INTRODUCTION

The injectability and mouldability of bone cements are properties of significance to the orthopaedic surgeon as they enable percutaneous delivery (access to bone is achieved via the needle puncture of the skin and the injection of the cement through the needle into the treatment site) for minimally invasive procedures. Inorganic bone cements can be shaped to the dimensions of bone defects while in a dough consistency and harden in situ, that is “set,” within the cavities that they fill. The setting reactions involve the dissolution of calcium-rich basic and phosphate-rich acidic species, and the subsequent precipitation of a more stable phase (Fukase, Eanes, Takapp, Chow, & Brown, 1990; Mirtchi, Lemaitre, & Terao, 1989) or hydrolysis of a metastable, stoichiometrically similar calcium phosphate to the final apatitic phase (Ginebra, Fernandez, et al., 1995; Bohner, 2005). The setting kinetics, rheological and mechanical properties of calcium phosphate cements have been extensively investigated and correlated with various factors that directly affect the dissolution, crystallization and growth of calcium phosphates including pH (Bohner, 1997), temperature (Liu, 2003), particle size and crystallinity (Fernandez et al., 1996, 1998; Gbureck, Dembski, Thull, & Barralet, 2005), water content (Xu, Quinn, Takagi, & Chow, 2002),
ionic strength (Şahin & Çiftçioğlu, 2013), surface charge (Gbureck, Probst, & Thull, 2002), concentrations of calcium phosphate ions (Wang & Nancollas, 2008; Komath, Varma, & Sivakumar, 2000) and chemicals that have affinity to them (Ten Huisen & Brown, 1997, Şahin & Çiftçioğlu, 2014). Two main types of calcium phosphate cements, hydroxyapatite and brushite-forming cements, undergo setting in quite different rates, the latter setting much more rapidly due to the water consuming reaction of relatively fast dissolving precursors, suiting the clinical requirements for vertebroplasty, that is being workable for about 5–10 min and harden in about 15 min (Heini & Berlemann, 2001).

Time dependencies of injectability and workability of calcium phosphate cements present obstacles in their processing during surgery. Measures of injectability are carried out by attempting to extrude the cement out of a syringe with a needle of a certain diameter at constant force (Khairoun, Boltong, Driessens, & Planell, 1998). During injection, the liquid–solid phase separation can occur which is a widely encountered problem during the processing of concentrated suspensions (Bohner & Baroud, 2005; Khairoun et al., 1998; Leroux, 1999). Changes in the formulations of calcium phosphate cements have been proposed to prevent the demixing of the paste by effective dispersion (Burguera, Xu, & Sun, 2008; Takagi, Chow, Hirayama, & Sugawara, 2003; Wang, Chen, Xiang, & Ye, 2007). In addition, setting kinetics is aimed to be controlled to prolong the injection period by using setting retarder chemicals (Barralet, Tremayne, Lilley, & Gbureck, 2005; Gbureck, Barralet, Spatz, Grover, & Thull, 2004; Ginebra, Boltong, Fernández, Planell, & Driessens, 1995). Such chemical setting retarders strongly modify the setting kinetics to the extent that ultimate mechanical properties may be compromised due to incomplete conversion to the product phase (Hofmann, Young, Gbureck, Nazhat, & Barralet, 2006).

Earlier studies have shown that the only available route to manipulate the setting kinetics of inorganic bone cements is chemically modifying their formulations and thus compromising their bioactivity. Recently, we reported the effect of deformation conditions on the rheological properties of brushite cement by utilizing small amplitude oscillatory rheometry (a.k.a. mechanical spectrometry) (Şahin & Kalyon, 2017). This technique resolves the mechanical behaviour of a suspension into the storage modulus ($G'$), representing the propensity to store the mechanical energy elastically in the solid phase, and the loss modulus ($G''$), representing the propensity to dissipate the mechanical energy viscously in the liquid phase. Thus, setting kinetics of a quiescent cement is revealed by monitoring the variations of the storage modulus at small oscillatory torsions with time. Here, it is shown that the setting kinetics of the calcium phosphate bone cements can be modified by the same drag-induced strains produced by torsion of cement samples and their flow behaviour can be controlled simply by implementing a deformation history immediately prior to their injection. Furthermore, an apparatus is proposed for this preshearing process which is capable of preshearing by oscillatory and steady torsions, and efficient delivery as a micro-extruder. The application of the demonstrated preshearing methods and devices has the potential to significantly enhance the ease of the injection of inorganic bone cements by manual or robotic deposition.

2 | MATERIALS AND METHODS

Brushite-forming calcium phosphate cement powder consisting of stoichiometric amounts of β-tricalcium phosphate (obtained from Sigma-Aldrich with purity of 96%) and monocalcium phosphate monohydrate (obtained from J.T. Baker with purity of 99.5%) was mixed with 1 wt% brushite seed (obtained from Sigma-Aldrich with purity of 98%) using a mechanical mixer for 15 min. The powder mixture batch was prepared daily and stored in a desiccator throughout the analyses. A 0.5M aqueous citric acid solution was prepared with deionized water and citric acid (obtained from Sigma-Aldrich with purity of 99.5%) to facilitate setting of brushite phase according to the following reaction:

$$
\beta-\text{Ca}_3\left(\text{PO}_4\right)_2 + \text{Ca}\left(\text{HPO}_4\right)_2\cdot\text{H}_2\text{O} + \text{7H}_2\text{O} \rightarrow 4\text{CaHPO}_4\cdot2\text{H}_2\text{O}
$$

All samples were prepared by mixing 1 g of precursor powder with 1 ml of citric acid solution (0.5M) using a sonicator for 60 s. For sonication, a Misonix XL2020 ultrasonic processor was used at 150 W to generate liquid jet streams resulting from ultrasonic cavitation. The samples of the calcium phosphate cement suspensions were freshly prepared and upon mixing were transferred immediately to the rheometer via a syringe for the characterization of their setting kinetics and associated rheological behaviour. Citric acid was employed in this study in order to slow down the setting kinetics and extend the setting curve to cover longer periods of time. Preliminary tests on brushite cement prepared under the same conditions without citric acid showed that the final setting time had been reached before the initiation of rheological testing. With citric acid, it was possible to extend the setting time significantly.

2.1 | Preshearing and subsequent characterization of the setting kinetics and rheological behaviour

Upon mixing of the ingredients, the cement suspension was immediately transferred to a rotational rheometer, that is an Advanced Rheometric Expansion System (ARES) Rheometer (available from TA Instruments). The dynamic properties of the bone cement were both modified and characterized as a function of time at different shearing modes and shear rates. This partitioning of the preshearing and characterization runs was done to apply the same measurement conditions for comparison of different shearing histories as explained elsewhere (Şahin & Kalyon, 2017). During rheological characterization and preshearing, the cement specimen was sandwiched between two aluminium discs (25 mm diameter), one of which either oscillates (consecutive clockwise and counterclockwise cycles) or rotates at constant angular velocity while the second disc remains stationary. Once the cement was ready, the following reaction:

$$
\beta-\text{Ca}_3\left(\text{PO}_4\right)_2 + \text{Ca}\left(\text{HPO}_4\right)_2\cdot\text{H}_2\text{O} + \text{7H}_2\text{O} \rightarrow 4\text{CaHPO}_4\cdot2\text{H}_2\text{O}
$$

All samples were prepared by mixing 1 g of precursor powder with 1 ml of citric acid solution (0.5M) using a sonicator for 60 s. For sonication, a Misonix XL2020 ultrasonic processor was used at 150 W to generate liquid jet streams resulting from ultrasonic cavitation. The samples of the calcium phosphate cement suspensions were freshly prepared and upon mixing were transferred immediately to the rheometer via a syringe for the characterization of their setting kinetics and associated rheological behaviour. Citric acid was employed in this study in order to slow down the setting kinetics and extend the setting curve to cover longer periods of time. Preliminary tests on brushite cement prepared under the same conditions without citric acid showed that the final setting time had been reached before the initiation of rheological testing. With citric acid, it was possible to extend the setting time significantly.
stationary. Various preshearing conditions were imposed on the bone cement formulation to investigate the role preshearing plays in the development of the subsequent rheological behaviour, setting kinetics and injectability.

For the oscillatory preshearing runs, the strain amplitude was kept within the linear viscoelastic strain (LVS) range at 0.04, 0.1 and outside LVS range at 1. The frequencies of 0.1, 1, 10 and 100 rad/s were applied for varying durations from 120 s to 2000 s. In the steady torsional mode of preshearing, the apparent shear rate that is imposed on the cement sample at the edge (at the free surface) is: \[ \dot{\gamma} = \frac{\omega R}{H} \], where R is the radius of the disc, H is the gap in between the two discs and \( \omega \) is the angular velocity of the upper disc. The apparent shear rate values that were imposed during steady torsional preshearing were 0.01 and 0.1. The gap, H, was kept constant at 1 mm during all oscillatory and steady preshearing and subsequent rheological characterization experiments, so that the surface to volume ratio of the apparatus does not change from run to run (wall slip which occurs upon setting is a function of the surface to volume ratio). The shear viscosity responses were obtained directly from the steady torsion runs and were compared to the oscillatory measurements according to the Cox–Merz rule, that is, the magnitude of complex viscosity measured at the LVS range nearly equals the zero-shear viscosity. (Kalyon, Dong-Woo, & Yu, 1988).

In all preshearing and subsequent rheological characterization runs, the temperature of the sample holder chamber was kept at 25°C and the free surface of the sample was sealed with a low molecular weight silicone oil to prevent the evaporation of water. Typically, transfer of the mixed cement suspension and sample holder adjustments took about two minutes so that the initiation of the rheological characterization or preshearing could be started within three minutes of the completion of the mixing process. Each experiment was replicated for at least three times to ensure reliability. Student’s t-distribution at \( p < .05 \) was used to calculate the variation as represented by the error bars for all data points. 95% confidence levels of the normally distributed setting kinetics data were taken into account as the setting period.

### 3 | RESULTS

In our previous study, we have seen that brushite cement setting quiescently in 0.5 M citric acid solution reaches the dough time (when cement can be shaped without sticking to the hand but also when it starts to thicken rapidly leading to poor injectability) in 300 s, the initial setting time (when a continuous, solid network structure forms by inter-growing crystals) in 540 s and the final setting time (when the microstructure is predominantly solid) in about 1,200 s. (circular data points in Figure 1). Also, the LVS limit was found to increase from 0.05 to 0.1 as setting progressed (Şahin & Kalyon, 2017). These parameters are conveniently determined from the variation of the dynamic rheological properties with time (\( \tan \delta = \frac{\eta''}{\eta'} \approx 0.5 \) at the dough time; \( G' \) rises exponentially at the initial setting time; and \( G' \) reaches a plateau at the final setting time) and with strain amplitude (\( G' \) remains constant until the strain amplitude reaches the LVS limit), respectively.

A marked difference between the dynamic rheological properties of the quiescent (non-sheared) and the presheared calcium phosphate cement suspensions both before and after the dough times is observed when the results for the preshearing at a mild strain amplitude of 0.04 are compared with that of the quiescent setting. To elaborate this observation, the setting rates for the quiescent and presheared samples were determined as a function of time by differentiating the sigmoidal equations that fit the storage modulus curves. As seen in Figure 1b, the 95% confidence intervals of these normal distribution curves are taken as the setting periods so that the 2.5 percentiles correspond to the initial setting times and the 97.5 percentiles correspond to the final setting times. Accordingly, the initial setting times of cement samples presheared at different frequencies within the LVS range showed small variation.

**FIGURE 1** Effect of oscillatory torsional strains applied at various frequencies (\( \omega \) in radians per second) and strain amplitudes (\( \gamma \)) on the setting kinetics of brushite cement as represented by the variation of storage modulus with time (a). The setting rate curves are obtained by taking the derivative of the setting curves, giving the initial (I) and final setting times (F) (b)
around 600 s. The injection periods defined by the dough times are seen in Figure 2 to extend with preshearing, the extension being inversely proportional to the applied oscillation frequency.

Generally, it is observed that the peaks representing the setting rates broaden, shorten and shift to later times as applied frequency decreases. The wide range of dynamic properties and setting times observed for various oscillation frequencies suggest that competing setting mechanisms dominate at different frequencies. For instance, diffusion enhancement similar to a temperature increase is pronounced at higher frequencies while setting receives small benefit from low frequencies, similar to the quiescent sample that undergoes slightly faster setting than the lowest frequency sample. The resulting net setting promoting effect as evident in the increasing peak heights with increasing oscillation frequency is attributed to an enhanced crystal growth rate as the left-hand side of the peaks reflects the changes in crystal growth rate at high initial supersaturations whereas dissolution is the rate-limiting mechanism at later stages of setting in calcium phosphate cements. (Fernandez et al., 1996; Şahin & Çiftçioğlu, 2014). Each different cement formulation is expected to exhibit different dependence on oscillation frequency, and a characteristic “setting promoting frequency limit” should be sought by similar measurements in order to control their setting rate.

The quiescent sample that was kept undisturbed before rheological testing developed the strongest crystal network \((G' > 2\text{MPa})\) within a setting time of 20 min. This is also indicated by the initial increase in loss modulus of the quiescent sample to a greater extent than the samples continuously sheared at the same temperature as seen in Figure 3a. Such relative rise in suspension viscosity is most likely caused by the increase in solid ratio and abundance of brushite crystal domains due to enhanced crystallization before dough time. The ratio of loss modulus to storage modulus (tangent \(\delta\)) indicates the proportion of oscillatory strain energy dissipated by the liquid matrix to the energy used for elastic deformation of the solid phase. Because brushite cement setting reaction is water consuming, setting not only produces a solid network but also depletes the water content of the cement suspension. Thus, tan \(\delta\) decreases gradually with time to a constant value as setting completes. As seen in Figure 3b, tan \(\delta\) of the quiescent cement suspension at its dough time (around 300 s when tan \(\delta < 0.5\)) is much less than those of the presheared suspensions and gradually decreases to the same minimum around 0.1 at a slower rate, that is it undergoes a shorter injection period. Hence, viscous dissipation consumes a greater portion of the oscillation energy applied to the presheared samples at the initial stages of setting. The constantly higher tan \(\delta\) for cement samples oscillated with the lowest frequency indicates that the weakest solid network develops at this preshearing condition. Conversely, the sample presheared at the highest frequency had accelerated viscosity and elasticity development particularly after the initial setting time as evidenced by the lower tan \(\delta\) values.

The effect of oscillatory torsional strain amplitude on the dynamic rheological properties as a function of time and hence the setting kinetics of brushite cement suspensions were also investigated at a mild oscillatory strain frequency of 1 rad/s with amplitudes ranging from LVS range (less than 10%) to a high strain amplitude of 100%. The comparison of viscosities that is shown in Figure 4a indicates that strain amplitude has a stronger effect on the microstructural evolution of brushite cement than frequency, due to the disrupting effect of higher mechanical energies applied outside the LVS range. Strain amplitudes up to 10% enable crystal structure development in the brushite cement samples of the studied composition at ambient conditions. Further increasing the strain amplitude above this LVS limit seems to result in gradual disruption of the inter-growing crystals as indicated by the prolonged setting time. The strain amplitude of 10% gives the sample a mechanical energy that is about 2.5 times higher compared to a strain amplitude of 4% at the constant frequency of 1 rad/s. Similarly, a 10-fold energy increase occurs between samples presheared at the same strain amplitude of 4% and frequencies of 0.1 rad/s and 1 rad/s. The consequent enhancement in the setting kinetics, as evident from the earlier rise of the storage modulus, is attributed to the intensified agitation in the LVS range with beneficial effects on the crystallization.
rate. Thus, it is seen that both of the control parameters of the oscillatory torsional strains, the frequency and the strain amplitude, promote setting kinetics of brushite cement in the presence of citric acid provided that the strain amplitude stays in the LVS range.

On the other hand, higher energy oscillations were seen to delay setting at similar low frequencies. Strain amplitude of 100% is well above the LVS limit of the set cement and as a result effectively disrupts the cement setting as seen in Figure 4a. Although the setting kinetics is slowed down in this case, it appears that crystallization has continued and developed a strong crystal network at a later time. Rather, intergrowth of crystals is reduced by the applied high mechanical energy. This is evident from the variation of tan δ in the reverse direction, that is increase in the loss modulus in comparison with the storage modulus for a lag period (Figure 4b).

Furthermore, steady torsional strains that increase constantly with time produce a much stronger retardation effect as seen in Figure 5 where shear viscosity for the steady torsion is compared with the magnitude of complex viscosity data for the oscillatory torsion which has a parallel variation to the storage modulus data. Oscillatory torsional strains much greater than the LVS range, as much as 10,000% at frequencies as much as 100 rad/s, produce retardation and subsequent recovery of the elasticity development, significantly broadening the workability window of fast setting brushite cement (data not shown for brevity). In addition, cyclic shifting of applied shearing frequency between a low and a high magnitude at a constant strain amplitude greater than the LVS range produced a similar effect that magnified with increasing number of cycles.

4 | DISCUSSION

The initial portions of the setting curves reveal that the quiescent samples reach the dough time faster compared to presheared
samples. After this period that cement remains fully injectable, presheared cement suspensions exhibit dynamic properties proportional to their oscillation frequency, that is the faster samples are oscillated within the LVS range, the faster their dynamic moduli and magnitude of complex viscosity develop. Rapid oscillation seems to provide a boost to brushite supersaturation after the dough times when the dissolution is expected to slow down and the supersaturation to decrease rapidly. Such initial setting retardation effect is beneficial for improving the injectability of cements and it can also facilitate faster setting of slow setting cements, particularly those with a high liquid/powder ratio.

Multiple physico-chemical mechanisms may be involved during the observed delaying of the initiation of setting for the cement suspensions presheared within the LVS range and promotion of the setting rates at the setting period:

1. crystal mobility and the associated delaying of crystal intergrowth;
2. viscous heat dissipation and the consequent rise in liquid temperature
   a. increase in diffusivities of ions
   b. reduction in the solubilities of the precursors;
3. mixing of precursors, seeds, citrate molecules and growing crystals with the setting liquid that is initially supersaturated with respect to calcium and phosphate ions and undersaturated with respect to citrate molecules.
   a. Increase in exposed surface area of the precursors and the associated
      (i) increase in dissolution rates
      (ii) increase in heterogeneous nucleation rates
      (iii) increase in adhesion between the liquid and the solid phase
   b. Reduction in the viscosity of the suspension due to deagglomeration (shear-thinning).

Brushite cement setting during the injection period is known to be governed mainly by the growth kinetics as the initial rapid dissolution of monocalcium phosphate monohydrate and that of accompanying β-TCP build supersaturation up (Alkhraisat, Marino, Retama, Jerez, & Lopez-Cabarcos, 2008; Şahin & Çiftcioglu, 2013). The quiescent samples are thought to crystallize more efficiently into a three-dimensional crystal network than the presheared samples lacking initial elasticity according to the dynamic rheological properties. Setting and crystallization rates may differ if the brushite crystals are kept as small, isolated domains by prevention of intergrowth. Apparently, this is the case for presheared samples with higher crystallization rate due to multiple beneficial effects on crystal nucleation (2a, 3ai–3aivii, 3bi).

Heterogeneous nucleation in calcium phosphate cements is known to shorten the supersaturation build-up time and extent (Yang, Troczynski, & Liu, 2002). In our study, nucleation kinetics are assumed to be the same for both quiescent and presheared samples because all samples initially contained 1 wt% of brushite seeds and the same heterogeneous nucleation kinetics. Therefore, samples start crystal growth as soon as supersaturation is built-up locally by the relatively slow dissolution of β-TCP. The less soluble β-tricalcium phosphate may dissolve completely depending on the solution pH, temperature, and the volume of water or may remain covered by the brushite crystals. Quantitative phase analysis of set cement samples revealed that the latter was the case and about 10% of the initial β-TCP residue remained undissolved in the quiescent samples as reported in our previous study (Şahin & Kalyon, 2017).

The overall dynamic rheological properties reveal that the initial slow setting rates of the presheared samples catch up with that of the quiescent samples around the initial setting time and exceed it during the setting period and on. This is attributed to the evolving cement microstructure that gets gradually depleted in calcium phosphate ions. This typically occurs at the maximum setting time that
corresponds to the inflection point of the sigmoidal setting curve which would otherwise be represented in the form of an exponential function of time. At this point, the setting kinetics shifts from growth controlled to dissolution and diffusion controlled as the crystals with surfaces exposed to the setting liquid rapidly transform to the product phase that limits the dissolution and diffusion of the precursor ions. Oscillatory preshearing within the LVS range and at high frequencies apparently remedies this kinetic limitation while oscillation with very low frequencies seems insufficient to speed up the transport of ions to the growth site.

When effective and complete mixing is achieved, surface area of the precursors that are in contact with the setting liquid increases due to uniform dispersion. Homogenization of the cement paste is generally accompanied by increases in its flowability and dissolution rate. It is indeed reported that oscillatory mixing decreases the magnitude and variability of calcium phosphate cement viscosity by shear-thinning and improved dispersion of the crystals (Baroud, 2004). Thus, the variation of viscosity for different preshearing frequencies is partially a result of variations in the extent of dispersion. It is expected to play a small role in the presheared cement suspensions because of the initial ultrasonication that involves rigorous cavitation for homogenization and the abundance of citrate molecules in the cement suspensions which facilitate dispersion via electrostatic stabilization. Viscous dissipation of oscillation energy and the resultant enhancement in diffusivities of calcium and phosphate ions seem to be the main reason for faster structure development at higher frequencies. Both initial ultrasonic mixing and 1 wt% brushite seed addition should reduce the contribution of diffusion mechanism in initial crystal growth. Diffusion is the rate-limiting step at the late stages when depleted calcium and phosphate ions in the setting liquid around the crystal network structure necessitate a transport mechanism as provided by oscillation applied at high frequencies.

On the other hand, the dissolution rates of β-TCP, brushite and crystal growth rate of brushite are strongly reduced due to interaction of citrate groups with both β-TCP and brushite crystals in multiple ways (Alkhraisat et al., 2008; Şahin & Çiftçioglu, 2014). In the presence of citrate, free calcium ion concentration and supersaturation are significantly reduced (Rosmaninho & Melo, 2006). It is reported that citrate addition also increases the supersaturation required for nucleation due to adsorption of citrate onto the newly formed calcium phosphate nuclei which, in turn, influences the size and geometry of the developing cement crystal lattice (Houwen, Cressey, Cressey, & Valsami-Jones, 2003). Citrate molecules also alter the charge of the calcium phosphate surfaces they adsorb to, hence stabilizing the rheological behaviour of calcium phosphate cement suspensions by mixed electrostatic and steric repulsion (Barralet, 2005). High surface charges induced by citrate groups also influence the ion exchange between the hydrate layer around the calcium phosphate particle and the particle surface itself (Giocondi, 2010). On the other hand, citrate addition in the form of citric acid has a slight promoting effect on brushite cement setting rate due to protonation of the aqueous suspension which increases both the dissolution and crystallization rates. The net effect of citric acid addition in a quiescently setting cement is the retardation of setting as the former mechanisms dominate for concentrated brushite cement suspensions.

It is not clear which citrate interaction mechanisms are altered by preshearing at various oscillation frequencies at the LVS range. The concentration of citrate molecules that are adsorbed on the surface exposed calcium atoms of β-TCP and brushite crystals may be increased by enhanced contact area with the liquid matrix at high oscillation frequencies. Brushite growth kinetics is mainly controlled by phosphate incorporation, and additives interfering with this step are known to regulate crystal growth. Adsorbed citrate molecules have to be removed during crystal growth to accommodate the competing HPO$_4^{2-}$ ion (Lindegren & Persson, 2009). Furthermore, a hydrate layer is present around brushite surfaces in contact with water, and citrate molecules preferentially adsorb on this layer as surfactants which require lower desorption energy than groups adsorbed on surface calcium ions (Giocondi, 2010). This may result in more citrate groups to accommodate on newly grown brushite crystals as setting progresses and permit more dissolution of exposed β-TCP surfaces, which may explain the faster setting kinetics of samples presheared at higher frequencies.

Comparison of the relative viscosity values for the sample presheared above the LVS limit with those of the samples presheared within the LVS range and not sheared at all reveals that the former yields during setting in accord with the non-linear viscoelastic strain theory. This mechanism of the setting retarding effect is indicated by the significant differences between tan δ of samples presheared at different strain amplitudes as given in Figure 4b, for example the portion of the mechanical energy consumed by the liquid matrix starts to increase for the higher strain amplitude of 100%, at an initial setting time of about 700 s. The fluctuation in tangent δ suggests that cement setting progressed at the initial state similarly to cement samples with higher rates, exhibiting a development in the solid network by crystal intergrowth. The abrupt reversal of the curve around 700 s indicates an arrest in the intergrowth mechanism, and its

![Figure 6](image-url)
continuous increase until 900 s is most likely associated with yield-
ing and the fracture of the intergrown crystals during this period.

This observation is also reflected by significant differences
between the shear stress responses of samples presheared at dif-
ferent strains and strain amplitudes as given in Figure 6. Although
much higher mechanical energy (≥10X) was applied at the highest
strain amplitude of 100%, the stress responses given by the micro-
structure are initially at the same level as those of cement samples
presheared near the LVS limit of 10%. As the measurements of the
small amplitude oscillatory rheometer represent the elastic and
viscous responses of the sample, parts of the applied mechanical
energy that are spent via alternative mechanisms, such as plastic
deformation or fracture, are not measured. Hence, the collapse of
the stress response for the strain amplitude of 100% is a reflection
of the collapse of the solid microstructure (as represented by G’)
upon yielding. This additional energy dissipation mechanism was
also observed in cement samples presheared at various shear rates
of steady torsions that exceeded the LVS limit as seen in Figure 6.

Steady torsional strains produce considerable retardation of
brushite cement setting even at relatively low shear rates of 0.01/s
and 0.1/s because of the steady increase in applied shear strains
with time. The wavy setting curve observed for steady shearing at
a rate of 0.1/s is an indication of the dynamically changing balance
between the constantly increasing shear strain and the differential
setting kinetics, that is the setting process, indicated by the time-de-
pendent variation of shear viscosity as seen in Figure 5 is retarded
as strains continuously exceed and reduce the LVS limit which is the
yield strength of the developing microstructure. Although this way
much of the energy is spent for reorganization of the cement micro-
structure without a network formation, it enables development of a
more robust network structure according to the faster recovery of
G’ to higher values observed after setting.

The preshearing applied by oscillatory strain amplitude of 100%
thus conditioned the cement to achieve a higher setting extent as
indicated by the higher maximum G’ values in Figure 4a. This im-
provement in crystallization kinetics is similar to the setting promo-
tion effect of oscillatory torsion within the LVS range and may be
attributed to the same mechanisms including surface exposure of
β-TCP and brushite crystals as a result of disruption of the rigid crys-
tal structure, increased contact area between the solid and the liq-
uid phases, and the associated change in concentrations of calcium,
phosphate and citrate ions due to dissolution and adsorption of
these species. Basically, these are the microstructural changes that
are responsible for the well-known thixotropy of calcium phosphate
cements (Liu, 2006). Therefore, from a broad perspective preshear-
ing is a means to exploit the thixotropy of the inorganic cement by
accurate control of applied torsional strains with respect to the pre-
cise characterization of its setting kinetics.

This method is expected to be generally applicable for inorganic
cements that have competing kinetic and thermodynamic me-
chanisms. The extents of preshearing effects for other inorganic ce-
ments at larger oscillation frequencies and strain amplitudes will be
studied next, as well as their dynamic rheological properties under
quiesscent conditions to elucidate their inherent setting kinetics and
microstructural evolution. Such database of characteristic rheologi-
cal properties are necessary for each inorganic cement formulation
in order to utilize the preshearing method and apparatus for their ef-
ficient processing. The basic apparatus that can effectively apply the
targeted preshearing strain history to tailor the setting kinetics and
cement viscosity is an unconventional oscillatory micro-extruder
(Şahin & Kalyon, 2018). It is aimed to modify the setting kinetics in
situ during a surgery or robotic deposition operation in order to fa-
cilitate mixing and injection/extrusion of the cement batch. A sche-
matic representation of the preshearing method and apparatus has
been shown in the graphical abstract.

5 | CONCLUSIONS

The two modes of preshearing, oscillatory and steady torsion, elicit
various physical responses of the dynamically evolving brushite ce-
ment suspension for a wide range of extents from setting promoting
effect for oscillatory torsion within the LVS range and setting delaying
effect outside the LVS range to setting retarding effect for steady tor-
sion. Oscillatory torsional strains enable control of the setting times
for both shortening and delaying them, depending on the difference
between the strain amplitude and the linear viscoelastic strain limit.
The strain amplitude is a critical parameter in oscillatory torsional
preshearing as a sudden change in dynamic rheological properties
which stems from structural break-up occurs around the LVS limit.
Oscillation frequency may be considered as a “fine-tuning” parameter
that accentuates the promoting or retarding effect to tailor the setting
times in preshearing. Steady torsional strains more effectively shuf-
le the microstructure at the expense of the setting time, especially
high shear rates truly producing a setting retardation effect. Such a
wide variety of modes for the mechanical control of setting kinetics
of aqueous inorganic cement pastes is a key finding that may enable
much more controlled processing of these materials during their in-
jection and robotic deposition. For this aim, a novel oscillatory micro-
extruder is proposed with the capability to apply both oscillatory and
steady torsion to a setting cement prior to delivery for the intended
application. Thus, in situ control of the setting kinetics and viscoelastic
character of the calcium phosphate cement is enabled.

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