AJNR Am J Neuroradiol 25:1286–1290, August 2004

Review Article

Bone Cements: Review of Their Physiochemical and Biochemical Properties in Percutaneous Vertebroplasty

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Percutaneous vertebroplasty is an effective treatment for aggressive vertebral hemangiomas, osteoporotic vertebral compression fractures, spinal metastases, and myelomas. As percutaneous vertebroplasty is more commonly performed to treat various forms of back pain, new or modified cements are being used. This review examines the physiochemical and biomechanical properties of various bone cements and additives.

Since the mid-1960s, bone cement, primarily polymethylmethacrylate (PMMA), has been increasingly used for orthopedic applications. The expanding number of potential procedures has led to the development of new cements with a wide variety of physiochemical and biomechanical properties. Determining the suitability of using a cement in an established or new procedure depends on an understanding of those properties, including their handling characteristics, antimicrobial effects, and interactions with surrounding bone. The current review focuses on the properties of various cements used for percutaneous vertebroplasty (PVP).

Percutaneous Vertebroplasty

Determining a cement's suitability depends in part on an understanding of the procedure for which it is being used. Developed in the mid-1980s, PVP is designed to stabilize a vertebral body that has been mechanically compromised (eg, by fracture, tumor, or metastases). During PVP, the patient is anesthetized and placed in the prone position. Under fluoroscopic or (rarely) CT guidance, an 11–13-gauge trocar is placed unipedicularly or bipedicularly into the affected vertebral body, and bone cement is injected. During injection, continuous lateral fluoroscopy is used to monitor for cement extravasation. When hardened, the cement helps stabilize the vertebral body and has been successful in alleviating pain in 75–85% of patients (1). It is not known whether the pain relief is secondary to the mechanical stabilization, chemical toxicity, or thermal necrosis of nerve tissue.

Received September 29, 2003; accepted after revision March 17, 2004.

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Properties of Bone Cements

Many cements are commercially available for orthopedic interventions (Table). Each has its own physical, chemical, and mechanical properties. Although some cements are approved for use in member states of the European Economic Area (CE marked) and other areas worldwide for use in vertebroplasty, no cement has yet been approved by the US Food and Drug Administration (FDA) for this use. Off-label use of FDA-approved cements opacified with additional barium has become common. Several FDA trials are ongoing to obtain approval for this indication.

Physical Properties of Unaltered Cement

Many reports have compared the physical properties (strength and stiffness) of some of the cements commonly used for PVP when they are prepared according to the manufacturer's instructions. One such study found that molded cylinders of Simplex P were stronger and stiffer than those made of Osteobond (2). However, because cement injected into the vertebral body may behave differently than that in molded cylinders and because the direct injection of cement into a vertebral body could alter the cement's performance, biomechanical testing of cadaveric osteoporotic vertebral bodies has been conducted. In one test, such vertebral bodies were compressed to determine their initial strength and stiffness and then mechanically crushed posterior to the anterior wall to simulate compression fractures (3). After vertebroplasty with Simplex P, Osteobond, or Cranioplastic containing additional barium (per the current standard of practice in off-label use), the vertebral bodies were retested. All three cements resulted in increased strength (beyond precrush levels), but only Simplex P and Osteobond restored initial stiffness (3).

Additives and Their Effects

Many clinicians modify the currently available cements to facilitate their use and improve their function. What follows is a summary of the cement additives in use and their physiochemical properties.

Cement manufacturers and contact information

Cement	Manufacturer	Contact Information
Allegiance	Cardinal Health, McGaw Park, IL	*www.cardinal.com* 1500 Waukegan Rd, McGaw Park, IL 60085-6827 Phone: 847-785-3366
BoneSource	Stryker Leibinger, Kalamazoo, MI	*www.strykercorp.com* 4280 Commercial Ave, Kalamazoo, MI 49002 Phone: 269-323-7700, Fax: 877-648-7114
Cranioplastic	Depuy International, Ltd., Blackpool, England	*www.codmanjnj.com* 325 Paramount Dr, Raynham, MA 02767-0350 Phone: 800-225-0460, Fax: 508-828-3070
Orthocomp	Orthovita, Malvern, PA	*www.orthovita.com* 45 Great Valley Pkwy, Malvern, PA 19355 Phone: 610-640-1775, Fax: 610-640-2603
Osteobond	Zimmer, Warsaw, IN	*www.zimmer.com* PO Box 708, 1800 West Center St, Warsaw, IN 46581-0708 Phone: 800-613-6131, Fax: 574-372-4988
Palacos	E. Merck, Darmstadt, Germany or Biomet, Inc, Warsaw, IN	*www.merck.com, www.biomet.com* Biomet, Inc., PO Box 587, Warsaw, IN 46581-0587 Phone: 574-267-6639 or 800-348-9500
Palacos E-Flow	Essex Chemie AG, Lucerne, Switzerland	*www.essex.ch.www.sch-plough.com* Essex Chemie AG, Weystrasse 20, PO Box CH-6000 Lucerne 6, Switzerland Phone: 41-41-418-16-16
Simplex P	Stryker-Howmedica-Osteonics, Mahwah, NJ	*www.strykercorp.com* 325 Corporate Dr, Mahwah, NJ 07430 Phone: 201-831-5000 or 800-447-7836
Sucour	ArthroCare (formally Parallax), Sunnyvale, CA	*www.arthrocare.com* 680 Vaqueros Ave, Sunnyvale, CA 94085-3523 Phone: 408-735-6363
Vertifix (US, Osteofirm in Europe)	WE Cook, Bloomington, IN William Cook Europe Cook Australia	*www.cookgroup.com* PO Box 489, Bloomington, IN 47402-0489 Phone: 800-468-1379 Denmark phone: 45-56868686, Brisbane phone: 61-7-3841-1188

Liquid Polymer

PMMA-based cements are prepared by mixing a powdered polymer and a liquid monomer. Each cement manufacturer recommends a specific monomer-to-polymer ratio, expressed as grams per milliliter. Changing the monomer-to-polymer ratio (ie, increasing the amount of liquid polymer) dilutes the cement, which increases the handling and injection times. However, doing so can affect the cement's properties, specifically strength and polymerization temperature, and it may affect monomer-induced neural toxicity (one of the proposed pain relief mechanisms for PVP). To our knowledge, the latter claim is as yet unsupported by data.

In one study, cylindrical specimens of Cranioplastic were prepared by using various monomer-to-powder ratios (0.40 to 1.07 mL/g) and tested to determine ultimate strength, compressive strength, and the ability to withstand mechanical stress (0.40 to 1.07 mL/g) (4). Results showed that all three measurements were highest at a mixture of 0.53 mL/g, close to the manufacturer's recommended ratio of 0.57 mL/g, and diminished when the ratio deviated in either direction. The study's authors estimated that the actual mixture ratio used in PVP is between 0.60 and 0.74 mL/g, resulting in a reduction in strength of 16% for this range of ratios (4).

Radiopaque Compounds

Radiopaque substances, such as tantalum powder, tungsten, barium sulfate, or zirconium dioxide, have been added to bone cements before injection to facilitate visualization under fluoroscopy and monitoring for possible cement extravasation (5–7).

Although tungsten and tantalum powder have been

added to bone cement in PVP (5, 6), little is known concerning their effect on the cement's physical and mechanical properties.

Studies on the addition of barium sulfate have produced conflicting reports: it has been reported to decrease the ability to withstand deformation under a load or fracture (8), to diminish some physical properties (tensile, compressive, and transverse bending strengths) (9), not to affect the ability to withstand shearing forces until it exceeded 50% of the total dry powder weight of the cement (surpassing the amounted added during PVP) (10), and to increase compressive strength (11).

Barium sulfate affects not only mechanical strength but also polymerization temperature. One study showed that the maximum polymerization temperatures for Simplex P with 30% and 60% barium sulfate by weight had maximum polymerization temperatures of 60°C and 44°C, respectively (10). Other work has shown no significant difference in peak polymerization temperature between a PMMA cement with 10% and 0% barium sulfate (9). Although Haas et al (9) did not observe statistically significant temperature changes, they found that dough time, handling, and setting times all significantly increased with the addition of 10% barium sulfate.

The addition of barium sulfate to PMMA also has been associated with significantly increased bone resorption (12, 13), which if occurring within the vertebral body, could negate the strengthening features of the cement and reduce the effectiveness of PVP. These findings led to the hypothesis that the increased bone resorption is caused by barium sulfate–enhanced macrophage-osteoclast differentiation (13).

The addition of zirconium dioxide to PMMA cements also has produced mixed results. One study reported that the addition caused a significant increase in bone resorption, although that increase was 50% less than that of cement-containing barium sulfate (12). Another study of PMMA with zirconium dioxide did not show a significant increase in bone resorption (13).

Antibiotics

Antibiotics are sometimes added to the cement powder before injection to minimize infection (6, 7). These additives, like barium sulfate and zirconium dioxide, can affect the mechanical properties of the bone cement. Research has shown that adding various types of antibiotics to bone cement, in quantities less than 2 g per standard packet of bone cement, does not adversely affect some of the cement's mechanical properties (compressive or diametrical tensile strengths), although quantities exceeding 2 g did weaken them (14, 15). These findings were substantiated by another report that showed the addition of 0.5 g of erythromycin and 0.24 g of colistin to Simplex P were not detrimental to the cement's fatigue life (16).

As with other additives, the addition of antibiotics to the cement has produced conflicting results. In one study, the addition of 2 g of powdered gentamicin, oxacillin, or cefazolin to 60 g of Simplex P or Palacos produced no statistically significant difference in terms of short-term (less than 40 days) compressive and tensile strengths compared with the cement without powdered antibiotics (17). However, another study found a significant decrease in mechanical strength between cements mixed with 250 or 500 mg of gentamicin in 6.25 or 12.5 mL of water and cements without aqueous antibiotics (15). Although these reports showed no deleterious mechanical effects from the addition of powdered antibiotics, provided the quantity was less than 2 g, other investigators have reported that compression strength was compromised by the addition of 2 g of antibiotics (gentamicin or keflin) per 60 g of Simplex P (18).

One alternative, already used by some physicians performing vertebroplasty, is the intravenous administration of antibiotics before vertebroplasty (19), which avoids the risk of potential changes to the cement's properties.

Pain Relief

Thermal necrosis of surrounding nerves has been postulated as a mechanism of pain relief in vertebroplasty. Research indicates that thermal necrosis of bone tissue occurs when temperatures surpass 50°C for more than 1 minute (20).

Deramond et al (21) measured temperatures at the anterior cortices, centers, and spinal canals of cadaveric vertebral bodies after bipedicular injections of Simplex P or Orthocomp (Bis-phenol glycidyl dimethacrylate/Bis-phenol ethoxy dimethacrylate/triethyleneglycol dimethacrylate, a matrix composite cement reinforced with glass-ceramic), both of which were prepared according to the manufacturer's specifications. They found that, at the central location, Simplex P injection was associated with significantly higher temperatures and with temperatures exceeding 50°C for significantly longer times (61.8°C $\pm$ 12.7, 3.6 minutes $\pm$ 2.1) than Orthocomp injection (51.2°C $\pm$ 6.2; 1.3 minutes $\pm$ 1.4) (21). However, measurements at the anterior cortex and spinal canal locations showed no significant difference between the two cements. In fact, at the latter location, the temperature of cement did not exceed 41°C in either cement. The authors hypothesized that, given their results, it was unlikely the pain relief from vertebroplasty was caused by intraosseous neural tissue damage (21).

Bone Adherence

PMMA cements cannot adhere to existing bone (22), but this disadvantage may not be as pertinent for vertebroplasty as for arthroplasty. Because the cement is injected directly into the bone, and not used as an adhesive agent in arthroplasty, cement loosening may not cause any noticeable problems. Results of one study indicated that, at long-term follow-up (average, 1.3 years) after vertebroplasty with PMMA cements, the vertebrae were stable with respect to compression and the degree of kyphosis (23). Only

one of 20 vertebral levels showed signs of cement compression; the remaining 19 showed no change in cement morphology (23). Another follow-up study (48 months after the procedure) showed no progression of vertebral deformity after vertebroplasty (24). However, if the cement loosens to such a degree that it compromises the structural integrity of the vertebral body, refracture of the vertebral body can occur around the injected cement (25).

Bone Formation and Other New Developments

Although research has shown that PMMA cements cannot induce new bone formation (23), some new bone cements show promise not only in terms of bone growth but also in terms of improved physical and mechanical properties, which could be beneficial for PVP. One recently developed cement consists of bioactive glass beads and a novel organic matrix of PMMA, which resulted in new bone formation around the beads and a significant increase in bending strength compared with PMMA cement without the beads (26). Curing time and polymerization temperatures were not reported. Adding a glass-ceramic powder and bisphenol-a-glycidyl methacrylate (Bis-GMA) resin to a PMMA-based cement has produced a bioactive acrylic bone cement that bonds directly to the bone after 4–8 weeks in vivo and has faster hardening times, lower curing temperatures, and significantly better physical properties (27).

In one study, investigators measured the stiffness and strength of fresh cadaveric thoracic and lumbar vertebrae injected with BoneSource (a hydroxyapatite bioactive bone cement) or Cranioplastic (a PMMA-based product) and then mechanically compressed (28). The vertebrae injected with Cranioplastic had significantly greater strength compared with strength in the prefractured state, whereas those injected with BoneSource regained initial strength. However, both Cranioplastic and BoneSource resulted in a lower stiffness in all vertebrae compared with initial measurements (28). A similar comparison of Simplex P and BoneSource showed that both cements resulted in significantly less stiffness than in the precompressed states (29). However, Simplex P injections resulted in significantly greater strength compared with prefracture measurements, whereas BoneSource restored the vertebrae to their initial strength (29). Despite these findings, in vitro studies comparing hydroxyapatite cements and PMMA products should be conducted to determine which is more suitable for use in vertebroplasty.

Simplex P and Orthocomp were studied with respect to their ability to restore strength and stiffness of the vertebral body (30). After initial measurements of strength and stiffness were made, mechanical compression was applied to osteoporotic cadaveric vertebral bodies posterior to the anterior wall. Vertebrae were then injected with Simplex P or Orthocomp and retested to determine their augmented strength and stiffness. Injection with Simplex P or Orthocomp significantly increased vertebral body strength compared with the initial measurements. Initial vertebral body stiffness was restored by using Orthocomp, but vertebral bodies augmented with Simplex P were significantly less stiff than in their precrush condition (30).

Similar studies have compared a PMMA cement (Palacos E-Flow) to a calcium phosphate experimental brushite cement (EBC) with respect to strength and stiffness (31). Osteoporotic vertebral bodies harvested from cadavers were measured, axially compressed, injected with either Palacos E-Flow or EBC, and then retested for strength and stiffness. Injections PMMA and EBC increased the average stiffness (in osteoporotic vertebrae only) by 174% (range, −10–159%) and 120% (range, 108–131%), respectively, and the average strength by 195% (range, 26–254%) and 113% (range, 104–126%), respectively. The study also showed that the cements' augmenting effects were proportional to the degree of filling, although the correlation was weak (31).

Novel work is underway with cements containing bone morphogenic protein (BMP), a protein that belongs to the transforming growth factor-β (TGF-β) superfamily and found in bone matrix (32). It is believed that BMP serves as a growth factor for adult articular cartilage matrix repair and synthesis. Although no work specific to PVP has been conducted, studies using BMP-impregnated cement implanted into bone have shown new bone or callus formation in a dose-dependent manner (33, 34). Additional research is required to determine what effect, if any, BMP has on the physical properties on the bone cement and its application in PVP.

Glossary

Compressive strength is a material's ability to withstand compressive loads without being crushed.

Fatigue strength is a material's ability to withstand varying and alternating loads.

Flexural strength is a material's ability to resist deformation under load.

Hardness is a material's ability to withstand indentation.

Impact strength is the energy needed to cause a material to fracture when struck.

Modulus of elasticity is the rate of the change in strain as a function of stress.

Stiffness is a material's rigidity.

Tensile strength is a material's ability to withstand tension without rupture.

Toughness is a material's ability to absorb energy and withstand shattering.

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