J Mater Sci: Mater Med (2009) 20:2427–2431
DOI 10.1007/s10856-009-3822-1

Real time monitoring of the polymerisation of PMMA bone cement using Raman spectroscopy

Christopher P. Hagan · John F. Orr · Christina A. Mitchell · Nicholas J. Dunne

Received: 26 September 2008 / Accepted: 10 July 2009 / Published online: 5 August 2009

Abstract In this investigation Raman spectroscopy was shown to be a method that could be used to monitor the polymerisation of PMMA bone cement. Presently there is no objective method that orthopaedic surgeons can use to quantify the curing process of cement during surgery. Raman spectroscopy is a non-invasive, non-destructive technique that could offer such an option. Two commercially available bone cements (Palacos® R and SmartSet® HV) and different storage conditions (4 and 22°C) were used to validate the technique. Raman spectroscopy was found to be repeatable across all conditions with the completion of the polymerisation process particularly easy to establish. All tests were benchmarked against current temperature monitoring methods outlined in ISO and ASTM standards. There was found to be close agreement with the standard methods and the Raman spectroscopy used in this study.

1 Introduction

Bone cements are acrylic based resins that were first used for joint arthroplasty surgery in 1958. Their function is to fill the space between the prosthesis and the bone, thereby fixing the prosthesis in place and acting as an interface between the bone and prosthesis allowing load to be transferred during activity [1].

C. P. Hagan · J. F. Orr · N. J. Dunne (✉)
School of Mechanical and Aerospace Engineering, Queens University Belfast, Stranmillis Road, Belfast BT9 5AH, UK
e-mail: n.dunne@qub.ac.uk

C. A. Mitchell
School of Medicine, Dentistry and Biomedical Sciences, Queens University Belfast, Grosvenor Road, Belfast BT12 6BP, UK

Bone cements are two component systems [2]. The powder component comprises pre-polymerised polymethyl methacrylate (PMMA), an initiator benzoyl peroxide (BPO) and a radiopaque component. The monomer, methyl methacrylate (MMA) is the main component of the liquid but an activator, dimethyl-para-toulidine (DMPT) is also included. A small amount of hydroquinone is added to ensure polymerisation of the liquid monomer does not take place during storage.

When the polymer powder and liquid monomer are combined a dough is formed and a free radical polymerisation reaction takes place (Fig. 1).

During polymerisation, the viscosity of the cement dough is continually changing, which results in variations in the handling characteristics of the dough [3]:

- *Mixing*—full integration of the powder and liquid components either by hand mixing or use of a mixing device.
- *Waiting*—after mixing, the cement viscosity is too low for working. At the end of this phase the cement can be handled without sticking to surgical gloves.
- *Working*—the time during which the cement can be manipulated, applied and the prosthesis inserted.
- *Setting*—the cement viscosity makes it hard to manipulate. At the end of this phase the cement is fully hardened. The setting time, as defined by ISO 5833 [4], occurs in this phase.

In joint arthroplasty surgery, the orthopaedic surgeon determines the stage of polymerisation of the bone cement by physical examination. This is very subjective and requires a high degree of experience [2]. If the surgeon is inexperienced there may be a need to consult the data included in the cement pack (Fig. 2), providing guidelines relating to the times of each handling phase for varying

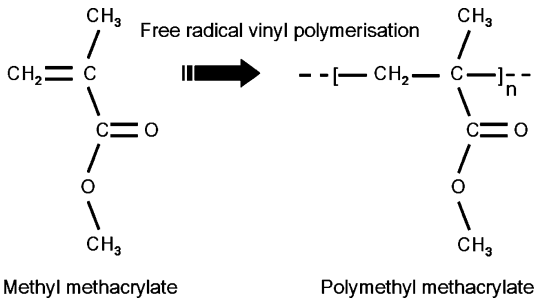

Fig. 1 Free radical polymerisation of MMA

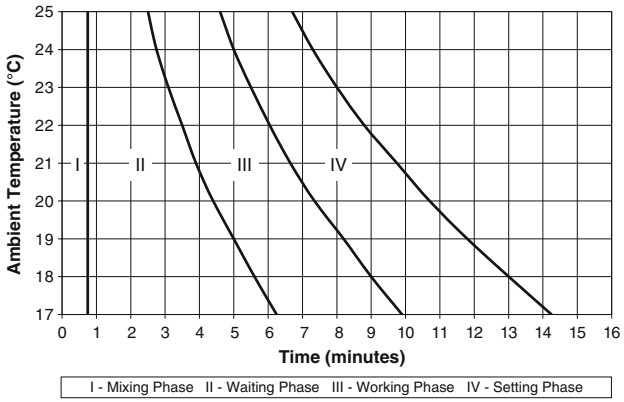

Fig. 2 Working curves of bone cement [12]

ambient temperatures. The data used to generate these polymerisation charts is primarily collated in accordance with the test protocol outlined in ISO 5833 [4].

Ambient temperature has a significant influence on the polymerisation reaction of the cement; 1°C increase in temperature reduces the total polymerisation time by approximately 1 min. Temperature is not the only factor that can affect the polymerisation of bone cement. Meyer et al. [5] investigated the change in powder to liquid ratio of the components. They found that a decrease in the ratio leads to an increased maximum polymerisation temperature and delays the dough and setting times. Similar results were found by Dunne and Orr [2] when they experienced a reduction in the powder to liquid ratio due to powder getting trapped in a groove in a mixing device. The normal powder to liquid ratio is 2:1 but it is possible that this will be slightly altered in surgery due to spillages or powder getting trapped and not incorporated into the mixture.

The dough time signals the beginning of the working phase [4], recognised as the time at which the mixture is able to separate cleanly from a gloved finger. He et al. [6] examined the effect that four different types of surgical gloves had on dough time measurements of PMMA bone cements as measured by ISO 5833 and ASTM F-451. They observed that using the different surgical gloves, dough time measurements time for Simplex P^{TM} cement varied by

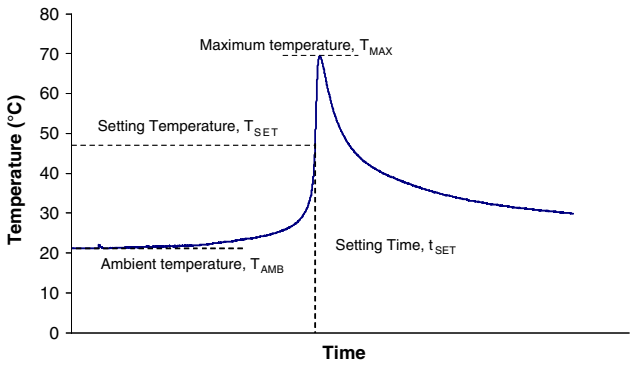

Fig. 3 Typical polymerisation temperature trace for bone cement [4]

up to 250%; the shortest at 3 min and the longest time 10.5 min. This study highlights the uncertainty that can arise in an operating theatre as to whether or not the cement mixture was ready for use. Similar ambiguity exists when determining the cement setting characteristics for acrylic bone cements. ISO 5833 [4] documents a method for determining the setting temperature and setting time for PMMA bone cement, taking advantage of the fact that chain propagation is an exothermic process. The temperature of the cement mixture is monitored throughout polymerisation and a temperature trace (Fig. 3) is produced. The setting temperature, T_{set} is determined using Eq. 1.

$$T_{set} = \frac{T_{amb} + T_{max}}{2} \quad (1)$$

where T_{amb} is the ambient temperature during polymerisation (°C) and T_{max} is the maximum temperature reached during polymerisation (°C). The setting temperature can then be used to find the setting time, t_{set} (min), the time taken to reach a temperature midway between ambient and maximum.

It is not practical to conduct the temperature monitoring technique according to ISO 5833 in a clinical environment as it requires at least 40 g of bone cement and would not provide any useful information during the surgical procedure because no thermal data can be quantified until full polymerisation has occurred.

To the authors' knowledge there is currently no test procedure or device that can be used to monitor the polymerisation of PMMA bone cement in a clinical setting. Successful studies have shown that ultrasonic technology can be applied to characterise the polymerisation of acrylic bone cement [2, 7]; Dunne et al. monitored the transition of PMMA cement through its phases of polymerisation [2]. Rehman et al. [8] investigated the application of Raman spectroscopy as a means of monitoring the polymerisation of novel bone cement comprising polyethyl methacrylate and butyl methacrylate. Raman spectroscopy is an analytical technique that is used to identify the modes of

vibration taking place in a molecular structure [9]. It can distinguish between these modes, allowing the different elements, chemical bonds and molecules present to be identified.

Raman spectroscopy has been used by Barnes et al. [10] to follow the polymerisation of dicyclopentadiene and Gulari et al. [11] to follow the bulk polymerisations of MMA and styrene. Other spectroscopic techniques can be used to follow polymerisation reactions but the best results seem to be found using Raman spectroscopy. This is possible because loss of the C=C bond is particularly easy to follow using Raman spectroscopy [9].

The purpose of this study was to monitor the polymerisation of commercially available PMMA bone cements using Raman spectroscopy. In parallel the polymerisation reaction of the PMMA bone cement was determined in accordance with ISO 5833 [4] Annex C: Determination of maximum temperature and setting time of liquid–powder mixture. If the two methods produce corresponding results it may be possible to develop further the use of Raman spectroscopy as a tool for monitoring the curing of PMMA with a view to developing a device that can be used in a clinical setting.

2 Materials and methods

2.1 Sample preparation

Two commercially available bone cements were analysed in this study: Palacos® R (Heraeus Kulzer, Germany) and SmartSet® HV (CMW Laboratories, UK). Five batches of Palacos® R were stored at 4 ± 1°C and five batches stored at 22 ± 1°C for at least 24 h prior to mixing. Five batches of SmartSet® HV were stored at 22 ± 1°C for at least 24 h prior to mixing. Each batch contained a single mix of cement consisting of 40 g powder and 20 ml liquid. All mixing aids and mixing devices were stored at ambient laboratory conditions (22 ± 1°C, 50 ± 2% relative humidity) for a minimum of 24 h prior to the cement constituents being mixed. All cement constituents were mixed using a Summit HiVac™ Syringe mixing system (Summit Medical Ltd., UK) under atmospheric conditions for 30 s, after which the dough was quickly transferred to the appropriate moulds to allow for monitoring.

2.2 Monitoring using Raman spectroscopy

Raman spectroscopy was carried out using a RamanStation Fusion (Avalon Instruments, UK). After the bone cement was mixed, 3 ± 0.5 g was transferred to a polymeric receptacle and placed in the spectrophotometer. On average, the cement was situated in the spectrophotometer approximately 90 s after the liquid monomer was added to the polymer powder. Raman spectroscopy was carried out using a RamanStation Fusion (Avalon Instruments, UK). An initial background scan was taken followed by a scan of the sample. Each scan consisted of six exposures of 5 s each, giving a total exposure time of 30 s. Scans were taken every 35 s for a period of 1 h. Upon completion of data collection, the spectra were analysed. By determining a sub-section of each spectra that did not demonstrate Raman scattering it was possible to obtain a spectral baseline (Fig. 4). The intensity of any peak was then calculated using Eq. 2.

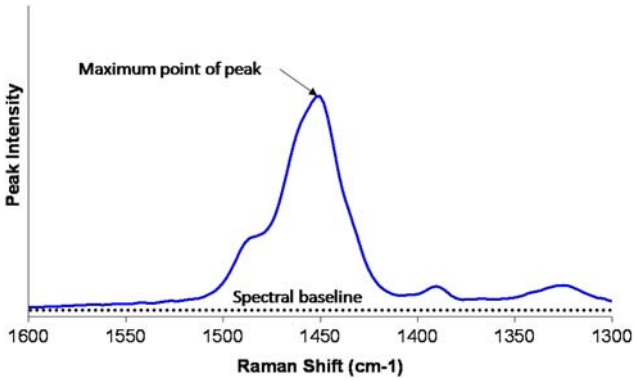

Fig. 4 Calculation of peak intensity

$$\text{Peak Intensity} = I_{\text{PEAK}} - I_{\text{BASE}} \quad (2)$$

where I_{PEAK} is the intensity of the highest point of the peak and I_{BASE} is the baseline intensity. For this study the peak of interest corresponded to the C=C bond, which was present at a Raman shift of 1,640 cm^{-1}.

2.3 Temperature monitoring

The remaining cement from each mix was used to measure maximum temperature and setting parameters (T_{set} and t_{set}) in accordance with ISO 5833 [4]. A polytetrafluoroethylene (PTFE) mould was used to contain the bone cement during polymerisation. A nickel–chromium–aluminium *k*-type thermocouple was used along with PicoLog Data Acquisition Software (Pico Technology Ltd., UK). The test equipment was stored in laboratory conditions for a minimum of 2 h prior to testing. The temperature of the cement was recorded at 1 s intervals for a period of 1 h and a temperature trace was collated.

3 Results and discussion

Figure 5 shows the intensity of the peak at a Raman shift of 1,640 cm^{-1} at four timepoints: 5, 10, 15 and 20 min after mixing. Figure 6 shows the typical variation in Raman

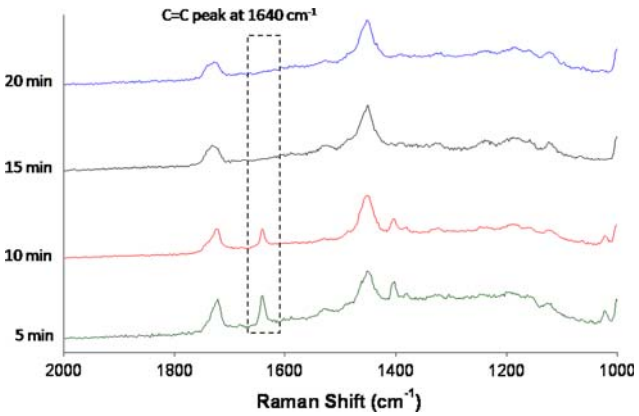

Fig. 5 Spectra of Palacos® R at 5, 10, 15 and 20 min after mixing (peak at 1,640 cm^{-1} highlighted)

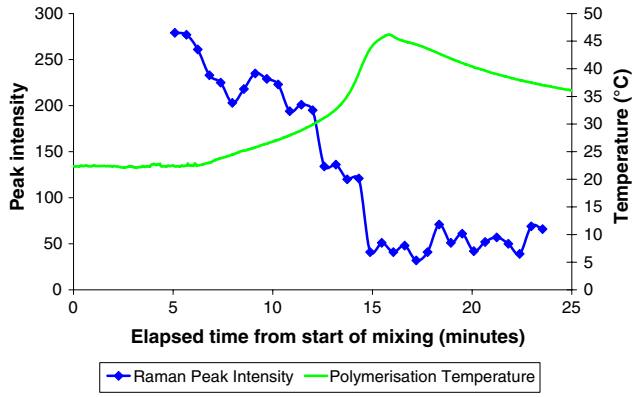

Fig. 6 Typical variation in Raman peak intensity and temperature trace of polymerising acrylic bone cement (Palacos® R bone cement stored at 4°C)

peak intensity and a typical polymerisation temperature trace of polymerising Palacos® R bone cement that had been stored at 4°C, respectively. It can be seen that initially the intensity of the Raman peak decreased as polymerisation reaction progressed. This is expected since it is known that this peak corresponds to the C=C bond, which is broken down during the propagation step of the polymerisation reaction. As time progresses, the peak intensity levels off to a plateau and remains stable. Since decreasing peak intensity is indicative of the diminishing number of C=C bonds, this stability indicates that chain propagation has completed and chain termination is the predominant polymerisation step occurring. If this is the case then the polymerisation of the bone cement has completed. For Palacos® R bone cement stored at 4°C, the time at which the plateau occurred, $t_{plateau}$ was 14.55 ± 0.38 min. The variation in peak intensities for the Palacos® R and SmartSet® HV bone cements stored under ambient conditions followed a similar trend to that shown in Fig. 6 with an initial decrease followed by a levelling off to a plateau.

From the polymerisation temperature trace measured in accordance with ISO 5833 [4], a t_{set} could be quantified. For Palacos® R stored at 4°C the average t_{set} was 13.19 ± 0.35 min. It was difficult to correlate the t_{set} to any point of reference from the Raman spectra. The t_{set} was obtained from the T_{set}, which represents the time point in cement polymerisation when approximately 90% of the reaction has occurred [4]. Of more interest and relevance is t_{max}, the time of T_{max}. Chain propagation is the exothermic step of the polymerisation reaction and therefore causes the temperature of the cement to increase. During the stage of the polymerisation reaction where termination is the principal step, the temperature decreases as the exothermic propagation step has ended and any heat already generated is dissipated to the surroundings. The t_{max} therefore indicates the transition between the propagation and termination steps and suggests that the polymerisation reaction has been completed. Kuehn [12] reported that at the time point when polymerisation reaches completion; the polymerisation temperature has usually reached its maximum. For Palacos® R bone cement stored at 4°C the average t_{max} was reached at 14.44 ± 1.18 min. t_{max} for Palacos® R bone cement stored at 4°C was found to be in close proximity to the time point when the Raman peak intensity levelled off. Similar trends were also noted for SmartSet® HV and Palacos® R when stored at 22°C (Table 1).

Since both the temperature maximum and the levelling off of the peak intensity suggest the completion of the polymerisation reaction of the PMMA bone cement, these results indicate that Raman spectroscopy could be used as a tool for real-time monitoring of the polymerisation of commercially available PMMA bone cements according to accepted time points for characterisation.

The findings of this study are in agreement with the results reported by Rehman et al. [8]. In both cases the polymerisation reaction was monitored in situ using Raman spectroscopy. The peaks monitored were in a similar location. This was to be expected as both studies used PMMA based materials and demonstrated similar structures, limiting the possible shifting of the C=C band. Both studies reported that the disappearance of the C=C peak coincided with t_{max}. However, a significant difference between this study and that by Rehman et al. is that they only obtained Raman spectra at 5-min intervals. Since the polymerisation reaction for PMMA bone cement is influenced significantly by environmental and operator factors [3] it is suggested that 5 min between each spectrum measurement is not sufficient for dynamic characterisation of the reaction. A shorter interval between spectra, such as the 35 s used in this study will improve the accuracy of predicting the completion of polymerisation, while maintaining the advantage of repeated measurements within each sample. Due to machine constraints used in this study,

Table 1 Polymerisation times as suggested by the three methods investigated

Technique used	Time (minutes)	Palacos® R (4°C)	Palacos® R (22°C)	SmartSet® HV (22°C)
Raman	$t_{plateau}$	14.55 ± 0.38	11.97 ± 0.88	13.50 ± 1.79
ISO 5833 [4]	t_{set}	13.19 ± 0.35	10.45 ± 0.76	12.25 ± 2.16
ISO 5833 [4]	t_{max}	14.44 ± 1.18	10.90 ± 0.72	12.79 ± 2.06

35 s was the shortest interval that could be used, but by taking spectra as close together as possible it allows the most information possible to be gained from the monitoring process.

It is worth considering that during polymerisation there will be some shrinkage in the cement and the topography of specimen may change [13]. This could affect the focus of the spectrometer, which in turn could influence the intensity of the spectra being recorded. It is possible to correct this problem by identifying a peak whose intensity will not change throughout polymerisation and calculating the C=C intensity as a ratio of this constant peak.

Other techniques that have been used to monitor the polymerisation of PMMA bone cements include the use of ultrasonic technology [2, 7]. This technique utilises the changing speed of sound through the cement as the viscosity changes throughout polymerisation. Again this testing can be carried out in situ, and can therefore give real time data on the polymerisation of the bone cement. An advantage, reported by both Dunne et al. [2] and Viano et al. [7], of the ultrasonic testing is that the velocity of sound through the fully polymerised cement can be used as a guide to predict the mechanical properties of the polymerised cement.

By looking in closer detail, Dunne et al. [2] were able to identify trends in the velocity of sound that related closely to the times quoted in the working curves for each cement. This would be beneficial in that it could allow the surgeon to know exactly when the working phase begins and ends. It is anticipated that with further investigation of the Raman data, it will be possible to identify trends in the variation in peak intensity that can be used to determine the different steps of the polymerisation reaction for PMMA bone cement.

4 Conclusions

Raman Spectroscopy was used to monitor the polymerisation reaction of PMMA based bone cement. This was compared with the more common temperature monitoring method outlined in ISO 5833. The Raman spectroscopy data indicated when the polymerisation reaction of the PMMA bone cement had ended. When compared to the temperature monitoring method, the results obtained using Raman spectroscopy were found to be in close proximity to the time of T_{MAX}. This indicates that Raman spectroscopy could be used as an alternative approach to monitoring the polymerisation of PMMA bone cement.

A problem with the ISO 5833 method is that it cannot be used in a clinical setting. This is because it requires a large amount of cement, i.e., 40 g, which could otherwise be used for the orthopaedic procedure, and does not yield any real time information. Raman spectroscopy can solve both these problems as a relatively small amount of cement, i.e., 3 g is required for the test and it indicates immediately when the polymerisation of the cement has ended.

References

1. Kuehn KD, Ege W, Gopp U. Acrylic bone cements: composition and properties. Orthop Clin N Am. 2005;36:17–28.
2. Dunne NJ, Xu Y, Makem J, Orr J. Ultrasonic characterisation of the mechanical properties and polymerisation reaction of acrylic based bone cements. Proc IMechE H. 2006;221:251–61.
3. Dunne NJ, Orr JF. Curing characteristics of acrylic bone cement. J Mater Sci: Mater Med. 2002;13(1):17–22.
4. ISO 5833. (International Organisation for Standards, Geneva, 2002).
5. Meyer PR, Lautenschlager EP, Moore BK. On the setting properties of acrylic bone cement. J Bone Joint Surg. 1973;55(1):149–56.
6. He S, Scott C, De Luise M, Edwards B, Higham P. Effect of choice of surgical gloves on dough time measurements of acrylic bone cement. Biomaterials. 2003;24(2):235–7.
7. Viano AM, Auwarter JA, Rho JY, Hoffmeister BK. Ultrasonic characterization of the curing process of hydroxyapatite-modified bone cement. J Biomed Mater Res. 2001;56(4):593–9.
8. Rehman I, Harper EJ, Bonfield W. In-situ analysis of the degree of polymerisation of bone cement by using FT-Raman spectroscopy. Biomaterials. 1996;17(16):1615–9.
9. Smith E, Dent G. Modern Raman spectroscopy—a practical approach. Great Britain: Wiley; 2005.
10. Barnes SE, Brown EC, Corrigan N, Coates PD, Harkin-Jones E, Edwards HGM. Raman spectroscopic studies of the cure of dicyclopentadiene (DCPD). Spectrochim Acta A. 2005;61:2946–52.
11. Gulari E, McKeigue K, Ng KYS. Raman and FTIR spectroscopy of polymerization: bulk polymerization of methyl methacrylate and styrene. Macromolecules. 1984;17:1822–5.
12. Kuehn KD. Bone cements—up to date comparison of physical and chemical properties of commercial materials. Berlin: Springer; 2000.
13. Orr JF, Dunne NJ, Quinn JC. Shrinkage stresses in bone cement. Biomaterials. 2003;24(17):2933–40.