Grafting of PMMA brushes on cross-linked PMMA nanospheres for use in novel two-solution bone cements

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Statement of Purpose: Novel two-solution cements containing cross-linked PMMA nanospheres as part of the polymer phase have been developed to optimize the material viscosity. This cement was shown to exhibit reduced viscosity, lower polymerization exotherm, longer setting time and lower concentration of residual monomer in comparison to a standard two-solution bone cement formulation [1]. In this work, PMMA brushes were grafted to the surface of cross-linked PMMA nanospheres in order to improve interfacial bonding of the beads to the cement matrix, allowing for complete substitution of the linear phase of the cement mixture. The first goal of this study was to develop a novel synthetic pathway, which allows for efficient surface modification of cross-linked PMMA nanospheres for grafting of PMMA nanospherical brushes at high densities. The second goal was to prepare two-solution cements with reduced monomer concentration and lower viscosities by the complete substitution of linear PMMA with PMMA brushes at higher polymer-to-monomer (P:M) ratios.

Methods: Grafting of PMMA brushes was performed through a multistage reaction scheme. Briefly, cross-linked PMMA nanoparticles (~300 nm in diameter) were surface modified via a series of reactions for attachment of aminoethyl acrylate groups that served as initiating sites for brush grafting. PMMA brushes were tethered on the surface of the nanospheres via free radical graft copolymerization of methyl methacrylate (MMA) in water using potassium persulfate (KPS) as the initiator[2]. To determine optimal brush molecular weight (M_w) for addition in two-solution cements, the reactions were performed at MMA concentrations of 2, 4 and 5 wt% with KPS concentrations varying from 0.4 to 1 wt%. The degree of modification in each reaction step was verified by NMR ^{1}H (Bruker DPX-300). M_w of grafted chains was determined by GPC (Waters 2414) with a multi-angle light scattering detector (miniDawn TREOS, Wyatt). The graft density and degree of stretching of brush compositions diluted in tetrahydrofuran was determined with dynamic light scattering (DLS, Wyatt). Selected brush compositions were added to two-solution cements, which were prepared as described previously[3]. Brush-cements prepared at increasing P:M ratios (1:1 to 1.2:1) were subjected to viscometry using a Brookfield Viscometer (DV-E). The concentration of residual monomer was measured with differential scanning calorimeter in isothermal mode (DSC 7, Perkin Elmer). The results were compared with a standard formulation containing linear PMMA (TSBC) and cements prepared with a mixture of PMMA nanospheres and linear PMMA.

Results: A higher degree of surface modification was achieved with this method, which allowed for high brush grafting efficiencies, as confirmed by NMR ^{1}H. The M_w of the grafts was observed to increase with an increase in the concentration of MMA up to 5 wt%. The composition 2 wt% MMA/0.4 wt% KPS showed appropriate M_w for the preparation of brush cements (110 kg/mol). DLS results revealed that brush densities on the nanospheres core decreased exponentially (R^2=0.97) with an increase in the M_w of the grafts, reaching a maximum grafting density at 2 wt% MMA/0.4 wt% KPS (1.02 chains/nm^2) and a minimum at 5 wt% MMA/0.4 wt% KPS (0.39 chains/nm^2). Brush stretching, determined by the ratio of brush thickness (h) to the radius of gyration (R_g) of grafts (h/R_g), exhibited a linear decrease with increasing M_w of grafts (R^2=0.72). This result points to a possible collapse of the higher M_w grafted chains onto the nanoparticle core due to the lower graft densities observed for these compositions. Cements prepared with brushes synthesized at 2 wt% MMA/0.4 wt% KPS allowed for a significant increase in the P:M ratio (up to 1.2:1) in comparison to the TSBC (0.9:1) and nanospheres cements (Figure 1). Brush cements prepared at P:M ratios of 1:1 and 1.1:1 exhibited significantly lower viscosities than nanospheres cements at the same P:M ratios. Residual monomer in the cement matrix was significantly reduced when PMMA brushes substituted the linear PMMA (2.5 wt% in comparison to12.5 wt% for TSBC). The decrease in residual monomer achieved with brush addition is a result of the increase in the polymer concentration in the mixture and higher degrees of monomer conversion.

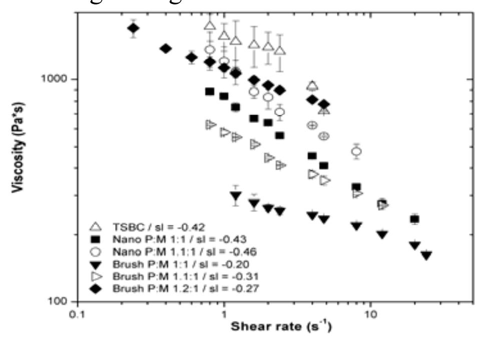

Figure 1. Viscosity versus shear rate of two-solution cements. The slopes (sl, from linear regressions) indicate the degree of shear-thinning.

Conclusions: This synthetic pathway showed advantages over other methods employed for efficient modification of PMMA particles[2] and grafting of PMMA brushes at high densities. The graft density was observed to vary with graft M_w, being tuned by simple variations in the concentrations of monomer and initiator, which ultimately allowed for cement viscosity reduction through maximum graft attachment and stretching. The addition of brushes synthesized via this method enabled the preparation of solutions at higher P:M ratios, which exhibited lower viscosities than the linear TSBC and nanospheres formulations. The addition of brushes also resulted in a significant decrease in the residual monomer concentration in cured cements. These cements will be characterized biomechanically in follow up studies.

References: 1. Rodrigues D et al. JBMR-B 2009;91:248-256.
2. Jayachandran KN et al. Eur Polym J 2000;36:743-749.
3. Rodrigues D et al. SFB Proceedings, San Antonio 2009.

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