CHANGES OF STRUCTURE AND PROPERTIES OF PMMA-BASED BONE CEMENTS WITH HYDROXYAPATITE AFTER DEGRADATION PROCESS

Anna Laska-Leśniewicz[1]* , Małgorzata
Raczyńska[1], Maciej Wrotniak[2] ,
Anna Sobczyk-Guzenda[1]

[1] Lodz University of Technology,
Department of Mechanical Engineering,
Institute of Materials Science and Engineering,
1/15 Stefanowskiego st., 90-924 Lodz, Poland
[2] Department and Hospital Department
of Orthopaedics, Silesian Medical University,
St. Barbara 5th Regional Specialised Hospital
in Sosnowiec,
Pl. Medyków 1, 41-200 Sosnowiec, Poland
*e-mail: anna.laska.lesniewicz@gmail.com

Abstract

PMMA-based bone cements are commonly used for implant fixation or as bone void fillers. Hydroxyapatite added as a filler to bone cement may positively affect the final properties of the material, in particular its biological properties. In this study, the preparation of poly(methyl methacrylate)-based bone cements with incorporated hydroxyapatite (HAp) is reported. The purpose of this article is to examine the properties of bone cements enriched with HAp filler (the concentration of 3wt% and 6wt%) and reveal the changes in the composites properties (chemical structure, surface morphology and distribution of HAp in the composite matrix, moisture absorption, hardness in Shore D scale) during the long-term incubation in the PBS (phosphate-buffered saline) solution at 37°C. The incubation lasted up to 21 days, but only the period when the changes actually occurred was analysed. The studies have shown that the samples containing HAp absorb more moisture and have a lower hardness. These characteristics vary depending on the concentration of HAp. There is no elution of HAp and ZrO_2 from the composite during the incubation. The surface morphology and chemical structure do not change during long-term studies. The obtained bone cements are characterized by high stability in the PBS solution.

Keywords: *bone cement, PMMA, hydroxyapatite, vertebroplasty*

Introduction

Bone cements have been widely used in medicine since the 1960s when joint replacements started to be common orthopaedic surgical procedures. The significant increase in physical activity among people over 50 years of age, a higher rate of obesity in the population, ageing of the population and perpetual rise of patients' demands combined with development of new implants used in treatment of osteoarthritis will result in a rise of numbers of joint replacements in next decades.

According to the latest data, osteoarthritis (OA) affects 240 million people globally, about 10% of men and 18% of women over 60 years of age [1]. There are both conservative and surgical methods of OA treatment, however the first one is still ineffective and cannot stop the OA progression. Therefore, the total joint replacement is the most successful method of osteoarthritis treatment reducing pain and improving the quality of life. The total hip replacement arthroplasty (THA) and total or uni-compartment knee arthroplasty (TKA, UKA) are the most common procedures in the everyday practice of orthopaedic surgeons. In both cases, the bone cement is to fasten the joint endoprosthesis. The final result of the treatment depends on a properly selected implant, accordingly to the patient's age, bone quality and future activity, their demands and expectations and indications for the operation. Therefore, selecting biomaterials that will provide the efficient and long-lasting stability of the implant is yet another aspect. In patients with osteoporosis, whose bone tissue is less resistant to physical stress, fixing bone cement is the most important factor that influences the implant lifespan and may provoke its early loosening.

Among other applications, bone cements are implemented to fill up minor bone cavities mainly in the facial area. They are also used in other medical procedures, such as vertebroplasty (VP) and kyphoplasty (KP) –that are preferred methods of treating stable, compression fractures of vertebral body. This type of vertebral fractures, combined with fractures of the proximal humerus and femoral neck, are the most frequent injuries in patients with osteoporosis. Both VP and KP are minimally invasive and designed mainly to relieve the pain, strengthen collapsed vertebrae and finally restore geometry of the vertebral column [2]. Furthermore, VP is a palliative method of treatment in pathological spinal fractures in the case of metastases of the vertebral column [3]. As the population in Europe is ageing and the statistics shows progressive osteoporosis, increased spinal fractures and joint problems, the development of such biomaterials as bone cements that will fully meet the requirements of bone rebuilding and bonding the implant with tissue seems to be inevitable [4].

Bone cements can be divided due to the materials they were made of. There are polymeric, phosphate-calcium-based, hydrogel and composite bone cements [5]. The most popular ones are cements based on poly(methyl methacrylate) (PMMA). They have long clinical history, therefore it is easier to predict their behaviour in the human body over the years. The PMMA cement exhibits biocompatibility and appropriate mechanical properties. Still, it is possible to develop composites so that the connection between the injected cement and surrounding tissue will improve. That is why bioactive bone cements with the addition of bioactive glass or hydroxyapatite are a particularly promising solution [6,7].

Requirements for bone cements are strictly related to their use. In the case of fixing endoprostheses, cement can form just a mechanical connection with the bone (without chemical bonding). According to the ISO norm (ISO 5833), its compressive strength must be higher than 70 MPa. For the bone defect reconstruction or filling, cements should also exhibit osteoconductive effects and support tissue regeneration. The material introduced into bone defects may be characterized by lower strength parameters, similar to the properties of natural spongy bone tissue (at least 30 MPa). PMMA-based cements are endowed with good mechanical properties (Young's modulus – 1800-2200 MPa, compressive strength – 75-105 MPa, bending strength – 60-75 MPa) and the ease of feeding resulting from good rheological properties [8,9].

In addition, the rheological properties of cement, its setting time and behaviour in contact with the physiological fluid are important. The chemical and granular composition has a significant impact on these parameters. The widespread use of bone cements in orthopaedics and facial-jaw surgery forces their modifications which will improve their biological and mechanical properties.

Polymeric cements are two-component systems – powder and liquid, whose weight ratio is about 2:1. The powder usually consists of poly(methyl methacrylate) (PMMA) or a copolymer of styrene and methyl methacrylate. In addition, a polymerization initiator – benzoyl peroxide and radiopaque agents – barium sulphate or zirconium dioxide are added. The liquid contains methyl methacrylate monomer (MMA), about 98% by weight. Additionally, bone cements may contain antibiotics, e.g. gentamicin or vancomycin, which increases the septicity of the medical procedure [10].

Unfortunately, PMMA cements are also burdened with negative effects on the human body. The biggest problems associated with their use include:
• exothermic reaction related to the mechanism of polymerization of this material,
• polymerization shrinkage,
• poor adhesion to the bone surface and inorganic substance,
• lower resistance to cracking (compering to natural bone),
• leaving 4-7% unreacted MMA monomers with toxic effects.

Composite bone cements are the answer to problems occurring mainly with PMMA-based cements. The selection of the reinforcement phase plays a key role for the strength and stability of the bone cement in the human body. The contribution of reinforcement (a filler) in the composites equals usually from a few to several percent by weight. Changes in material properties may be noted even after minor addition of a filler (such as 1%wt) but there is no obvious correlation that can be simply stated about all reinforcement types. In the case of such fillers as bovine bone pulp, bone-substitute material and Al_2O_3, the significant changes in mechanical properties and the polymerisation course are found in samples with a filler quantity of more than 5% [11]. What is more, the type and amount of a filler determines the polymerization course, the material solidification and its behaviour in contact with the tissue. The addition of bioactive glass, hydroxyapatite or calcium triphosphate results in a decrease in compressive properties (slight deterioration of strength properties), it reduces porosity and improves fracture toughness. Composites containing starch are characterized by better degradation and resorbability [12].

Hydroxyapatite (HAp) – $Ca_{10}(PO_4)_6(OH)_2$ naturally occurs in human bones. It is slightly soluble in water and resilient in tissues, therefore it facilitates the integration of tissues and bone restoration. The introduction of hydroxyapatite into the polymer phase may increase biocompatibility and facilitate performing biomechanical functions. Additionally, bioactive HAp particles can act as anchors for the composite - bone bonds, which ensures good restoration of the living tissue and promotes bone growth around the implant [13]. Moreover, according to the research, the bone cement based on poly(methyl methacrylate-co-styrene) filled with HAp has a lower exothermic effect during the curing process and a higher degree of conversion (which means a lower residual monomer amount) than the cement without this addiction [14,15]. The HAp addition also influences the mechanical properties of bone cement, but it is hard to clearly estimate the trend.

The aim of the present study was to describe and characterise the novel composite bone cements in terms of the chemical composition and structure, surface morphology, moisture uptake and changes in hardness over different time of incubation in a buffer at 37°C. The new materials described in this work are based on the commercial PMMA bone cement loaded with a biocompatible and bioactive hydroxyapatite powder (HAp) that was precisely selected and synthesised.
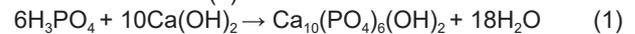
Materials and Methods

Materials
Commercial bone cement is used as a polymeric matrix of the tested samples. The chemical composition of bone cement (BC) is presented in TABLE 1.

TABLE 1. Chemical composition of commercial basic bone cement.

Powder phase (26 g)	Poly(methyl acrylate, methyl methacrylate)
	Zirconium dioxide
	Benzoyl peroxide
	Colouring agent E141 – Chlorophyll
Liquid phase (10 ml)	Methyl methacrylate
	N, N-dimethyl-p-toluidine
	Hydroquinone

Hydroxyapatite powder, a filler in the created bone cement, was synthesized via the chemical wet method i.e. precipitation. The process was based on the experiments carried out by Afshar and co-workers [16] via the following chemical reaction (1):

$$6H_3PO_4 + 10Ca(OH)_2 \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 18H_2O \qquad (1)$$

As it was calculated, for the synthesis approx. 50 g of powdered HAp and 37 g of calcium hydroxide ($Ca(OH)_2$, Chempur) was added to 4 liters of distilled water and mixed for 1 hour at 40°C (± 2°C). Then, 34.6 g of orthophosforic acid (H_3PO_4, POCH) was gradually poured into the mixture at the speed of 1 drop per second. At that stage, it was crucial to control the temperature (40 ± 2°C) and the pH value (above 9). If pH came closer to 9, a small amount (10 ml) of ammonia solution 25% (POCH) was added. After the synthesis, the sediment was purified at least 10 times in order to get rid of the ammonia solution. Then, the synthesized HAp was dried at room temperature. Final steps were milling and sifting (screening). The material was milled in the planetary ball mill (Retsch, Germany) and sieved in the laboratory sifter (Morek Multiserw, Poland) to get the proper particle size of 25-50 µm.

Dulbecco's phosphate-buffered saline (PBS, Corning Media) without calcium and magnesium was used to immerse all the bone cement samples for the experiments.

Preparation of bone cements
The three types of specimens were prepared for examinations: (1) the control sample – the commercial bone cement without hydroxyapatite (Osteopal® plus), (2) the 3%HAp/BC - the commercial bone cement with 3wt% HAp, (3) the 6%HAp/BC - the commercial bone cement with 6wt% HAp. The composition of all specimens is presented in TABLE 2.

TABLE 2. Composition of specimens.

Sample name	Powder phase		Liquid phase	Powder/Liquid Ration
	Bone Cement	HAp		
Control sample (Bone Cement – BC)	3 g	-	1.154 ml	2,6
3%HAp/BC	3 g	0.126 g	1.154 ml	2,7
6%HAp/BC	3 g	0.261 g	1.154 ml	2,83

The novel bone cements were prepared in three steps. Firstly, the powder phase of the commercial bone cement was precisely mixed with synthesised HAp powder in proper amounts. Then, the new powder phase was manually mixed, using a spatula, with the liquid in a small glass beaker for 30-40 s at room temperature. Finally, the material was transferred into silicon moulds. The samples were prepared as cylinders of measuring 6 mm or 12 mm in diameter and 2 mm in height.

Degradation test

Three types of specimens (the control sample BC, the 3%HAp/BC, the 6%HAp/BC) were subjected to degradation tests. The samples (cylindrical shape, ø6 mm) were soaked in the PBS buffer and kept in an incubator at 37°C for different periods of immersion. i.e. 7 days, 21 days, 42 days. After the incubation, the samples were preliminarily dried with a paper towel and then left at room temperature. The incubated specimens were tested, using the following techniques:

- Scanning Electron Microscope (SEM) – morphology of the sample surfaces,
- Energy Dispersive X-ray Spectroscopy (EDS) – elemental composition and maps of the distribution of elements,
- Furrier Transform Infrared Spectroscopy (FTIR) – chemical structure,
- Shore D hardness test after 7 and 21 days of incubation,
- Moisture uptake after 7-day, 21-day and 42-day immersion in the buffer.

Morphology of the bone cements

The surface morphology of the composite bone cements was examined on the JSM-6610LV Scanning Electron Microscope (SEM, JEOL USA). The samples were observed right after preparation (before the incubation) and after being soaked in PBS for 21 days. To obtain clear images the samples were covered in a thin (10 nm) layer of gold. The detailed images of two different magnifications (x100 and x1000) were obtained under high vacuum and at 20 kV accelerating voltages.

Elemental composition of bone cements

The composition of the cements was confirmed via EDS. The additional module X-MAX 80 (Oxford Instruments) attached to the JEOL JSM-6610LV scanning electron microscope was used for the EDS X-ray microanalysis. The 20 kV acceleration voltage was used for the measurements. The scanning time of 7 min, the resolution of 2048 px and the excitation time of 100 μs/px were set for the measurements. The maps of the distribution of selected elements were made.

Chemical structure

For studies of the chemical structure of the samples, the Nicolet IS 50 FT-IR Spectrophotometer (FTIR, ThermoScientific) was used. The system was equipped with deuterated tri-glycine sulphate (DTGS) KBr beam splitter. The special reflection attachment (DRIFT type) with the incidence angle of 90° was used for the measurements. The FTIR spectra of absorbance over the wavelength range of 4000-400 cm^{-1} with the resolution of 4 cm^{-1} were measured.

Hardness test

The indentation hardness of the specimens was determined by means of the durometer (Shore hardness scale D) according to the norm ISO 868:2003. The tests were conducted using the manual durometer MC-DX/D (max: control measuring instruments). Ten independent measurements were taken for each sample. The samples were tested before the immersion in PBS and after the immersion of 7 and 21 days.

Moisture uptake

The cement samples (small cylinders of 6 mm in diameter and height of approx. 3 mm) were soaked in PBS at 37°C, up to 42 days. The moisture uptake (MU) was calculated according to the equation: (1) [12].

$$MU = [(m_{ti} - m_i)/m_i] \times 100 \qquad (1)$$

m_i – initial mass (before immersion)
m_{ti} – sample mass after i immersion days.

Results and Discussions

The morphologies of the studied bone cements are presented in FIG. 1. At the x100 magnification, there are no significant differences between the samples with varied HAp additions and the control sample (the bone cement without HAp). In the samples containing hydroxyapatite there are small white particles visible in the pictures (FIG. 1B and FIG. 1C). The morphologies, investigated at the low magnification, confirm the non-defected structure in all the specimens. Therefore, it can be deduced that the HAp addition does not adversely affect the material structure and the bone cements preparation proceeds correctly.

There are three characteristic structures visible in the images presented in FIG. 2: zirconium dioxide ZrO$_2$, PMMA and HAp. ZrO$_2$ creates the bright, sizeable, cauliflower structures. PMMA can be recognised as spherical, bubble-like and dark-grey grains. HAp is noticeable as tiny irregular shapes, bright shreds on the surface. It is worth recalling that both zirconium dioxide and HAp act as fillers in the created bone cements. Their regular distribution and degree of fineness have a strong impact on the mechanical properties of the composite. The content of zirconium dioxide in the composite is 40wt%, which is many times more than the HAp amount. It is also clearly visible that the amount of zirconium is higher than HAp (even considering 6%HAp specimen). What is more, the zirconium tendency to agglomerate is observed. The size of the zirconium dioxide agglomerates was estimated to be of 20-30 μm and is significantly larger than HAp grains (about 1-2 μm). It cannot be unequivocally stated that any of the components eluted during the incubation. The comparison of the morphology before and after the immersion does not reveal any visible changes.

The distribution of such elements as zirconium, calcium and phosphate is illustrated in the maps (FIG. 3). The control sample contains only zirconium, there are no maps for Ca and P, as it does not contain HAp. The maps of the 3%HAp/BC and the 6%HAp/BC confirm the occurrence of hydroxyapatite in their structures. In all the specimens, Zr, Ca and P show the tendency to agglomerate, they create clusters that are quite unevenly distributed in the material.
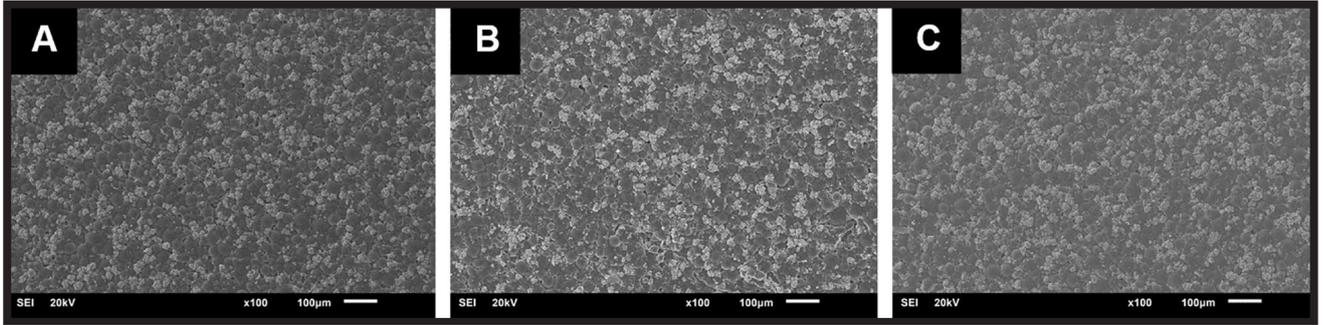
FIG. 1. Morphology of the prepared bone cements (A – control BC sample, B – 3%HAp/BC, C – 6%HAp/BC).
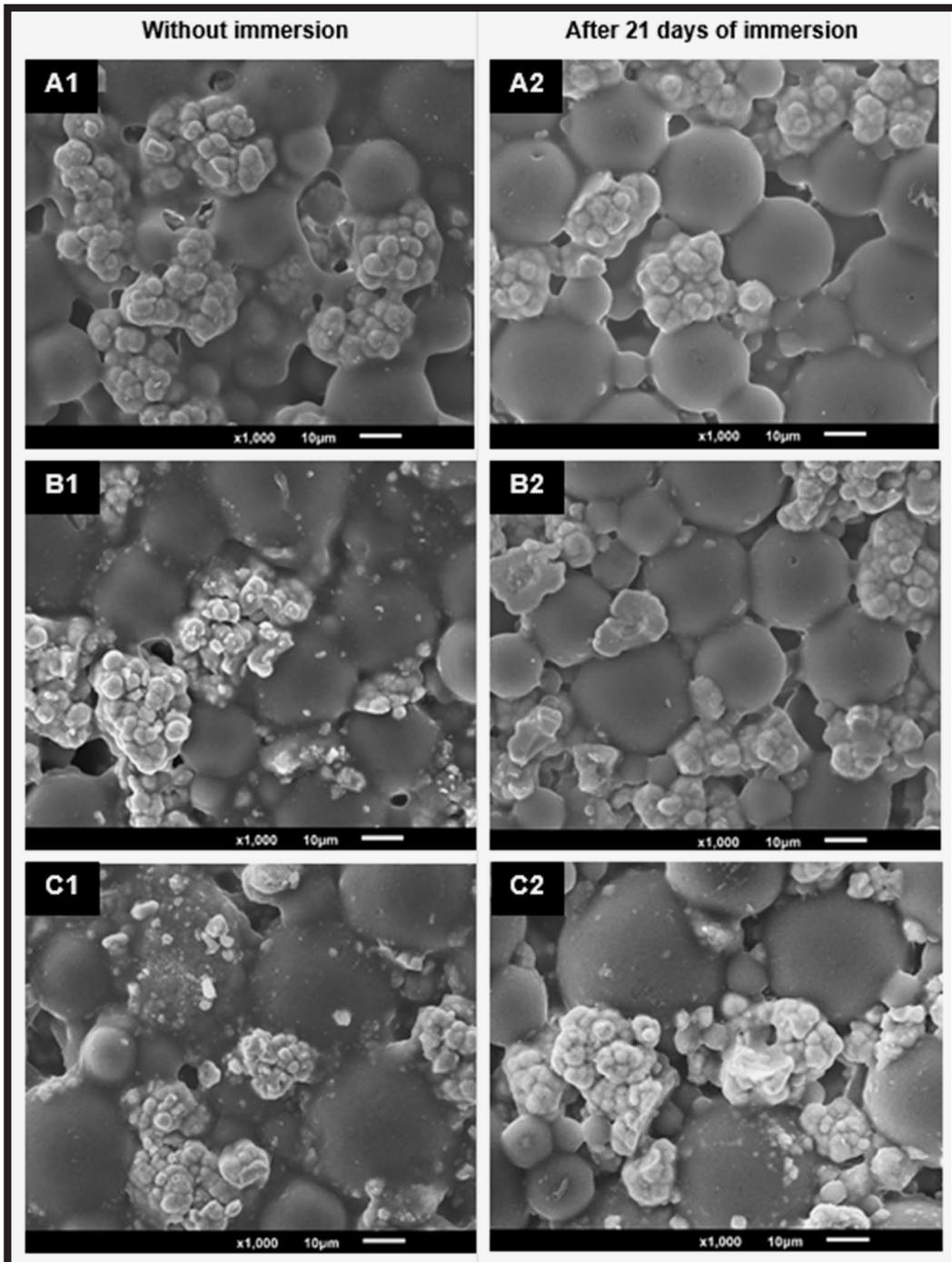

FIG. 2. SEM images before and after immersion in PBS (A1 – control BC sample before immersion, A2 – control BC sample after immersion; B1/ B2 – 3%HAp/BC before/after immesion; C1/C2 – 6%HAp/BC before/after immesion).
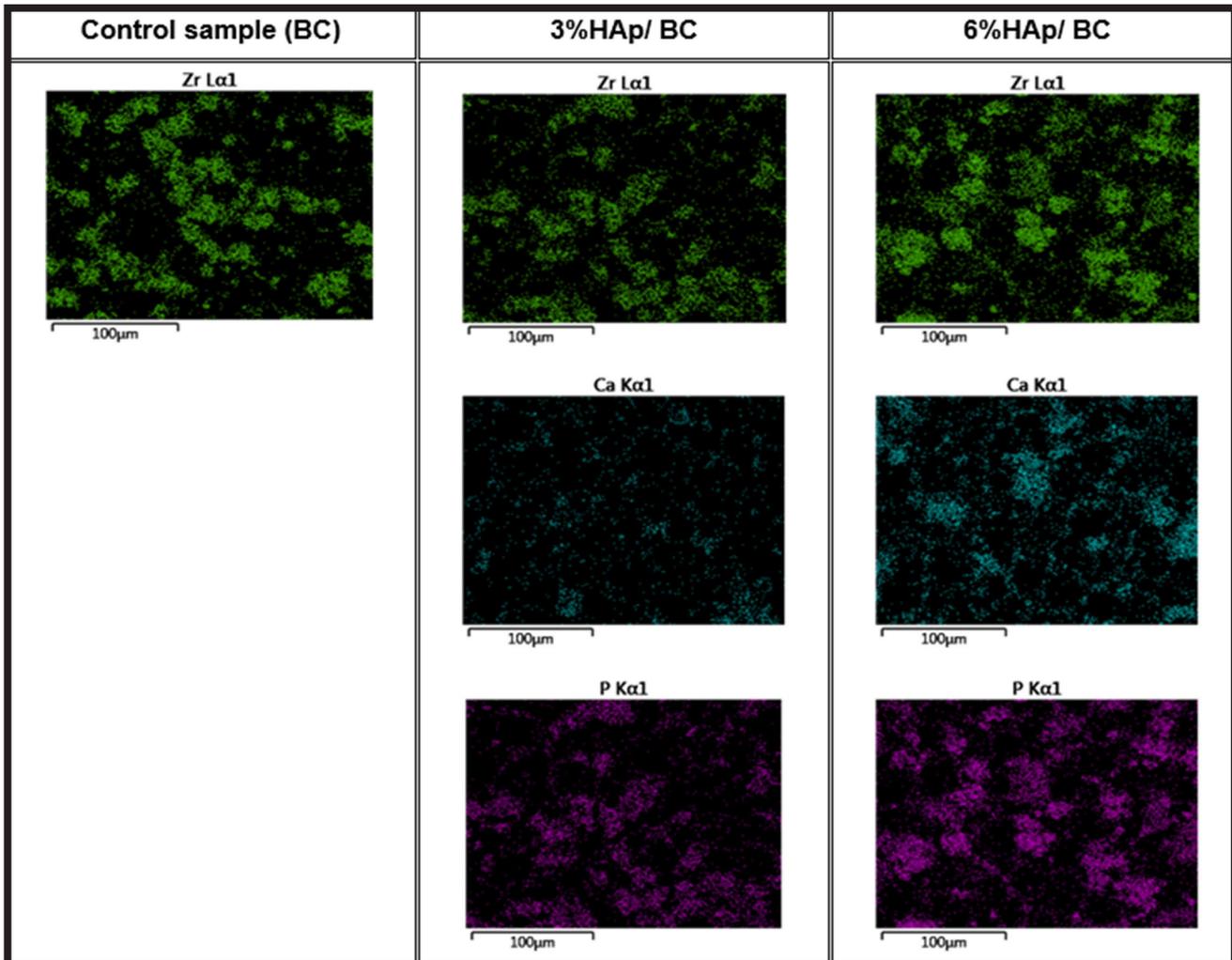
FIG. 3. Maps of the distribution of zirconium, calcium and phosphate in all tested samples.

The maps were also prepared after the 21-day immersion in the PBS solution. There was no visible elution of either HAp or zirconium dioxide over time. In FIG. 4 there are visible agglomerates of calcium. The tendency to agglomerate increases with the higher content of HAp. After the incubation the amount of calcium noticeably rises over 1wt% in both the sample types (3%HAp/BC and 6%HAp/BC).

FIG. 5A depicts the FTIR spectra for the bone cement samples. Based on the spectra, it can be concluded that a minor HAp addition slightly affects the chemical structure of the material.

As expected, the collected FTIR spectra display peaks characteristic for the bone cements based on poly(methyl methacrylate) (FIG. 5). The most prominent peaks occur at 1729 cm^{-1} and from 2750 to 3000 cm^{-1} corresponding to C=O stretch and -CH$_2$, -CH$_3$ stretch, respectively. The peak at 3000 cm^{-1} decreases with the rising amount of HAp in the samples.

The characteristic peaks for Zr-O at 750, 610 and 430 cm^{-1} are visible in all the spectra, which confirms the presence of that kind of a radiopacifier agent.

For the 3%HAp/BC and the 6%HAp/BC spectra the wide and visible peak at 857 cm^{-1} can be attributed to ions HPO$_4^{2-}$ present in HAp. The peak rises substantially with the increasing HAp content. Another peak at 1083 cm^{-1} changes similarly. It represents ions PO$_4^{3-}$ present in HAp.

The peak at 565 cm^{-1} is generated by benzene rings and the other three bands come from the O-H bond in alcohols and phenols. Such groups are present in compounds that regulate the initiation and kinetics of polymerization (benzoyl peroxide, hydroquinone, N, N-dimethyl-p-toluidine). These substances are not inert to living organisms and their amount should be vestigial. All the visible differences are related to the chemical composition of the prepared bone cements and changes in the HAp/polymeric matrix ratio.

The peak at the wavelength of 716 cm^{-1} is visible in each spectrum, but it is slightly wider and less pointy in the 6%HAp. It is connected with the Ar-OH bond in phenols (present in the hydroquinone structure). The mentioned change is related to another peak (at the wavelength of 716 cm^{-1}, generated by P$_2$O$_7^{4-}$) that merges with it. It seems that, as a result of the HAp precipitation, the trace amount of other ions was noted (absent in the HAp structure).

The peak at the wavelength of 1012 cm^{-1} which decreases with the increasing HAp amount represents the C-O bonds in esters.

The minor, slightly visible peak at the wavelength of 565 cm^{-1} and more visible peaks at 3629, 3830, 3946 cm^{-1} slightly decrease with the increasing HAp content and are less visible in the 6% specimen spectra. The peak at 565 cm^{-1} is generated by benzene rings and the other three bands come from the O-H bonds in alcohols and phenols. Such groups are present in the compounds that regulate the initiation and kinetics of polymerization (benzoyl peroxide, hydroquinone, N, N-dimethyl-p-toluidine). These substances are not neutral to living organisms and their amount should be limited.
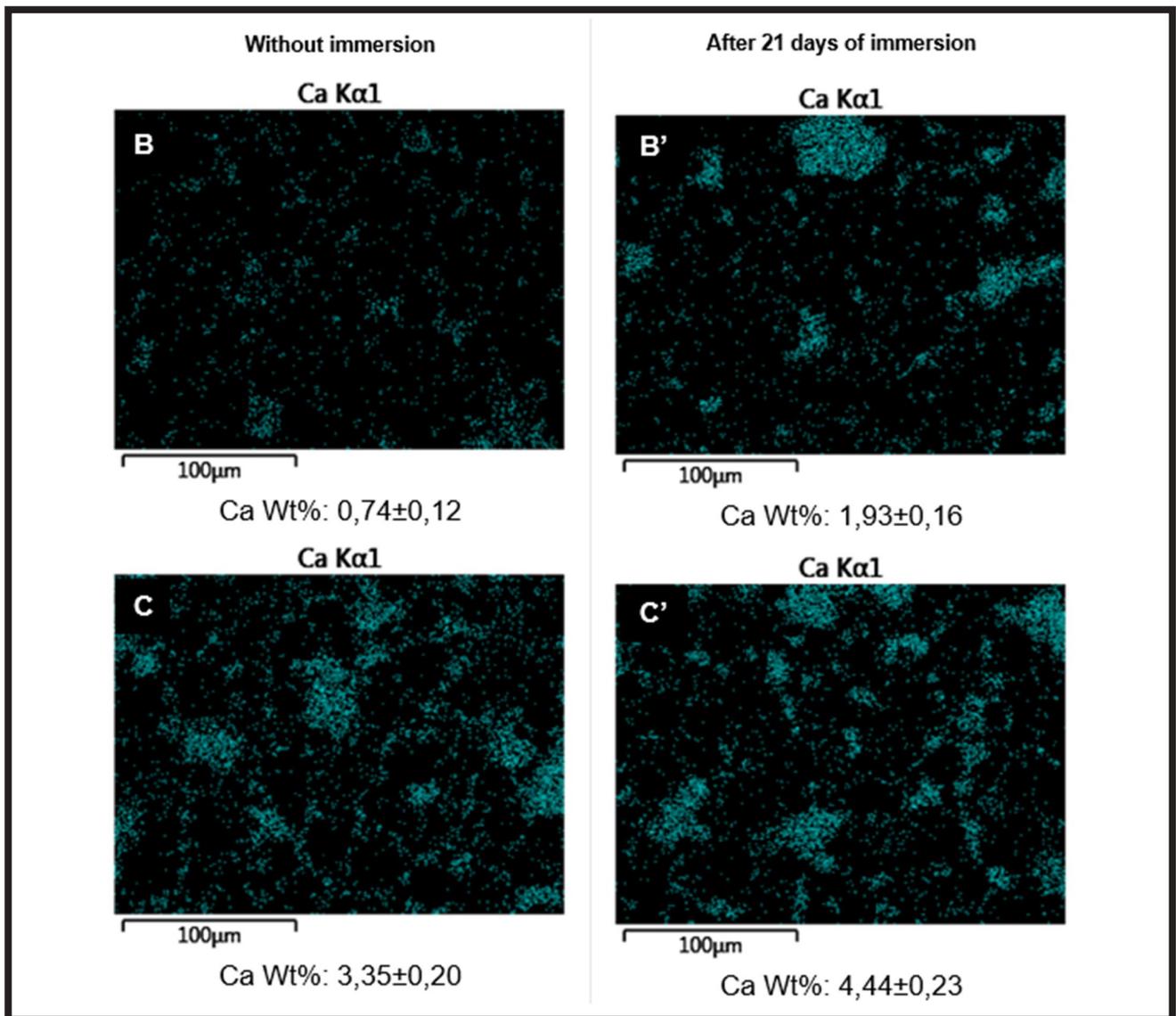
FIG. 4. Maps of calcium distribution before and after immersion in PBS (A1 – 3%HAp/BC before immersion, A2 – 3%HAp/BC after immersion, B1 – 6%HAp/BC before immersion, B2 – 6%HAp/BC after immersion).

FIGs 5B-5D show the spectra of all the types of bone cements after different immersion time. The analysis of the control sample spectra (bone cement) does not reveal any significant changes. In contrast, the spectra of the samples containing HAp display clearly visible changes.

The trend of the observed changes cannot be unambiguously determined. Non-schematic changes in peak values that represent bonds in HAp and polymeric bone cement matrix are most likely related to minor changes in the composition and the HAp distribution in heterogeneous samples.

Before the incubation, the highest hardness value was noticed for the control sample – the bone cement without hydroxyapatite (FIG. 6). The higher amount of HAp was the lower hardness. The differences in hardness between the bone cements with HAp are slight. After the incubation there were some changes in the hardness values. In general, the storage in PBS worsens the samples hardness. Those changes may be partly connected with the moisture uptake of the bone cements. Small molecules of water absorbed into the bone cement between the long chains of poly(methyl methacrylate) act as a "plasticizer" of the polymer structure. Most probably, the addition of a ceramic filler such as HAp increases the inhomogeneity and influences the mechanical properties of the composites.

The moisture uptake results (FIG. 7) show that the cement is getting filled by liquid most at the beginning of the immersion, regardless of its composition. The tests indicate that the largest increase in mass, i.e. the greatest moisture uptake at that time, which is coherent with the literature [12,17]. The amount of the absorbed solution gradually decreases over time. However, another process should be taken into consideration that has an impact on the specimen mass – the release of residual monomer. Since the PMMA matrix is hydrophobic, it is possible that the mass values of the absorbed moisture and the released monomer are comparable. One can assume that the released monomer amount is higher than the absorbed moisture weight. The weight changes vary, depending on the HAp content. The 6%HAp weight increased twice as much as the control sample on the 7th day of measurement. The 3%HAp weight grew one and a half times more than the control. The most significant change in weight was recorded for the specimens with HAp, this phenomenon is related to the heterogeneous structure of the composite with the highest value of a ceramic filler. Water easily penetrates a porous, heterogeneous structure with the well-developed area of the phases boundary between the PMMA matrix and the filler. The more numerous the heterogeneities are, the more spaces where water can be accumulated.
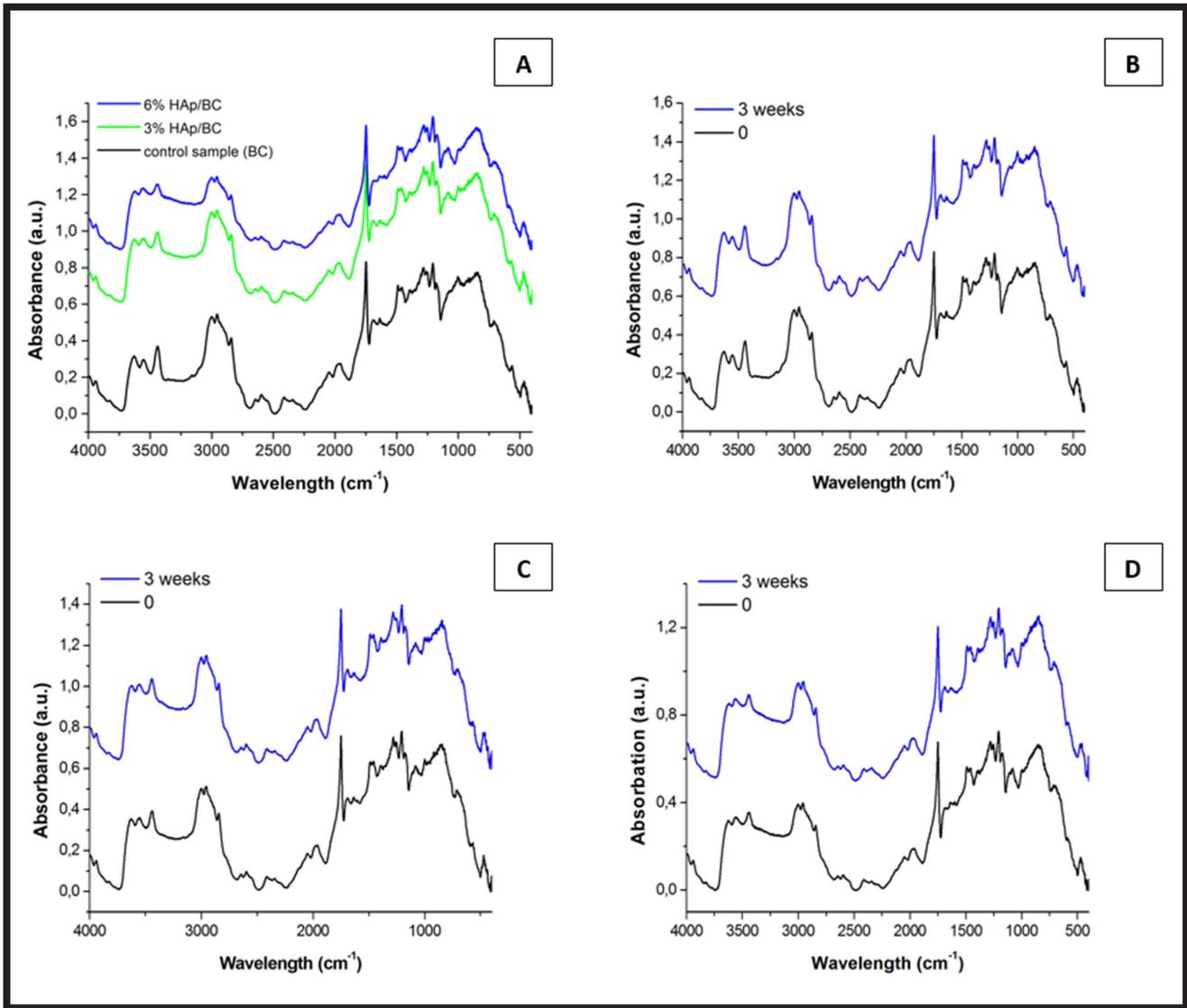
FIG. 5. FTIR spectra (A – spectra of all prepared samples before immersion, B – spectra of control sample over immersion time, C – spectra of 3%HAp/BC over immersion time, D – spectra of 6%HAp/BC over immersion time).
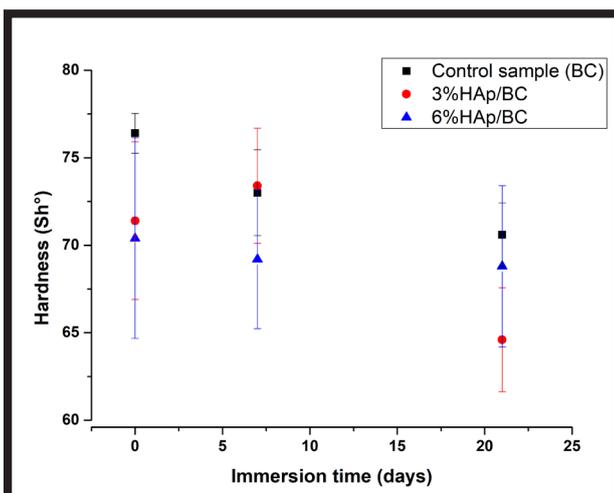

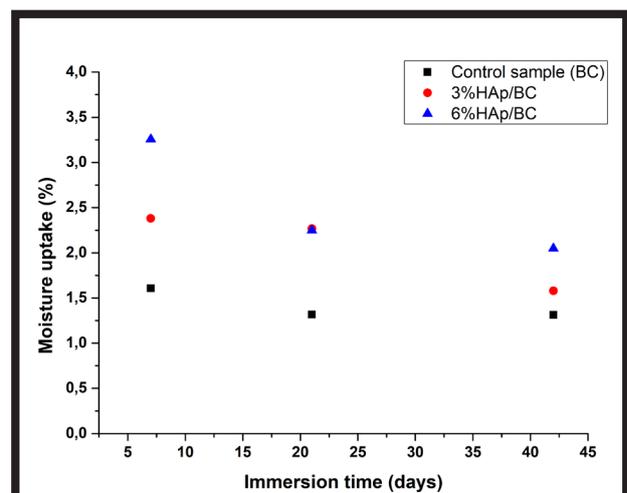**FIG. 6. Changes in hardness (Shore D scale) after immersion in PBS buffer.**

FIG. 7. Moisture uptake over different immersion time.

Conclusions

Hydroxyapatite is a ceramic filler that can be used in polymer-based bone cements. It may improve poor biological properties of those biomaterials, especially by enhancing osseointegration between the living bone and an artificial implant.

The morphology and the chemical structure of the prepared samples – the bone cements without and with hydroxyapatite have insignificantly changed over time of the PBS incubation. However, the amount of calcium increased under the liquid conditions. After the FTIR analysis, it may be concluded that there are no big differences in the position or magnitude of intensity peaks after the samples immersion, indicating that hardly any new chemical groups were formed. The chemical structure analysis revealed unexpected features of precipitated HAp. Despite the strict compliance with the procedure, additional phosphate ions were observed. The SEM images and the maps of the sample composition draw attention to another issue. The ceramic filler (HAp) is significantly less finely divided than zirconium dioxide (ZrO_2). This feature may affect the properties of the entire bone cement. However, HAp is distributed more evenly and has a smaller tendency to agglomerate than ZrO_2. Unfortunately, it is also noticeable that the most common location of HAp is in the phases boundary and the HAp adhesion to other compounds is weak.

The PMMA-based bone cements also undergo changes in mechanical properties during the incubation. The extent of these changes can be attributed to the moisture uptake, the cement composition and the immersion time. A typical change is an increase in the sample mass. Regarding the moisture absorption test, it can be estimated that the HAp addition enhances the moisture absorption, which may affect the material structure, worsen the mechanical properties and accelerate the cement degradation in the future.

Exact changes are difficult to assess due to the simultaneous occurrence of another process affecting mass – the release of residual monomer (MMA) into the solution.

The differences in hardness are not enormous but these changes are problematic in time. This factor influences the growth of adjacent bone tissue and variable mechanical properties of the material may lead to the implant loosening in the human body. Therefore, taking into account the rapidity of these changes, the sample filled with a large amount of the filler (6% HAp and 3% HAp) seem to be the best solution.

What is more, too high concentration of the HAp filler may worsen the injectability, which is a crucial factor for medical applications. Since the results of the study indicated changes in the polymerization process depending on the HAp content, the appropriate selection of components that regulate the kinetics, course and initiation of this reaction is also worth considering.

Acknowledgement

ORCID iDs

A. Laska-Leśniewicz: https://orcid.org/0000-0002-0546-0378
M. Wrotniak: https://orcid.org/0000-0002-4329-8623
A. Sobczyk-Guzenda: https://orcid.org/0000-0003-1583-4238

References

[1] A.E. Nelson: Osteoarthritis year in review 2017: clinical, Osteoarthritis and Cartilage 26 (2018) 319-325.

[2] C. Robo, C. Ohman-Magi, C. Persson: Compressive fatigue properties of commercially available standard and low-modulus acrylic bone cements intended for vertebroplasty. J. Mech. Behav. Biomed. Mater. 82 (2018) 70-76.

[3] A. Delpla, L. Tselikas, T. De Baere, S. Laurent, K. Mezaib, M. Barat, O. Nguimbous, C. Prudhomme, M. Al-Hamar, B. Moulin, F. Deschamps: Preventive Vertebroplasty for Long-Term Consolidation of Vertebral Metastases, Cardiovasc Intervent Radiol 42(12) (2019) 1726-1737.

[4] E. Hernlund, A. Svedbom, M. Ivergård et al.: Osteoporosis in the European Union: medical management, epidemiology and economic burden. Arch Osteoporos. 8(1-2) (2013) 136.

[5] A. Balin: Cementy w chirurgii kostnej, Wyd. Politechniki Śląskiej (2016) 13-23.

[6] J. Łukaszczyk: Polimerowe i kompozytowe cementy kostne oraz materiały pokrewne, cz. I. Klasyczne cementy metakrylanowe i ich modyfikacja. Polimery 49(2) (2004) 79-88.

[7] J. Łukaszczyk, M. Śmiga-Matuszowicz: Polimerowe i kompozytowe cementy kostne oraz materiały pokrewne, cz. II. Kompozycje resorbowalne i wykazujące aktywność biologiczną. Polimery 55(2) (2010) 83-92.

[8] A. Boger, K. Wheeler, B. Schenk: Clinical investigations of poly(methyl methacrylate) cement viscosity during vertebroplasty and related in vitro measurements. Eur Spine J 18 (2009) 1272-1278.

[9] M. Jayabalan, K. Shalumon, M. Mitha: Injectable biomaterials for minimally invasive orthopaedic treatments. J Mater Sci: Mater Med 20 (2009) 1379-1387.

[10] W. Jiranek, A. Hanssen, A. Greenwald: Antibiotic – loaded bone cement for infection prophylaxis in total joint replacement. J. Bone Joint Surg. Am 88 (2006) 2487-2500.

[11] J. Włodarski: Wpływ wypełniaczy na właściwości wytrzymałościowe kompozytowych cementów kostnych. Kompozyty 5 (2005) 78-82.

[12] C. Aubrun-Fillatre, F. Monchau, P. Hivart: Acrylic bone cement and starch: botanical variety impact on curing parameters and degradability. Material Science and Engineering C 69 (2016) 1328-1334.

[13] A. Sobczak, Z. Kowalski: Materiały hydroksyapatytowe stosowane w implantologii. Czasopismo Techniczne. Chemia 104 (1) (2007) 149-158.

[14] L. Morejón, J.A. Delgado, N. Davidenko, E. Mendizábal, E.H. Barbosa, C.F. Jasso: Kinetic effect of hydroxyapatite types on the polymerization of acrylic bone cements. International Journal of Polymeric Materials and Polymeric Biomaterials 52(7) (2010) 637-654.

[15] L. Morejón, A.E. Mendizábal, et al.: Static mechanical properties of hydroxyapatite (HA) powder-filled acrylic bone cements: Effect of type of HA powder. J. Biomed. Mater. Res. B Appl. Biomater. 15, 72(2) (2005) 345-352.

[16] A. Afshar, M. Ghorbani, N. Ehsani, et al.: Some important factors in the wet precipitation process of hydroxyapatite. Materials and Design 24 (2003) 197-202.

[17] W.N. Ayre, S.P. Denyer, S.L. Evans: Ageing and moisture uptake in polymethyl methacrylate (PMMA) bone cements. J. Mech. Behav. Biomed. Mater. 32 (2014) 76-88.