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An ultrasonic pulse-echo technique for monitoring the setting of $CaSO_4$-based bone cement

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Abstract

We present a new ultrasonic technique for monitoring the entire setting process of injectable bone cement. The problem with existing standards is their subjectivity. Because of this the results are not comparable between different research groups.

A strong advantage with the proposed technique is that it is non-invasive and non-destructive, since no manipulation of the cement sample is needed once the measurement has started. Furthermore, the results are reproducible with small variations.

The testing was performed on calcium sulfate cement using an ultrasonic pulse-echo approach. The results show that the acoustic properties of the cement are strongly correlated with the setting time, the density, and the adiabatic bulk modulus. The measured initial and final setting times agree well with the Gillmore needles standard. An important difference compared to the standards, is that the technique presented here allows the user to follow the entire setting process on-line.

Keywords: Ultrasound; Pulse-echo; Bone cement; Calcium sulfate; Setting time

1. Introduction

Injectable bone cements [1] based on calcium sulfate ($CaSO_4$) and calcium phosphates are potential materials for bone defect filling and reinforcement of osteoporotic bone. They are especially suitable for filling fractured vertebras thanks to their good injectability even through small needles. The cements are biodegradable and replaced by new bone tissue with time. The calcium sulfate phase resorbs in 4–6 weeks in the body and leaves pores in the material where bone tissue may penetrate and accelerate the resorption of the calcium phosphate phase. All the material is estimated to be resorbed within 6–12 months.

Many different test methods are used today to characterize injectable cements and set materials for biomedical applications. Most of the test methods, such as compression, flexibility, and tensile strength tests, are objective and controlled by international standards. However, there is no such standard to test the setting time of the cement. Currently, there exist two standardized methods for setting time testing: (a) Vicat needle [2] (ASTM C191-92) and (b) Gillmore needles [3] (ASTM C266-89) but both of them are based on visual examination which make them subjective. A significant difference between the results of the same material measured by two different users has been shown. For example, the same research group has reported three different results for the same cement, i.e. Norian SRS, 27 min [4], 22 ± 1 min [5] and 8.5 ± 0.5 min [6], respectively. According to the US Food and Drug Administration this cement "sets in approximately 10 min" [7]. Similar variations in the results have also been reported for other cements such as Cementek (34 min [4], 36 min [5] and 17 ± 1 min [6]) and BoneSource (19 min [4] and 20–25 min [8]). Note that these cements are all based on calcium-phosphate cements, but the problems are the same for the cement material used in the measurements in this paper. This becomes a problem when it comes to comparing results from different researchers and research groups, which further motivates the search for a new, objective measurement method.

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Moreover, there are no standards or limits neither in setting time nor in strength that define the material properties needed to close the wound without complications when implanted. Gillmore needles measure one initial (I) and one final (F) setting time of hydraulic cements. According to Driessens et al. [9] the clinical meaning of Gillmore needles is that the cement should be implanted before (I) and that the wound can be closed after (F). The paste should not be deformed between (I) and (F) because in that stage of the setting process any deformation could induce cracks. The desired time for (I) is about $4 \leqslant I \leqslant 8$ min and the desired time for (F) is about $10 \leqslant F \leqslant 15$ min [10]. Most cements do not fulfill the last requirement and Sarda et al. [11] suggests, using rheology measurements, that the material probably reaches a sufficient strength to withstand the pressure during wound closing long before the (F) time. Since the operation time is not only important in the patient's point of view but also economically, there is a need of a good standard that define the true time needed for the cement to set into a sufficiently strong material.

Recently, Viano et al. [12] presented an ultrasonic technique for the characterization of bone cement based on polymethylmethacrylate (PMMA). Their method uses the broadband attenuation of pulsed ultrasound (BUA) and the speed of sound within the cement to determine when the cement is set. They use two ultrasound transducers in a through-transmission setup. The BUA and speed of sound vary dramatically during the setting process and this shows that the acoustic properties of the materials can be used to characterize different types of bone cement. Although the BUA is very sensitive to variations in viscoelastic properties of the material, there is no immediate connection between the BUA value and the actual mechanical properties of the material.

The purpose of the work presented in this paper is to show that an ultrasonic pulse-echo technique can be used to follow certain properties of the cement, on-line, during the setting of $CaSO_4$-based cements. The method is based on low-intensity pulsed ultrasound which makes it a non-invasive and non-destructive method. The method takes advantage of the fact that the acoustic properties of a material are closely related to its mechanical properties. Emphasis is on measuring the setting time of the cement, by following how some properties change as functions of the setting time. Once the material is set, and its mechanical properties stabilize, this will also be reflected in the measured acoustic parameters. The acoustic impedance at the interface between the measurement cell and the cement, and the speed of sound within the cement, are measured directly. These two properties are then used to determine the adiabatic bulk modulus and the density of the material. Unlike the Gillmore needles standard, the proposed technique does not define the setting time as when the material has a certain strength, but when the chemical reaction stops. This makes the ultrasonics technique less dependent on which type of material is used.

Section 2 describes the experimental setup as well as some of the theory behind the method. In Section 3 we present experimental results from measurements on calcium sulfate dihydrate, CSD ($CaSO_4 \cdot 2H_2O$). These results are then compared with results obtained using the Gillmore needles standard.

2. Materials and methods

In this section we describe the materials used in the experiments and the basic principles behind the proposed ultrasonic technique.

2.1. Materials

α-Calcium sulfate hemihydrate (CSH) powder (30 g) (Bo Ehrlander AB, Gothenburg, Sweden) was mixed with an aqueous solution of 2.5% (by weight) of Na_2HPO_4 at a liquid-to-powder (L/P) ratio of 0.32 ml g^{-1}, during 1 min, to form a paste. During the setting CSH hydrates into CSD following the reaction:

$$CaSO_4\tfrac{1}{2}H_2O + \tfrac{3}{2}H_2O \rightarrow CaSO_4 \cdot 2H_2O. \quad (1)$$

The mixing time was 1 min, after which the paste was considered homogeneous. Thereafter it was put inside the measurement cell (Fig. 1) and formed so that it completely covered the area of the transducer surface. The ultrasonic measurement was started 3 min after the mixing started, and after a total of 5 min the whole measurement setup was immersed in water. The data acquisition then continued for 2 h, with one pulse-echo measurement every 20 s. All measurements were performed in a climate chamber at 37°C.

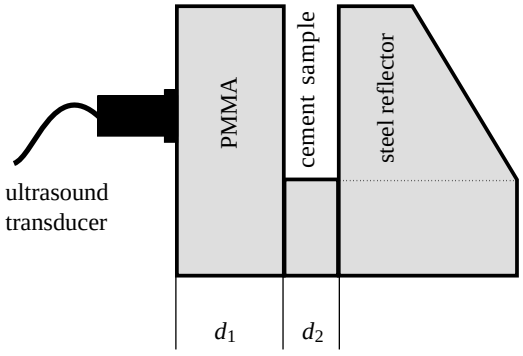

Fig. 1. Device for ultrasonic pulse-echo measurements used in the experiments.

2.2. Setting time with Gillmore needles

A reference experiment was made in compliance with the Gillmore needles standard in order to compare the new ultrasonic technique with the existing standard. CSH powder (5 g) was mixed with 1.6 ml of the Na_2HPO_4-solution ($L/P = 0.32$ ml g^{-1}) during 1 min to form a paste. To perform the setting time test it was then put in moulds and tested according to the Gillmore needle standard [3]. The initial setting time (I) is defined as the time when a 0.3 MPa static pressure does not leave a visible print on the surface of the cement. The final setting time (F) is the corresponding time for a static pressure of 5 MPa.

2.3. Acoustic measurement principle

The principle of the method presented in this paper is to measure the acoustic impedance at the interface between a material with known acoustic properties and the cement. This together with the speed of sound in the cement is then used to calculate density and adiabatic bulk modulus of the cement. In this section the details of the measurement principle will be described in detail.

When a sound wave encounters a boundary between two materials with different acoustic properties, part of the acoustic energy will be reflected back towards the transmitter, and part of the energy will continue into the second medium. How much of the acoustic energy that is reflected back depends on the difference in specific acoustic impedance between the two layers. The acoustic impedance, Z (Pa s m^{-3}) can be related to an analogue electrical system in a similar way as voltage is related to sound pressure and current is related to particle or volume velocity. The specific acoustic impedance, z, of a material has the unit pressure/particle velocity (Pa s) and is very useful in calculations involving transmission and reflection of sound waves [13]. In the rest of this paper the term acoustic impedance is referring to the specific acoustic impedance. Fig. 1 shows the measurement cell used in the experiments. An ultrasound transducer was mounted on the surface of a Plexiglass (PMMA) buffer. This was first introduced by Lynnworth [14] as a method to measure density of liquids. An overview of other pulse-echo setups can be found in [15].

In the setup, the transducer is first used to transmit a short ultrasound pulse with a center frequency of 2 MHz. The same transducer is then used as a receiver to record the reflected echoes. The electrical pulses recorded with the transducer are then sampled at a sampling frequency of 200 MHz and transferred to a computer. Fig. 1 shows the measurement cell, and Fig. 2 shows an example of the received signal when the measurement cell is filled with cement. The first echo, $x_1(t)$ is from the PMMA/cement interface and the second echo, $x_2(t)$, comes from the interface between the cement and the steel reflector.

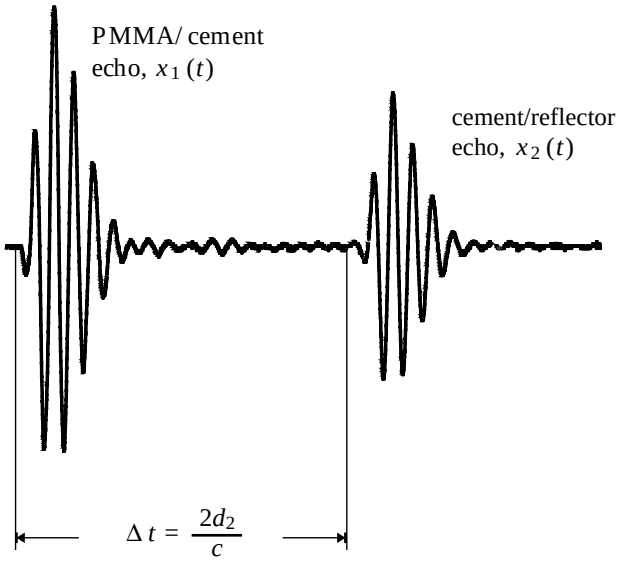

Fig. 2. Reflected pulse from PMMA/cement interface, $x_1(t)$ and reflected pulse from cement/reflector interface, $x_2(t)$, respectively. The time delay between is denoted Δt.

The ratio of the amplitude of the first echo $x_1(t)$ to a corresponding echo measured in a calibration experiment in pure water gives the acoustic impedance of the cement. The time of flight of the second echo, $x_2(t)$, and the thickness of the cement sample gives the speed of sound in the cement. These two properties can then be used to determine the density and the adiabatic bulk modulus, β, of the cement. The adiabatic bulk modulus can be written as [16]

$$\beta = C - \frac{4G}{3}, \tag{2}$$

where the compression wave modulus, C, and the shear wave modulus G as

$$C = \lambda + 2\mu, \tag{3}$$

$$G = \mu, \tag{4}$$

where λ and μ are the Lamé constants of the solid material. The bulk modulus is related to how an isotropic material is affected by a pressure applied from all directions, and thus a relevant measure of the mechanical strength of the material. In order to determine both the shear and the compression modulii it is necessary to measure both the shear wave velocity and the compression wave velocity. In the current setup only a compression wave transducer is used, and therefore it is only possible to determine the bulk modulus.

The reflection coefficient $R_{p,c}$ is defined as the amount of reflected acoustic energy at the PMMA/cement

interface. That is,

$$R_{p,c} = \frac{A_c}{A_w} R_{p,w}, \tag{5}$$

where $R_{p,w}$ is the reflection coefficient for a PMMA/water interface, A_c is the amplitude of the PMMA/cement echo, and A_w is the amplitude of a corresponding echo measured in pure water. The reflection coefficient [13] for water is given by

$$R_{p,w} = \frac{z_w - z_p}{z_w + z_p}, \tag{6}$$

where z_w and z_p are the known acoustic impedances of water [17] and PMMA [18], respectively.

The amplitude of the echoes is calculated by first taking the discrete Fourier transform (DFT) of the sampled pulses, then calculating the amplitude ratio A_c/A_w for all frequencies within the bandwidth of the pulse, and finally averaging this to obtain an average value of the attenuation.

Once the reflection coefficient is known the acoustic impedance of the cement sample can be calculated as

$$z_c = z_p \frac{1 + R_{p,c}}{1 - R_{p,c}}. \tag{7}$$

In order to determine the speed of sound in the cement, the two echoes $x_1(t)$ and $x_2(t)$ are cross-correlated. The maximum of the cross-correlation corresponds to the time-shift Δt between the two pulses. Since the propagation distance, d_2, of the pulse is known, the speed of sound is $c = 2d_2/(\Delta t)$.

From the speed of sound, c, and the acoustic impedance, z_c (Eq. (7)) of the cement, the density, ρ, and the adiabatic bulk modulus, β, are given by

$$\rho = \frac{z_c}{c}, \tag{8}$$

$$\beta = c^2 \rho. \tag{9}$$

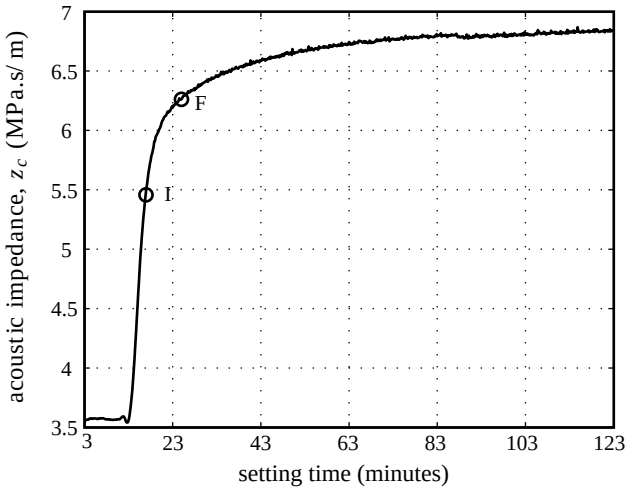

Fig. 3. Acoustic impedance of CSD as a function of the setting time.

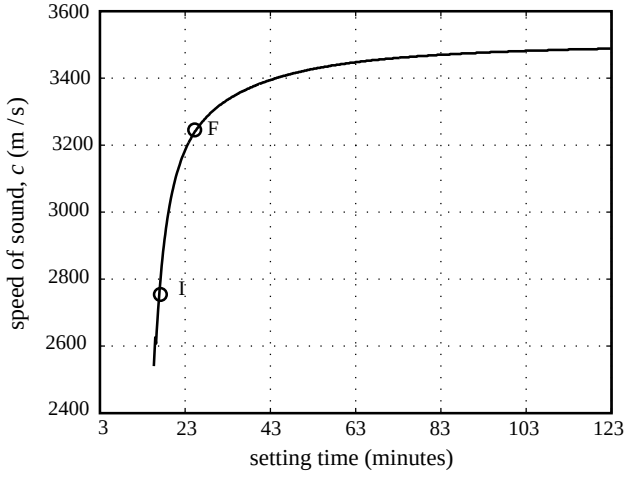

Fig. 4. Speed of sound in CSD as a function of the setting time.

3. Results

Using the pulse-echo technique described in the previous section it is possible to measure the acoustic impedance and the speed of sound in the cement sample, on-line, during the setting of the cement. Fig. 3 shows the acoustic impedance at the PMMA/cement interface as a function of the setting time. The figure clearly shows that when the cement is set, the rate of change of the acoustic impedance decreases. The (I) and (F) times obtained with the Gillmore needles method are also marked in the figure, and they were determined to be 17 and 25 min, respectively.

Fig. 4 shows the speed of sound in the cement as a function of the setting time. The speed of sound was obtained by cross-correlating the echo from the steel reflector with the echo from the PMMA/cement interface. In the early stages of the setting process, most of the sound energy was absorbed by the cement and thus the second echo was very weak. For this time interval it was therefore not possible to determine the sound velocity accurately.

Fig. 5 shows the adiabatic bulk modulus as a function of the setting time. This was calculated from the speed of sound and the acoustic impedance using Eq. (9). The adiabatic bulk modulus is a property related to the elasticity and compressive strength of the material. Using only compressional sound waves, it is not possible to completely solve for the different modulii of the material [19].

Using the measured values of the acoustic impedance and the speed of sound, it is also possible to determine the density of the cement at the PMMA/cement interface. The results are shown in Fig. 6. The figure shows

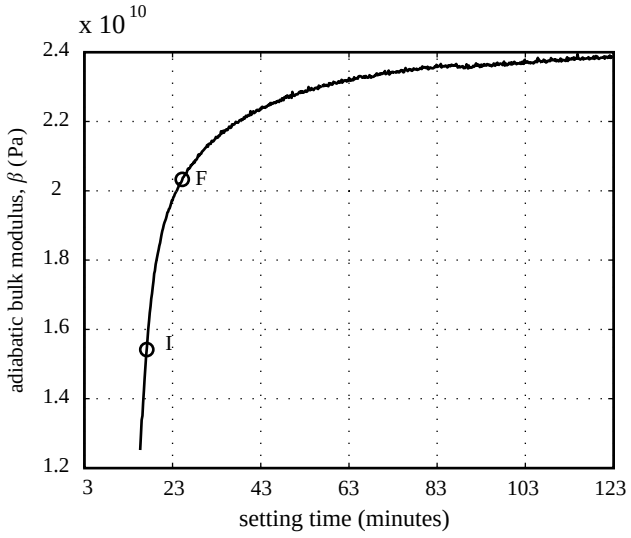

Fig. 5. Adiabatic bulk modulus of CSD as a function of the setting time.

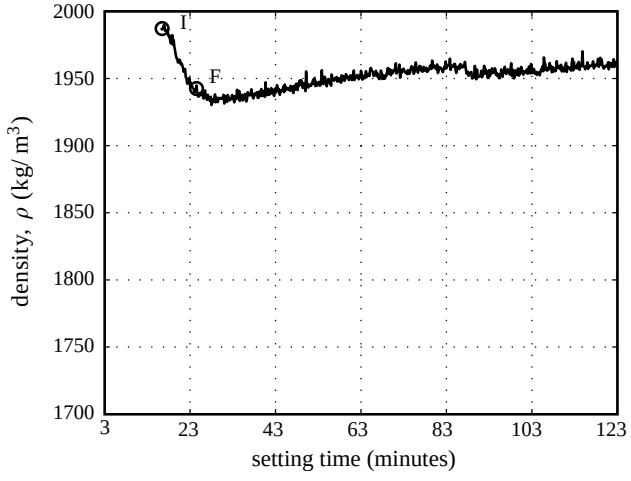

Fig. 6. Density of CSD as a function of the setting time.

that there is a sudden decrease in density between the (I) and (F) times, measured with the Gillmore needles standard. The slow increase in density in the time interval 20–120 min, was about 1.6%, which is in the same range as the documented shrinkage observed by others [20,21]. The exact shrinkage depends on how the cement is prepared, and under what conditions the setting takes place.

4. Discussion

There are several reasons why a non-invasive and non-destructive method that can objectively measure the actual mechanical parameters of the cement is preferred over the existing standards. Finding a method for determining the setting time accurately is important, since it has implications on when the surgeon may close the patient's wound. If the surgeon is able to close the wound earlier, this is not only good from an economical point of view, but also reduces the risk of medical complications. Since the standards are based on visual examination of the cement surface, the measured setting time can give very different results depending on who is making the experiment.

The existing standards define the setting time as when the surface of the material is strong enough to withstand a certain pressure. This has, however, in many cases little or nothing to do with if setting reaction has stopped or not. In this aspect, the ultrasonic method is more appropriate, since it shows when the acoustic properties of the material are no longer changing. Because the acoustical and mechanical properties are strongly correlated, this indicates that the underlying chemical reaction has also stopped. An important difference from the standards is thus that the proposed technique reports mechanical properties as a function of time, but the actual setting time is not based on a fixed value of, for example, the mechanical strength.

Another drawback using these test methods is the large volumes of cement required in these standards. The Vicat Needle and the Gillmore Needles standards demand a volume of 133 and 41 cm^3, respectively. This requirement is, however, never met when using the standards, since it leads to a significant waste of expensive cement. Because of this, many researchers have developed their own, in-house techniques for determining when the cement has set. The volume required in our measurement cell was 20 cm^3, which is less than in for the standards, but still rather large. The size of the cell can, however, be reduced further without loss of information. Furthermore, using this technique it is also possible to measure other properties about the cement than just the setting time. Looking in more detail at the backscattered sound, it should also be possible to asses the porosity of the material. During different stages of the setting process, the crystal structure of the cement changes. Cavities and boundaries between different crystals will give rise to partial reflections from within the crystal structure of the cement. This is visible in the measurements as changes in the shape and length of the reflected pulses.

The use of longitudinal pressure waves allows the determination of the adiabatic bulk modulus of the material. This modulus is a combination of parameters that characterize the compressive strength and the elasticity. There is, however, no way to solve for these parameters using the information in the reflected pulses. Modifying the experimental setup slightly, it should be possible to use both longitudinal and shear waves. The

combination of these makes it possible to solve for several mechanical parameters of the material. An example of this type of setup was proposed by Freemantle and Challis [16] as a technique to monitor curing adhesive.

The results obtained with Gillmore needles agree well with the results from the ultrasonic technique. The (*I*) time (17 min) was found during the fast increase in the Figs. 3–5. However, this is the most critical part of the curve where small errors in time change the result significantly. Since the Gillmore needles method is inaccurate, large differences may be obtained in results from different users. The (*F*) time (25 min) is found just when the curves attain the plateau, which shows good correlation between the two test methods. After the (*F*), time no large changes are seen in either of the Figs. 3–5, which indicates that the (*F*) time gives a good value of the time when the final properties of the cement are obtained.

In the case of the density, however, the results show a completely different behavior (Fig. 6). The (*I*) time is found as the first point in the figure while the (*F*) time corresponds to its lowest point. As seen in the figure we cannot determine the speed of sound in the cement at the beginning of the experiment. This is because the wet paste attenuates most of the sound energy and thus no second echo, from the cement/reflector interface, is obtained. The first measurable point corresponds in this case to the (*I*) time. This problem could be overcome in two ways. One is to use an ultrasound transducer with lower frequency, since the attenuation increases with increased frequency. Another solution is to increase the energy of the transmitted pulse. The major risk with the second approach is that an increased sound pressure might also affect the setting of the cement.

Using our test parameters the (*I*) time corresponds to the first point when the attenuation of the cement is sufficiently low to obtain a second echo. This is probably due to a rapid change in the crystal structure during a short period around this time. The (*F*) time is found at the point of the curve where the end of the hydration and the beginning of the shrinkage process is detected. During shrinkage the density increases slightly. The measured value of the final density after 2 h differs slightly from theoretical values found in, for example, [17]. The exact density, however, depends on both the liquid-to-powder ratio and if the density is measured in dry or wet conditions.

The experimental results presented in this paper are for CSD cement only, see Eq. (1). The results clearly show the feasibility of using ultrasound to measure the setting time, as well as determining some of the mechanical properties of the material. Future work will involve evaluating the proposed technique for other cement mixtures.

5. Conclusions

In this paper we have presented an ultrasonic pulse-echo technique that can be used to measure the setting time, the density, and the adiabatic modulus of calcium sulfate based bone cement.

The method is easy to use and the testing can be made throughout the entire setting process without having to move or otherwise manipulate the cement sample. There are no indications that the sound affects the cement structure during setting, since the results are in line with those obtained by Gillmore needles. As opposed to the existing standards, where the initial setting period is measured at two points, the proposed technique shows the development during the entire setting process.

Most important, the results obtained with the ultrasonic technique are reproducible and completely objective, which makes it possible to compare results between different researchers.

Moreover, the acoustic method could be implemented to be operated at the operation theater as a way to avoid batch-to-batch differences of cement material, if necessary.

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