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Adhesion Behavior of Ti–PMMA–Ti Sandwiches for Biomedical Applications

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The "stress-shielding" problem, common with metallic implants, may be solved by using biocompatible sandwiches with a polymeric core between two metallic skin sheets. To achieve such sandwiches, a process route has been developed, beginning with the grafting of poly-(methyl-methacrylate) (PMMA) on titanium (Ti) sheets via the "grafting from" technique. Grafting resulted in variable thicknesses of PMMA on the Ti sheets. Hot-pressing was used to prepare semi-finished Ti–PMMA–Ti sandwiches. The adhesion was achieved by the interpenetration between PMMA sheet and the grafted PMMA chains. Investigation was carried out to understand the influence of the grafted PMMA thickness on the adhesion strength. Similar adhesion strengths were found for the sandwiches despite variable grafted PMMA thicknesses, indicating a successful grafting of PMMA on large-scale Ti sheets. The adhesion followed the autohesion theory, where a time-dependent increase in adhesion strength was found for the sandwiches.

INTRODUCTION

The complexity of the human body always makes it as challenging for any host material to perform as the native organ. This makes implant development a very challenging task. For example, in the case of craniomaxillofacial (CMF) implants, the most commonly used ones are based on titanium (Ti),[1,2] but even such alloys do not fulfil all the desired criteria. The high stiffness of Ti causes a mismatch in load distribution between the implant and neighboring bone, also known as "stress-shielding", which results in bone resorption of the neighboring bones and, ultimately, in implant failure.[3] On the other hand, polymers, such as poly-(methyl-methacrylate) (PMMA), are also intensively used materials for CMF implants, but PMMA clearly lacks the mechanical properties needed for implant applications.[4]

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As monomaterials alone do not fulfil all the properties needed to become an ideal implant, one way to circumvent this problem is by the application of hybrid systems, i.e., by merging different biocompatible materials. Hybrid materials such as sandwich-structured composites can minimize the problems, as, in such structures, the mechanical properties can be easily modulated by changing the skin-to-core material ratios.[5,6] These composites are quite popular in the automotive and aerospace industries, but the major problem in their application for the biomedical sector is the bonding between the metal and the polymer sheets. Where, in industrial sectors, epoxy resins are used as an adhesive agent to improve the bonding between the skin and the core material, this is not feasible for biomedical purposes due to their cytotoxicity.[7] In an effort to minimize this problem, an innovative "grafting from" approach has been developed by Reggente et al.,[8] in which grafted PMMA has been used as an adhesive agent, and the interpenetration and reptation between polymer chains of the bulk PMMA and the grafted PMMA have provided the

necessary adhesion strength.[9–11] In cytotoxicity studies, this approach was found to be biocompatible.[12]

The success of the grafting from approach for polymer autohesion (van der Waals interaction between similar polymers) is based on the grafting density and length of the grafted polymers. In previous studies, it was found that highly dense grafted polymers result in decreased adhesion, as it leads to overlapping of grafted chains, thus preventing interpenetration.[13–15] Thus, the grafted chain density should be in a regime where they can easily move and interpenetrate in the adhering polymer. As polymer autohesion is also a time-dependent process, by increasing the processing time, the degree of bonding between the polymers will also increase.[16,17] Therefore, to achieve a strong adhesion strength, longer times are required. Based on the literature known to the authors, the influence of the grafted polymer thickness on the adhesion strength achieved after a long-timescale autohesion process has not yet been investigated.

Thus, in this study, the effect of contact time and the grafted PMMA thickness on the adhesion behavior of a Ti–PMMA–Ti sandwich has been investigated.

MATERIALS AND METHODS

Sample Preparation

Ti sheets (DIN A5 size, 0.15 mm thick, roughness 0.5 ± 0.1 μm), cut from Grade 2 Ti were used. The samples were cleaned by sonication in acetone, ethanol, and deionized water for 10 min each. The solvents were purchased from Carlo Erba.

In order to graft PMMA onto Ti sheets, a three-step strategy (Fig. 1) was carried out following a previous work.[18] The first step is activation to increase the content of hydroxyl groups on the Ti surface. Second, a phosphonic acid derivative, used as a polymerization initiator, was grafted onto the substrates as an anchoring group. And third, surface-initiated atom transfer radical polymerization was employed to grow PMMA chains.

Alkali-Activated Ti Surfaces

The cleaned Ti surfaces were activated by immersing the samples in a 2.0-M concentrated aqueous sodium hydroxide (NaOH) (Carlo Erba) solution for 1 h at 80°C and 300 rpm in a Teflon beaker.[19] During the activation reaction, the Ti samples were suspended in the reactive media with a Teflon wire, avoiding any possible contact between them.

Initiator-Modified Ti Surfaces

After rinsing with deionized water, the alkali-activated Ti samples were suspended in a Schlenk tube containing 0.5 mM concentrated initiator aqueous solution to covalently graft it onto the surface of the samples. This was a synthesized bromoisobutyrate-undecyl-1-phosphonic acid ($C_{15}H_{30}O_5PBr$),[20] an initiator required for the polymerization. The reaction was performed for 24 h at 95°C and 300 rpm under reflux. The grafting reaction was carried out in the dark to avoid side reactions caused by the well-known photocatalytic activity of titanium dioxide.[21,22] At the end of the reaction, the samples were sonicated in dichloromethane and deionized water for 15 min each, to remove the initiator physisorbed on the Ti surface.

Polymer-Coated Ti Surfaces

The initiator-modified Ti samples were transferred in a Schlenk tube where the ATRP of the methyl-methacrylate (MMA) took place. For a typical polymerization, a molar ratio of [1]:[5]:[5]:[5] was used for [Initiator]:[CuBr]:[PMDETA]:[malononitrile], respectively. The reagents were added in this order:

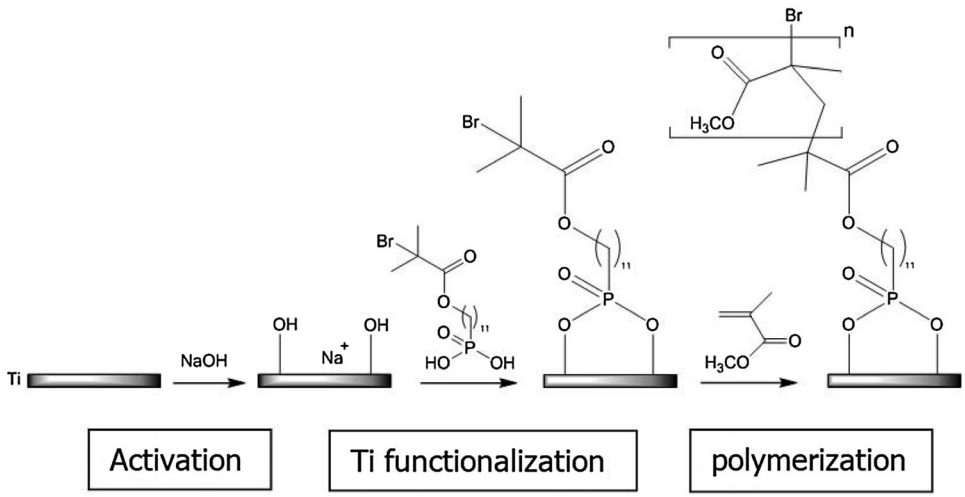

Fig. 1. Three-step strategy used to design the polymer-coated Ti surfaces.

- First, copper bromide (Cu(I)Br) (Sigma Aldrich), anisole (Acros Organics) and pentamethylene-diethyl-triamine (PMDETA) (Acros Organics) were incorporated into the media, which was stirred to obtain a green, homogeneous solution.
- Second, malononitrile (Acros Organics) was then included in the reactive media to enhance the polymerization rate.[20,23] The solution immediately turned dark.
- Third, 5.3 M of MMA (Acros Organics), purified from its stabilizer by column chromatography on basic aluminium oxide (Acros Organics), was added to the reactor. The monomer was kept cold in a refrigerator for 20 min before removal and purification.

Finally, the system was degassed one more time by alternating vacuum and argon. The reaction was performed for 24 h at 35°C and 300 rpm under argon in 5.3 M concentrated monomer solution. At the end of the reaction, the samples were rinsed carefully and sonicated for 10 min in methanol to stop the polymerization, and to remove the catalyst's residues (e.g., copper bromide derivatives and PMDETA) and the unreacted monomer.

Cross-Section Analysis

The sample was coated with a copper layer using an ion beam cross polisher (Hitachi IM4000+) to determine the top of the sample. Then, the cross-polishing was carried out from the sample's back side using 6 keV Argon ions to protect the PMMA coating by the Ti; very few were exposed to the ion beam. The surface morphology was investigated by scanning electron microcopy (SEM; CrossBeam® Workstation AURIGA-Zeiss 405 Microscope).

On visual inspection of the PMMA-grafted Ti sheets, a variation in the color/shade of the grafted PMMA can be observed (Fig. 2). Moreover, the SEM cross-section images were performed on three zones, labeled A, B, and C, and the grafted PMMA thicknesses were estimated. The effect of these differences on the adhesion was investigated in the next steps.

Ti–PMMA–Ti Sandwich Adhesion Investigation

Sandwiches were prepared, combining commercial PMMA (Plexiglass 0F301, 0.5 mm thick) and PMMA-grafted Ti sheets via hot-pressing (MAN 1000 kN hydraulic press). In the initial study, keeping p = 2 bar, and T = 150°C constant, time steps 5 min, 90 min, and 120 min were applied to determine the optimum bonding conditions. B-zone-grafted PMMA was used for all the cases.

For investigation of the variation of the grafted PMMA thicknesses on the adhesion strength, sandwiches were prepared using all the possible combinations of grafted PMMA thicknesses. Based on previous studies, the A–A sandwich was used as control.[18] The hot-pressing conditions applied for these cases were kept constant with p = 2 bar, T = 150°C, and t = 120 min.

The adhesion strength was investigated via pull-off tests. Here, sandwiches were initially attached to stainless steel bars using a two-component adhesive (3M scotch-weld DP 390). Before testing, the adhesive was cured at 60°C for 24 h. The samples were finally mounted in a universal testing machine, and tests until rupture were performed at a constant velocity of 0.1 mm/min.

RESULTS AND DISCUSSION

PMMA Grafting on Ti surface

The adhesion is linked to the build-up of the interface of the Ti/grafted polymer. At the start, NaOH treatment allows the formation of a nanostructured and porous layer of sodium titanate (step

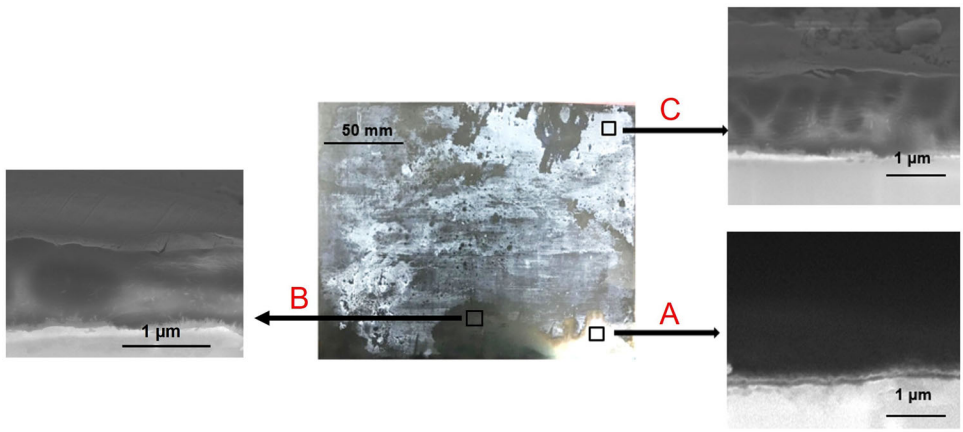

Fig. 2. Variation in grafting of PMMA on Ti sheets. *Left* PMMA grafting on DIN A5 sheet, and *right* cross section SEM images of the three grafted zones, *A*, *B*, *C*. The thickness of the PMMA varied from approximately 200 nm to >1 μm determined by cross-section SEM: *A zone* had grafted PMMA thickness of approximately 200 nm; *B zone* had a thickness of approximately 1 μm, and *C zone* had a thickness of approximately 2 μm.

1 in Fig. 1). Its thickness and porosity strictly depend on the reagent concentration and on the time of the reaction. The sodium titanate layer creates an open porosity which will establish a further mechanical interlocking between the growing polymer layer and the substrate.[2,24,25] Indeed, the formation of titane-oxygene-phophore (Ti–O–P) bonds (step 2 in Fig. 1) are produced by the interaction between the surface hydroxyl and phosphonic acid groups. Finally, the PMMA-grafted Ti surface (step 3 in Fig. 1) was obtained by spreading the PMMA chains into the initiator-modified Ti surface. As shown in Fig. 2, this resulted in the variation of grafted PMMA thicknesses over the complete Ti surface of size A5. Zone A had a grafted PMMA thickness of approximately 200 nm, zone B of approximately 1 μm, and zone C of approximately 2 μm.

Adhesion Behavior of Ti–PMMA–Ti Sandwiches

The adhesion strength between the interfaces of the Ti–PMMA–Ti sandwiches depends on the interlocking conditions between the Ti–PMMA grafted and PMMA commercial foils. Merging the parts, the adhesion strength increased linearly with processing time from approximately 4 MPa to 20 MPa, when the hot-pressing time was increased from 5 min to 120 min (Fig. 3). After visual inspection of the fractured samples, an adhesive mode of failure could be detected in the case of a shorter processing time (5 min). In this case, the PMMA foil was not found at the side of delamination, whereas for longer processing times (90 min and 120 min), an adhesive-cohesive mixed failure was observed (Fig. 4). Indeed, delamination occurred within the bulk PMMA which could be found on both interfaces of the sandwich. Moreover, investigating the influence of different thicknesses of the grafted PMMA, no significant effect could be found, and an adhesion strength of approximately 20 MPa was obtained in all the cases (including control) (Fig. 5), and mixed failure resulted for all the cases.

As mentioned in various literature, polymer autohesion is a time-dependent process, which can be divided into two parts: intimate contact, i.e., the full contact of surfaces, and cohesion, i.e., the formation of entanglements between polymers.[16,26,27] Thus, the adhesion strength increases with time. This phenomenon was also observed in the experimental results. Here, it should be mentioned that pressure is required only to get the surfaces into full contact, and, afterwards, cohesion is only temperature- and

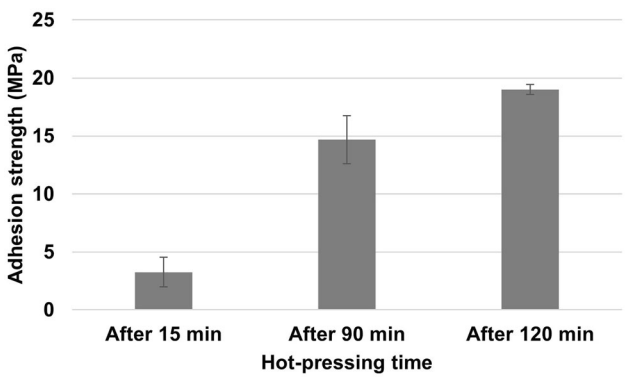

Fig. 3. Adhesion strength of Ti–PMMA–Ti sandwiches (B zones) after different hot-pressing times (T: 150°C, p: 2 bar). The adhesion strength significantly improved with time from approximately 4 MPa to approximately 20 MPa.

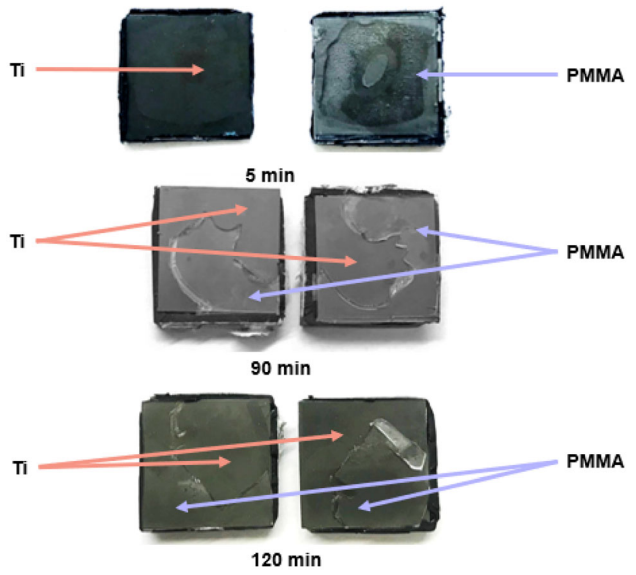

Fig. 4. Fractured Ti–PMMA–Ti surfaces after pull-off tests. The difference in failure mechanism with respect to time can be seen. Where, after 5 min of hot-pressing failure, was pure adhesive (no bulk PMMA on one side), at 90 and 120 min of hot-pressing, an adhesive–cohesive mixed-failure was found (bulk PMMA residue on both sides).

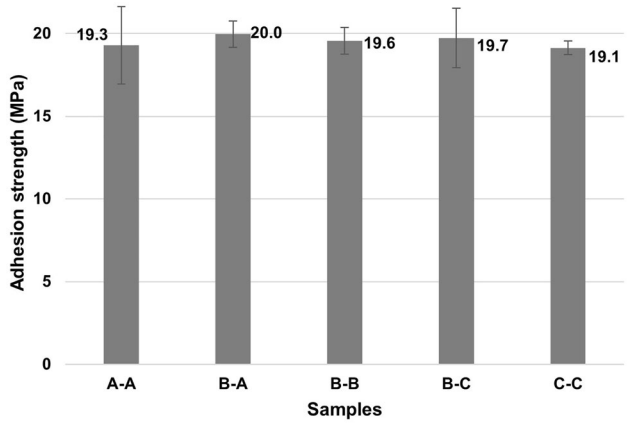

Fig. 5. Adhesion strength of Ti–PMMA–Ti sandwiches prepared by combining different thicknesses of PMMA grafted Ti zones. *A* grafted PMMA thickness is approximately 200 nm, *B* approximately 1 μm, *C* approximately 2 μm. Abbreviation *B–A* means the combination of type A on one side with type B on the other side of the sandwich.

time-dependent. Thus, with higher temperature, the same adhesion strength can be reached in shorter times. However, in the thermal analysis of PMMA, bubble formation was found to be a major problem above 150°C, thus. this was the temperature limit used for all the cases. While a higher density of the grafted polymer caused problems in getting stronger adhesion in other studies,[13–15] this was not observed in the current one. A possible reason could be the longer processing time used for the process. Where, in a short timescale, a high density could cause problems in reptation and interpenetration of the polymers, if a sufficient amount of time is provided, this problem can be avoided. It can also be found in the pull-off test results (Fig. 3). The delaminated surface after 5 min of hot-pressing showed an adhesive failure, which shows that the bulk PMMA was not able to adhere properly with the grafted PMMA. This situation changes with increasing the processing time, where an adhesive–cohesive mixed failure was found, which was also followed for all the different grafted zones (A, B, C) combined sandwiches. With 120 min of hot-pressing, the adhesion strength was also similar for all the sandwich combinations, where an adhesive–cohesive mixed failure was obtained for all the cases. It can be stated that the degree of autohesion was almost the same for all cases irrespective of the grafted PMMA thickness. It becomes clear that the influence of the grafted polymer thickness is irrelevant by the application of long timescales for polymer autohesion. The study shows that, once the minimum thickness is obtained for a successful adhesion, any inhomogeneity in thickness of the grafted polymer does not play a big role for a good bonding afterwards.

CONCLUSION AND OUTLOOK

In this study, the influence of grafted PMMA thickness and autohesion time on the adhesion behavior of biocompatible Ti–PMMA–Ti sandwiches was investigated.

The grafted PMMA was used as an adhesive to prepare Ti–PMMA–Ti sandwiches by a hot-pressing process for biomedical applications. During the adhesion strength analysis, a time-dependent adhesion behavior was observed, following the literature on cohesion. No adhesion difference was observed based on the grafted PMMA thicknesses, which could have been caused by the long hot-pressing time provided for the sufficient interpenetration, and by entanglements between the bulk PMMA and the grafted PMMA. Moreover, it can be stated that metal–polymer sandwiches developed using grafted polymers as adhesive layers have the potential to be used at a larger scale in the future.

The next challenge for these sandwiches is their shaping to complex parts, as such polymers are brittle in nature at room temperature. So, in future studies, the shaping conditions of these sandwiches to achieve custom-shaped implants will be investigated.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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