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Liquid-solid phase transition alloy as reversible and rapid molding bone cement

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ABSTRACT

Acrylic bone cement has been an essential non-metallic implant used as fixing agent in the cemented total joint arthroplasty (THA). However, the currently available materials based mainly on polymethylmethacrylate (PMMA) still encounter certain limitations, such as time-consuming polymerization, thermal and chemical necrosis and troublesome revision procedure. Here from an alternative way, we proposed for the first time to adopt the injectable alloy cement to address such tough issues through introducing its unique liquid–solid phase transition mechanism. A typical cement along this way is thus made of an alloy Bi/In/Sn/Zn with a specifically designed low melting point 57.5 °C, which enables its rapid molding into various desired shapes with high plasticity and ultimate metallic behaviors. The fundamental characteristics including the mechanical strength, biocompatibility and phase transition-induced thermal effects have been clarified to demonstrate the importance of such alloy as unconventional cement with favorable merits. In addition, we also disclosed its advantage as an excellent contrast agent for radiation imaging on the bone interior structure which is highly beneficial for guiding the surgery and monitoring the therapeutic effects. Particularly, the proposed alloy cement with reversible phase transition feature significantly simplifies the revision of the cement and prosthesis. This study opens the way for employing the injectable alloy materials as reversible bone cement to fulfill diverse clinical needs in the coming time.

1. Introduction

Bone cement has long been an important biomedical material applied in the orthopedic surgery [1]. In a number of total joint replacements (TJRs), the implant is generally cemented in bone using acrylic bone cement (ABC). Although it was revealed that uncemented fixation has become widely used in total joint replacements (TJRs), especially in total hip joint replacements (THJRs) [2], cemented fixation remains the gold standard in total knee arthroplasty (TKA) [3] and the rate of cemented THJR can achieve 90% in some countries [4]. Based on such advantages like biostability, good mechanical properties, accurate implantation, low cost [5] and other comparable properties to that of uncemented replacement, cemented arthroplasties are attracting tremendous interests among the worldwide researchers. However, acrylic cement works mainly depending on the time-consuming polymerization process [6]. Its exothermically high polymerization and unreacted monomer release can cause the target bones to subject to thermal and chemical necrosis, coupled with shrinkage of the cement during polymerization [7–9]. This may further contribute to the failures in joint replacements due to aseptic loosening [10–15]. And in general, radiological imaging has served as an efficient tool to monitor the healing process after surgery. Barium sulfate or zirconium dioxide is often adopted as radiopacifier in most of the commercial bone cements [15,16]. On the other hand, due to the incompatibility between metal salt and acrylic material, the addition of the metal salt would result in the heterogeneity of cement [17]. Some studies suggest that these inorganic particles can cause mechanical weakness [18,19] and even become fatigue crack initiation sites in the cement [20].

In addition, TJRs with cement has been proven to be a safe operation with high success rate in relieving pain and recovering function. In spite of that, a proportion of failures among them are inevitable as time goes on. Although the revision rate with cemented is lower than that with cementless replacement, revision

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of cemented fixation remains a significant concern worth of emphasizing since its appearance over ten years [3]. Usually, the revision requires some specialized manual instruments and sophisticated technical skills for the surgeons. The commonly adopted means for removing prosthesis and cement include the sliding trochanteric osteotomy, the extended trochanteric osteotomy (ETO), the extended proximal femur and the cortical windows [21–26]. Clearly, these methods require surgeons to cut femurs, such as the ETO that involves the removal of 1/3 of the femoral shaft [25], which not only weakens the remaining bone but also accompanies with complications [21,22]. Undoubtedly, revision of a failed cemented THA maintains a big challenge so far.

In principle, appropriate bone cement is generally characterized by proper injectability, rapid setting, adequate stiffness, bioactivity, low setting temperature, and radiopacity [27] etc. Here, aiming to find out a generalized way to simultaneously achieve the above goals, we are dedicated to propose a distinctive metal material which can easily shift between liquid and solid phase and demonstrate its capability as bone cement with multi-functions. In fact, many previous continuous studies have been launched on metal as biomaterials used in orthopedics, such that stainless steel, cobalt alloy, titanium and titanium alloy are the most commonly used [28–30]. However, these metal materials are common in their extremely high melting points to be above 1000 °C and low plasticity which would encounter big trouble in forming various shapes *in situ*. Here from an alternative way, we proposed for the first time the low melting point metal as bone cement. As is noted, the eutectic alloy which was first reported as a suitable solder has the melting temperature as low as 60 °C [31]. Currently, the eutectic alloys composed of Bi, In, Sn and Zn have been supplied as lead-free solder materials. And the melting point for a specific alloy varies with different proportion of metal compositions. Molelans et al. have investigated the thermal properties of ternary and quaternary alloy system with these four elements [32]. Their data shows that the melting point of quaternary system is lower than that of ternary alloy. Moreover, the alloy with composition of 35.0Bi-48.6In-16.0Sn-0.4Zn owns the lowest melting point among Bi–In–Sn–Zn alloy with other proportions. All these characteristics remind us that such eutectic alloy could be utilized as a high quality bone cement.

In this work, we present the alloy composing of 35.0Bi-48.6In-16.0Sn-0.4Zn as bone cement and revealed the fundamental mechanisms thus involved. Such material is found to be easily shaped into various forms at the low temperature to fit for different shapes of defects. Compared to the conventional cement, alloy cement features simple preparation and operation, rapid setting, low peak temperature and excellent radiopacity. Its mechanical strength and biocompatibility were also determined and clarified here. Uniquely, the liquid–solid phase transition of this alloy cement enabled its easy implanting and removal from the bone bed which in fact offers a highly flexible and reversible surgical process with evident clinical importance. This mechanism allows reversion much easier and controllable, and favors to prevent remaining bones from more damages as well.

2. Materials and methods

2.1. Composition of alloy bone cement

The present liquid–solid phase transition alloy bone cement was composed of bismuth (Bi), indium (In), tin (Sn) and zinc (Zn) metals with purity of 99.99 percent, and they were prepared with a corresponding weight ratio of 35%, 48.6%, 16% and 0.4%, respectively. The weighted metals were then added into the beaker and heated at 400 °C for 24 h to make the target alloy. To increase the homogeneity of the components, the mixture were stirred using a magnetic stirrer at 70 °C for 4 h when they were all melted. Finally, the obtained alloy cement could be stored at room temperature in solid state for a long time. The device utilized for the injection was an ordinary medical syringe without needle.

2.2. Plasticity evaluation of liquid–solid phase transition alloy cement

Firstly, the flow characteristics of Bi/In/Sn/Zn alloy were demonstrated by studying the dropping process. The liquid alloy cement was prepared by heating the solid cement until melted. The liquid alloy cement was injected via 1 ml syringe, and the piston was forced to form droplet. The metal droplet fell vertically to the platform at room temperature. The high-speed camera (NR4-S3) was employed to record the dropping process at 500 fps (frames per second). And the viscosity of alloy cement was measured by using RHEOTRONI C VIII torsional oscillation viscometer (Tokyo Industry Kabuskiki Kaisha, Tokyo, Japan). To evaluate the plasticity, we injected the melting alloy cement into different letter molds. The molds with height of 3.5 cm were placed on the heating platform with 70 °C to keep the cement in liquid state during the filling process. After the molds were filled with cement, remove them from the platform and leave them at room temperature. Then cooling for about 10 min, the molding alloy was released from the molds.

2.3. Metallurgical analysis and immersion test

The solidified alloy discs with a diameter of 12 mm were employed for XRD analysis. Measurements were performed using a diffractometer (X' Pert PRO MPD, PANalytical, the Netherlands) at room temperature (21 °C) with Cu Kα monochromatic radiation at 40 kV and tube current of 40 mA. Data was collected at 0.02° (2θ) intervals over a 2θ range of 0-90°. Features on the XRD pattern were identified using the pattern library Powder Diffraction File by the software MDI Jade 5.0.

Immersion tests were carried out with element and microstructure analysis. Five alloy cement cylinders, 4.8 mm in diameter, and 5 mm in thickness were prepared and treated with 2000-grit abrasive paper. Cylindrical specimens were soaked in Hanks' solution at 37 °C. The relationship between volume (V, mL) of the solution and the apparent surface of the specimen (S, mm^2) satisfies the equation V=S/10 [33]. The specimens were taken out from the solution after 1, 2, 5, 9 and 14 days immersion, and the concentration of alloying elements (Bi, In, Sn and Zn) within solution were obtained by ICP-MS (Inductively Coupled Plasma Mass Spectrometry, Thermo XSeries II ICP-MS, Thermo Fisher Scientific, Germany). Before and after 14-day soaking, topography analysis of specimens was performed by SEM (Hitachi S-4300, Japan). The compositions of precipitates in the microstructures were determined by EDS with SEM.

2.4. Mechanical characteristics evaluation

Cylindrical specimens (12 mm in diameter, 15 mm in length) were prepared for compression testing and the specimens for bending test were made as rectangular with a length of 100 mm, width of 20 mm, and thickness of 8 mm, respectively. A four-point bend test was adopted to determine the bending strength and bending modulus at room temperature. The specimens were cured within molds at room temperature for 24 h. Three specimens of cement were used for each test. The values of ultimate compressive strength and bending strength were measured using a universal testing machine MTS-SANS CMT5000 (CMT5000, SANS, MTS Systems Corp., China) at a cross-head speed of 0.5 mm/min. The bending strength (F_{bend}) was calculated by Equation (1) and the bending modulus (E) was determined by Equation (2) [34], i.e.

$$F_{bend} = \frac{3Fc}{bh^2} \tag{1}$$

$$E = \frac{\Delta Fc}{4fbh^3}\left(3l^2 - 4c^2\right) \tag{2}$$

where, F is the maximum force during the bending process; b and h are the width and thickness of the specimens, respectively; c represents the distance between the inner and the outer loading points (20 mm) and l is the distance between the outer loading points (60 mm); f denotes the difference between the deflections under two points (90 N and 270 N) which are placed on linear portion of the stress–strain plot and ΔF denotes the load range of corresponding two points (270 N-90 N = 180 N).

Fatigue tests were conducted in air at room temperature [35], using a material test machine (Instron 8874, Instron Corp., Canton, MA). Here, a dumbbell type test specimen with cylindrical cross-section was prepared and its configurations and sizes were provided in Fig. 1b [36,37]. Each specimen was subjected to a uniaxial constant-amplitude fully reversed (tension-compression) loading with a sinusoidal waveform to a maximum stress of ±15 MPa. The cyclic load was applied at a frequency of 5 Hz. Fatigue testing continued until the specimen was fractured. Before failure, the maximum number of cycles, N_f was recorded.

To further determine the present material's fracture toughness (K_{IC}), according to the ISO 12737-2005 standard, three rectangular compact tension specimens have been prepared and machined [38]. Fig. 1c gives the specimen's specified geometrical dimensions with a width of 32 mm and a thickness to width (B/W) ration of 0.5 [39,40] The crack resistance tests have been performed by using a typical machine named MTS-SANS CMT5000 (CMT5000, SANS, MTS Systems Corp., China) at room temperature with a displacement rate of 2 mm/min. In addition, the fracture surface was measured with the aid of a high-performance scanning electron microscope (SEM, FEI Quanta 200, Netherlands). Based on the above measured data, we can