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Comparison between the polymerization behavior of a new bone cement and a commercial one: modeling and *in vitro* analysis

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The polymerization behavior of a new bone cement based on poly(ethylmethacrylate), hydroxyapatite powder and *n*-butylmethacrylate monomer and a commercial cement have been studied. Polymerization kinetics were analyzed by means of differential scanning calorimetry (DSC). DSC data have been used to evaluate a phenomenological model describing the cure kinetics of this new bone cement. The kinetic model coupled with the energy balance was then used to obtain temperature and degree of conversion profiles in the bone–cement–prosthesis system, under non-isothermal conditions, as function of initial temperature and thickness of the cement. Material properties, boundary and initial conditions and the kinetic behavior were the input data for the numerically solved heat-transfer model. The modeling results have been compared with *in vitro* results.

1. Introduction

Acrylic bone cements are widely used for prosthetic component fixation in total joint replacement surgery. Cements permit the immediate fixation of a prosthesis, but many short and long-term effects are connected with their use. Acrylic monomers are highly reactive and release considerable heat during polymerization, thus tissue necrosis may occur giving rise to damage to the cement/bone interface. This interface is considered to be a weak point often responsible for failure of the total joint replacement [1]. However, high levels of unreacted monomers which are slowly released by the cement, may also be responsible for tissue damage. For these reasons, the properties and performance of acrylic-based bone cements and the supporting bone are strongly dependent on the polymerization kinetics. A quantitative correlation between the temperature profiles and the degree of conversion across the bone–cement–prosthesis system, as a function of the process variables, is necessary because the final properties of the cement are highly influenced by the processing variables (mixing procedure, temperature and the geometry of the prosthesis and of the cavity). The only way to obtain a cement with repeatable properties is to control these variables fully [2].

In this paper, the isothermal and non-isothermal polymerization behavior of a new bone cement, based on poly(ethylmethacrylate) (PEMA) powder and *n*-butylmethacrylate (*n*-BMA) developed at the IRC in Biomedical Materials and of CMW1 (C.M.W. Laboratory, UK), based on poly(methylmethacrylate) powder and methylmethacrylate monomer are described.

The reaction kinetics were analyzed by differential scanning calorimetry (DSC) and the data obtained are used for the quantitative determination of the rates of polymerization in isothermal and non-isothermal conditions. The experimental data were used to evaluate the parameters of a phenomenological kinetic model. In the second part, the kinetic model is coupled with a heat transfer model. The heat-transfer model was obtained by applying an energy balance across the prosthesis, bone and cement in order to predict the temperature in these parts and the degree of conversion in the cement as a function of the setting time, during non-isothermal polymerization. The full model was used to study the effects of different thicknesses and initial temperatures of the cement on the temperature and degree of conversion profiles across the bone–cement–prosthesis system. Material properties, boundary and initial conditions and the kinetic behavior are the input data of the heat-transfer model that is solved numerically. *In vitro* experiments of bone cements polymerization have been done and the results are compared with the modeling results.

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2. Materials and methods

The experimental IRC bone cement (IRC) used in this investigation was based upon poly(ethylmethacrylate) powder (PEMA), hydroxyapatite (HA) powder and *n*-butylmethacrylate (nBMA) monomer. The amount of HA powder, corresponding to a weight fraction of powder of 40% (12.7% by volume), was added in such a way as to maintain the polymer to monomer weight ratio at 2:1. HA powder was added as reinforcement in an attempt to increase both the fatigue and the flexural properties of this new cement [3]. CMW1 (C.M.W. Laboratory UK) is a clinically used bone cement based upon poly(methylmethacrylate) powder and methylmethacrylate monomer. The reaction kinetics were studied using Perkin–Elmer DSC7 and Mettler DSC30 differential scanning calorimeters. Dynamic scans at different heating rates and isothermal measurements in the temperature range 10–35 °C, were carried out for 30 or 50 min.

DSC measurements enable the determination of the degree of polymerization. It may be assumed that the heat evolved during the polymerization reaction is proportional to the overall extent of reaction given by the fraction of reactive groups consumed. Using this approach, the degree of reaction, α, is defined as

$$\alpha = H(t)/H_{\text{tot}} \tag{1}$$

where $H(t)$ is the heat developed in a DSC experiment between the starting point and given time, t; H_{tot} represents the total heat developed, and is calculated by integrating the total area under the DSC curve in a non-isothermal experiment.

Isothermal DSC experiments show that the developed heat, H_{is}, is lower than H_{tot}, thus indicating the presence of unreacted monomer. A maximum degree of conversion, $\alpha_{\max}$, may be introduced

$$\alpha_{\max} = H_{\text{is}}/H_{\text{tot}} \tag{2}$$

It was found that $\alpha_{\max}$ increases with increasing isothermal polymerization temperature according a linear law

$$\alpha_{\max} = p + qT \quad \text{for} \quad T < T_{\text{gmax}} \tag{3a}$$

$$\alpha_{\max} = 1 \quad \text{for} \quad T > T_{\text{gmax}} \tag{3b}$$

where p and q are empirical constants and T_{gmax} is the glass transition temperature of the full polymerized system.

A dynamic DSC scan of a sample previously subjected to a dynamic DSC scan does not show a residual peak, indicating that the sample is fully polymerized. When the scan temperature approaches T_{gmax}, $\alpha_{\max}$ goes to 1.

Many complex models have been reported in the literature for the polymerization of methacrylate [4–6]. However, as the onset of the gel effect is shifted to the start of the reaction, it is possible to use a simplified kinetic model. A simple pseudo-autocatalytic expression, previously proposed for polyester and acrylic thermosetting resins, may be used [7, 8]

$$\mathrm{d}\alpha/\mathrm{d}t = K(\alpha_{\max} - \alpha)^n \alpha^m \tag{4}$$

where n and m are non-temperature dependent constants and K is a temperature dependent rate constant described by an Arrhenius equation

$$K = K_0 \exp(-E/RT) \tag{5}$$

where K_0 is a constant, E is the activation energy, R is the gas constant and T is the absolute temperature.

In a bone–cement system, non-isothermal conditions occur because of the high exothermic nature of the reaction, particularly with thick cement layers. To predict the temperature profiles and thus the degree of cement conversion as a function of the setting time during the non-isothermal polymerization, we have combined the appropriate kinetic model with the energy balance, thus allowing for the inclusion of material thicknesses, the initial temperature differences between the components, and the ability of different materials to dissipate heat [9]. In the femur, the system can be modeled as an infinitely long symmetrical cylinder and

$$\frac{\partial\theta}{\partial t^*} = \mathrm{De}_{\text{i}}\left(\frac{\partial^2\theta}{\partial r^{*2}} + \frac{1}{r^*}\frac{\partial\theta}{\partial r^*}\right) \qquad i = \text{b, p} \tag{6}$$

where θ is a dimensionless temperature, r^* is the radial dimension, b and p indicate the properties of bone and prosthesis, respectively, and De_{i} is the dimensionless diffusion Deborah number, given by:

$$\mathrm{De}_{\text{i}} = k_{\text{ri}} t_{1/2} \rho_{\text{i}} Cp_{\text{i}} (\Delta r_{\text{i}})^2 \qquad \text{i} = \text{b, p} \tag{7}$$

where k_{ri} is the conductivity, ρ_{i} is the density and Cp_{i} is the specific heat.

The Deborah number represents the relative importance of the heat transferred by conduction with respect to the heat accumulated in the material. In the cement

$$\frac{\partial\theta}{\partial t^*} = \mathrm{De}_{\text{c}}\left(\frac{\partial^2\theta}{\partial r^{*2}} + \frac{1}{r^*}\frac{\partial\theta}{\partial r^*}\right) + St_{\text{c}}\frac{\mathrm{d}\alpha}{\mathrm{d}t^*} \tag{8}$$

where

$$St = \frac{Q_{\text{tot}}}{[(T_{\text{ref}} - T_0)Cp_{\text{c}}]} \tag{9}$$

is the Stefan number, expressing the relative weight of the latent heat associated with the chemical reaction with respect to the accumulation of heat in the material. α is obtained from Equation 4. These equations were solved using implicit finite differences.

The *in vitro* experiments were performed using a thick Teflon cylinder mold (Fig. 1). The cylinder base was kept at 37 °C to simulate body temperature; present in the cylinder three layers, parallel to the base, were present: cortical bone, cement and a stainless steel disc. The top of the cylinder was closed by a Teflon disc. Thermocouples were positioned at the different interfaces to record the temperature during the polymerization.

The cement thickness and the insertion temperature were varied. Two different initial temperatures were considered: 5 °C (pre-cooled cement) and 18 °C (ordinary room temperature). Each case is considered with three different cement thicknesses: 3, 5 and 7 mm. In all cases the cortical bone was 8 mm thick and the

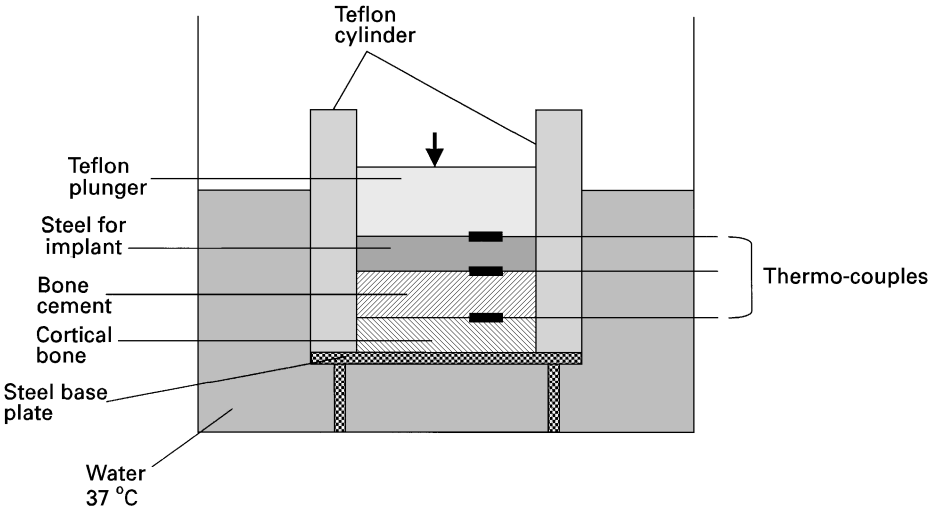

Figure 1 Experimental model representing a one-dimensional heat flow from bone cement to implant and bone.

stainless steel plate 10 mm thick. The model was thus assumed to give a one-dimensional thermal model of bone, bone cement and implant in the shaft of a long bone.

3. Results and discussion

For the IRC bone cement and CMW1, H_{tot} were 100 and 123 J g^{-1}, respectively, by averaging the reaction heats measured in the non-isothermal experiments. The total heat for the cement based on *n*BMA monomer is lower than that for PMMA cement and the polymerization heats of MMA and BMA are 576 and 418 J g^{-1}, respectively [10]. This gave parameters for the kinetic model shown in Table I. As the temperature increased, the rate of reaction increased, giving higher peak which occurred earlier and the degree of conversion increased reaching 0.88 and 0.84 at 35 °C for IRC and CMW1, respectively.

Figs 2 and 3 show the profiles of temperature, as a function of polymerization time, at the bone/cement interface for the three different thicknesses (initial temperature 18 °C) for IRC and CMW1, respectively. For both cements the higher the starting temperature, the higher the maximum temperature reached and the greater the degree of conversion. During the polymerization of the IRC cement, the temperature is always below 50 °C, reaching a maximum of 49 °C for the thickest cement layer. The degree of conversion was above 90% for all three cement thicknesses. The increasing cement thickness increased the maximum temperature and the degree of conversion. Pre-cooling the cement to 5 °C resulted in a temperature below 48 °C

TABLE I Parameters of the kinetic model for the bone cements

Parameter	IRC	CMW1
n	1.14	1.064
m	0.98	0.98
$\ln(K_0)$	9.4	9.1574
E_a/R (K)	4000	3763

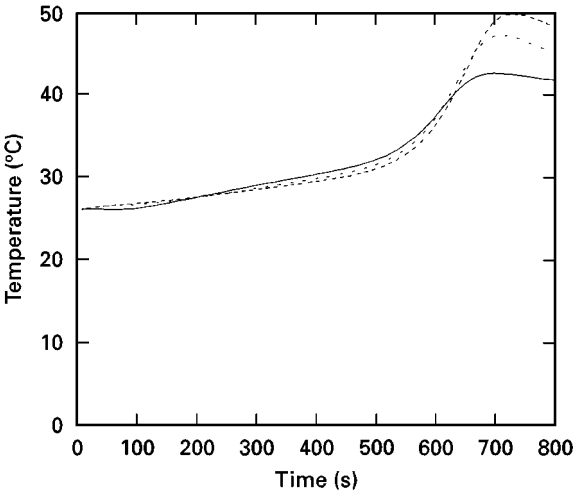

Figure 2 Results of the numerical simulation: polymerization time dependence of temperature at the bone/cement interface for three different thicknesses (initial temperature 18 °C) for IRC cement. (——) 3 mm, (- - -) 5 mm, (---) 7 mm.

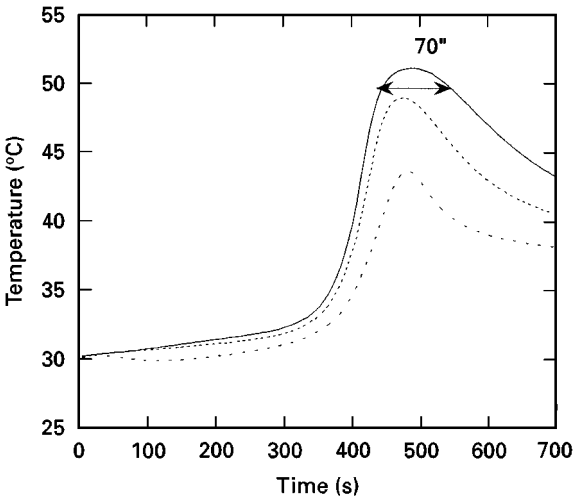

Figure 3 Results of the numerical simulation: polymerization time dependence of temperature at the bone/cement interface for three different thicknesses (initial temperature 18 °C) for CMW1. (- - -) 3 mm, (---) 5 mm, (——) 7 mm.

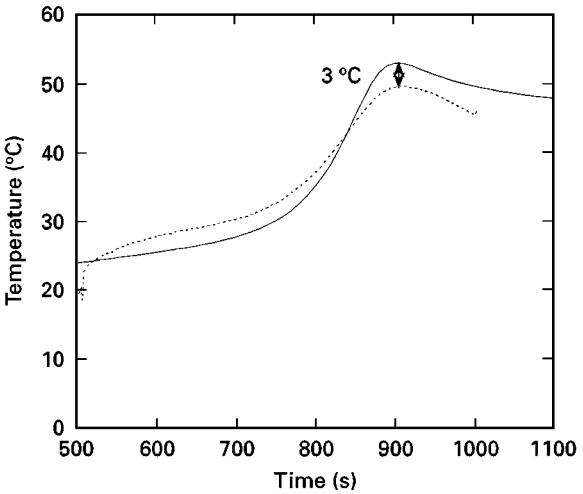

Figure 4 Comparison between (– – –) *in vitro* and (——) modeling results: polymerization time dependence of temperature at the bone/cement interface (initial temperature 18 °C, thickness 7 mm) for IRC cement.

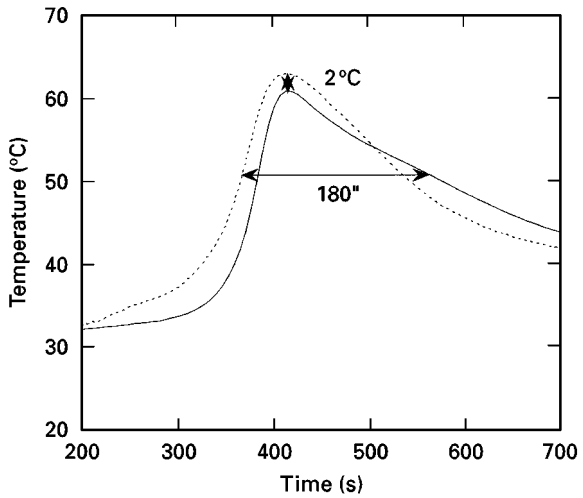

Figure 5 Comparison between (– – –) *in vitro* and (——) modeling results: polymerization time dependence of temperature at the bone/cement interface (initial temperature 18 °C, thickness 7 mm) for CMW1.

and a degree of conversion above 90%, only slowing the polymerization [9].

For CMW1, the temperature was higher than 50 °C for a cement thickness of 7 mm and initial temperature of 18 °C, so problems of tissue necrosis could arise [11]; the degree of conversion was always below 85%.

Figs 4 and 5 show the comparison between the results of the modeling and *in vitro* polymerization for both cements. The model predicts well the temperatures obtained during the *in vitro* polymerization.

4. Conclusion

The isothermal and non-isothermal polymerization of two bone cements have been studied. A simple phenomenological model was successfully used to describe the polymerization reaction of cement. This model was integrated with an energy balance to predict temperature and degree of conversion across the bone–cement–prosthesis system. The characteristics of the PEMA cement (low exotherm and low glass transition temperature) resulted in the temperature at the bone/cement interface being below 50 °C, but gave conversion rates above 90%. The commercial cement (CMW1) reaches a temperature higher than 50 °C for thick layers and a conversion less than 85%. Therefore, this simulation shows that the application of IRC cement should not produce problems of tissue necrosis from either thermal or chemical stimuli, unlike CMW1. The *in vitro* results are in agreement with the modeling results.

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