

Vertebroplasty and kyphoplasty – advantages and disadvantages used bone cement of PMMA

P. Choryłek

Department of Polymer Processing, Faculty of Mechanical Engineering and Computer Science, Czestochowa University of Technology, Al. Armii Krajowej 19c, 42-201 Czestochowa, Poland
Corresponding e-mail address: chorylek@itm.pcz.pl

ABSTRACT

Purpose: This paper is a review of literature where the analyses of the commonly used bone cements were carried out especially: methods of manufacturing, surgical techniques, mechanical properties, biocompatibility studies as well as possibility of improvement some properties by using additives.

Design/methodology/approach: The aim of this publication is the analysis of the state of knowledge and treatment methods on compression fractures, approximation of the specifics of compression fractures, presentation of minimally invasive percutaneous surgical techniques, description of features of the most common used bone cement on matrix Poly(methyl methacrylate) – (PMMA) and presentation cement parameters which affect potential postoperative complications.

Findings: In considering to review of actual state of knowledge there is a need to find the additives which allow: to reduce the polymerization temperature, improve the biocompatibility as well as mechanical properties. During the studies it was found that the additive which can meet the requirements is glassy carbon in form of powder.

Practical implications: Discussion allows to prepare samples during practical work with new kind additives in composite with bone cement as matrix.

Originality/value: The original in this discussion is the possibility to improve fundamental properties of the selected bone cements by using different than commonly used additives.

Keywords: Vertebroplasty, Kyphoplasty, Bone cement, PMMA, Compression fractures

Reference to this paper should be given in the following way:

P. Choryłek, Vertebroplasty and kyphoplasty – advantages and disadvantages used bone cement of PMMA, Journal of Achievements in Materials and Manufacturing Engineering 92/1-2 (2019) 36-49.

BIOMEDICAL AND DENTAL ENGINEERING AND MATERIALS

1. Introduction

Spine compression fractures are relatively frequent and characteristic type of fracture, in which the vertebrae are

collapsed and as a result the vertebral body are decreased. These fractures involve damage of vertebral body, leading to their collapse and reduction of their height (Fig. 1). They can be occurred by injuries, when spine is subjected to very

high force, with consequently is subjected to compression and damage. Compression fractures may be triggered also by others factors as osteoporosis, diseases decreasing quality of osseous tissue, such as another metabolic diseases or bone tumours. Front part of vertebral body is usually damaged and bone cancellous located inside it, it is collapsed and fragmented. Vertebral body is richly nerved and in a consequence compression fracture causes strong pain, appearing at the time of the injury. Pain usually intensifies in a standing position and walking time, while relief is brought in a lying position. Significant damaged vertebral body may cause fragmentation his back part which moving to the lumen of spinal canal, it can compress and damage nerve structure which are in its lights. In this situation apart from strong spine pain in place of fractures may occur neurological disturbances in the form of a sensory disturbances or paralysis.

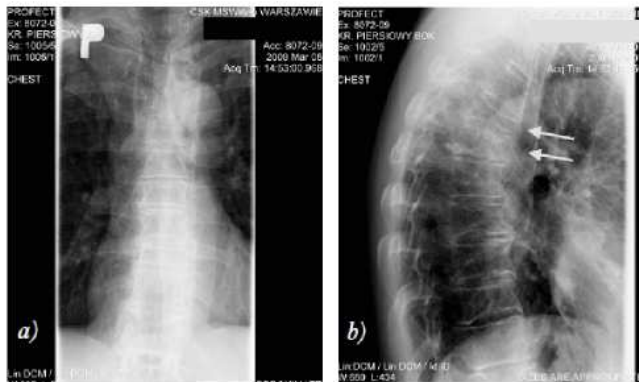


Fig. 1. X-ray of the thoracic spine. Projections AP (a) and lateral (b). Compression fractures of Th5 and Th6 shafts [1]

Osteoporosis is systemic bone disease, which is characterized by decreased bone density, what increases the risk of fractures (Fig. 2). concerning mainly people over 50 years old, with two-fold predominance of women. Increased calcium absorption from bones and disturbances cancellous bone structure, lead to focus microcracks in vertebral body and in a consequence to compression fractures. In osteoporosis compression fractures are arisen as a result of inconsiderable injury or spontaneously while performing daily activities, such as getting up from bed or sneezing. Osteoporotic compression fractures may process without specific visible symptoms, however there are usually painful symptoms within fractured bone. Fractures, in particularly concerning many vertebrae may lead to arise Thoracic Hyperkyphosis deformation. Such arise of thoracic hump in some cases may be the reason of significant decrease function on breathing circulation

system. Most of the patients are noticed that pain caused by compression fracture is decreasing as the time is passing. At around 1/3 patients suffer from compression permanent complains caused by compression fractures.

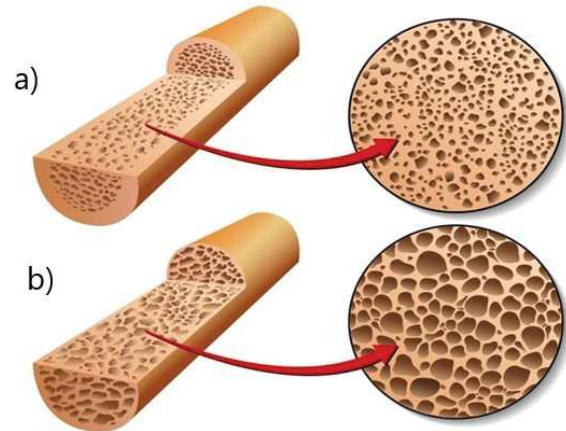


Fig. 2. Correct density of healthy bone (a) and reduced density in a result of osteoporosis (b) [2]

There are not ailments of neurological spinal cord side effects or neurological nerve root caused by compression fractures in a result of osteoporosis contrary to traumatic fractures. Compression fractures are the most often located in lower parts of thoracic spine (Th10-Th12) and within the upper parts of lumbar vertebrae (L1-L2).

The final diagnosis of fracture is based on total diagnosis conduction, involving detailed medical interview, neurological researched and necessary neuroimaging test.

According to it, the back column of spine and the ligaments apparatus is untouched, such fracture may be considered as a stable fracture. So far such fractures have been treated in a conservative treatment involving staying in bed, resting and usage pharmacological therapy, as well as orthopaedic corset. At Present beyond above mentioned techniques, compression fracture are treated by minimally invasive surgery of vertebroplasty and kyphoplasty [3-10].

Vertebroplasty and kyphoplasty as minimally invasive techniques have been adapted to compression fractures treatment of vertebral body with the usage of polymeric cements bones on matrix PMMA. Above mentioned cement used for compression stabilization of fractured vertebral body must be at justed to specific biomechanical and biological requirements. This material is deposited in the area that is load-bearing environment, it must be able to withstand cyclic and static complex loading patterns. This review focuses on discussion bone cement on matrix PMMA properties used in Vertebroplasty and kyphoplasty and explanation potential complications connected with using cement.

2. Vertebroplasty and kyphoplasty

First surgeries of percutaneous vertebroplasty were made in France by Deramond in 1984. This procedure is based on injection bone cement under pressure into vertebral body through a cannula. However, this procedure is not restored heights of fractured vertebral body. Bone cement is cured on polymerization process after injection and stabilises fractured vertebrae, increases mechanical strength, provides relief in pain and improves life comfort. Vertebroplasty procedure is minimally invasive what is particularly important in case of elderly patients with coronary diseases and it is carried out mainly of local anaesthesia. Advantage of local anaesthesia is maintaining constant contact with the patient, this allows to detect neurological complications rapidly and to react immediately. Vertebroplasty is the procedure which provides pain relief within several dozen minutes [11-14].

Kyphoplasty in contrast to vertebroplasty may restore height of fractured vertebrae through inflate balloon inside wedge decreased vertebral body, before cement injection. Kyphoplasty is used particularly in cases while occurred angular deformation of spine and advanced kyphosis appearing in a result of compression of fractures. This procedure is based on insert high-pressure into the balloon, by means which there is a possibility of moving away boundary plates in fractured vertebral body, which makes it possible partial restored height of vertebral body. In the result cavity higher viscosity bone cement is injected than in Vertebroplasty procedure and lower pressure, what decreasing the risk of cement leakage apart from vertebral body [1].

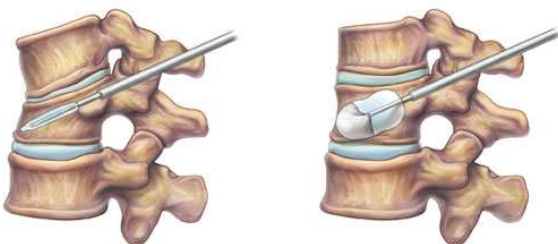


Fig. 3. Diagram showing the differences between the technique a) vertebroplasty b) kyphoplasty – expanding the balloon inside vertebral body [15]

Vertebroplasty and kyphoplasty are different primarily by surgical technique (Fig. 3). Vertebroplasty is based on injection liquid of the bone cement on matrix PMMA under pressure to collapsed space fractured vertebra, whereas kyphoplasty procedure consists of created cavity inside

vertebral body by means of balloon, and next controlled filling cavity by semi-cured bone cement (Fig. 4). Differences surgical techniques both procedures determined differ handling properties to cements [16].

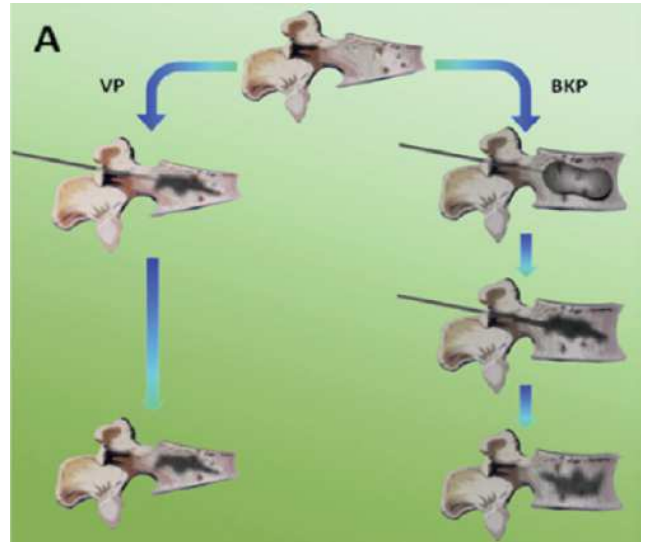


Fig. 4. Scheme present differences in vertebroplasty and kyphoplasty techniques [17]

3. Advantages and disadvantages of bone cement usage on matrix PMMA

For 50 years the most known polymeric bone cement has been cement on matrix PMMA, which has been widely used in various medical fields, mainly in orthopaedic surgery, traumatology and maxillo-facial surgery. In orthopaedics it is used for example in total joint replacement surgery, vertebroplasty, kyphoplasty and traumatic surgery. Bone cement is used for fixing and bonding implants, filling bone defects, stabilizing complex fractures [18-21].

Requirements concerning mechanical properties of bone cement depends on what functions will be performed in the body of the man. Cements which are used for filling bone defects, must have compressive strength no less than 30 MPa, this value is determined through compressive strength cancellous bones. In contrast to the bone cements used for filling defects bone, bone cements used for fixing endoprosthesis should have much higher compressive strength worth minimum 70 MPa.

Bone cements irrespective of their use must be characterized by biocompatibility, good biomechanical strength and stiffness. Bone cement cannot cause infection

in the body's environment and have to be radiopaque because a lot of surgical techniques, in particularly

vertebroplasty and kyphoplasty are based on fluoroscopy (Fig. 5) [14].

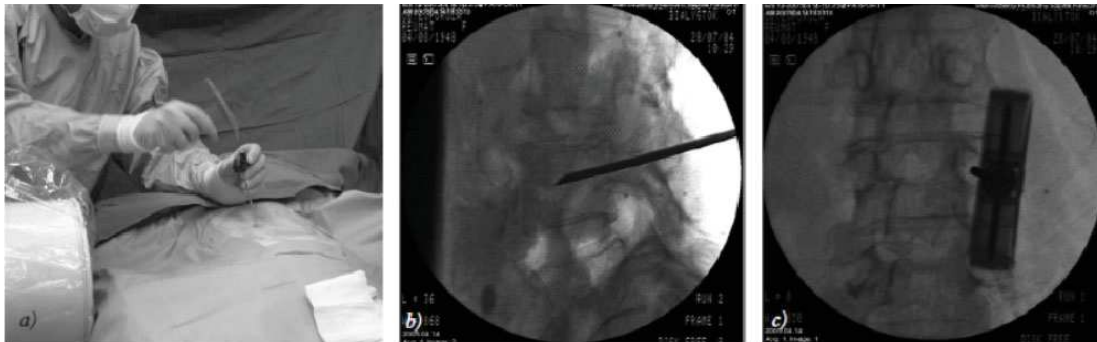


Fig. 5. Vertebroplasty: (a) insertion of the needle into the vertebral body, (b) X-ray view in the lateral projection, (c) X-ray preview in the AP projection [15]

At first in 1958 John Charley used self-curing bone cement PMMA to total hip joint replacement. Since this surgery, PMMA has been the most common used material for reduction bone defects during orthopaedic treatment [17].

Treatment using PMMA is giving fast effects and good mechanical stability within a few minutes. According to it, PMMA bone cements have been applied in minimally invasive techniques such as vertebroplasty and kyphoplasty [14]. Acrylic bone cements have a lot of advantages such as good handling properties, biointegrity, good biotolerance, appropriate biomechanical properties and strength. On the other hand this material has disadvantages, which includes:

- high polymerization temperature,
- exuding of toxic monomer,
- cement shrinkage,
- shrinkage of cement whereas polymerization process,
- porosity of polymeric materials.

Two-component system bone cement is composed of liquid component and powder component (Fig. 6). Liquid phase of acrylic bone cement contains monomer MMA and inhibitor, while powder contains copolymers MMA, activator and zirconium dioxide or barium sulphate to provide radio-opacity. Antibiotics are often added to composition of cement for example gentamicin to prevent infections. After mixing the two components, the polymerization process begins, and with its course self-cured of the cement occurs.

Polymerization is exothermic process, that causes the increase of temperature of cement during self-cured cement, what is very unfavourable from medical point of view. Polymerization temperature significantly exceeds the temperature of protein coagulation and may cause to

necrosis of surrounding tissues. Due to the rapid degree of polymerization of the cement, its viscosity increases rapidly, resulting in a short working time (about 2-5 minutes), depending on the temperature of the components, the environment and the composition. When the polymerization process is over, the cement temperature drops and cures. Polymerization process is reaction, which proceeds according the radical mechanism (Fig.7) [14,18,22,28].

Bone Cement for Spinal Applications



Fig. 6. Mainly cement components are liquid monomer MMA and powder contain copolymers, activator and radiopacity substances [23]

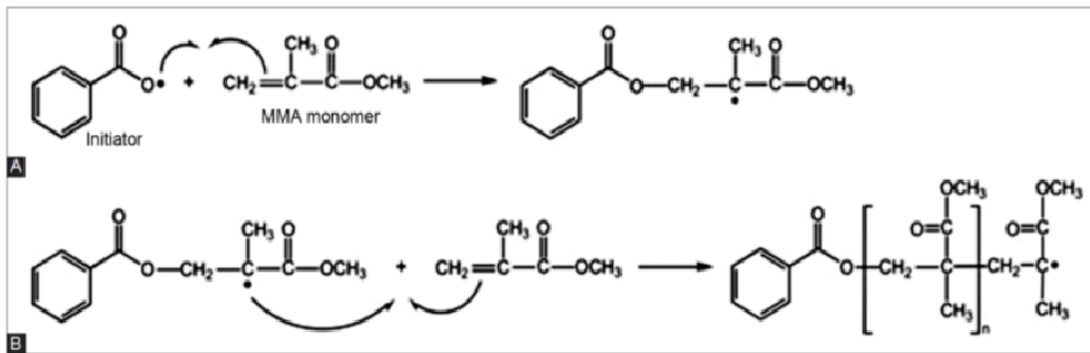


Fig. 7. Scheme polymerization reaction initiated benzoyl peroxide [14]

In order to decrease rate of polymerization process, and thus extended injection time, the cooling operation of the mixture is carried out, which concerns cooling components of mixture in the refrigerator 12-24 hours before surgery. It is noticed that the reduction of the temperature of the components has a large impact on the rate of the polymerization reaction [14]. Bone cement on matrix PMMA count of biotolerance groups of materials because in cured cement remains around 4-7% unreacted monomers, which show toxic properties. Polymer without any additives can be considered bioinert materials, stabilizers, softeners may cause that materials will show toxic properties [18,24,25].

Self-curing cement is polymerization reaction, therefore there is a volume shrinkage while self-curing process of the cement. Volume shrinkage formed during polymerization process is theoretically 6-7%, however it is smaller in reality due to air content. The present air in the mixture causes higher porosity, as a result there is a decrease mechanical properties [14]. Effective method of reducing porosity is homogenization of components mixture in reduced pressure conditions.

The various additives are also impacted on mechanical properties and connections. Cement can have Antibiotics additives as a preventive measure against infections, which can be appeared whereas surgery. The studies have shown, that mechanical properties cured PMMA can change depending on kind and amount of antibiotic. It has been reported that there are no significant effects on mechanical properties a smaller amount of antibiotics than 2 g per cement serving, whereas a bigger amount than 2 g of antibiotics it can significantly reduce them. The studies also have shown significantly reduce of mechanical properties cement mixed with aqueous solution of antibiotic compare with antibiotic additives as powder [16,26,27].

Cement used in Vertebroplasty and Kyphoplasty is enriching with radiopaque substances to improve

visualization of flow whereas injection and quick detection of possible leakage. However, increased content radiopaque substances such as barium sulphate or zirconium dioxide have unfavourable impact on mechanical strength. Barium sulphate or zirconium dioxide agglomerates may initiate fatigue cracking, and thus have a negative impact on fatigue crashing of cement. In the conducted studies, in which static and mechanical behaviour were tested bone cement with a larger content barium sulphate, it was shown, that addition 10% barium sulphate in powder per serving of cement are not significantly impact on its mechanical strength. However, focused barium sulphate particles, when increasing content to 30%, it is causing decrease in its tensile strength and fatigue strength [14,29]. The effect on mechanical properties of acrylic cement have:

- chemical composition,
- external factors for example the ambient temperature,
- types and quantities of additives,
- impurities e.g. blood and tissue debris,
- aging of the material.

4. Analysis of problems occurring after surgery

Despite the high efficacy of vertebroplasty and kyphoplasty treatments, as with any treatment may also have an adverse effect in the form of side effects and complications.

4.1. Leakage of cement

One of significant postoperative problem is cement leakage outside vertebral body. Cement may get out

through damaged or through venous plexuses to intervertebral disc (Fig. 8), paraspinal soft-tissues, episcleral veins or intervertebral holes. Cement leakage may also cause oppression of the Dural sac or nerve roots. Roots or meningitis are transient and usually resolve after pharmacological treatment and standard conservative treatment. The most serious but rare complication associated with cement leakage is leakage into the vertebral canal, which can cause spinal cord damage [10,30], pulmonary embolism [10,31-38], and cardiac embolism [39]. The most common leaking of the cement is asymptomatic [40]. Only one case of permanent root pain observed in the patient was presented in the literature [41], while spinal cord injury was reported in two cases that required rapid decompression. Unfortunately, one of them ended in permanent damage to the core [42, 43].

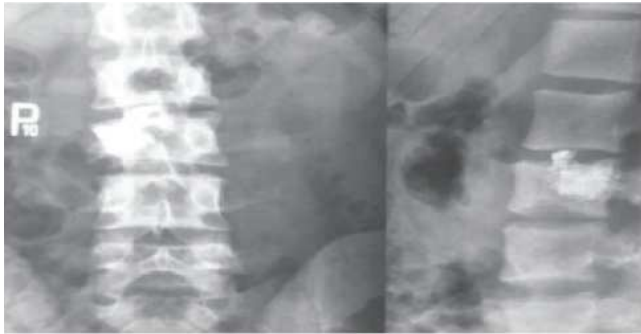


Fig. 8. Cement leakage to intervertebral space [49]

In the aim of eliminate to the threats of patient's life as a result postoperative problems, it is recommended routine X-rays of the chest after vertebroplasty surgery [43]. Factors affecting cement leakage include, among others, bone permeability, bone porosity, bone marrow viscosity and cement viscosity. The cement viscosity is a parameter that can be controlled and therefore also reduces the risk of cement leaking out of the vertebral body.

It has been shown that the use of low and medium viscosity cement increases the possibility of leakage. Effective stabilization of compression may be achieved through usage high viscosity cement, and thus minimizing risk of cement leakage and related in complications in vitro [44,45]. On the other hand use of high viscosity cement require using many more injection forces, it may lead to weaker filling of cavity with cement [46] or complications such as extravasation marrow to cardiac system. Viscosity is probably the most important parameter responsible for cement leakage outside the vertebral body [46].

4.2. Changing spine biomechanics and creating new fractures

Vertebroplasty and kyphoplasty effectively prevent the occurrence of new fractures within the operated vertebrae. In literature has been reported only one case of fracture of the treated vertebra, which, most likely resulted from applying not enough volume of bone cement to the treated vertebra [47]. Unfortunately, the increase in the frequency of vertebral fractures adjacent to vertebrae treated with cement compare to other vertebrae is worrying. Cracking of vertebrae adjacent to vertebrae after vertebroplasty and kyphoplasty procedures may result from increased pressure on other weakened vertebrae [48].

4.3. Other complications

The polymerization reaction is an exothermic reaction so the high temperature accompanying cement hardening can cause thermal damage to the nervous tissue, and it cannot be ruled out that it is the main cause of pain relief in treated patients.

There were also noticed rib fracture with patients, which resulted mainly from advanced stage of osteoporosis in patients and the position of patient during procedure [48,49].

5. Development opportunities of acrylic bone cements

Many research centres in the country and around the world conduct research to develop cement polymers with better strength properties, making attempts to introduce non-polymeric admixtures for acrylic cements such as: carbon fibres, aramid fibres, polyurethane, polyethylene, steel and glass fibres, apatite powder, ceramic glass or starch. The development of polymer composites for medical applications to obtain better biomaterials as synthetic bone substitutes is the future direction [18,50]. The main purpose of presented studies are to reduce the temperature of the polymerization process of cements and the adverse effect of excessive temperature.

5.1. Ceramic additives

For many years, ceramic materials have been used in medicine for various types of implants, such as dental implants or elements of endoprostheses in acetabular joints. Al_2O_3 oxide bioceramic, as well as pure undoped

PMMA, are bio-active materials. Given the high strength of this material in a wide temperature range, it can be assumed that the addition of oxide ceramics to polymer cement can lower the temperature of its polymerization during curing, which significantly exceeds the temperature of protein coagulation, and can reduce polymerization shrinkage without significantly affecting the mechanical properties. Polymer composites with the addition of ceramics have a much higher coefficient of thermal conductivity than undoped cement [51]. Comparing temperature coefficients for Al_2O_3 $a = 32.4 \times 10^{-3} \text{ m}^2/\text{h}$, which is much higher than PMMA for which it has a range of $a = 0.1-1.5 \times 10^{-3} \text{ m}^2/\text{h}$ and thermal conductivity coefficients λ which for ceramic are also higher than for PMMA and are respectively, for Al_2O_3 $\lambda = 29-30 \text{ W/mK}$ and for PMMA $\lambda = 0.19 \text{ W/mK}$, thanks to which ceramic molecules that do not participate in the exothermic polymerization process can lower the polymerization temperature by taking away some of the heat of the polymerization process [18,52-54].

In manuscripts [53,56-57] attempts have been made to modify bone cements with ceramic powder with two different granulations: 10-20 μm , particle size similar to the particle size of the cement powder component, and 0.3 μm granulation, which aimed to increase the boundary surface between the admixture particles and the polymer matrix, causing a higher rate of heat absorption by such molecules. In the presented research, it has been shown that admixture of ceramic powder has a positive effect on the volume shrinkage associated with the polymerization process. The linear expansion coefficient for Al_2O_3 ceramics has the range of $\alpha = 7.4-7.6 \times 10^{-6} \text{ K}^{-1}$ and is much smaller than for PMMA where $\alpha = 60 \times 10^{-6} \text{ K}^{-1}$ which reduces the volume shrinkage during the curing process of cement mass. In a study conducted by Balin it was observed that cement modified with ceramic reduced the linear shrinkage by about 30%, and this phenomenon was explained by reducing the percentage of monomer in cement mass and filling this mass with oxide ceramic particles that inhibit the cement mass shrinkage [18,54,55].

The addition of ceramic powder influenced the change of mechanical properties of the tested acrylic bone cements. There has been a slight increase in the modulus of elasticity in the conditions of bending, stretching and compression of the modified surgical cement. The research shows that cement doping with more than 2 g per 40 g portion of cement makes it difficult to form cement mass, which may adversely affect the anchoring of cement in bone pores. Changes in mechanical properties with small additions of oxide ceramics are important from the point of clinical application [18,53-55,58].

The modification method of the polymer composite and the change of the heat release conditions should not cause a deterioration of the strength properties and should not reduce the durability of cement. Another important aspect is also the amount of the additive, which should not exceed a few percent, because larger amounts may increase the cement viscosity which is unfavourable and may hinder the process of bone cement implantation. Adding hard particles to the brittle PMMA polymer matrix favourably enhances the composite and increases the modulus of elasticity [18].

5.2. Carbon additives

Thanks to the development of the technology of carbonaceous material structure modification, the use of this group of materials in implants in reconstructive surgery increases, as evidenced by the large number of research and publications related to these materials.

Starting materials to produce one of the glassy carbon grades are thermosetting resins such as furfuryl alcohol, phenol-formaldehyde resins or crosslinked polymers. Glassy carbon is an amorphous variety of carbon. Despite the fact that it does not have the structure characteristic of glassy amorphous bodies, it possesses some specific features of glassy substances, such as brittleness or the presence of closed micropores. The characteristic features of this type of carbon is the glassy fracture and the ability to conduct electricity and heat. Important features of glassy carbon from the point of view of bone cement supplement is its excellent biocompatibility. Due to its porosity, it acts as a scaffolding for bone growth [18,57]. The amorphous form of carbon has appropriate mechanical properties, which are suitable for performing the function of a synthetic bone substitute in the body, in places where compressive stresses act. Modified cement has excellent biocompatibility, whereas research on rabbits show that bone ingrowth in the pores of the glassy carbon implant in the rabbit organism occurred only after 3 weeks. An increase in bone density was also observed. Bearing in mind the specificity of glassy carbon, beneficial for the organism and for the mechanism transferring the bone-implant system load, numerous attempts are made to modify the surgical cement with glassy carbon [60,61,62].

Modification of bone cements with glassy carbon has a beneficial effect on the polymerization process temperature, reduction of volumetric shrinkage, improvement of biocompatibility and reduction of cyclic creep characteristic of cement on a polymer matrix. When comparing the thermal properties of amorphous carbon and PMMA, the formation of PMMA-glassy carbon composite increases the thermal conductivity ratio as compared to

undoped PMMA. By combining the thermal conductivity coefficients of PMMA for which $\lambda = 0.19$ W/mK, glassy carbon $\lambda = 188-220$ W/mK, which is much larger than the PMMA coefficient itself, it can be concluded that non-polymerizing glassy carbon molecules can receive part of the heat during the polymerization process. In research [63,64], the polymerization process of two BIOMET V and BIOMET Plus cements doped with glassy carbon in different mass shares was investigated. This research confirmed the beneficial effect of glassy carbon in acrylic cement on lowering the polymerization temperature having a negative impact on surrounding tissues, it was also observed that a larger mass fraction of glassy carbon reduces the polymerization temperature, shortens curing time of cement and increases its viscosity which is not favourable from the point the view of its application to bones using a pressure applicator. However, after comparing the linear thermal expansion coefficient, where for PMMA $\alpha = 60 \times 10^{-6} \text{ K}^{-1}$ and for glassy carbon is much lower and amounts to $\alpha = (1.5-3.0) \times 10^{-6} \text{ K}^{-1}$, a glassy carbon admixture added to the bone cement, a decrease in linear shrinkage by about 34% during curing of modified cement as compared to unmodified was shown [63-64].

Admixtures of glassy carbon also had an effect on the mechanical properties of cements. The research showed a lower plastic deformation capacity of doped cement compared to unmodified cement. What is more, it was observed that both modified and unmodified bone cement showed an increase in the toughness value after ageing in Ringer's solution, as well as under the influence of X-ray radiation. In [65,66] it was suggested that the increase in impact strength of samples aged in Ringer's solution was explained by the penetration of Ringer's solution with the increase in ageing time, which caused the monomer to be released and thus composite plasticity. For samples aged with X-ray radiation, the increase in impact strength was explained by the increased monomer release, which was responsible for the increase in cement plasticity. All mechanical properties of glassy carbon-modified cements met the basic requirements for surgical cements [67-71]. The research has also shown that physical modification of acrylic cement reduces the tendency to creep during cyclic loads and reduces the tendency to cement cracking [72].

5.3. Additives that improve cement bioactivity

Biocompatibility is an inherent feature of biomaterials, it means that they cannot cause negative reactions in the body. From currently applied acrylic bone cements, in addition to the mentioned biocompatibility, bioactive features are also expected. Bioactive features in relation to

cements are considered in two antimicrobial approaches and stimulation of osseointegration. Many current research is related to the improvement of cement bioactivity, this is due to the fact that every surgical procedure is associated with the risk of a bacterial infection. Modification aimed at changing the properties of bioactive bone cements has to ensure anti-infective safety during surgery, as well as during convalescence [18-21,73,74].

Bioactivity in the antimicrobial aspect

Modifications of cement composition to improve bioactivity and improve bio-functional properties cause additional complications such as too quick release of bioactive admixture into the tissue environment, destruction of modifier by polymerization reactions, leaching of bioactive additives through body fluids, resulting in low efficiency of modified cements and a short therapeutic period. Another important aspect when modifying bioactive cement additives is the change of physical and mechanical, as well as functional properties therefore it is important to carry out interdisciplinary research on the modified cement [21,75-77]. The literature has noted the use of various additives to increase bioactivity in antimicrobial capacity, among others, such as [76-81]:

- antibiotics,
- silver ions,
- silver nanoparticles,
- copper nanoparticles,
- xylitol,
- chitosan nanoparticles.

For antibiotics, the release of the additive depends on many factors, such as the type of cement, viscosity and porosity of cement, as well as the method of preparing the antibiotic, its type and amount [80-82]. Due to the continuous increase in bacterial resistance to antibiotic therapy, research is being conducted to search for new alternative modifications of biomaterials that improve antimicrobial bioactivity [80,82].

An alternative to antibiotics may be nanoparticles of metals such as silver and copper [20], and chitosan nanoparticles. Cement modified with nanometal Ag and Cu showed bactericidal activity, whereas chitosan nanoparticles prevented the survival of live bacteria on the surface of cement modified with chitosan [81,82]. On the other hand, silver nanoparticles are characterized by a broad spectrum of antimicrobial activity, low bacterial resistance. It is concluded that microorganisms are unlikely to develop resistance to silver. Nanoparticles owe bioactive properties to high activity which is coupled with their dispersed metallic phase, continuous motion and the

absence of attached anionic groups. Preliminary research presented in [81] shows that the addition of 0.5% AgNPs (Silver nanoparticles) shows an inhibition of biofilm by 83.1% for *S. Epidermidis* and 76.7% for *S. aureus*. However, compared to the biofilm inhibition tests, Kirby Baura and Time-Kill tests showed the lack of antimicrobial activity of modified cements against *S. aureus* and *S. epidermidis*. In research [81,83], it was suggested that this type of AgNPs modified cement is probably ineffective in situations where active infection is already present, e.g. in reimplantation. Cement modified with Ag nanoparticles also showed a slight reduction in the change in mechanical properties, although the modified material met the requirements for surgical cement. The addition of silver nanoparticles also resulted in a two-fold increase in cement curing time [81,83].

Bioactivity in the osseointegration aspect

Many research centres direct their research towards improving the bioactivity of cement in the aspect of osseointegration. The osseointegration process consists in penetrating the bone cell biomaterial and its proliferation into pores. This process is long-term, but it allows a permanent structural and functional connection between bone tissue and implant [79,84,85]. Polymer bone cement is a porous material, but its osseointegration with tissues is very low. Existing commercial bone cements, apart from the absence of osseointegration, cause major complications after percutaneous vertebroplasty and kyphoplasty procedures, such as fractures of adjacent vertebrae, pulmonary embolism or myocardial infarction. Due to the lack of osseointegration of acrylic bone cement caused by short bioactivity, cement cannot be combined with natural bone [76,77]. In the aspect of improving osseointegration, bone cement modifications using admixtures have been reported in the literature [79]:

- Bioactive ceramics,
- Hydroxyapatite,
- Bioglass.

In vivo research of modified cements with the above-mentioned admixtures have shown stimulation of the osseointegration process and improvement of its quality. Cements modified with bioglasses are the most promising because they generate extracellular and intracellular bone tissue responses. Modification of cements with bioglasses results in a more stable osseointegration process, and promotes the colonization of stem cells of bone tissue, as well as soft tissues and their proliferation. The modified cement shows better bioactivity [79].

Postoperative vertebrae also differ in mechanical strength. When comparing the modulus of elasticity at

normal human spinal cord compression, which is 50-800 MPa, [86-88] and the elastic modulus of compression of the cemented vertebra which is 2000-3700 MPa [89,90], it can be concluded that the main cause of fractures of neighbouring vertebrae is pressure on neighbouring vertebrae through increased stiffness of cemented vertebrae [91-94]. The decreased modulus of elasticity under compression and the improvement of bioactivity are shown in the studies [93,94]. In the literature, attempts have been made to modify bone cement with mineralized collagen. It has been observed that the addition of the MC additive, which shows good osseogenic activity to commercial surgical cements, significantly improves its mechanical properties as well as cytocompatibility. Chinese researchers, Cui and Qui [93-97], conducted in vitro animal tests, which also confirmed the improvement of the modulus of elasticity and osseointegration of the modified MC bone cement. It was observed that new tissues gradually grew into the porous structure of cement after the absorption of collagen by the bones. Modified cements showed better pre-osteoblast proliferation and adhesion compared to unmodified cements, which increases the ability to bone cement integration in vertebrae and can effectively protect against cement being torn from damaged vertebrae. The decrease in compression of the modulus of elasticity and the stiffness of the cemented vertebrae results in less pressure of the treated vertebrae on the adjoining vertebrae, and at the same time reduces the risk of secondary fracture of the neighbouring vertebrae. MC modification did not have a significant impact on the change of handling properties and the time of cement curing.

6. Conclusions

Transdermal surgical techniques are widely used to treat compression spinal fractures caused by various pathologies such as primary and secondary osteoporosis, hemangioma or multiple myeloma. Vertebroplasty and kyphoplasty treatments are minimally invasive and at the same time very effective methods to treat vertebral compression fracture. Both treatments effectively reduce pain, although this mechanism is not fully explained. Bone cement on the PMMA matrix is currently the most frequently used filling material due to its advantages. It should also be remembered that current cements available on the market are not ideal materials and have several significant disadvantages. The treated vertebral body filled with cement is much stiffer than untreated vertebrae and does not undergo elastic deformations which may lead to fractures of neighbouring vertebrae, whereas high

polymerization temperature may lead to necrosis of surrounding tissues. Modification of cement to improve its functional properties as a filler of spinal compression fractures is the key to improving the patient's health. Certain cement properties, such as the polymerization rate and the cement curing time, can be modified by lowering the operating temperature or earlier cooling of mixture components. An ideal modified bone cement should be characterized not only by good handling properties, injectability and adequate mechanical strength but it should also have better biocompatibility, lower polymerization temperature that does not cause tissue necrosis, and reduced modulus of elasticity which after curing would favourably influence stress distribution and prevention of fractures of neighbouring vertebrae treated segments. Modifications should also include the ability to integrate cement with autogenous bone tissues of treated patients. Modification of cements with various admixtures such as oxide ceramics, glassy carbon, mineral collagen or nanoparticles of Ag and Cu metals may improve defects of currently used commercial cements.

Vertebroplasty and kyphoplasty can improve the quality of life of patients and physical activity through mechanical stabilization of fractures and thermal necrosis of nerve endings, thus leading to almost immediate and significant pain reduction.

The need for reconstruction as part of bone surgery continues to grow as the population ages, so there is an increase in demand for synthetic orthopaedic materials. This demand results from the fact that in many cases it is not possible to perform autotransplantation, due to the lack of this material or the danger of transmission of infection. Synthetic materials based on composite structures allow for better imitation of organic structures through continuous improvement. Therefore, there is a clear demand of the market for this type of materials and the need for further development of these materials and for studies on the behaviour of various materials and their modifications in the long-term use.

Physical and chemical modification of commercial cements used in medicine is a very widely used direction of currently conducted research works. Addition of cements with various additives significantly influences the change of their mechanical and rheological properties. Understanding these dependencies will help to use them safely and consciously in different types of injuries of patients at different ages.

Based on the information in the article, attempts will be made to dope commercial bone cements with glassy carbon and mineralized collagen (1-3%) and compared to currently used commercial surgical cements.

References

- [1] M. Zawadzki, J. Walecki, K. Kordecki, I. Nasser, *Interventional radiology: vertebroplasty and kyphoplasty*, *Acta Bio-Optica et Informatica Medica* 15/1 (2009) 70-72 (in Polish).
- [2] Website: <https://polki.pl/zdrowie/choroby,jak-uniknac-osteoporozy,10402497>, Access in: 14.12.2018.
- [3] E. Czerwiński, B. Frańczuk, P. Borowy, *Problems of osteoporotic fractures*, *Medicine after Diplom* 13 (2004) 42-49 (in Polish).
- [4] E. Czerwiński, P. Działak, *Evaluation of osteoporosis and fracture risk*, *Orthopedics, Traumatology, Rehabilitation* 2 (2002) 127-134 (in Polish).
- [5] J.A. Kanis, O. Johnellm, A. Oden, A. Dawson, C. De Laet, B. Jonsson, *Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds*, *Osteoporosis International* 12 (2001) 989-995.
- [6] N.B. Watts, S.T. Harris, H.K. Genant, *Treatment of painful osteoporotic vertebral fractures with percutaneous vertebroplasty or kyphoplasty*, *Osteoporosis International* 12 (2001) 429-437.
- [7] A.A. Ismail, T.W. O'Neill, C. Cooper, J.D. Finn, A.K. Bhalla, J.B. Cannata P. Delmas, J.A. Falch, B. Felsch, K. Hoszowski, O. Johnell, J.B. Diaz-Lopez, A. Lopez Vaz, F. Marchand, H. Raspe, D.M. Reid, C. Todd, K. Weber, A. Woolf, J. Reeve, A.J. Silman, *Mortality associated with vertebral deformity in men and women: results from European Prospective study (EPOS)*, *Osteoporosis International* 8 (1998) 291-297.
- [8] P.J. Meunier, *Osteoporosis: diagnosis and management*, Martin Duniz, 1998.
- [9] Z. Kotwica, A. Saracen, *Vertebroplasty*, *West Pomeranian Specialist Hospital „MEDICAM”*, Gryfice, 2009, 31-59 (in Polish).
- [10] N. Przybyłko, D. Kocur, R. Sordyl, W. Ślusarczyk, A. Antonowicz-Olewicz, W. Kukier, M. Wojtacha, K. Suszyński, S. Kwiek, *Vertebroplasty in vertebral compression fractures - literature review*, *Academiae Medicae Silesiensis*, 68/5 (2014) 375-379 (in Polish).
- [11] N. McArthur, C. Kasperk, M. Baier, M. Tanner, B. Gritzbach, O. Schoierer, W. Rothfischer, G. Krohmer, J. Hillmeier, H.-J. Kock, P.-J. Meeder, F.X. Huber, *1150 kyphoplasties over 7 years: Indications, techniques, and intraoperative complications*, *Orthopedics* 32 (2009) 90.
- [12] S. Masala, R. Mastrangeli, M.C. Petrella, F. Massari, A. Ursone, G. Simonetti, *Percutaneous vertebroplasty in 1,253 levels: Results and long-term effectiveness in a single centre*, *European Radiology* 19 (2009) 165-171.

- [13] M. Weisskopf, M. Weikopf, J.A. Ohnsorge, F.U. Niethard, Intravertebral pressure during vertebroplasty and balloon kyphoplasty: An in vitro study, *Spine* 33 (2008) 178-82.
- [14] P.-L. Lai, L.-H. Chen, W.-J. Chen, I.-M. Chu, Chemical and Physical Properties of Bone Cement for Vertebroplasty, *Biomedical Journal* 36 (2013) 162-167.
- [15] Website: http://allspine.com/eng/treatment/treatment_01_09.html, Access in: 09.04.2019.
- [16] I.H. Lieberman, D. Togawa, M.M. Kayanja, Vertebroplasty and kyphoplasty: Filler materials, *Spine Journal* 5/6 (2005) 305-16S.
- [17] Z. He, Q. Zhai, M. Hu, C. Cao, J. Wang, H. Yang, B. Li, Bone Cements for percutaneous vertebroplasty and balloon kyphoplasty: Current status and future developments, *Journal of Orthopedic Translation* 3 (2015) 1-11.
- [18] A. Balin, *Cements in bone surgery*, Publisher of the Silesian University of Technology, Gliwice, 2016 (in Polish).
- [19] I. Koh, A. López, A.B. Pinar, B. Helgason, S.J. Ferguson, The effect of water on the mechanical properties of soluble and insoluble ceramic cements, *Journal of the Mechanical Behavior of Biomedical Materials* 51 (2015) 50-60.
- [20] J. Slane, J. Vivanco, J. Meyer, L.H. Ploeg, M. Squire, Modification of acrylic bone cement with mesoporous silica nanoparticles; Effect on mechanical, fatigue and absorption properties, *Journal of the Mechanical Behavior of Biomedical Materials* 29 (2014) 451-461.
- [21] M. Wekwejt, B. Świeczko-Żurek, The bioactivity of modified bone cement: literature review, *Engineer and Medical Physicist* 6/4 (2017) 261-268 (in Polish).
- [22] A. Kozłowska, Research on the polymerization conditions of acrylic mass as implants, *Polymers in Medicine* 7/3 (1997) 137-177 (in Polish).
- [23] Website: https://www.osartis.de/media/bonosinject_e_0718_osartis_final_1.pdf, Access in: 09.04.2019.
- [24] A. Balin, Material-conditioned adaptation and durability of cements used in bone surgery, *Science Notebooks of Silesian University of Technology: Metallurgy* 1610/69 (2004) (in Polish).
- [25] J. Marciniak, *Biomaterials*, Publisher of the Silesian University of Technology, Gliwice, 2013 (in Polish).
- [26] E.P. Lautenschlager, J.J. Jacobs, G.W. Marshall, P.R. Meyer Jr., Mechanical properties of bone cements containing large doses of antibiotic powders, *Journal of Biomedical Materials Research* 10 (1976) 929-938.
- [27] E.P. Lautenschlager, G.W. Marshall, K.E. Marks, J. Schwartz, C.L. Nelson, Mechanical strength of acrylic bone cements impregnated with antibiotics, *Journal of Biomedical Materials Research* 10 (1976) 837-845.
- [28] K.D. Kuehn, W. Ege, U. Gopp, Acrylic bone cements: Composition and properties, *Orthopedic Clinics of North America* 36 (2005) 17-28.
- [29] D.J. Theodorou, S.J. Theodorou, T.D. Duncan, S.R. Garfin, W.H. Wong, Percutaneous balloon kyphoplasty for the correction of spinal deformity in painful vertebral body compression fractures, *Clinical Imaging* 26 (2002) 1-5.
- [30] Y.J. Chen, T.S. Tan, W.H. Chen, C.C. Chen, T.S. Lee, Intradural cement leakage: a devastatingly rare complication of vertebroplasty, *Spine* 31 (2006) 379-382.
- [31] D.H. Choe, E.M. Marom, K. Ahrar, M.T. Truong, J.E. Madewell, Pulmonary embolism of polymethyl methacrylate during percutaneous vertebroplasty and kyphoplasty, *American Journal of Roentgenology* 183 (2004) 1097-1102.
- [32] K.Y. Yoo, S.W. Jeong, W. Yoon, J. Lee, Acute respiratory distress syndrome associated with pulmonary cement embolism following percutaneous vertebroplasty with polymethylmethacrylate, *Spine* 29 (2004) 294-297.
- [33] K. Francois, Y. Taeymans, B. Poffyn, G. Van Nooten, Successful management of a large pulmonary cement embolus after percutaneous vertebroplasty: a case report, *Spine* 28 (2003) 424-425.
- [34] J.S. Jang, S.H. Lee, S.K. Jung, Pulmonary embolism of polymethylmethacrylate after percutaneous vertebroplasty: a report of three cases, *Spine* 27 (2002) 416-418.
- [35] B. Padovani, O. Kasriel, P. Brunner, P. Peretti-Viton, Pulmonary embolism caused by acrylic cement: a rare complication of percutaneous vertebroplasty, *American Journal of Neuroradiology* 20 (1999) 375-377.
- [36] M. Freitag, A. Gottschalk, M. Schuster, W. Wenk, L. Wiesner, T.G. Standl, Pulmonary embolism caused by polymethylmethacrylate during percutaneous vertebroplasty in orthopaedic surgery, *Acta Anaesthesiologica Scandinavica* 50 (2006) 248-251.
- [37] J.N. MacTaggart, I.I. Pipinos, J.M. Johanning, T.G. Lynch, Acrylic cement pulmonary embolus masquerading as an embolized central venous catheter fragment, *Journal of Vascular Surgery* 43 (2006) 180-183.
- [38] G. Baroud, M. Crookshank, M. Bohner, High-viscosity cement significantly enhances uniformity of cement filling in vertebroplasty: an experimental

- model and study on cement leakage, *Spine* 31 (2006) 2562-2568.
- [39] P. Shridhar, Y.F. Chen, R. Khalil, A. Plakseychuk, S.K. Cho, B. Tillman, P.N. Kumt, Y.J. Chun, A review of PMMA bone cement and intra-cardiac embolism, *Materials* 9 (2016) 821.
- [40] K.D. Harrington, Major neurological complications following percutaneous vertebroplasty with polymethylmethacrylate. A case report, *Journal of Bone and Joint Surgery* 83 (2001) 1070-1073.
- [41] C. Cyteval, M.P. Sarrabere, J.O. Roux, E. Thomas, C. Jorgensen, F. Blotman, J. Sany, P. Taourel, Acute osteoporotic vertebral collapse: open study on percutaneous injection of acrylic surgical cement in 20 patients, *American Journal of Roentgenology* 173/6 (1999) 1685-1690.
- [42] M. Wenger, T.M. Markwalder, Surgically controlled, transpedicular methyl methacrylate vertebroplasty with fluoroscopic guidance, *Acta Neurochirurgica (Wien)* 141 (1999) 625-631.
- [43] J.S. Jang, S.H. Lee, S.K. Jung, Pulmonary embolism of polymethylmethacrylate after percutaneous vertebroplasty: a report of three cases, *Spine* 27/19 (2002) 416-418.
- [44] G. Baroud, R. Falk, M. Crookshank, S. Sponagel, T. Steffen, Experimental and theoretical investigation of directional permeability of human vertebral cancellous bone for cement infiltration, *Journal of Biomechanics* 37 (2004) 189-196.
- [45] B. Meng, M. Qian, S.X. Xia, H.L. Yang, Z.P. Luo, Biomechanical characteristics of cement/gelatin mixture for prevention of cement leakage in vertebral augmentation, *European Spine Journal* 22 (2013) 2249-2255.
- [46] S. Aghyarian, L.C. Rodriguez, J. Chari, E. Bentley, V. Kosmopoulos, I.H. Lieberman, D.C. Rodrigues, Characterization of a new composite PMMA-HA/Brushite bone cement for spinal augmentation, *Journal of Biomaterials Application* 29 (2014) 688-698.
- [47] P.F. Heini, B. Walchli, U. Berlemann, Percutaneous transpedicular vertebroplasty with PMMA: operative technique and early results. A prospective study for the treatment of osteoporotic compression fractures, *European Spine Journal* 9 (2000) 445-450.
- [48] J. Osieleniec, E. Czerwiński, S. Zemankiewicz, Vertebroplasty and kyphoplasty in the treatment of osteoporotic vertebral fractures: expectations and fears, *Advances in Osteoarthrology* 14/2 (2003) 1-8 (in Polish).
- [49] T. Wądek, A. Nobis, M. Paściak, Complications of percutaneous vertebroplasty, *Journal of Spine Surgery* 1/21 (2011) 59-64 (in Polish).
- [50] K.A. Mann, D.L. Bartel, T.M. Wright, A.H. Burstein, Coulomb frictional interfaces in modeling cemented total hip replacement: a more realistic model, *Journal of Biomechanics* 28 (1995) 1067-1078.
- [51] R. Mala, A.S. Ruby Celsia, Bioceramics in orthopaedics: A review, in: S. Thomas, P. Balakrishnan, M.S. Sreekala (Eds.), *Fundamental Biomaterials: Ceramics*, Woodhead Publishing, 2018, 195-221.
- [52] A. Balin, M. Sozańska, J. Toborek, Z. Gajda, Application of scanning microscopy and X-ray microanalysis for description of the admixture surgical cements fracture, *Journal of Medical Informatics & Technologies* 2/2 (2001) 75-83.
- [53] A. Balin, J. Myalski, G. Pucka, J. Toborek, Influence of admixtures of ceramic material on the physicochemical properties of surgical cement, *Polimers* 51/11-12 (2006) 852-858 (in Polish).
- [54] J. Okrajni, A. Balin, Estimation of the ceramic admixture influence on the polymerization temperature of surgical cement, *Proceedings of the VII International Conference „Medical Informatics and Technologies”*, *Journal of Medical Informatics and Technologies* 6 (2003) 127-135.
- [55] K.E. Oczóś, *Shaping ceramic technical materials*, Rzeszow University of Tehchnology Publishing House, Rzeszów, 1996 (in Polish).
- [56] A. Balin, Mechanisms of cracking and durability of new biomaterials used as fillers in bone hip surgery, Report on the research project KBN No. 7 T08E 029 16, 1999-2000 (in Polish).
- [57] A. Balin, J. Toborek, J. Myalski, Physical properties of surgical cement modified with ceramic, *Acta Bioengineering and Biomechanics* 1/1 (1999) 51-54 (in Polish).
- [58] A. Sudo, M. Hasegawa, A. Fukuda, A.J. Uchida, Treatment of Infected Hip Arthroplasty With Antibiotic-Impregnated Calcium Hydroxyapatite, *The Journal of Arthroplasty* 23/1 (2008) 145-150.
- [59] E. Fitzer, From polymers to polymeric carbon – a way to synthesize a large variety of new materials, *Pure and Applied Chemistry* 52/7 (1980) 1865-1882.
- [60] V.T. Tarvainen, H. Pätäälä, T. Tunturi, I. Paronen, K. Lauslahti, P. Rokkanen. Bone growth into porous glassy carbon implants, *Acta Orthopaedica Scandinavica* 56 (1985) 63-66.
- [61] V.T. Tarvainen, T.O. Tunturi, I. Paronen, K.R. Lauslahti, E.T. Lehtinen, P.U. Rokkanen, J.

- Rautavuori, P. Törmälä, H.V. Päätiälä, Glassy carbon implant as a bone graft substitute: an experimental study on rabbits, *Clinical Materials* 17/2 (1994) 93-98.
- [62] K.L. Elias, R.L. Price, T.J. Webster, Enhanced functions of osteoblasts on nanometre diameter carbon fibers, *Biomaterials* 23/15 (2002) 3279-3287.
- [63] A. Balin, Research on increasing the durability of composite biomaterials for orthopedics, Research Project No. N N518 383837, 2009-2012 (in Polish).
- [64] E. Kolczyk, Durability of polymer cement for use in orthopedics, PhD Thesis, Silesian University of Technology, Katowice, 2010 (in Polish).
- [65] P. Colombi, Fatigue analysis of cemented hip prosthesis: model definition and damage evolution algorithms, *International Journal Fatigue* 24 (2002) 895-901.
- [66] S.R. Tatro, G.R. Baker, K. Bisht, J.P. Harmon, A MALDI, TGA, TG/MS, and DEA study of the irradiation effects on PMMA, *Polymer* 44 (2003) 167-176.
- [67] A. Balin, Preliminary results of surgical cement modification with glassy carbon, *Physiotherapy* 2/16 (2008) 63-69.
- [68] A. Balin, The effect of a glassy carbon additive to surgical cement on its durability and adaptation in the organism, *Engineering of Biomaterials* 18/131 (2015) 12-31 (in Polish).
- [69] A. John, A. Balin, The influence of bone cement modified with glassy carbon on effort state of pelvic joint after reconstruction, Proceedings of the 16th International Conference „Mechanics”, Kaunas, 2011, 143-148.
- [70] A. Balin, G. Junak, Investigation of cyclic creep of surgical cements, *Archives of Materials Science and Engineering* 28/5 (2007) 281-284.
- [71] A. Balin, G. Junak, Low-cycle fatigue of surgical cements, *Journal of Achievements in Materials and Manufacturing Engineering* 20/1-2 (2007) 211-214.
- [72] E. Kolczyk, A. Balin, Application of the rheological model for the assessment of the influence of glassy carbon admixture on the cyclic creep of surgical cement, *Current Problems of Biomechanics – Scientific Papers of the Department of Applied Mechanics* 3 (2009) 99-104.
- [73] M. Wekwejt, B. Świczko-Żurek, M. Szkodo, Requirements, modifications and test methods of bone cement - literature review, *European Journal of Medical Technologies* 16/3 (2017) 1-10.
- [74] I. Koh, Y. Gombert, C. Persson, H. Engqvist, B. Helgason, S.J. Ferguson, Ceramic cement as a potential stand-alone treatment for bone fractures: an in vitro study of ceramic–bone composites, *Journal of the Mechanical Behavior of Biomedical Materials* 61 (2016) 519-529.
- [75] J. Martínez-Moreno, C. Mura, V. Merino, A. Nácher, M. Climente, M. Merino-Sanjuán, Study of the Influence of Bone Cement Type and Mixing Method on the Bioactivity and the Elution Kinetics of Ciprofloxacin, *Journal of Arthroplasty* 30/7 (2015) 1243-1249.
- [76] G. Massazza, A. Bistolfi, E. Verné, M. Miola, L. Ravera, F. Rosso, Antibiotics and cements for the prevention of biofilm-associated infections, in: *Biomaterials and Medical Device - Associated Infections*, Woodhead Publishing Limited, 2015, 185-197.
- [77] A.C. Matos, L.M. Gonçalves, P. Rijo, M.A. Vaz, A.J. Almeida, A.F. Bettencourt, A novel modified acrylic bone cement matrix. A step forward on antibiotic delivery against multiresistant bacteria responsible for prosthetic joint infections, *Materials Science and Engineering C* 38 (2014) 218-226.
- [78] P. Prokopovich, R. Leech, C.J. Carmalt, I.P. Parkin, S. Perni, A novel bone cement impregnated with silver-tiopronin nanoparticles: its antimicrobial, cytotoxic, and mechanical properties, *International Journal of Nanomedicine* 8 (2013) 2227-2237.
- [79] M. Miola, M. Bruno, G. Maina, G. Fucale, G. Lucchetta, E. Vernè, Antibiotic-free composite Bone cements with antibacterial and bioactive properties. A preliminary study, *Materials Science and Engineering C* 43 (2014) 65-75.
- [80] E. Paz, P. Sanz-Ruiz, J. Abenojar, J. Vaquero-Martin, F. Forroiol, J.C. Del Real, Evaluation of elution and mechanical properties of high-dose antibiotic-loaded bone cement: comparative ‘in vitro’ study of the influence of vancomycin and cefazolin, *Journal of Arthroplasty* 30/8 (2015) 1423-1429.
- [81] J. Slane, J. Vivanco, W. Rose, H.L. Ploeg, M. Squire, Mechanical, material, and antimicrobial properties of acrylic bone cement impregnated with silver nanoparticles, *Materials Science and Engineering C* 48 (2015) 188-196.
- [82] S.C. Shen, W.K. Ng, Y.C. Dong, J. Ng, R.B.H. Tan, Nanostructured material formulated acrylic bone cements with enhanced drug release, *Materials Science and Engineering C* 58 (2016) 233-241.
- [83] B. Świczko-Żurek, The influence of biological environment on the appearance of silver coated implants, *Advances in Materials Science and Engineering* 12/2 (2012) 245-250.

- [84] H. Tan, S. Guo, S. Yang, X. Xu, T. Tang, Physical characterization and osteogenic activity of the quaternized chitosan-loaded PMMA bone cement, *Acta Biomaterialia* 8/6 (2012) 2166-2174.
- [85] R. Ormsby, T. McNally, P. O'Hare, G. Burke, C. Mitchell, N. Dunne, Fatigue and biocompatibility properties of a poly(methyl methacrylate) bone cement with multi-walled carbon nanotubes, *Acta Biomaterialia* 8 (2012) 1201-1212.
- [86] X. Banse, T.J. Sims, A.J. Bailey, Mechanical properties of adult vertebral cancellous bone: Correlation with collagen intermolecular cross-links, *Journal of Bone and Mineral Research* 17 (2002) 1621-1628.
- [87] F.J. Hou, S.M. Lang, S.J. Hoshaw, D.A. Reimann, D.P. Fyhrrie, Human vertebral body apparent and hard tissue stiffness, *Journal of Biomechanics* 31 (1998) 1009-1015.
- [88] E.F. Morgan, H.H. Bayraktar, T.M. Keaveny, Trabecular bone modulus-density relationships depend on anatomic site, *Journal of Biomechanics* 36 (2003) 897-904.
- [89] S.M. Kurtz, M.L. Villarraga, K. Zhao, A.A. Edidin, Static and fatigue mechanical behavior of bone cement with elevated barium sulfate content for treatment of vertebral compression fractures, *Biomaterials* 26 (2005) 3699-3712.
- [90] L.E. Jasper, H. Deramond, J.M. Mathis, S.M. Belkoff, Material properties of various cements for use with vertebroplasty, *Journal of Materials Science: Materials in Medicine* 13 (2002) 1-5.
- [91] F. Grados, C. Depriester, G. Cayrolle, N. Hardy, H. Deramond, P. Fardellone, Long-term observations of vertebral osteoporotic fractures treated by percutaneous vertebroplasty, *Rheumatology* 39 (2000) 1410-1414.
- [92] A.T. Trout, D.F. Kallmes, K.F. Layton, K.R. Thielen, J.G. Hentz, Vertebral endplate fractures: An indicator of the abnormal forces generated in the spine after vertebroplasty, *Journal of Bone and Mineral Research* 21 (2006) 1797-1802.
- [93] H.J. Jiang, J. Xu, Z.Y. Qiu, X.L. Ma, Z.Q. Zhang, X.X. Tan, Y. Cui, F.Z. Cui, Mechanical properties and cytocompatibility improvement of vertebroplasty PMMA bone cements by incorporating mineralized collagen, *Materials* 8 (2015) 2616-2634.
- [94] M. Bai, H. Yin, J. Zhao, Y. Li, Y. Yang, Y. Wu, Application of pmma bone cement composited with bone-mineralized collagen in percutaneous kyphoplasty, *Regenerative Biomaterials* 4 (2017) 251-255.
- [95] Z.Y. Qiu, I.S. Noh, S.M. Zhang, Silicate-doped hydroxyapatite and its promotive effect on bone mineralization, *Frontiers of Materials Science* 7 (2013) 40-50.
- [96] T. Li, X. Weng, Y. Bian, L. Zhou, F. Cui, Z. Qiu, Influence of Nano-HA coated bone collagen to acrylic (Polymethylmethacrylate) bone cement on mechanical properties and bioactivity, *PLoS One* 10 (2015) 012-018.
- [97] J. Wu, S. Xu, Z. Qiu, P. Liu, H. Liu, X. Yu, F.-Z. Cui, Z. R. Chunhua, Comparison of human mesenchymal stem cells proliferation and differentiation on poly(methyl methacrylate) bone cements with and without mineralized collagen incorporation, *Journal of Biomaterials Applications* 30 (2016) 722-731.