Theoretical and Experimental Investigation of the Production of PMMA-Based Bone Cement

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Summary: Poly(methyl methacrylate) (PMMA)-based polymers have been extensively used for manufacturing of artificial bone cements for treatment of osteoporosis. A typical bone cement recipe contains methyl methacrylate, which polymerizes *in situ* during cement application. An inherent problem of this reaction is the high amount of heat released during the cement preparation, which may lead to irreparable damage of living tissues. Optimization of PMMA-based bone cement (PMMABC) recipes is thus an important step towards safe and reliable clinical usage of these materials. A theoretical and experimental investigation is performed here to unveil the influence of some preparation variables on the production of PMMABC and to allow for future optimization of the PMMABC recipe. It is shown that the degree of mixing of the components of the recipe plays a fundamental role on the development of the temperature profile. For this reason, the PMMABC obtained with the *in-situ* blending of PMMA and barium sulfate during the suspension polymerization leads to much better homogeneity of the final test pieces and improved control of the temperature profile.

Keywords: biomaterials; bone cement; mixing; PMMA; suspension polymerization

Introduction

Polymers constitute an important class of materials intended for biomedical applications, being largely used in medicine, biotechnology, and in the cosmetics and food industries.[1] When compared to other materials, such as metals and ceramics, polymers present a unique advantage, which lies in the fact that polymers may be synthesized to attend specific required characteristics for a certain application.[2] Among the polymeric materials normally used in biomedical applications, poly(methyl methacrylate) (PMMA)-based resins have played a prominent role due to their optical and physical properties, excellent biocompatibility and easiness of manipulation. Applications include blood pump devices and reservoirs, membranes for blood dialyzers, implantable ocular lenses, contact lenses, and bone and denture materials.[3]

PMMA gained fame in orthopedics due to the Judet brothers, who pioneered the production of PMMA prosthesis for bone reparation.[3] In 1958, John Charnley made the first significant use of PMMA for the support of medullar portions of total hip replacement, although there is a long history of applications in general surgery, which dates back into the 1940's.[4]

PMMA-based bone cement (PMMABC) is prepared during the application through the free radical bulk polymerization of MMA monomer, initiated by the decomposition of benzoyl peroxide (BPO) and activated by N,N dimethyl-p-toluidine (DMPT).[5] The recipe also contains a

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prescribed amount of barium sulfate ($BaSO_4$), which is used to render the cement X-ray opaque, and PMMA particles, which are used to increase the viscosity of reaction medium and to accelerate the polymerization reaction due to gel effect.

The bone cement preparation reaction begins by mixing the recipe components in a vessel. The system viscosity and the reaction rate increase quickly due to the gel effect, which is greatly enhanced by the presence of the PMMA particles. When a suitable viscosity (or degree of polymerization) is reached, the mixture is delivered to the patient. An inherent problem of this reaction is the high amount of heat released during the bone cement preparation, which may cause the reaction temperature to increase above 100 °C, possibly leading to irreparable damage of living tissues.[6]

PMMABC has been extensively studied in the past and there are many reports in the open literature about the influence of some preparation variables on the evolution of reaction variables (temperature and conversion) and on the final properties of the produced PMMABC.[5–13] Some of the analyzed preparation variables were the operation room temperature, the type and characteristics of the used pre-polymer, the monomer to powder ratio, the type and amount of radiopaque agent, and the amount of BPO and DMPT used. In spite of that, fundamental knowledge about how variables affect the bone cement preparation is not available yet, as much of the developed work is based on empirical cause-effect analysis of experimental observations.

Meyer *et al.*[7] verified that the maximum temperature reached during bone cement preparation can be minimized by reducing the operating room temperature. This indicates how important heat transfer effects may be during the bone cement preparation in a real application environment. Haas *et al.*[8] showed that, by using minimum amount of MMA monomer and maximum amount of PMMA particles, the polymerization rate and heat released during the reaction can be minimized. This can be easily explained in terms of the reduction of the MMA concentrations. It was also reported that the final compressive strengths of bone cements prepared with MMA(liquid)/PMMA(powder) mixtures varying from 0.33 to 0.66 mL/g were essentially the same. Nevertheless, Bellkok *et al.*[9] showed that the increase of the monomer-to-powder ratio may significantly reduce the ultimate compressive strength, the yield stress and the compressive modulus of the final cement.

Pascual *et al.*[6] found out that it is possible to improve the characteristics of PMMABC and control the observed reaction temperature peak through manipulation of the particle size distribution of PMMA. Liu *et al.*[10] showed that PMMA powders of different average particle sizes and average molecular weights produce PMMABCs with different mechanical properties. These results indicate that the final bone cement performance may depend on the initial bone cement formulation and on the properties of the PMMA powder. It was also shown that the molecular weight of PMMA may be reduced during sterilization due to scission of PMMA chains.[11] Besides, other variables, such as porosity, may also affect the mechanical performance of PMMABC.[12] In fact, Ries *et al.*[12] showed that there is an inverse relationship between fracture toughness and pore size.

Mechanical toughness of bone cement is strongly affected by the content of residual monomer (which acts as a plastifying agent[5]), the bone porosity[6] and the molecular weight of the polymer obtained.[14] The final content of residual monomer is partially due to the glass effect, which prevents total monomer conversion.[15] The formation of pores is a consequence of the fast evaporation of the monomer during the polymerization reaction and of the air entrapped during the mixing of the solid and liquid components of the recipe.[6] Barros[16] showed that the amount of pores in the PMMABC depends on the preparation technique, as also discussed by Lewis.[17]

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Vazquez *et al*.[5] studied the influence of BPO and $BaSO_4$ on the bone cement preparation. BPO plays an important role in the reaction kinetics. They observed the increase of the temperature peak and the decrease of setting time when the BPO concentration was increased. This can be explained by the increase of free radical concentration in the reaction medium. Vazquez *et al*.[5] also observed that the tensile modulus of the bone cement progressively decreases with the increase of the concentration of $BaSO_4$ in the reaction medium. This indicates that the amount of X-ray contrast in the final cement material should be minimized. On the other hand, Kurtz *et al*.[13] verified that the addition of $BaSO_4$ does not necessarily compromise the static and fatigue properties of PMMABC used for the treatment of vertebral compression fractures.

It is clear that, in order to obtain a PMMABC with appropriate characteristics, it is necessary to understand and control the process variables that affect final properties of the bone cement, including porosity, content of residual monomer, temperature profile during the reaction and molecular weight and particle size of PMMA. For this reason, the literature reports a number of mathematical modeling investigations, which have been carried out to allow for improved understanding of the bone cement preparation. The evolution of the temperature profile during the reaction normally is the investigated process variable, as it can be monitored in-line in the real application environment.[18–20] However, available modeling studies are based on modeling approaches that do not emphasize the importance of heat transfer and of the gel effect to explain the evolution of reaction variables.

An experimental and theoretical study is carried out in this work to provide better understanding of the bone cement preparation. This may be regarded as a first step towards the development of a methodology for PMMABC preparation that will allow for proper control of temperature profiles during the polymerization reaction in the real application environment. Experiments were performed at different operation conditions in order to evaluate the role of monomer and BPO purification, PMMA particle sizes and the mixing technique of the recipe components on the evolution of the reaction temperature. A mathematical model based on a typical free-radical polymerization mechanism is proposed to simulate the evolution of reaction temperatures during the bone cement preparation. It is shown that the proposed model is able to describe available experimental data very well and that heat transfer to surroundings and initial PMMA content of the recipe play fundamental roles on the evolution of reaction temperatures.

Experimental

Materials

MMA (Rhodia) was distilled at low pressures. BPO purchased from Fluka (97% pure on a dry basis) was used as received or purified. Purification was performed by dissolution of BPO powder in chloroform at room temperature, followed by re-crystallization in cold ethanol. BPO particles were then filtered and dried at room temperature under vacuum. DMPT (Aldrich) and $BaSO_4$ (Isofar) were used without further purifications.

Three PMMAs were used for the bone cement preparation, as described in Table 1. PMMA 1 (Aldrich) was obtained

Table 1.
PMMA characterization.

PMMA	Diameter (μm)	Mw $\times 10^{-3}$ (Dalton)	Mn $\times 10^{-3}$ (Dalton)	Polydispersity
PMMA 1	75–300	1736	1389	1.25
PMMA 2	5–10	301	148	2.03
PMMA 3	35–50	602	330	1.83

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commercially, whereas PMMA 2 and PMMA 3 were synthesized through free-radical suspension polymerization, using poly (vinyl alcohol) - PVA (Vetec) - as suspension agent and BPO as initiator.

Casting Mold

Cylindrical test pieces for analysis of mechanical performance were molded in accordance with the ASTM D 695 – 85 (25.4mm tall and 12.7 mm diameter). Figure 1 shows the mold and some of the obtained test pieces.

PMMA Particles

Two suspension polymerization runs were performed to produce PMMA particles for preparation of bone cements. PMMA 2 consists of pure poly(methyl methacrylate). PMMA 3 is an *in situ* blend of poly(methyl methacrylate) and $BaSO_4$, added to the reactor vessel as a suspension in the MMA monomer. Reactions were carried out in a glass stirred heated reactor. Firstly, an aqueous solution of PVA was delivered to the reactor. After temperature stabilization, a solution of BPO in MMA monomer (which may contain the suspended $BaSO_4$ particles) was added into the reactor. Figure 2 shows a typical MEV microscopy of a final PMMA 3 particle. Figure 2 shows some of the much smaller $BaSO_4$ particles placed on the final particle surface.

Bone Cement

PMMABC were produced through free-radical bulk polymerization using an initiator (BPO)-activator (DMPT) system. The reactions were carried out in small 50-mL glass vessels. Solid and liquid components were weighed separately. Solid materials were mixed manually before addition of liquid components. Afterwards, the solid and liquid mixtures were mixed manually in the glass vessels. Mixing was conducted as normally performed in real surgery rooms. A thermocouple was placed in the center of the reaction medium in order to monitor the temperature profile during the reaction.

Test Pieces

Test pieces were prepared following the same methodology used for bone cement preparation. However, after homogenization of the reaction medium, the mixture was carefully shed into the mold in order to avoid air bubble formation. Figure 1b shows the mold and some of the obtained test pieces. The toughness compression tests were carried out using a universal test machine INSTRON, model 4204. The used cell was able to support up to 5000 N of strength.

Mathematical Modeling

A mathematical model for the bone cement preparation is developed. The model takes into account mass and energy balances and is based on a classical kinetic mechanism for free radical polymerization of MMA.[21–23] The only significant difference is the fact that initiation may take place at

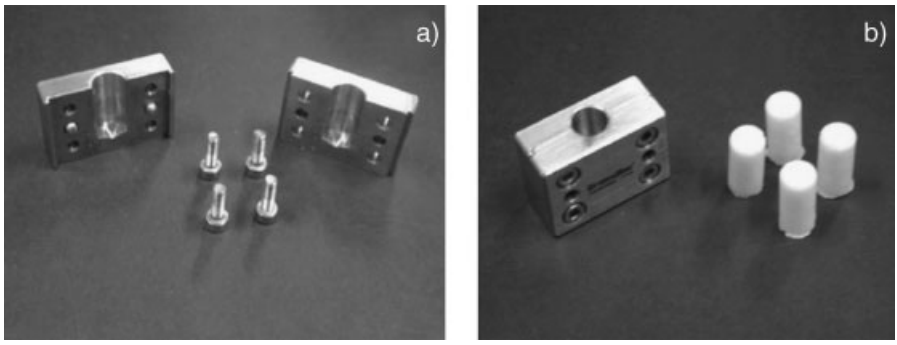

Figure 1.
Casting mold (a) opened and (b) closed and some test pieces obtained.

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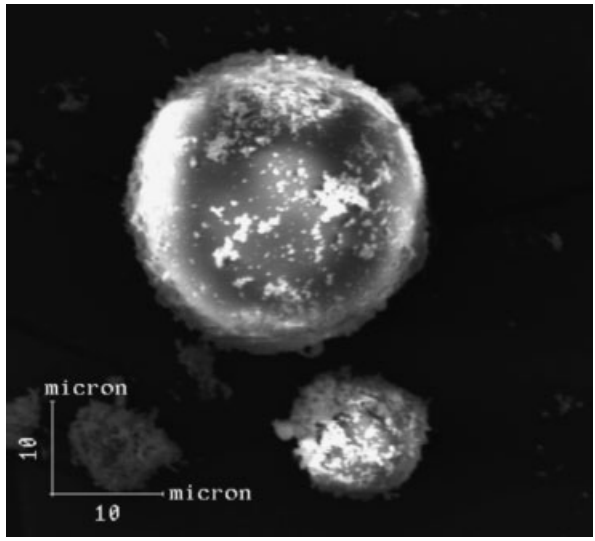

Figure 2.
MEV analysis of PMMA 3 particles.

low temperatures due to the presence of an initiation activator agent (DMPT).[24–26] As acknowledged by the literature,[24–26] the redox system activator/initiator mechanism is not well understood. Besides, it is uncertain whether the activator species are indeed consumed or not during the reaction. It should be pointed out, though, that the stoichiometric coefficients are not known precisely even when it is assumed that the activator species are consumed. From a practical point of view, though, the trajectories are not very sensitive to the activation step because initiation occurs mostly by thermal effects. The generation of radicals by the activator is only important when the temperature is very low (for reaction kick-off). This is because of the large temperature variations and the strong gel-effect of the MMA bulk polymerizations which control the dynamical evolution of reaction rates.

The reaction mechanism comprises the following steps:
Initiation:

$$At + I \xrightarrow{k_a(T)} At + 2R_0\cdot,$$

$$I \xrightarrow{k_d(T)} 2R_0\cdot,$$

$$R_0\cdot + M \xrightarrow{k_i(T)} P_1\cdot.$$

Propagation:

$$P_i\cdot + M \xrightarrow{k_p(T)} P_{i+1}\cdot, \quad i \geq 1$$

Termination:

$$P_i\cdot + P_j\cdot \xrightarrow{k_{tc0}(T)} \Lambda_{i+j}, \quad i,j \geq 2$$

$$P_i\cdot + P_j\cdot \xrightarrow{k_{td0}(T)} \Lambda_i + \Lambda_j. \quad i,j \geq 2$$

It is assumed that the quasi-state steady hypothesis is valid for radicals, that termination takes place solely by disproportionation, that the activator promotes the degradation of the initiator, and that the reactivity of macroradical P_i depends only on the last added monomer unit (terminal model). Therefore, the mass balances for monomer, initiator and activator and the energy balance are given by:

$$\frac{dM}{dt} = -k_p(T)[P\cdot]M, \tag{1}$$

$$\frac{dI}{dt} = -k_d(T)I - k_a(T)[At]I, \tag{2}$$

$$\frac{dAt}{dt} = 0, \tag{3}$$

$$\rho c_p V(1+\varepsilon)\frac{dT}{dt} = (-\Delta H)k_p(T)[P\cdot]M - \alpha UA(T - T_{amb}), \tag{4}$$

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where $[P\cdot]$ represents the molar concentration of free radicals $P\cdot$, and is given by:

$$[P\cdot] = \left(\frac{f[I](2k_a(T)[At] + 2k_d(T))}{k_t(T)}\right)^{1/2}, \quad (5)$$

ε represents the external thermal capacitance factor[27] and αUA represents the heat transfer coefficient between reactor and environment. The external thermal capacitance factor represents the ratio of the thermal capacitance of externals (e.g. tube walls, connections, valves, recycling pump, *etc.*) to that of the reaction mixture. The formulation for the external thermal capacitance presented assumes that the externals are in thermal equilibrium with the reactor contents.[27] All physical parameters and kinetic constants described in the model equations are shown in Table 2.

In order to take the gel-effect into account, the termination rate constant is assumed to depend on both the reaction temperature and the monomer conversion, as proposed by Ross and Laurence.[33] The termination constant is rewritten as follows:

$$k_t(T) = k_{t0}(T)g_t(T) \quad (6)$$

where $g_t(T)$, the gel-effect function, is given by

$$g_t = \begin{cases} 0.10575\exp(17.5\upsilon_f - 0.01715(T - 273.15)), & \upsilon_f > \upsilon_{ftc} \\ 2.3\cdot 10^{-6}\exp(75\upsilon_f), & \upsilon_f \le \upsilon_{ftc} \end{cases} \quad (7)$$

where υ_f is the total free volume and υ_{fc} is a critical free volume, given by:

$$\upsilon_f = \upsilon_{f_{MMA}}\nu_{MMA} + \upsilon_{f_{PMMA}}\nu_{PMMA}, \quad (8)$$

$$\upsilon_{ftc} = 0.1856 - 2.965 \cdot 10^{-4}(T - 273.15). \quad (9)$$

Free volumes of MMA and PMMA are given by:

$$\upsilon_{f_{MMA}} = 0.025 + 0.001(T - 167), \quad (10)$$

$$\upsilon_{f_{PMMA}} = 0.025 + 0.00048(T - 387). \quad (11)$$

Results and Discussion

Parameter Estimation

Equation (4) presents two thermal parameters, representing the heat transfer to the environment (αUA) and the external thermal capacitance factor (ε). These parameters were estimated by fitting simulated temperature profiles to observed experimental profiles for experimental runs performed without reaction (without the initiator / activator system). In a typical heat transfer experiment, equal amounts of MMA (inhibited with 2 wt% of hydroquinone in order to avoid spontaneous thermal polymerization) and PMMA were

Table 2.
Parameters describing the MMA polymerization.

Parameter	References
$k_p(T) = 7.0\cdot 10^9\exp(-6300/RT)$ cm^3/mol s	[28]
$k_d(T) = 6.94\cdot 10^{13}\exp(-29220/RT)$ s^{-1}	[29]
$kt(T) = 1.76\cdot 10^{12}\exp(-2800/RT)\cdot g_t(T)$ cm^3/mol s	[28]
$\rho_{MMA}(T) = 0.9654 - 0.00109(T - 273.15) - 9.7\cdot 10^{-7}(T - 273.15)^2$ g/cm^3	[30]
$\rho_{PMMA}(T) = \frac{\rho_{MMA}(T)}{0.754 - 9\cdot 10^{-4}\cdot(T - 343.15)}$ g/cm^3	[30]
$\rho_{BaSO_4} = 4.50$ g/cm^3	[31]
$c_{p_{MMA}} = 0.490$ cal/g K	[30]
$c_{p_{PMMA}}(T) = 0.339 + 9.55\cdot 10^{-4}\cdot(T - 298.15)$ cal/g K	[30]
$c_{p_{BaSO_4}} = 0.104$ cal/g K	[31]
$\Delta H = 137.70$ cal/g	[32]
f = 0.6	Mean value from various references in [28]

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mixed inside the glass vessel. Then, the system was heated until 100 °C with a hot air blower. Afterwards, heating was interrupted and temperatures were allowed to decrease through natural heat exchange with the surroundings. It may be observed that simulated and experimental temperature profiles agree fairly well after estimation of thermal parameters, as shown in Figure 3. Table 3 presents the estimated thermal parameters.

Figure 3 indicates that heat transfer to the surroundings may be extremely important for control of the temperature profile during real applications, as significant temperature decrease may be observed during the typical time span of the bone cement preparation (10 to 20 minutes). Therefore, it may be advisable to standardize the temperature conditions and glass flask properties during preparation of bone cements.

All kinetic constants were obtained from the literature,[34] with exception of the kinetic constant related to initiator decomposition due to the activator, k_a. This rate constant was estimated by fitting simulated and experimental temperature profiles in an experimental run containing 58.4 % (w/w) of PMMA pre-polymer, 38.9% (w/w) of MMA, 1.5% (w/w) of DMPT and 1.2% (w/w) of BPO. It may be observed that simulated and experimental temperature profiles agree fairly well after the estimation of parameter k_a (Figure 4). Table 3 presents the estimated correlation for k_a.

Table 3.
Parameter estimates.

Parameter	Value
αUA	0.017cal/K/s
ε	0.095
k_a	$7.0 \times 10^2 \exp(-6300/RT)$ cm^3/mol/s

Bone Cement Preparation

The set of experimental runs carried out in this work are shown in Table 4. According to Table 4, it may be concluded that both MMA purification through distillation (cf. runs 1 and 2) and BPO purification through re-crystallization (cf. runs 2 and 4) do not affect significantly the evolution of the temperature profiles. These are very important results because they indicate that other preparation variables are much more influential than the initial purity of the reagents, which has to be controlled basically for clinical purposes.

The effect of the initiator/activator system on the course of the polymerization can be verified by comparing runs 2 and 3. It may be observed that the temperature

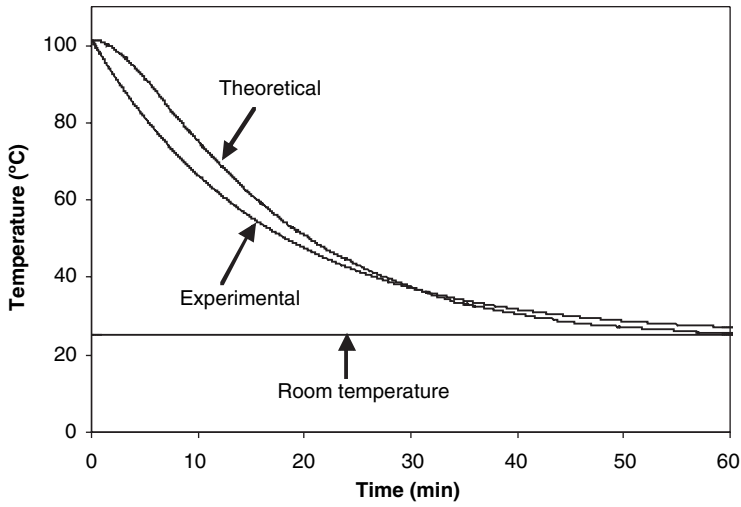

Figure 3.
Simulated and experimental temperature profiles after estimation of thermal parameters.

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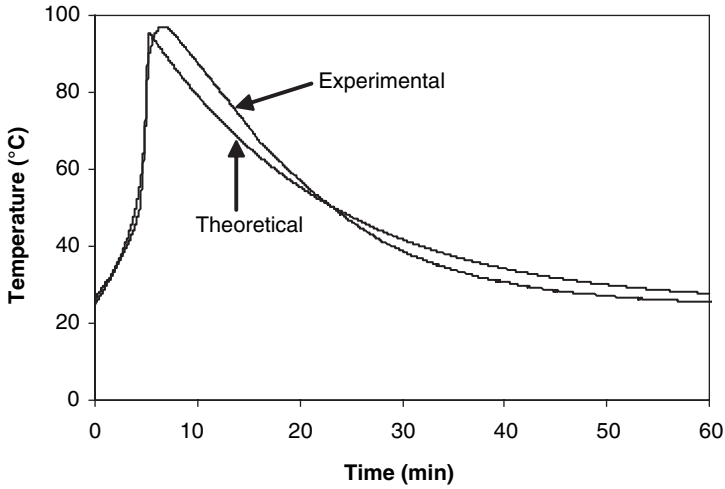

Figure 4.
Simulated and experimental temperature profiles after estimation of k_a.

profile, measured in terms of the temperature peak and peak time, is very sensitive to the amount of the initiator/activator system added to the reaction medium. This is also a very important result because it indicates that the initiator/activator ratio can be used for design, control and optimization of the temperature profile.

Experimental runs 2 and 5 illustrate the effect of adding PMMA pre-polymer into the reaction medium. It may be observed that the temperature peak obtained in run 2 is higher than that obtained in run 5. It should be noticed that part of the heat of reaction released during run 5 was used to warm-up the PMMA pre-polymer. In spite of that, temperature peaks do not vary considerably in these experimental runs, which may lead to the conclusion that the polymerization reaction in run 5 was more complete, mainly due to enhancement of the gel effect. The gel effect causes the acceleration of reaction rates and, therefore, acceleration of rates of heat release and reduction of final residual monomer contents.

Another important point to be addressed is the effect of the average particle size of the PMMA pre-polymer on the reaction course. Run 6 was performed with the same recipe as run 5, except for the fact that PMMA particles

Table 4.
Experimental runs.

Run	m_{MMA} (g)	m_{DMPT} (g)	m_{BPO} (g)	m_{BaSO4} (g)	m_{PMMA} (g)	PMMA	Peak T (°C)	Peak t (min)
1	10.04*	0.41	0.32	–	–	–	67	4.1
2	10.01	0.41	0.33	–	–	–	69	3.9
3	10.05	0.22	0.15	–	–	–	55.5	8.6
4	10.02	0.42	0.30**	–	–	–	72	4.4
5	10.09	0.40	0.30	–	5.00	PMMA 1	64	5.8
6	10.00	0.42	0.32	–	5.08	PMMA 1***	72	5.0
7	10.00	0.43	0.30	5.01	–	–	50	4.8
8	10.04	0.43	0.31	3.30	11.70	PMMA 2	83	6.4
9	10.01	0.40	0.34	15.01		PMMA 3	103	6.0

* Non-distilled monomer.
** Purified initiator.
*** Ground PMMA.

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size in run 6 was reduced by means of grinding. It was verified that the use of smaller particles cause significant increase of polymerization rates and, consequently, of the attained temperature peak, as already reported in the literature.[6] This indicates that heat and/or mass transfer effects, probably related to the dissolution of the polymer material in the reaction medium, should be taken into account during the analysis of the bone cement preparation. Although this effect has been neglected in the model proposed here, it is analyzed in detail in a companion paper.[35]

Experimental run 7 illustrates the presence of $BaSO_4$ powder in the reaction medium. Comparing to run 2, it may be observed that $BaSO_4$ powder plays a considerable role on absorbing reaction heat released during polymerization. Besides, it was observed experimentally that usage of high amounts of solids in the bone cement recipe, mainly $BaSO_4$, cause inefficient and heterogeneous mixing, thus leading to production of porous and poorly mixed bone cement material, as shown in Figure 5a. The dark spots in Figure 5a indicate the existence of local high concentrations of initiator, which is undesirable.

In order to improve the mixing of bone cement constituents, which is an important problem for commercial products, batches of *in-situ* mixtures of $BaSO_4$ embedded in PMMA pre-polymer were prepared. PMMA pre-polymer obtained by this technique (PMMA 3) was extremely efficient for producing homogeneous bone cements (Figure 5b), also improving the reaction temperature profile (Figure 6). Figure 6 clearly indicates that the *in-situ* preparation of PMMA and $BaSO_4$ leads to more complete and faster monomer consumption, as indicated by the higher temperatures (rates of heat release).

Figure 7 shows the comparison between experimental and simulated temperature profiles during the bone cement preparation, as discussed previously. It is shown that experimental and modeling results agree very well during the polymerization. The estimated model parameters were the overall heat transfer coefficient and the reactor external thermal capacitance. This mathematical model may be used now for more detailed investigation of the role played by each one of the constituents of the bone cement recipe. For instance, Figure 8 shows simulated temperature profiles for increasing amounts of PMMA pre-polymer. It can be observed that it is possible to control both the temperature peak and the reaction time through manipulation of the relative amounts of the bone cement constituents. As the PMMA content increases, the temperature peak moves towards shorter reaction times because of the significant gel effect of the PMMA polymerization. Based on Figure 8 and on a

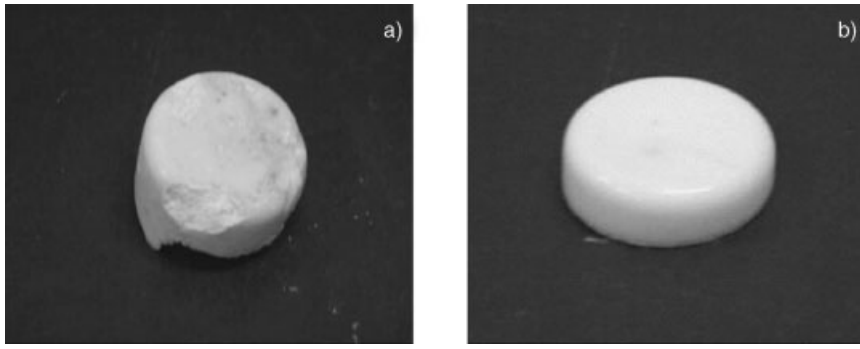

Figure 5.
PMMABC (a) $BaSO_4$ powder and PMMA particles added to the reactor and (b) $BaSO_4$/PMMA (PMMA 3) added to the reactor.

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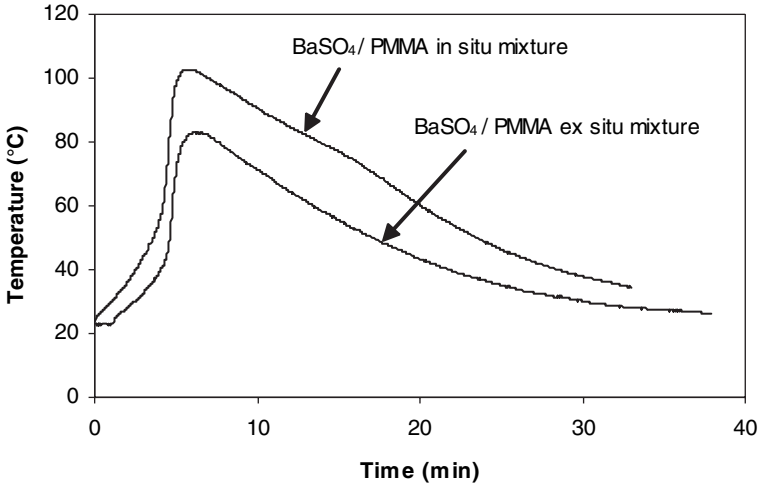

Figure 6.
Experimental temperature profiles showing the efficiency of mixture *in situ* of $BaSO_4$ powder.

typical preparation time of 15 minutes, it is possible to conclude that the initial PMMA content should be around 40 wt%. In this case, the cement should be introduced into the bone tissue about 5 minutes after the observation of the temperature peak. It is certain that other performance indices should be taken into consideration simultaneously, such as the residual monomer content and the system viscosity, but Figure 8 shows very clearly that the proposed model can be very useful for the design of PMMABCs.

Bone cements synthesized from the PMMA pre-polymer mixed *in situ* with $BaSO_4$ (experiment run 9) presented the best optical/mechanical properties among the recipes tested in this work. This recipe was used to prepare the test pieces for toughness compression essays. The bone cement prepared resisted without crack up to the maximum limit strength of cell used

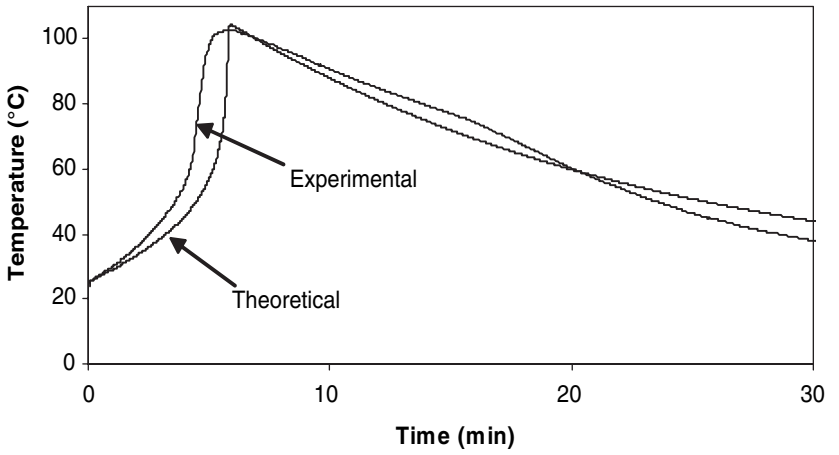

Figure 7.
Experimental and theoretical temperature profiles.

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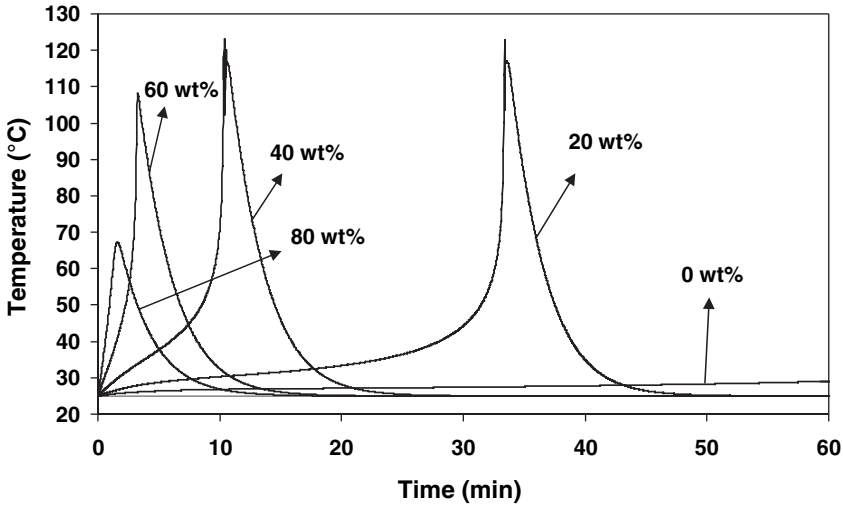

Figure 8.
Simulated temperature profiles for increasing amounts of PPMA pre-polymer.

in the test. Therefore, for the time being, the PMMABC prepared in this work with the proposed recipe is able to resist up to 5000N of strength applied without cracking, indicating the excellent performance of the prepared bone cements.

Conclusion

It was shown that a simple mathematical model is capable of describing the main features of the PMMABC synthesis and, therefore, that the model can be used for quantitative analysis of the bone cement preparation. It was shown that the properties of the pre-polymerized PMMA (particle size, molecular weight, and relative amount) are of fundamental importance for the proper interpretation of the evolution of temperature profiles during bone preparation. Particularly, it was shown that the mixing degree of the recipe constituents is one of the most important variables during bone cement preparation. For this reason, the *in-situ* preparation of mixtures of $BaSO_4$ and PMMA pre-polymer particles leads to PMMABC with better characteristics, as far as residual monomer and morphological properties are concerned. It was also shown that heat transfer to the surroundings and the gel effect exert significant influence on the course of the polymerization and should not be neglected in models intended for description of bone cement preparations in real applications.

Notation

M	monomer molecule or monomer mass
I	initiator molecule or initiator mass
At	activator molecule or activator mass
$[At]$	molar concentration of activator
$[P_i^{\cdot}]$	molar concentration of free radical $P_i\cdot$containing i units of monomer
$[P\cdot]$	total molar concentration of free radical $P_i\cdot$
$R_0\cdot$	free radical produced by degradation of initiator
f	initiator efficiency
g_t	gel effect correlation for k_t
k_a	kinetic constant for activation of initiator
k_i	kinetic constant for initiation of free radical
k_d	kinetic constant for initiator decomposition

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k_p	kinetic constant for propagation
k_t	kinetic constant for termination
c_p	heat capacity
V	volume reactor
T	temperature
T_{amb}	ambient temperature

Greek Characters

αUA	global heat transfer coefficient to the ambient
ε	thermal external capacitance factor
ΔH	heat of reaction for propagation
ρ	density
Λ_i	polymer formed with length i
Λ_j	polymer formed with length j
Λ_{i+j}	polymer formed with length i + j
υ_f	free volume
υ_{fMMA}	free volume of MMA
υ_{fPMMA}	free volume of PMMA
υ_{ftc}	critical free volume for termination
υ_{MMA}	volume fraction of MMA
υ_{PMMA}	volume fraction of PMMA

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