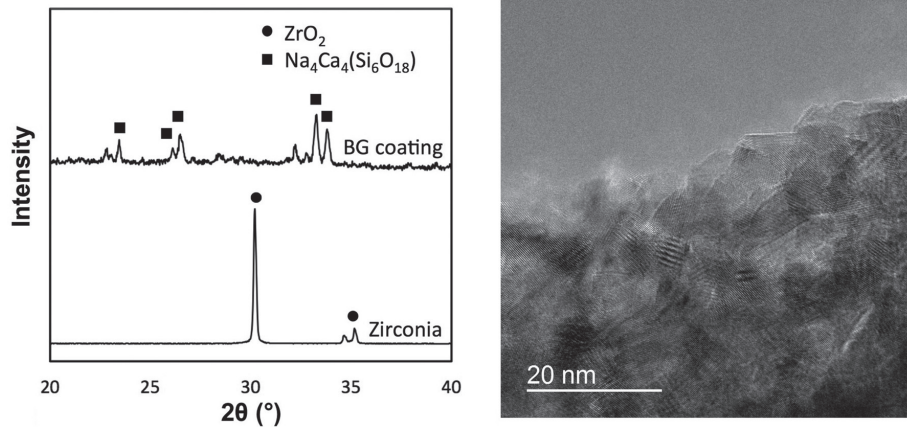


Fig. 6 XRD patterns of the zirconia sample before and after BG coating and TEM image for the coating layer.

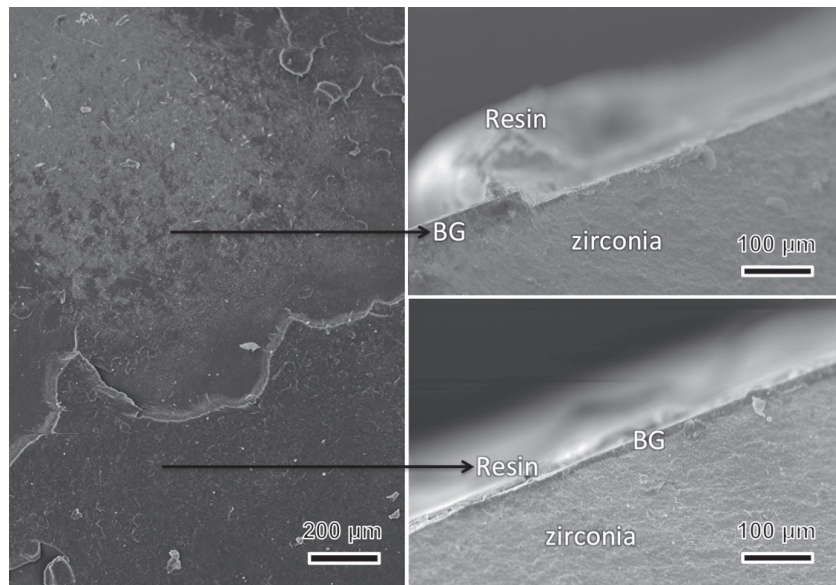


Fig. 7 SEM fractography images of the BG coated zirconia samples adhesion test.

MPa, respectively. The flexural strength before and after one-time BG coating did not significantly differ ( $p$ -value=0.527).

#### Cell response

Figure 8 shows the morphology of MC3T3-E1 cells cultured on each sample after 3 h and 2, 4 and 6 days culture the cells. Cells were extended on the coating layer after 3 h and 2, 4 and 6 days incubation. The SEM images for cell morphology were mentioned that cells were spread on the BG coated sample surface and the surface almost covered by extracellular matrix and the extra cellular matrix speared between cells in the BG coated samples. Also the SEM images mentioned that the cells number increased by time for all samples before

and after coating especially for 6 days culture sample before coating and among all non-coated samples.

Figure 9 demonstrates the histogram for cell viability test done by utilizing MC3-T3-E1 cells and MTS viability assay on the zirconia plates before and after BG coating. The histogram indicated that the viability of BG coated zirconia has significant difference even after 2 proliferations compared to untreated zirconia. Also the proliferation result for the samples after 4 and 6 days proliferation revealed that the difference between the BG coated and non-coated samples are increasing.



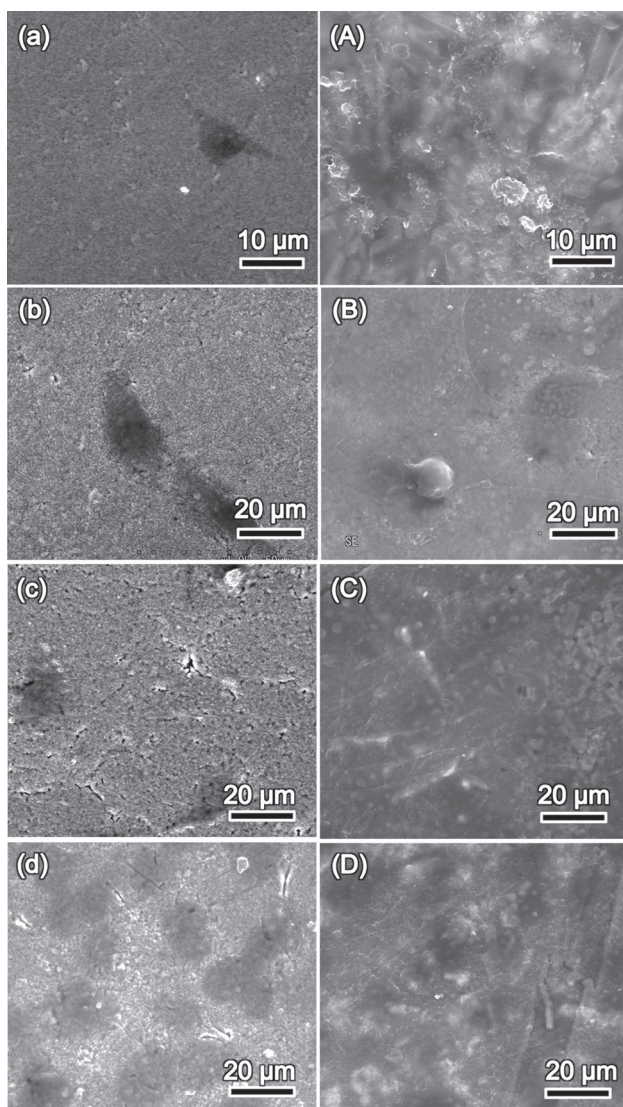


Fig. 8 SEM images of the cell morphologies for the zirconia samples without BG coating and after 3 h (a), 2 (b), 4 (c) and 6 days (d) cell culture and with BG coating after 3 h (A), 2 (B), 4 (C) and 6 days (D) cell culture.

## DISCUSSION

Recently the medical applications for the zirconia bioceramics are growing however the zirconia known as a bio-inert material. The BG coating is one of the effective methods to fabricate biodegradable and bioactive coating on the bio-inert zirconia surface. However, there are several difficulties in the BG coating by using BG powder. For example, the zirconia bulk with complicated shape is difficult to cover homogeneously by BG powder before sintering. This study assessed the hypothesis that BG layer could be prepared by vacuum sol-dipping method. The vacuum sol-dipping, sintering and drying

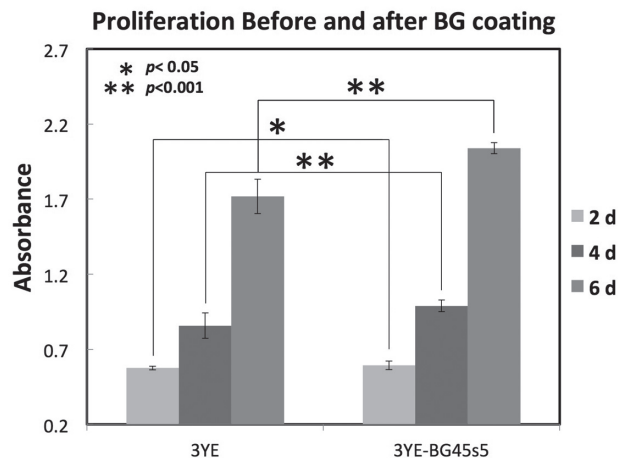


Fig. 9 The histogram of the cell viability after 2, 4 and 6 days cell culture for the zirconia samples before and after BG coating.

time durations were kept constant as described in the coating method, however the surface morphology and sintering temperature and sol-dipping counts effects on the coating layer coverage ability were investigated in this study. Surface morphology of the zirconia substrates played main role on the surface coverage ability of the BG coating layer. For example, the roughness of the as-sintered samples (shown in Fig. 4) was enough to cover the surface by BG coating layer only after one-time vacuum sol-dipping. Against polishing of substrates decreased the surface roughness and reduced the wettability of substrate surface therefore the coating layer could not cover the surface even 5 times vacuum sol-dipping. The sintering temperature was next effective parameter to have a homogenous BG coating layer on the surface. As it was revealed in the Fig. 3 the sample sintered at 900°C showed that the BG coating layer could not melt completely after 1 h therefore the sintering temperature was increased to 1,000 and 1,100°C and it was confirmed that the amount of melted BG was increased. The temperature that the all coated BG was melted and the experiment showed repeatable result was 1,200°C.

It is possible to coat the zirconia with BG in different thicknesses. The BG coating could be used to postpone the exposing bulk material and the thickness will affect the degradation time and ion release durability<sup>29,30</sup>. The adhesion of the BG coating to the zirconia surface is the parameter that gains the researchers attention. The adhesive strength of BG coated sample mainly came from the mechanical adhesion strength between coating and substrate<sup>34</sup>, that was approved by the failure morphology shown in Fig. 6. The major failure mode of BG coated sample was adhesion failure that occurred between the coating and substrate and there were some parts of mixed failure that occurred in the BG coating layer and also, Niu *et al.* have reported a similar mechanism for adhesion failure<sup>35</sup>. On the other hand,

the effect of the chemical bond between zirconia surface and the BG could not be negligible. Scott and Gray-Munro believe that the organosilanes have main role in BG-substrate bond through the Si– to Metal–O<sup>36</sup>. And it is clear that the zirconia ceramic surface containing a large number of Metal–O– compound that could be a suitable site to bond with Si–. Based on this opinion if the sol could cover the zirconia surface before sintering then BG coating adherent to the zirconia surface will be improved.

MC3T3-E1 cells morphology images indicated that cell spread and cover the surface by extracellular matrix very quickly. Even the transparent BG coating makes the photography very difficult. Cell viability result for the zirconia substrates before and after BG coating<sup>37</sup> especially 45S5 BG coating<sup>38</sup> was confirmed previous studies findings.

The introduced method for BG coating on the zirconia in this study containing several advantages such as easy to proceed and the strong adherent to the zirconia surface, adjust the thickness and same phase structure with the BG powder derived from sol-gel method.

## CONCLUSION

Strongly adhered homogenous 45S5 BG coating layer with 55±7 MPa adhesive strength was prepared on the rough as-sintered zirconia substrate by only one-time vacuum sol-dipping method followed by sintering at 1,200°C for 1 h. The thickness of BG coating layer was adjustable by number of coatings. The phase structure of the prepared BG coating after sintering was same with the 45S5 BG reported in previous articles. Cell morphology and cell viability result confirmed that the BG coated samples have superior response to cell compare to the non-coated zirconia.

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