The role of polymethylmethacrylate bone cement in modern orthopaedic surgery

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Polymethylmethacrylate remains one of the most enduring materials in orthopaedic surgery. It has a central role in the success of total joint replacement and is also used in newer techniques such as percutaneous vertebroplasty and kyphoplasty.

This article describes the current uses and limitations of polymethylmethacrylate in orthopaedic surgery. It focuses on its mechanical and chemical properties and links these to its clinical performance. The behaviour of antibiotic-loaded bone cement are discussed, together with areas of research that are now shedding light upon the behaviour of this unique biomaterial.

Polymethylmethacrylate (PMMA) was first employed by orthopaedic surgeons over 60 years ago and remains a key component of modern practice. The material is not strictly a cement, but a grout. The understanding of its properties has evolved and progressed alongside the advance of the specialty, and has indirectly helped improve implant design, particle science, cell biology and biomechanics. Fixation of components in total joint replacement with cement was followed by applications in fracture and tumour surgery, and latterly, percutaneous vertebroplasty.

The use of acrylic by orthopaedic surgeons is likely to continue, and knowledge of the properties and applications of this material remains essential.

Polymethylmethacrylate was unveiled by the chemical industry in 1843 and named ‘acide acrylique’ on account of the acid smell of the monomer. In 1936 it was noted that mixing ground polymer with monomer produced a dough that could be manipulated and moulded; hence it became one of the early biomaterials. Early applications were in dentistry. In 1945 and 1950 respectively, Scales and Herschell and Judet and Judet employed PMMA prostheses of the femoral head for arthritis of the hip. Its use as a grout to improve implant fixation was pioneered in 1953 by Haboush. However, the major breakthrough in the use of PMMA in total hip replacement (THR) was the work of Charnley in 1970 who used it to secure fixation of the acetabular and femoral components and to transfer loads to bone.

Chemistry

The structure of methylmethacrylate monomer allows polymerisation at room temperature to produce solid PMMA. The avidity of the polymer to dissolve in monomer aids this reaction. The contents of commercial packs of cement, including additives, are listed in Table I. The molecular weight of PMMA varies between proprietary brands and according to the method of sterilisation. Gamma radiation shortens the polymer chains, probably affecting many mechanical properties, but this does not occur with ethylene oxide sterilisation.

Working properties and viscosity

The dynamic viscosity (η) of fluids is denoted by shear stress (F)/shear rate (S) [η = F/S]. Fluids are designated as Newtonian if shear stress is linearly related to shear rate. Cement in its liquid phase of curing behaves as a non-Newtonian fluid with viscosity decreasing as shear rate is increased. This is called pseudoplastic or shear thinning behaviour. However, the viscosity of all cements increases during polymerisation as the polymer chains lengthen. Manufacturers can alter the viscosity of cement by changing the molecular weight, by using co-polymers, and by varying the methods of sterilisation. In addition, the curing process itself can be controlled by altering the proportions of the initiator (Toluidine) and the monomer, and this can change the working properties.

The cement must be liquid enough during the working phase to be forced through a...
delivery device and then flow under pressure to penetrate
the interstices of cancellous bone, achieving micro-inter-
lock.10,15 Manufacturers produce cements of varying vis-
cosities:14

Low. These have a long waiting phase of three minutes,
also known as a sticky phase. The viscosity rapidly
increases during the working phase and the hardening
phase is one to two minutes long.

Medium. There is a long waiting phase of three minutes,
but during the working phase, the viscosity only increases
slowly. Hardening takes between one minute 30 seconds,
and two minutes 30 seconds.

High. A short waiting/sticky phase is followed by a long
working phase. The viscosity remains constant until the
end of the working phase. The hardening phase lasts
between one minute 30 seconds and two minutes.

High viscosity cements are therefore forgiving for the
surgeon and are in predominant use in the United King-
dom.16 However, the rates of curing are very sensitive to
environmental factors. Low ambient temperatures during
storing and mixing,17 and high humidity both prolong
setting time.18

Heat production during polymerisation
The polymerisation of PMMA is exothermic.14 Catalysts
form free radicals which break the covalent C=C bonds of
the monomer, allowing them to bind to the lengthening
polymer chains. This reaction releases 52 KJ/mole of mono-
mer, equating to heat production of 1.4 to 1.7 × 108 J/m3 of
cement.14

The production of heat by the curing cement has been
studied in vitro and in vivo and modelled using finite ele-
ment analysis.19 In vitro studies have shown that the pro-
duction of heat is increased by thicker cement mantles,
higher ambient temperatures and an increased ratio of
monomer to polymer.17 Recorded temperatures range
between 70°C and 120°C.20 Collagen denatures with pro-
longed exposure to temperatures in excess of 56°C, and the
risk of causing thermal damage to bone has been raised by
several authors.20,21

However, in vivo studies have recorded lower peaks of
temperature.14 In 1977, Reckling and Dillon22 measured
the temperature at the bone cement interface in 20 THRs.
The maximum temperature was 48°C but the range of the
rise was from 3° to 17°C. These modest rises were attrib-
uted to the cooling effects of the local blood supply, the
metallic stem, the large surface area of the interface and
poor thermal conductivity of the cement. Harving, Soballe
and Bunger23 recorded temperatures above 56°C but only
for two to three minutes. Even if such temperatures may
sometimes be reached, animal studies have indicated no
adverse effects.24

Nevertheless, concerns regarding thermal and chemical
injury persisted and much effort was expended on low exo-
therm alternatives. Boneloc (Biomet Inc., Warsaw, Indiana)
was a methylmethacrylate/n-decylmethacrylate/isobotinyl-
methacrylate (MMA/DMA/IBMA) co-polymer cement. Its
setting temperature was 58°C in vitro.25 However, clinical
results were poor with a rate of aseptic loosening of 34% at
three years because of abnormal visco-elastic behaviour.26
Chemical changes made to the composition of cement can
therefore have profound effects upon function, as can
manipulation of the mix of the constituents, a feature that
has been exploited for specific indications such as percuta-
neous vertebroplasty.

Percutaneous vertebroplasty
This procedure is increasing in popularity. There are over
700 000 osteoporotic vertebral compression fractures each
year in the USA, one third being symptomatic. They repre-
sent a difficult problem in management and are predicted to
increase fourfold by 2050.27

Percutaneous vertebroplasty was originally developed as
a treatment for angiomas,3 but its application to the osteo-
porotic spine has been shown to provide significant and
prolonged relief of pain.4 It controls the symptoms of com-
pression fractures by recreating mechanical stability.28 The
technique involves the percutaneous transpedicular injec-
tion of low viscosity biomaterial into the vertebral body
guided by an image intensifier. It has become common prac-

<p>| Table I. Commercial constituents of bone cement |</p>
<table>
<thead>
<tr>
<th>Constituent</th>
<th>Role</th>
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<tbody>
<tr>
<td><strong>Powder components</strong></td>
<td></td>
</tr>
<tr>
<td>Polymer</td>
<td>Polymethylmethacrylate</td>
</tr>
<tr>
<td>Co-polymers (e.g. MA-MMA*)</td>
<td>Alter physical properties of the cement</td>
</tr>
<tr>
<td>Barium sulphate or zirconium dioxide</td>
<td>Radio-opacifiers</td>
</tr>
<tr>
<td>Antibiotics†</td>
<td>Antimicrobial prophylaxis</td>
</tr>
<tr>
<td>Dye (e.g. chlorophyll)</td>
<td>Distinguish cement from bone</td>
</tr>
<tr>
<td><strong>Liquid components</strong></td>
<td></td>
</tr>
<tr>
<td>Monomer</td>
<td>Methylmethacrylate monomer</td>
</tr>
<tr>
<td>N,N-dimethyl-p-toluidine (DMPT)</td>
<td>Initiates cold curing of polymer</td>
</tr>
<tr>
<td>Benzoyl peroxide</td>
<td>Reacts with DMPT to catalyse polymerisation</td>
</tr>
<tr>
<td>Hydroquinone</td>
<td>Stabiliser preventing premature polymerisation</td>
</tr>
<tr>
<td>Dye (e.g. chlorophyll)</td>
<td>Distinguish cement from bone</td>
</tr>
</tbody>
</table>

* MA-MMA, methacrylate-methylmethacrylate
† plain bone cements do not contain antibiotics
tice for clinicians to alter the mix constituents of the PMMA in order to facilitate the procedure. To ease injection they reduce viscosity by increasing the liquid to powder proportions of the mix. As detailed earlier, this would seem likely to increase the maximum setting temperature and setting time of cement, a cause for concern when considering the adjacent neurological and vascular structures. Another practice is the addition of extra opacifiers (barium sulphate, zirconium dioxide or powdered tungsten) to help with radiological visualisation. These departures from traditional practice may significantly reduce the compressive strength of the resulting cement, the former by reducing polymer chain concentrations and the latter by introducing multiple stress risers.

Care should be taken when performing such unpredictable alterations especially as the mechanical properties of new percutaneous vertebroplasty biomaterials have now been described.

Potential pitfalls of polymethylmethacrylate cement

Apart from thermal necrosis there are other concerns:

1) aseptic loosening is suggested to be a result of monomer-mediated bone damage.

2) during end-polymerisation there is volumetric shrinkage of the cement potentially compromising the bone/cement interface. Using a fluid displacement model, Charnley observed that the volume of cement increases to a maximum during polymerisation, before shrinking slightly, though not to its initial volume. Again this may be a largely theoretical concern,

3) there is a conflict between the stiffness of cement and the adjacent bone. The Young’s modulus is 0.5 GPa to 1 GPa for cancellous bone, 15 GPa to 20 GPa for cortical bone, 2 GPa for cement, 1 GPa for titanium and 220 GPa for cobalt chrome. The cement may provide a shock-absorbing layer between elastic bone and a stiff implant. The conflict between degrees of stiffness is therefore much greater for uncemented implants.

4) in some instances, the cement mantle and its interfaces may be the weak link in the construct. The bone/cement interface is the key to the survival of a THR. The combination of matt-surfac ed collared femoral stems and poor cementing technique are intrinsic to the failure of some implants. Polished collarless tapered stems have generally performed better.

5) cement particles were once considered a biological cause of aseptic loosening. However, Charnley believed that failure was mechanical in nature and that cement remained inert. Wear particles are now seen as primary initiators of the biological reactions in aseptic osteolysis.

The performance of cemented THR is strongly supported by both registry figures and clinical research. This reflects the practice of surgeons in many countries who are comfortable with their cementing technique. The mechanical characteristics of PMMA are key to this success.

Mechanical considerations of polymethylmethacrylate in total hip replacement

The implants in THR transmit load to the bone through their interfaces. Cemented implants can transmit sustained loads over a larger area than uncemented prostheses. Charnley demonstrated that the interface area of a cemented stem was approximately 13 m² (83.9 cm²). This was 65 times greater than the original uncemented calcar bearing stems.

Cemented implants have two interfaces, the implant/cement junction and the bone/cement interface, both of which ensure preservation of mechanical stability. Success depends upon the surgical technique, the design of the implant and the properties of the cement. Cemented acetabular components, generally made of ultra high molecular weight polyethylene (UHMWPE) (Young’s modulus of approximately 1 GPa), have a closer stiffness to cement and bone than they do to metal stems. Macro-interlock with cement is achieved using deep grooves in the UHMWPE, and most are overlapped to assist cement pressurisation. Transmitted forces are predominantly compressive with some shear. Charnley based the principles of ‘low friction arthroplasty’ on limiting these dangerous shear stresses.

Many different philosophies of design have been applied to cemented stems. The main differences between them occurs in the texture of shape and surface, which determine the nature and magnitude of forces at the interfaces because of the way they interact with cement. The survival of the bone/cement interface governs the outcome of cemented THR.

Stem design

It is beyond the scope of this article to describe in detail experimental and clinical data relating to different stem designs. There are two predominant options, the matt textured (sometimes collared) or shape-closed design, and the polished collarless tapered or force-closed design. Upon loading, shape-closed designs transmit high shear, some tensile and low compressive stresses to both sets of interfaces. By contrast, force-closed designs have much lower shear stresses and as the wedge shape engages, compressive radial stresses predominate. These latter designs, exemplified by the Exeter stem (Stryker Orthopaedics, Mahwah, New Jersey), have serendipitously exploited the viscoelastic properties of PMMA. The surface finish is critical and matt versions of the stem have higher failure rates than polished versions despite identical geometry.

Mechanical properties of polymethylmethacrylate

Polymethylmethacrylate is a brittle, notch sensitive material. In the context of THR its relative properties are crucial. Its modulus of elasticity (Young’s modulus) is usually tested in tension and is approximately 2400 MPa. This is approximately ten times lower than that of the surrounding cortical bone and 100 times lower than that of the
Table II. Mechanical properties of three leading cement brands

<table>
<thead>
<tr>
<th>Property</th>
<th>Value range (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultimate tensile strength</td>
<td>36 to 47</td>
</tr>
<tr>
<td>Ultimate compressive strength</td>
<td>80 to 94</td>
</tr>
<tr>
<td>Bending strength (4 point configuration)</td>
<td>67 to 72</td>
</tr>
<tr>
<td>Shear strength (ASTM D732)</td>
<td>50 to 69</td>
</tr>
<tr>
<td>Mean fracture toughness (Kic)</td>
<td>1.52 to 2.02 (MPa/m)</td>
</tr>
</tbody>
</table>

* Three leading cement brands, Simplex P, Palacos R, CMWI
† ASTM D732, American Society for Testing and Materials standard D732 protocol for testing the strength of acrylic materials
‡ Kic, mean fracture toughness of brittle materials

Visco-elastic properties of polymethylmethacrylate

The visco-elastic properties of bone cement are creep and its ‘inverse’ stress relaxation, which are both time and temperature dependent.

Creep. This is the deformation of a material under constant load. Under constant load a material capable of creep will deform by an amount dependent on the size of the load and the length of time it is applied. The rate of loading is also important, where visco-elastic materials demonstrate a higher Young's modulus at higher loading rates. Stress relaxation. This is the time-dependent change in stress within a material under constant strain. The force needed to maintain a set deformation will reduce with time if stress relaxation occurs.

Polymers demonstrate features of both elastic solids and viscous liquids under conditions of low strain and hence are described as visco-elastic. At a molecular level, relatively weak non-covalent bonds exist between adjacent polymer side-chains, and these may be breached, resulting in visco-elastic properties. Mathematical models have been applied to this behaviour.

At the implant level the trend towards polished tapered stem designs has been facilitated by the visco-elastic properties of PMMA. Robust evidence from both finite element analysis and laboratory studies indicates that the subsidence of a stem within the cement mantle by the process of creep protects the vital bone/cement interface and hence the replacement overall. This is supported by excellent clinical results using such a combination of components. Those who favour shape-closed designs have not exploited visco-elastic behaviour and have indeed taken measures to reduce it by altering the cement.

The visco-elastic behaviour of PMMA is therefore increasingly under investigation. The creep behaviour of leading cement brands can differ significantly even though their static properties are similar. In vivo, cement is bathed in water which permeates the PMMA and acts as a plasticiser (internal lubricant). Plasticisers, which include unreacted monomer and lipids, increase the creep of the cement. The use of co-polymers with high hydrophilicity, such as methacrylate-methylmethacrylate (MA-MMA) copolymer in Palacos cement (Heraeus Medical Gmbh, Hanau, Germany), also increases creep. Polymethylmethacrylate continues to polymerise for weeks after implantation and the creep is higher in this younger cement. The constraint of the proximal femur has a profound limiting influence on the visco-elastic properties.

An increased understanding of the effects of additives to cement upon creep is now developing. Antibiotics increase the creep of PMMA and this appears to be related to the porosity of the cement. There is much yet to be discovered in this field.
Antibiotic-loaded acrylic cement

In 1970 Buchholz and Englbrecht incorporated gentamicin in PMMA for the treatment of infection in prosthetic joints. Initially the antibiotic was added by hand, and subsequently during manufacture, making antibiotic-loaded acrylic cement widely available as part of antimicrobial prophylaxis in primary arthroplasty. There is valid evidence to support the prophylactic use of antibiotic-loaded acrylic cement which remains standard practice in the United Kingdom, Western Europe and Scandinavia, and is in transition in the USA. In 2003 the Food and Drug Administration accepted the use of three commercial antibiotic-loaded acrylic cements in the second stage of revision surgery for prosthetic joint infection. Their use in primary total joint replacement remains unauthorised. The American Academy of Orthopaedic Surgeons has produced guidelines regarding the use of antibiotic-loaded acrylic cement and advises its use as a prophylactic measure only in cases where the patient has significant risk factors for infection.

The use of antibiotic-loaded acrylic cement in joint replacement provides short- to medium-term protection against prosthetic infection. It aims to overlap with, and then replace, the prophylaxis provided by peri-operative intravenous antibiotics. To achieve this it must be released from cement in high enough concentrations to exceed the minimum inhibitory concentration of potential colonising bacteria.

The elution behaviour of acrylic bone cement has been studied extensively. Gentamicin is the most common additive because it has, amongst other features, a good spectrum of concentration-dependent bactericidal activity, thermal stability and high water solubility. In 1980, Wahlig and Dingeldein gave robust evidence of gentamicin release from Palacos cement for up to five and a half years in patients who had undergone THR. Following this they collaborated with Buchholz in a trial assessing the release of differing concentrations of gentamicin from Palacos cement in patients with a THR. Palacos/gentamicin was established as an ideal antibiotic delivery system. Others have confirmed reliable release of gentamicin from Palacos R (Heraeus Medical GMBH) cement (0.5 g per 40 g mix). However, concerns about antibiotics in cement still persist: Induction of antibiotic resistance. In 1989 Hope et al found that 90% of Staphylococcal strains isolated from infected hip replacements were resistant to gentamicin but if plain cement had been used at the initial operation the rate was only 16%. Other studies have confirmed that antibiotic-loaded acrylic cement reduces infection in total joint replacement at the price of increasing resistance.

Hypersensitivity and toxic side effects. These problems have not been demonstrated clinically, even though they have been postulated.

Unsuitable antibiotics. Many antibiotics have been shown either to be heat labile or to cause deleterious effects upon cement. The former include flucloxacillin, and possibly other penicillins, chloramphenicol and tetracyline. An example of the latter is rifampicin, preventing setting for several days.

Prolonged release of antibiotic. Despite the aim of achieving early and total release, all in vitro studies show that only 5% to 8% of the added antibiotic is ever freed.

Clinical studies have shown a low concentration of release of gentamicin in failing THRs up to 25 years after the primary operation, a potent stimulus for antibiotic resistance.

Adverse effects on the mechanical strength of polymethylmethacrylate. There is a large body of work available on this issue. Antibiotics should neither be added in liquid form nor to the monomer, as this can lead to a 40% reduction in compressive strength in vitro.

The addition of 2 g of gentamicin, cloxacillin or cefazolin to a 40 g mix of polymer has no significant effect on the short-term mechanical properties of Simplex-P (Stryker Orthopaedics) and Palacos-R (Heraeus Medical GMBH) cements.

Studies confirm that a 5% addition of antibiotic gives the optimal balance between elution and mechanical properties.

There remain a number of deficiencies in the literature regarding the behaviour of antibiotic-loaded acrylic cement. Most mechanical studies have assessed the static short-term mechanical properties. These are less clinically relevant than the fatigue life or visco-elastic properties. Single antibiotic additives have usually been the focus of mechanical studies but this trend is now changing as the need for antibiotic combinations becomes recognised as a result of the prevalence of multi-resistant bacteria. There is a need for continued research into the effects of single and multiple antibiotic additives upon the static and visco-elastic properties of PMMA. These should be performed, where possible, under standardised conditions and should reflect modern techniques of cement preparations.

Polymethylmethacrylate bone cement continues to have numerous uses in orthopaedic practice. Clinicians have acquired understanding of many of its properties through both chance and direct research. Continued research is still needed into its long-term mechanical behaviour and its interaction with additives such as antibiotics or radio-opacifiers.

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