PAPER

To study the effects of nano-additives and nano-indentation variables on viscoplastic behaviour of a polymeric orthopaedic bone cement

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Abstract
PMMA-based orthopaedic cement is an essential medical grade material in the modern healthcare system which has been widely used for the fixation of prostheses in total joint replacement surgeries. A PMMA bone cement is an intrinsically viscoplastic biomaterial, and a review of its constitutive material models seems to be of great importance to design, functionalize and improve the properties of these biomaterials. In this article, using the simultaneous analyses of experimental nano-indentation results and finite element simulation of a well-known two-layer viscoplasticity model, the effect of adding three types of nano-additives including hydroxyapatite (HA), Alumina (Al2O3), and single-walled carbon nanotubes (SWCNTs) on the viscoplastic behaviour of the cement was examined. Additionally, the effect of the experimental conditions such as loading rate, holding time and unloading rate on the viscoplastic behaviour of the cement was investigated. Making an analogy between the numerical and experimental results, the optimal constitutive material model for each case study was obtained. Moreover, by comparing the results with the condition where no nano-additives were added into the cement matrix, the effectiveness of the nano-supplements on the constitutive model was evaluated.

Introduction
Polymethyl methacrylate (PMMA-based) bone cement has been long one of the most useful biomaterials in various orthopaedic and trauma surgeries. The material design and engineering of PMMA cement components for the best are of the utmost importance and require a full understanding of the biological and mechanical properties. Having profound knowledge of intrinsic material behaviours of the PMMA cement and its composites enables designers to confidently design and manufacture more advanced bone cement, benefiting users worldwide. The main functions of bone cement are to immobilize the implant components in the bony skeleton and even to transfer the in vivo loads from the implant to the bone [1]. However, low compatibility with the host tissue and relatively poor mechanical properties of the cement are the primary problems that can have a detrimental effect on its overall performance, facilitating the chance of implant loosening [2]. In this regard, there are three weak zones in the prosthesis/cement/bone configuration (i.e. cement/bone interface, the bone cement itself and cement/implant interface), which are more susceptible to mechanical failure in comparison with the other parts of the system. Cement failure may lead to post-surgery complications that make surgical recurrence inevitably [3, 4]. To address this, the incorporation of additive biomaterials into PMMA-based cement is one of the most efficient solutions to overcome the aforementioned drawbacks [5–18].

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Quan et al[5] prepared a biocompatible PMMA/hydroxyapatite (HA) nano-composite bone cement by adding up to 40 wt% of (PMMA-co-MPS) modified HA. The resultant cement led to an increase in mechanical properties such as compressive strength, flexural strength and flexural modulus with modifying the modification degree of HA. Paz et al[6, 7] characterized the mechanical properties such as bending strength, flexural modulus, compression strength, fracture toughness and fatigue performance of a PMMA-based bone cement reinforced with the functionalized graphene (G) and graphene oxide (GO) nano-sized powders with loadings ranging from 0.1 to 1.0 wt%. It was observed that loading a small amount of graphene and graphene oxide (≤ 0.25 wt%) improved the mechanical performance of the cement, especially the fracture toughness and fatigue performance. Bao et al[8] fabricated PMMA bone cement by employing MPS (methacrylopropyltrimethoxysilane)-functionalized ZrO₂ particles as an inorganic filler into the cement powder component. ZrO₂ particles with surface vinyl groups exhibited a good dispersion in the fabricated bone cement, leading to an enhancement in the bending strength of the bone cement products.

Yerro et al[9] synthesized the acrylic PMMA resin strengthened by attaching the silanized alumina whiskers with self-healing agents into the cement matrix. The nano-indentation results revealed the significant increases in both reduced elastic modulus and hardness of the cement by ~65% and ~90% for composites with silanized whiskers, respectively. Khan et al[10] evaluated the static and dynamic mechanical properties such as creep, recovery, and stress relaxation of PMMA cement composites enriched by GO sheets in two groups of GO loading i.e. 0.025 wt% and 0.05 wt%. Analysis of variance test results indicated that although the elastic modulus and nano-hardness in both groups were not significantly different from those of pure-PMMA, the compressive strength increased considerably. The dynamic mechanical properties suggested an effective role of GO in polymerization with PMMA. Pahlevanzadeh et al[11] prepared and characterized PMMA bone cement modified by monticellite (Mon) and carbon nanotubes (CNTs). A better mechanical performance was obtained for the PMMA/ Mon/ CNT compared to PMMA and PMMA/ Mon types of bone cement. Desirable bioactivity was also seen in the types of bone cement having Mon and CNTs, whereas the neat cement exhibited poor bioactivity. In another attempt to develop the mechanical properties of PMMA types of cement[12], various low-loadings of mesoporous silica nanoparticles (MSNs) were embedded into the cement matrix. Flexural and nano-indentation measurements showed that incorporating low particles of MSNs had minimal effect on such properties of the cement. In reverse, the micro-indentation experiment revealed that the addition of MSNs considerably increased the micro-hardness. No significant effect was also seen for the stress relaxation and creep properties of the nano-composite types of cement.

Bone cement is inherently a viscoelastic/plastic material that exhibits both elasto-plastic and viscous behaviours which should be considered by orthopaedic implant designers[19]. Over the years, some surveys of viscoelastic properties of PMMA types of cement have emerged[19, 20] but there have been a limited number of studies, in which the comprehensive viscoelastic/plastic models have been concerned. The establishment of an accurate constitutive material model for types of bone cement and their composites seems to be a real challenge recently. It comes from the fact that a better understanding of the cement material model, in both short-term and long-term properties, has a directional link with orthopaedic implant design and can, therefore, help to enhance clinical applications.

In this study, a series of finite element (FE) analyses of a two-layer viscoplasticity model and experimental data are integrated to provide an important insight into the effect of incorporating three types of well-known nano-additives including hydroxyapatite (HA), Alumina (Al₂O₃) as well as single-walled carbon nanotubes (SWCNTs) on the viscoplastic behaviour of the bone cement. Further, polymers (like PMMA) exhibit that their material properties can be clearly affected by nano-indentation loading conditions such as loading rate, holding time and unloading rate[21]. Therefore, here, a wide range of above-mentioned conditions was also employed to examine the sensitivity of nano-indentation measurements to these experimental parameters using an FE analyzer. The variation of these nano-indentation parameters results in the appearance of some distortions, e.g. ‘nose phenomenon’, in the load-displacement curve that requires an explanation involving viscoplasticity dependent behaviour.

**Methodology: simulations and constitutive material model**

A commercially-available FE analyzer package (ABAQUS 6.14, SIMULIA Corporation, Providence, RI, USA) was used to simulate the nanoindentation experiment. For the sake of simplicity, indenter and specimens were modeled by 2D axisymmetric geometries. A cone-shape rigid indenter, with a half angle of 70.3 and the same projected area-versus-depth function according to the standard Berkovich tip, was used to model nano-indentation indenter. A highly fine mesh was constructed under the contact area and around the indenter’s tip to more precisely define the stress distribution. Each specimen was meshed using a set of 3878 four-node bilinear axisymmetric quadrilateral continuum elements (CAX4R) and 4149 nodes. In a nano-indentation technique, an indenter tip moves vertically
down onto the specimen surface and squeezed into a specific site of the sample by applying an upward loading profile. In this sense, when the applied load attains the pre-set maximum value, the indenter is held at this condition for a predefined short time to minimize the influences of material rate-dependent behaviour. Finally, the load is decreased until partial or complete relaxation would occur. In the present work, three above-mentioned phases of nano-indentation including 30 s loading, 10 s holding, and 30 s unloading times were simulated in the FE analyzer under conditions similar to the experimental procedure. Moreover, in order to study the sensitivity of the cement load-displacement curves to the nano-indentation variables, a set of different values of loading conditions was applied. Figure 1 displays a schematic of load-time curve including three steps i.e. loading, holding and unloading times so that all of them were changed to clarify such sensitivities.

It is worth noting that the Oliver and Pharr method is the most well-known approach to obtain mechanical properties of given material from loading-unloading curves. This method assumes that the unloading segment of nano-indentation is purely elastic behaviour [22]. Recent studies, however, have been reported that inconsistency between Oliver-Pharr assumption and intrinsic viscoelastic-plastic feature of polymers may cause some errors in the estimation of material properties [23]. Therefore, in order to overcome this problem and to have a reliable material model taking the time-dependent behaviour of the cement into account, a two-layer viscoplasticity model was simulated in an FE solver based on what was described in our previous paper [4]. Figure 2 shows the one-dimensional idealization of the two-layer viscoplasticity model. This model comprises a time-independent (elastoplastic) network which is in parallel with a time-dependent (viscoelastic) network. In the model, $K_p$ denotes the elastic modulus of the elastoplastic network, $K_v$ is the elastic modulus of the viscoelastic network, $\sigma_y$ presents the yield stress, $H'$ is the power-law hardening with work hardening exponent, and finally, $A$ & $n$ are the Norton creep parameters. With reference to the one-dimensional idealization, a parameter $f$ is also defined as the ratio of the elastic modulus of the viscoelastic network ($K_v$) to the instantaneous modulus ($K_p + K_v$) i.e.:

$$f = \frac{K_v}{K_p + K_v}$$  \hspace{1cm} (1)

Figure 1. A schematic of the load-time curve in order to assess the sensitivity of the cement load-displacement curve to the experimental variables in nano-indentation measurements by varying three steps.

Figure 2. A one-dimensional idealization of the two-layer viscoplasticity model. (All parameters are introduced in the text).
The total instantaneous stress of the network can simply be computed as:

\[ \sigma = \sigma_p + \sigma_v \]  

(2)

where \( \sigma_p \) and \( \sigma_v \) are the elastoplastic and viscoelastic stresses, respectively. Assuming linear isotropic elastic elements for elastic parts of the network, the total instantaneous strain can be presented as (see [4] for more details):

\[ \varepsilon = \varepsilon_e + f \varepsilon_v + (1 - f) \varepsilon_p \]  

(3)

where \( \varepsilon_e \) is the addition of elastic strains of both network branches, \( \varepsilon_v \) is the strain corresponding to the viscoelastic network, and \( \varepsilon_p \) is the plastic strain corresponding to the elastoplastic network, respectively.

Based on the Norton-Hoff rate law and under certain condition, one can obtain a relationship for the time-dependent viscoelastic stress as (see [4] for more details):

\[ \sigma_v = \left( \frac{\varepsilon_v}{A} \right)^{\frac{1}{n}} \]  

(4)

**Results and discussion**

According to the consideration given in the previous section and as shown in figure 2, the parameters \( A \) and \( n \) are directly related to the damping features of the viscoelastic network of the two-layer model while the parameter \( f \) represents the ratio of viscoelastic stiffness to total stiffness of the model (see equation (1) also). In what follows, via the carefully planned design of combining experiments and FE simulation results, the optimal values of these parameters are measured for three types of bone cement containing certain percentages of nano-additives. It should be noted that the fraction of nano-additives was selected based on data in the research background, which generally indicated the best behaviour was achieved with these amounts of supplements. The values of the elastic modulus and the load-displacement curves for PMMA bone cement [4] and its nano-composites including PMMA/HA [16], PMMA/\( \text{Al}_2\text{O}_3 \) [15] and PMMA/SWCNTs [14] types of cement were borrowed from the experimental data reported in previous studies. All types of bone cement and nano-additives are set out in detail in table 1. The value of Poisson’s ratio was also considered to be 0.3 [3, 4].

In figure 3, the sample obtained from the addition of 10 wt\% HA nano-particles to the bone cement was examined and the results of the nano-indentation test were extracted. Next, the most consistent behaviour with the experimental results was determined by performing FE simulations and by considering the viscoplastic two-layer viscoplasticity model. By comparing the results, the optimal parameters were selected and then the effect of variation in each parameter on the behaviour—when the other two parameters were kept constant—was investigated.

| No. | Composite | Bone cement | Additive | References |
|-----|-----------|-------------|----------|------------|
| 1   | Neat PMMA| EUROFIX GUN® | —        | [4]        |
| Powder (60 g) | Liquid (30 ml) | PMMA 52.6 g | MMA 29.6 ml |
| BPO 1.4 g | N,N DMPT 0.4 ml |
| BAS 6.0 g | HQ 20 ppm |
| 2   | PMMA/HA  | EUROFIX GUN® | —        | [16]       |
| The same composition with No.1 (above). | Bovine hydroxyapatite |
| Purity | Size (nm) | \( \geq 98 \) wt\% | \( \sim 30 \) |
| 3   | PMMA/\( \text{Al}_2\text{O}_3 \) | EUROFIX GUN® | —        | [15]       |
| The same composition with No.1 (above). | Alumina (Tecnan®, Spain) |
| Purity | Size (nm) | \( \geq 99 \) wt\% | \( 10-20 \) nm |
| 4   | PMMA/SWCNT| Simplex-P® | —        | [14]       |
| Powder (40 g) | Liquid (20 ml) | PMMA 30.0 g | MMA 19.5 ml |
| Co-polymer 6.0 g | N,N DMPT 0.5 ml |
| BAS 4.0 g | HQ 1.5 mg |

### Table 1. Details of all types of bone cement and their nano-additives used in this article.

BPO: Benzoyl peroxide; BAS: Barium sulphate; DMPT: Dimethyl p-toluidine; HQ: Hydroquinone; D: Diameter; L: Length.
In figures 4 and 5, with the same way mentioned above, the most consistent parameters of the two-layer viscoplasticity model were obtained for the samples produced by the addition of 3 wt% of Al$_2$O$_3$ and 0.15 wt% of SWCNTs nano-additives to the bone cement, respectively. Figure 6 represents a prototype of the stress/depth distribution of PMMA nano-composites in nano-indentation simulation.

As expected, in figures 3–5 the trends of behaviour with parameter variations are similar to those were previously studied for the PMMA-based bone cement in [4]. In other words, any increase in parameters $A$, $n$, and $f$—when the other two parameters are kept fixed—resulted in greater penetration of the indenter into the sample. The increase of the mentioned parameters decreased the stress supported by the viscoelastic network and due to being parallel of the networks, the stress in the elastic-plastic network became larger, which in turn increased the penetration.

One notable difference in figures 3–5 with that was previously presented in [4] for the PMMA-based bone cement is the presence of the nose in some graphs (especially for SWCNTs sample) in unloading segments. To justify this, it should be noted that firstly, according to [14, 24–27], the primary reason may be the intrinsic viscous property of the cement. Secondly, for better observation, using the model presented in [4], and with the
same conditions as mentioned for the tests of that reference, the values of loading, holding and unloading times for the PMMA-based bone cement sample were simulated. The results of the simulation were drawn in figure 7.

As shown in figure 7, the increase in the loading, holding and unloading times of the test led to more penetration, but clearly, the growth in unloading time aggravated the nose phenomenon. This figure revealed that the standard time to obtain a reliable and correct result in a nano-indentation measurement may vary for different materials and samples.

**Conclusion**

Using a set of experimental nano-indentation data and a series of FE simulations, the effect of incorporating three types of well-known nano-additives including hydroxyapatite (HA), Alumina (Al₂O₃), and single-walled nanotubes (SWCNTs) on the viscoplastic behaviour of the PMMA-based cement was investigated. The behaviour comparison index was chosen according to the constants of the equation of a well-known two-layer viscoplasticity model that has also been used in the research background. Similar qualitative trends were seen in
Figure 5. The effect of variation of the viscoplasticity model parameters (a): $A = 1.00 \times 10^{-7}$, $f = 0.73$ are kept constant), (b): $n$ ($A = 1.00 \times 10^{-7}$, $f = 0.73$ are kept constant), and (c): $f$ ($n = 2.00$, $A = 1.00 \times 10^{-7}$ are kept constant) on the load-depth diagram of the cement produced by the addition of 0.15 wt% of SWCNTs nanotubes.

Figure 6. (a) The Stress (MPa), and (b) displacement ($\mu$m) distributions of PMMA/Al$_2$O$_3$ cement nano-composites during nano-indentation at $t = 30$ s.
the behaviours of the case studies with ones previously obtained for a PMMA-based bone cement without any additives. Specifically, any increase in model constants i.e. $A$, $n$, and $f$—when the other two parameters were kept fixed—resulted in greater depth in the load-displacement curve. Although $A$ and $f$ values readjusted to PMMA nano-composites with different nano-additives, parameter $n$ had almost no obvious change in all case studies and it was approximately equal to 2. This insensitivity of parameter $n$, as a conjecture, might come from the constancy of the ratio $\frac{\ln(f)}{\ln(A)}$. To confirm this hypothesis, however, more and more investigations are required and such surveys should be performed further. On the other hand, it was revealed that any increase in the loading, holding and unloading times intensified the penetration, but noticeably, the increase in unloading time aggravated the nose phenomenon.

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*Figure 7.* The load-displacement diagrams for the two-layer viscoplasticity model with same conditions of [4] at different values of (a) loading time (holding (10 s) and unloading (30 s) times are kept constant), (b) holding time (loading (30 s) and unloading (30 s) times are kept constant), and (c) unloading time (loading (30 s) and holding (10 s) times are kept constant).
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