Advanced Structured Materials

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Biomaterials and Medical Devices

A Perspective from an Emerging Country

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Biomaterials in Orthopaedics

Ferdiansyah Mahyudin, Lukas Widhiyanto and Hendra Hermawan

Abstract In general knowledge, orthopaedic surgery treats the disease and injuries of musculoskeletal system including bone fractures, anomalies, degenerative disease, tumor, and infection. Significant difference in orthopaedic cases occurs between developed and developing countries. In the latter, the majority of cases are caused by injury and infection. Most surgical treatment needs the use of implants for both traumatic and reconstructive procedures. Orthopedic implants can be selected from metals, polymers and ceramics or their combination. in Indonesia, certain type of orthopaedic implants have been produced locally but still cannot fulfill the high demand. The current technology used by local manufacturers has some limitations in production capacity and product variety mainly for complex implants like arthroplasty. Collaboration in R&D activities on orthopaedic implants is on-going between local manufacturers with universities and government institutions under the assistance of orthopaedic surgeons. This collaboration receives a full support from the Indonesian Government as it aligns with the national programme on supporting local products and the new general health insurance programme which covers every citizen of Indonesia.

Keywords Biomaterials · Bone implant · Injury · Manufacture · Orthopaedic · Surgery

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1 Introduction

Orthopaedic is a branch of medical science that concerns with promotion, prevention, investigation, and treatment of disease and injury of musculoskeletal system by medication, physical therapy and surgery. Scope of orthopaedic field includes congenital anomaly, degenerative disease, tumor, injury, arthritis and inflammation, infection, muscle weakness and sensory disturbance (Salter 1999). There are significant differences in orthopaedic cases between developed countries and developing countries. In developed countries, the majority of orthopaedic cases are caused by degenerative diseases such as osteoarthritis and canal stenosis of spine. On the other hand, in developing countries, most cases are caused by trauma and infection. Orthopaedic surgeon is a profession that frequently applies implants in their practice. Orthopedic implants consist of traumatic implants, which can be used as internal fixation in trauma cases, and also reconstructive implants, that can be used to replace damaged bone and joint structure thus recovering the function as well. The material used for orthopedic implants can be selected from various options such as metals, polymers and ceramics or the combination of two or more.

2 The Most Common Orthopaedic Problems in Indonesia

Currently, the life expectancy in Indonesia has increased. Indonesia is one of the countries in the world that has rapid industrial and economic growth, as well as increasing growth in education level. Those changes bring a shift to the pattern of diseases in Indonesian. Nowadays, trauma and infectious diseases are still the dominant cases in the field of orthopedics. Trauma cases are closely related to traffic accidents and occupational hazard, for example in construction work. While, the infection cases are closely related with the level of environmental health, level of welfare and also the level of public education.

In line with the growth of economic and the society welfare, the degenerative disease that closely links with aging, the metabolic diseases which are influenced by changes in lifestyle and diet, and cancer are growing and start to become major diseases in the developing countries including Indonesia. Cause of death has also changed. Death caused by heart attacks and cancer have equaled and even exceeded deaths due to infection.

Looking at the tendencies described above, in the not too distant future the pattern of diseases in Indonesia would resemble the case in developed countries, where cases of infection and trauma will be decreased and replaced by degenerative, metabolic and cancer diseases. The incidence of orthopaedic cases in Indonesia is high and mostly due to traffic accidents. Most of Indonesian people use private vehicle, especially motorcycles (Fig. 1). Mass transport is still not provided very well therefore cheap and high flexibility vehicle is the best choice. The number of motorcycles has grown very fast in 10 years and becomes the highest cause of traffic accidents in Indonesia.

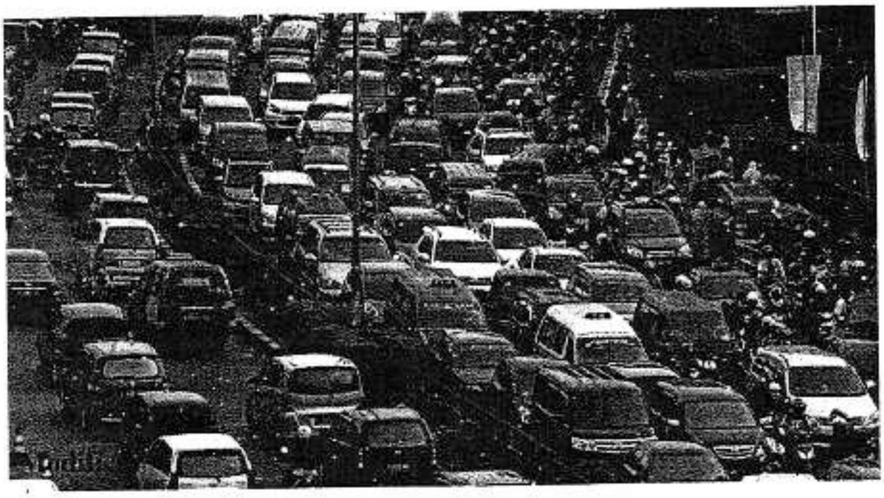

Fig. 1 Typical traffic condition in Indonesian main cities during rush hours, where motorcycles slipping around cars risking their own safety (Photo credit: Letter view.com)

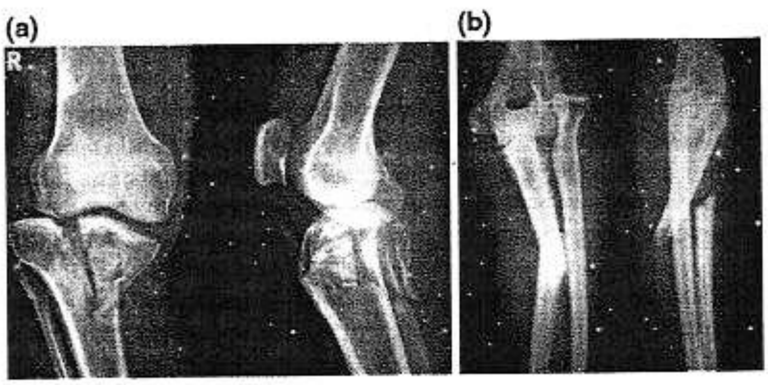

Fig. 2 Examples of frequent fracture cases due to traffic accidents: a lower leg fracture; b forearm fracture (Courtesy of Dr. Soetomo General Hospital, Surabaya)

Accidents are counted for the third death cause in Indonesia that lead to bone fractures and disability. Fractures happen more commonly to men compared to women under the age of 45 years old. They are often associated with sports, work, or injuries caused by motor vehicles. While in elderly, women are more often than men to experience fractures which associate with increasing incidence of osteoporosis due to hormonal changes at menopause. According to data recorded at the Department of Orthopaedic and Traumatology, Airlangga University—Dr. Soetomo General Hospital, Surabaya, from October 2009 to October 2012 there were as many as 7,134 patients admitted to the emergency room because of fractures (Fig. 2).

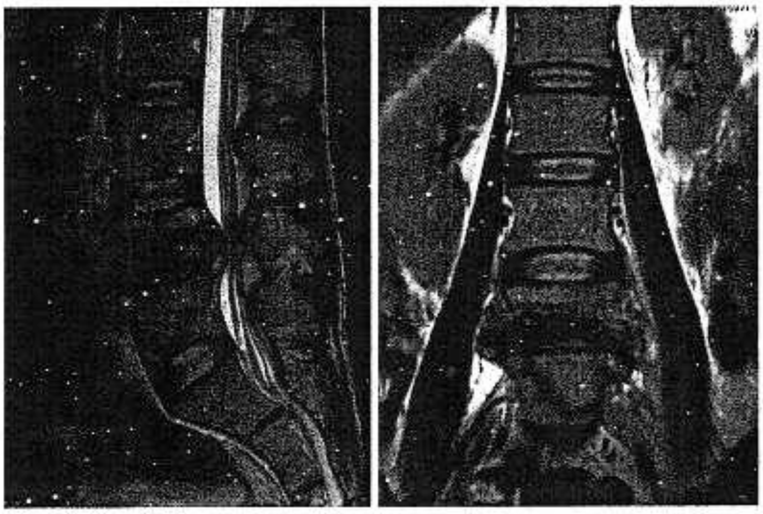

Fig. 3 Typical MRI pictures of the TB of the spine (Courtesy of Dr. Soetomo General Hospital, Surabaya)

The increase in the degree of welfare, education and intensive government healthcare program has considerably lowered the incidence of cases of infection in Indonesia although infection is still the second most common case in orthopaedics. It is mostly caused by mycobacterium infection such as tuberculosis (TB). The second most frequent TB infection following the lung TB is an infection of the bone. TB of the spine is still a major problem in Indonesia. TB of the spine (Fig. 3) will cause destruction of the bone, causing kyphotic deformities and compression of the spinal cord and eventually paralysis of the extremities. In addition to spinal tuberculosis, there are also infection to the joints, especially the hip joint and the knee.

In line with the increasing life expectancy in Indonesia, there is also an increased incidence of degenerative cases. Degenerative musculoskeletal diseases that have a relatively high incidence and cause of morbidity in patients is a degenerative joint disease (osteoarthritis) and osteoporosis (Fig. 4). Osteoarthritis is characterized by symptoms of joint pain, especially after activity, stiff joints and decrease of range of motion. Osteoarthritis can occur in all joints of the body, but the most debilitating is the one that affects large joints of the body such as the knee joint, hip joint and spine.

Osteoporosis is a disease that occurs due to disturbances in bone mineralization, causing bones to become susceptible to fracture. The disease is common in women after menopause. Pathologic fractures due to osteoporosis is most common in the spine, pelvis and wrist joints. The incidence of osteoporosis in Indonesia in age less than 70 years for women as much as 18–36 %, while men 20–27 %, for age above 70 years for women 53.6 %, men 38 % (Tirtarahardja et al. 2006). Osteoarthritis (OA) is the most common joint degenerative disease in the society, especially in elderly. Indonesia belongs to the 10 countries with a large elderly population.

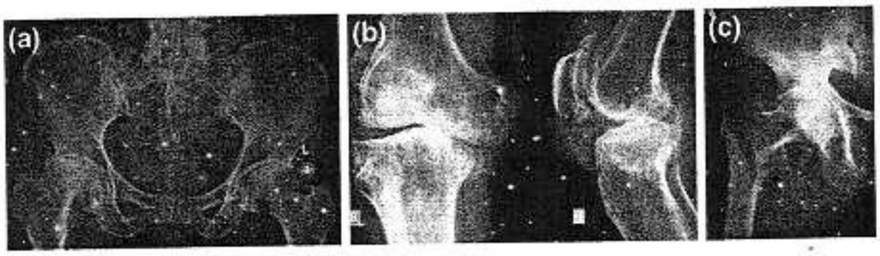

Fig. 4 Degenerative cases commonly found in Indonesia: **a** osteoarthritis of the hip; **b** osteoarthritis of the knee; **c** pathological femoral neck fracture caused by osteoporosis (Courtesy of Dr. Soetomo General Hospital, Surabaya)

In 1991, the number of people aged over 60 years was already 16 million, and is rapidly increasing. A population-based survey in a rural setting in Indonesia reported that the prevalence of radiographic OA of the knee in subjects aged 15 years and above was as high as 15.5 % among men and 12.7 % among women (Soeroso et al. 2005; Darmawan et al. 1992).

3 Surgical Intervention and Implants

3.1 Biomaterials in Orthopaedic Surgery

Biomaterials are commonly used in orthopaedic field. Firstly, it is used for augmentation of bone such as in the cases of fracture treatment. Secondly, they are also in very good use in replacement and reconstruction of musculoskeletal organs like joints, ligaments, intervertebral disc, resected bone due to malignancy, and defective joints due to degenerative changes (Grimm 2003). The definition of biomaterials itself is any material intended to perform the function of an organ or a tissue partly or completely in living organisms. Those which are usually used in orthopaedic are commonly called implants (Koksal 2014).

Biocompatibility, appropriate design, manufacturability, mechanical reliability, biological stabilities, special properties such as tensile strength, yield strength, elastic modulus, corrosion and fatigue resistance, surface finish, creep, and hardness, resistance to implant wear and aseptic loosening and corrosion of implants are all contributing to characteristic of implants. There are several basic requirements that need to be fulfilled in order for the devices to function properly (Patel and Gohil 2012). The main biomaterials used in orthopaedic surgery are divided into two groups: metals and non-metals.

Metals
The use of metals for orthopaedic devices started long time ago. In the 17th century, metals have started been used, and later on, in the 18th century a metal screw

implant was used for the first time. Metals have their main applications in load-bearing systems such as hip and knee prostheses and for the fixation of internal and external bone fractures. The metallic implants that are widely used in orthopaedic surgery are: low carbon grade austenitic stainless steels, titanium (Ti) and its alloys, and cobalt-chromium (Co-Cr) alloys.

Stainless Steels: Like any steel, it is an iron-carbon alloy. Alloying elements were added and contributed to the ability of stainless steel to resist corrosion. The first biomedical 18-8 steel alloy contained vanadium (V) but subsequent studies indicate that it provides the alloy with insufficient corrosion resistance, and therefore the medical use of vanadium steel has been discontinued (Ivanova et al. 2014). Further study yielded new resistance property in which modern corrosion resistant (stainless) steel is made by adding typically 18 wt% of Cr, which resulting in a thin Cr oxide (Cr_2O_3) film on the surface and 8 wt% of nickel (Ni) which contributes to austenite phase formation in the alloy. This Cr_2O_3 film is characterized by its low chemical reactivity and displays a self-healing capability in contact with oxygen. Based on phase composition, these steels are classified into three categories: austenitic, martensitic or ferritic stainless steels. They considered as the good choice for number of biomedical applications. In practice, stainless steels are used predominantly in temporary implant devices, such as fracture plates, screws, and hip nails, although stainless steel also is used in some Charnley-style femoral components for hip replacement. The microstructure of austenitic stainless steels is characterized by its gamma (γ) phase with faced-centered cubic structure which contributes excellent workability (both forming and machining) and non-magnetic properties. Those belong to this group are the types 302, 316 and the famous 316L which remains popular as an implant material and a low-cost alternative compared to Ti and Co-Cr alloys (Buhagiar and Dong 2012). Despite its special attributes, there is some downward of stainless steels such as the reported Ni toxicity to the host organism, and vulnerability of the alloy to pitting and crevice corrosion as well as stress-corrosion cracking. Therefore, the use of stainless steels is generally limited to temporary use as biomedical devices despite its role in modern use as orthopaedics and load-bearing implants (Buhagiar et al. 2012).

Ti and its Alloys: They are commonly used for dental and orthopaedic implants. Different alpha and beta structure leads to three different structural types of Ti alloys: alpha (α), alpha-beta (α-β), and metastable β and β-phase alloys. Their excellent corrosion resistance is a result of inert TiO_2 film formation on their surface. For dental implants, commercially pure (CP) Ti, typically with single-phase alpha microstructure, is commonly used, while Ti6Al4 V, with a biphasic alpha-beta microstructure, is most commonly used in orthopaedic applications. The presence of aluminum (Al) and V alloying elements not only contributes to the mechanical stability but also improves the microstructure of alpha-beta in relation to CP Ti. These properties are modulated by heat treatment and deformational works. Despite Ti and its alloys combine a range of excellent properties, i.e. mechanical properties, corrosion resistance, fatigue-corrosion resistance, low density and relatively low modulus, their processing is not easy whether it is machining, forging or heat treating (Navarro et al. 2008). The β-phase in Ti alloys tends to exhibit a much lower Young's modulus than that of the α-phase, therefore it satisfies most of the necessities or requirements for orthopaedic applications. However, the presence of Al and V in long term use of Ti alloys (especially Ti64) poses potential hazard of toxicity. The release Al and V ions from the alloys has been associated with the potential for Alzheimer and neuropathy disease (Patel and Gohil 2012).

Co-Cr Alloys: These alloys, which have been used for many decades, can be basically categorized into two types: Co-Cr-Mo alloys [Cr (27–30 %), Mo (5–7 %), Ni (2.5 %)] generally used in dentistry and artificial joints; and Co-Ni-Cr-Mo alloys [Cr (19–21 %), Ni (33–37 %), and Mo (9–11 %)] mostly used for making the stems of prostheses of heavily loaded joints, such as knee and hip (Patel and Gohil 2012). Involvement of heat during processing of Co-Cr-Mo alloys modifies the alloy's microstructure and leads to the alteration of electrochemical and mechanical properties of the alloys. In term of corrosion resistance, Co-Cr alloys are considerably superior to stainless steels as it demonstrates better performance in chloride-rich environment. However, the corrosion products of Co-Cr-Mo, especially the possible release of Cr ions is potentially more toxic than that of stainless steel 316L (Chen and Thouas 2015).

Polymers

Apart from metals, polymers, the organic or inorganic materials that form large chains made up of many repeating units, are extensively used in joint replacement components. Currently the most used polymers in joint replacements are: ultrahigh molecular weight poly(ethylene) or UHMWPE, poly(methyl methacrylate) bone cement or PMMA, thermoplastic poly(ether ether ketone) or PEEK, and bioabsorbable type of polymers.

UHMWPE: Being used since early 1960s, it is a semi-crystalline polymer with roughly half of its chains is structurally organized in crystalline lamellae and the balance is entangled in a random amorphous state. At the body temperature, this polymer behaves between its glass transition temperature and melting point, enabling unique viscous amorphous behavior combined with a solid-like crystalline phase. The microstructural arrangement of UHMWPE provides desirable material properties for use in total joint arthroplasty, including wear, strength and fatigue resistance in comparison with other polymeric materials. Therefore, UHMWE is used as a bearing surface in total joint arthroplasty (Ansari et al. 2015). However, UHMWPE is not a perfect material because small amount of fluids can be bound which makes discoloration of components as retrieved from infected sites. It is subjected to fatigue failure and displays a tendency to creep for long-term applications, though this is reduced in its highly cross-linked form. Highly cross-linked and thermally treated UHMWPE is generally acknowledged as the special structure for hip arthroplasty. Since the introduction of its first-generation, clinical performance of highly cross-linked implants is generally considered successful, though there has been a small number of reports on the rim fractures of some thinner liners implanted at high abduction angles. Highly cross-linked UHMWPE is currently less used in the knee owing to the inherent reduction in ductility and fracture resistance as the result of irradiation used to initiate the cross-links, despite its superior mechanical performance (Ong et al. 2014).

PMMA: In 1970s, Charnley introduced the use of acrylic plastic bone cement made from PMMA (Leong and Lu 2004). PMMA cement is formed by mixing liquid monomer and powdered polymer which produce an exothermic reaction at temperature of 48–56° C in vivo. The monomer component varies a little among different available preparations while the powder typical contains polymer, copolymers of different molecular weights, initiator, radio-opacifier, accelerator, and antibiotics and dye (Duffy and Shafritz 2011; Webb and Spencer 2007). Antibiotics and barium are added in order to reduce the risk of infection and increase radiographic visualization, respectively. Being available in both high-viscosity and low-viscosity preparation, PMMA does not adhere to bone or metal, but rather acts as a grout, interdigitating between the bony trabeculae and increasing the contact area. Its elastic modulus lies between 1–4 GPa which is close to that of cancellous (10–2,000 MPa) and cortical (10–20 GPa) bones. PMMA has viscoelastic properties that demonstrate an increase of stiffness with higher rates of loading, as well as creep and stress relaxation. It reaches its strongest point under compression (Wright and Maher 2008).

PEEK: It is a semicrystalline thermoplastic consisting of an aromatic molecular chain interconnected by ketone and ether functional groups. In orthopedic applications, PEEK has been utilized for bearing surfaces, fracture fixation plates, total joint arthroplasty parts, and spinal implants. In addition, PEEK is widely used for interbody fusion cages or components in spine fixation systems. PEEK is radiolucent which facilitates assessment of the surgical site with plain radiography, CT or MRI (Li et al. 2015). Due to its high quality and imperviousness to degradation, PEEK materials are utilized as a part of a wide assortment of mechanical applications. PEEK can be utilized as a part of an unfilled state, with added substances, for example, carbon or fired strands, or with bioactive added substances, for example, hydroxyapatite. Unfilled PEEK has a flexible Young's modulus of 4 GPa, but a composite (filled PEEK) could has a higher elastic modulus than that of Ti alloy (110 GPa). By filling 30 % weight with carbon fiber, PEEK composite can reach a versatile modulus of 20 GPa, while at 68 % reaches 135 GPa (Abdullah et al. 2015; Schwitalla and Muller 2013).

Bioabsorbable Polymers: Some polymers are resorbable in their nature and are suitable for initial fixation and stabilization. In orthopaedic surgery, bioabsorbable polymers are commonly used when the permanent presence of a device is not needed or desired, such as sutures, suture anchors, fracture fixation pins, and bone screws. Over time, these implants will undergo resorption through hydrolysis process at a predetermined rate, lose their mechanical integrity and becomes less stiff and loses its ability to support a load. During this process, the load is transferred increasingly through the healing tissue. Therefore, the rate at which the bioabsorbable polymer device loses integrity is an important consideration (Burg et al. 2000; Farraro et al. 2014). Bioabsorbable polymers can also provide a mean of releasing drugs locally to the surgery site. The rate of drug elution can be designed to correspond to the factors affecting healing or bone regeneration process. Some of the most frequently used bioabsorbable polymers are poly(glycolic acid), poly(lactic acid), and copolymers derived from them. The process of natural hydrolysis in the body will degrade these polymers to yield glycolic acid or lactic acid monomers, respectively (Ulery et al. 2011). Poly(glycolic acid) has higher elastic modulus of 7 GPa compared to that of 46-poly-L-lactic of 2.7 GPa, but poly(glycolic acid) has shorter degradation time of 6–12 months compared to that of the latter which degrades after 24 months. Elastic modulus and degradation time can be modulated by varying copolymer formulations, for instance, a formulation of half lactic acid and half glycolic acid results into low elastic modulus of 2 GPa and very short degradation time of 1–2 months (Middleton and Tipton 2000).

Ceramics

Ceramics are polycrystalline materials made of metallic and non-metallic elements bound by ionic or non-ionic bonds with occasional covalent bond, and are characterized by both brittleness and hardness. Many types of ceramic materials are used in practice and they are generally divided into two large groups: inert ceramics such as alumina (dense aluminum oxide), zirconia (zirconium oxide), calcium sulfate, and pyrolytic carbon; and bioactive ceramics that are designed to induce a reaction from the surrounding tissue such as hydroxyapatite, β-tricalcium phosphate, and silica-based or calcium-based bioglasses.

Inert Ceramics: Alumina has a very low coefficient of friction when articulated against UHMWPE due to its high wettability that reduces friction and provide self-lubrication during articulation. The combination of low friction, improved lubrication, and reduced wear has led to the popularity of alumina as a bearing surface for the femoral head in total hip replacement (Garino 2013; Piconi 2011). Zirconia is stronger and denser than alumina, and it can be polished to a finer surface finish, resulting in lower wear rates than alumina in a laboratory setting. Zirconia is also used as femoral bearing surfaces in total hip implants and in powdered form as a radiopacifier in some formulations of PMMA bone cement. Unlike alumina, zirconia should not be used in ceramic-on-ceramic articulations. A high rate of early fracture of zirconia heads has led to a large recall, hence the use of zirconia as bearing surface subsequently decreased. However, newer zirconia-toughened alumina matrix composites have been developed to provide greater strength and fracture toughness than alumina alone (Chang 2014; Heyse et al. 2012).

Bioactive Ceramics: These materials possess special characteristic that allows a formation of bonding with living tissue. They take advantage of the tissue's cellular physiology and structural component materials to induce bone remodeling, growth, and integration into the implant (Rahaman 2014). An ideal bioactive ceramic would actually spur bone growth adjacent to the implant, promote integration of the bone with the implant structure, and gradually biodegrade as healthy bone tissue replaces the artificial structure. Calcium-based ceramics (such as calcium phosphate, calcium sulfate, and hydroxyapatite) and bioglasses are two general categories of bioactive ceramics that have been developed. Bioglass is mineral rich structure that can be tailored to optimize the tissue response. Hydroxyapatite ($Ca_{10}[PO_4]_6\ [OH]_2$) is a logical choice for an osteophilic substrate since it is naturally occurs in bone mineral. Hydroxyapatite coatings have been used for decades both in dental and orthopaedic applications. As commonly occurs with bioactive agents, there was initial enthusiasm for coating the entire implant with hydroxyapatite to provide strong fixation to surrounding bone. However, over time it became apparent that hydroxyapatite is best used tactically to enhance regional bone fixation. In total hip replacement implants, for example, hydroxyapatite coating is best used around the implant shoulder, which is the most important region for robust bone apposition and implant fixation (Bose et al. 2015). β-tricalcium phosphate ($Ca_3[PO_4]_2$) and bio-glasses are usually utilized as a part of basic applications (e.g. filling cancellous bone defects), for bone graft replacement as substitutes or extenders, and especially as an aide to fracture repair or fusion in the setting of trauma, orthopaedic oncology, or spine surgery (Goff et al. 2013; Hartigan and Cohen 2005). The fillers are available in forms including granules, pastes, and malleable sheets.

3.2 *Types and Applications of Orthopaedic Implants*

Orthopaedic surgeons are the most common users of implants for treating, improving, or replacing anatomical elements of musculoskeletal system. Various implant sizes and shapes are used which are determined by the location and the disease to be treated. Metal implants consist of many types of plate and screw systems, intramedullary nail system, pedicle screw system that are used for fracture and reconstruction of bone and spine (Fig. 5). Polymer implants mostly used for biodegradable screw, while hydroxyapatite ceramic is used as a bone graft to accelerate bone healing. Certain implants use a combination of biomaterials such as

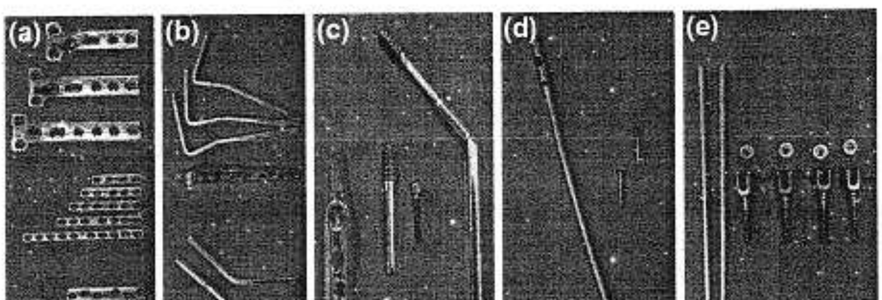

Fig. 5 Various types of implants used for traumatic purposes: **a** plates in various types and sizes; **b** angled-blade plate, commonly used for proximal or distal femoral fractures; **c** dynamic hip screw, widely used for cases in proximal femoral fracture; **d** interlocking nail, suitable for long bone fracture of lower extremity; and **e** pedicle screw and rod, used for posterior spine stabilization (Courtesy of Dr. Soetomo General Hospital, Surabaya)

the case of a total joint replacement that combines metal and polymer or ceramic. In general, implants used by orthopaedic surgeon are divided into: traumatic implants mainly for fracture fixation; and reconstructive implants which are used to replace body parts damaged by a disease such as osteoporosis. In Indonesia, the most used type is currently the traumatic implants, but gradually the use of reconstructive implants also begins to increase with the aging Indonesian population.

Traumatic Implants

Due to high incidence of trauma cases in Indonesia, traumatic implants are still the most frequent type of implants used in Indonesia. These include screws, plates, nails, and pins either to be used as internal or external fixation of fractures (Fig. 6). External fixator is preferable to be used for open fracture with severe soft tissue injuries in order to stabilize the fracture comminution and to handle the risk of postoperative infection. In the case of extramedullary fixation, plates are combined with screws above and below the fracture or using rods or nails inserted into medullary canal through the fracture site (Ito et al. 2015).

Like any other living tissue, bone responds to environmental and physiological changes. When bone grows, there is an increase of extracellular matrix material to the endosteum and periosteum layer. This will result in bone growth of both in length and diameter. Wolff hypothesized in 1892 that under continuous loading bone will grow better. Bone that does not get enough loading will lose its mass, while bone experiencing greater load will increases its mass in response to reduce stress (Frost 1994). Throughout life time, the process of removal and replacement of bone occurs continuously, known as remodelling. In fracture healing, this

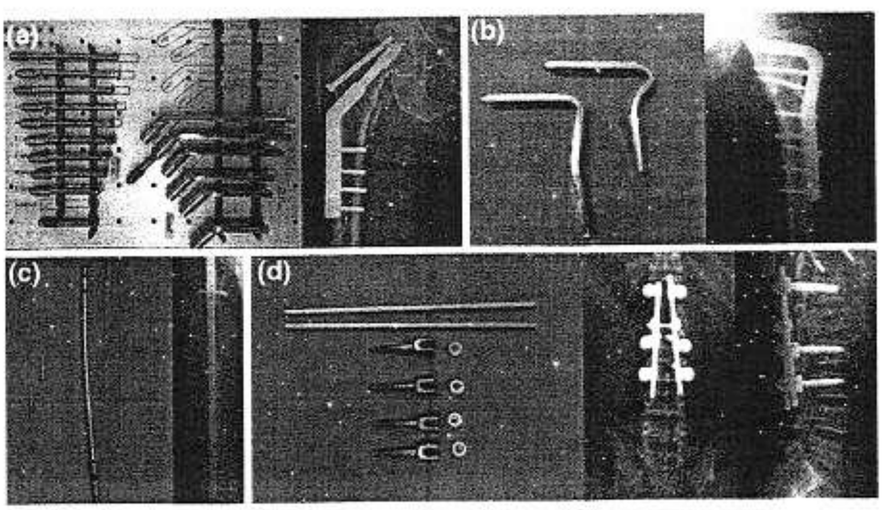

Fig. 6 Application of traumatic implants: **a** angled-blade plate for proximal femoral fracture, **b** dynamic hip screw for femoral neck fracture, **c** intramedullary nail used in femoral shaft fracture, **d** pedicle screw and rod applied for lumbar stabilisation (Courtesy of Dr. Soetomo General Hospital, Surabaya)

process enables the recycling process to occur continuously on the bone and into healthy tissue to prevent the accumulation of micro fractures that can lead to failure of the bone structure (Grimm 2003).

Fracture can heal with or without the formation of external callus depending on the mechanical environment supporting the healing process. The one that is fixed more anatomically and more rigidly will heal without the formation of external callus whereas that of being less rigidly fixed will form external callus. In overall, the process of fracture healing requires a suitable and favorable biological and mechanical environment (Cunningham 2001). A higher mechanical resistance of metallic implants (i.e. Young's modulus) compared to cortical bone leads to a decrease in mechanical stress received by the fracture site, known as stress shielding effect. In long-term fixation, this condition will result in increased bone resorption surrounding the implants. This device-related osteopenia or osteoporosis is caused by the increasing activity of osteoclast in respond to stress-shielding effect. This effect must be avoided in order to maintain good bone strength and it is advisable to remove the implant after certain period of bone union especially in weight-bearing bone (Ito et al. 2015).

When an implant is strained under continuous stress, it will reach a point of ultimate resistance which will result in failure when the point is surpassed (Fig. 7). One of the most commonly encountered failure is fatigue where cyclic load, which does not necessary to be massive, cause a repeated stress below ultimate strength leading to crack propagation and ultimately fracture (Kanchanomai et al. 2008; Mann and Allen 2013). In details, fatigue failure occurs at three stages: crack initiation, propagation and finally the catastrophic manifestation when the crack reaches a critical length of which the remaining material cannot withstand the applied stress (Rabbe and Anquez 2013). Under fatigue condition, the number of stress cycles that the material can withstand is inversely proportional to the magnitude of the applied stress; that is, the number of stress cycles the material can withstand increases as the stress intensity is reduced (Mann and Allen 2013). When environment is in favor to enhance crack formation, for example in exposure of

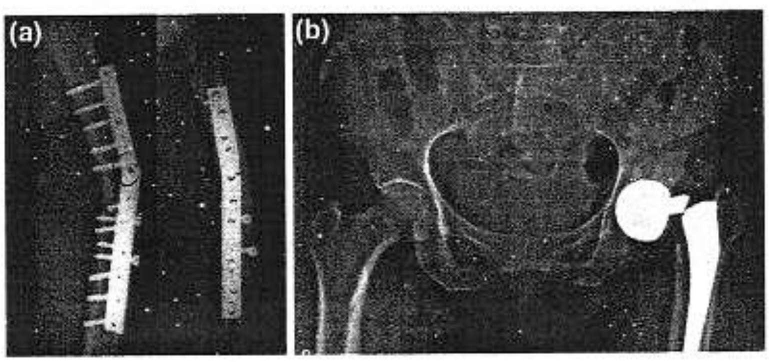

Fig. 7 Failure of implants: **a** fracture of a plate; **b** fracture on hemiarthroplasty of a hip joint (Courtesy of Dr. Soetomo General Hospital, Surabaya)

implants to scratches and nicking, the fatigue failure will be more rapidly reach and the device life span will be greatly reduced. Any factor that arrests or slows down crack propagation will increase fatigue life. In a certain composite system, a crack propagates through a fiber-reinforced matrix will stop when it reaches the boundary of a strong fiber within the matrix. The crack will remain stagnant until enough damage accumulates to move the crack through the fiber (Wright and Maher 2008).

The environment inside human body is physically and chemically different from the ambient condition. Consequently, a metal that performs well (inert or passive) in the air may suffer a severe corrosion in the body. Corrosion creates two problems: (1) it often leaves behind damaged regions on the surface of orthopaedic implants that act as stress risers, markedly decreasing implant strength; and (2) it releases to the surrounding environment corrosion products that can adversely affect biocompatibility, cause pain, swelling, and destruction of nearby tissue. Orthopaedic implants can be susceptible to several corrosion modes, depending on their geometry and manufacturing history, the in vivo conditions under which they perform, and the presence of surface defects (Chen and Thouas 2015; Wright and Maher 2008). The most common forms of corrosion are uniform corrosion, intergranular, galvanic, pitting, fatigue corrosion and stress corrosion cracking. Corrosion process is determined by two factors: (1) thermodynamic driving forces, which cause corrosion (oxidation and reduction) reactions; and (2) kinetics, which determines the rate of those reactions. The thermodynamic driving force corresponds with the energy required or released during a reaction, while the kinetics barriers are related to factors that impede or prevent corrosion reactions from taking place (Jacobs et al. 1998; Manivasagam et al. 2010). Oxide film formed on the surface of metallic materials plays an important role as an inhibitor for the release of metallic ions. During corrosion process, the composition of oxide film changes according to reactions at the interface of metal surface and living tissue, and hence this film plays a very important role, not only for corrosion resistance but also for tissue compatibility (Manivasagam et al. 2010).

Reconstructive Implants

Artificial joints are indicated for patients with severe destruction of any joints from those on small fingers to hips or knees caused by trauma, osteoarthritis or tumors. The affected joints are therefore replaced by prosthetic devices in order to restore its normal function and eliminate pain. Figure 8 shows example of various implants used in reconstructive surgeries. Hip prostheses consists of two separate components, namely the femoral and acetabular parts. The femoral part itself is further constructed by two main parts which are the head and the stem. Unlike the femoral part, the acetabular one can be separated into the cup and its liner. Materials used for making the components can come from metal alloys such as Co-Cr-Mo or Ti alloys, or ceramics and polymers. Since the invention of early prostheses by Charnley in 1970s, the most widely used combination for bearing surfaces is the metal-on-poly(ethylene). This combination is consistently being developed for all the prostheses to improve its design and techniques of implantation. The metal-on-poly(ethylene) bearing has become the most favorable and the gold standard in hip prostheses as it proved its safety, predictability and cost-effectiveness. However, the risk of complication caused by the presence of poly(ethylene) debris remains a major concern and downside. The debris might lead to accumulation of cytokines and proteolytic enzymes which causes peri-prosthetic osteolysis. In the end, this process may lead into the most feared complication of implant failure due to aseptic loosening. Several measures had been taken to minimize the complication caused by the debris by improving the wear resistance through gamma irradiation. However, despite the effort of minimizing the complication, there has been shift of interest towards the use of metal-on-metal bearings (Knight et al. 2011).

Due to the risk of metal toxicity, cancer development, hypersensitivity reaction and prosthetic loosening, metal-on-metal bearing was abandoned in 1970s. However, it was later found out that the cause of failure of the early model of this prosthetic was not due to the nature of the bearing material itself but rather caused by improper design and implantation technique. The metal-on-metal bearing is favorable than the metal-on-poly(ethylene) since it has better wear resistance (~ 60 times more resistant), lower brittleness of the femoral head component, better joint stability (due to larger possible head diameter), lower incidence of dislocation, and lower osteolytic and peri-prosthetic inflammation reaction. However, there is possible risk from debris released from metal-on-metal bearing. The released metal ions increase the Co and Cr ions blood level three to five times higher, even though the long-term effect is still being investigated (Zywiel et al. 2011; Drummond et al. 2015).

Due to issue of wear resistance and friction problem in the two previously mentioned bearings, ceramic-on-ceramic bearing was then introduced by using alumina and zirconia as the materials. This type of bearing is more superior to metal or poly(ethylene) counterparts in term of hardness, scratch resistance, and inert characteristic of the debris. Ceramic bearing is very suitable for active and mobile patients as it has very good durability and low friction. The low friction comes from its hydrophilic property which improve lubrication on its surface. However, apart from its superiority, the cost of ceramic bearing is higher. The adverse complication might occur as a result of loose body presence. This loose body usually originates from chipped parts of the contact surface when improper technique of insertion is applied or when head dislocation occurs (Zywiel et al. 2011; Macdonald and Bankes 2014).

Apart from the characteristic of the bearing surface materials, the interface between bone and prostheses is not less important. There are two kind of bone-implant fixation: cementless and cemented fixations. Cementless implants provide better possibility for revision surgery when needed and they also have better soft tissue preservation when being implanted. When cement is not used, the implants must have special characteristics on their surface to ensure fixation (i.e. porous or grit-blasted surface). The most recent special surface in cementless prostheses is the use of hydroxyapatite coating that promotes bone growth onto the implant surface, therefore increases fixation strength. On the other hand, cement is used as space filler rather than as glue. Cemented implants use methacrylate cement

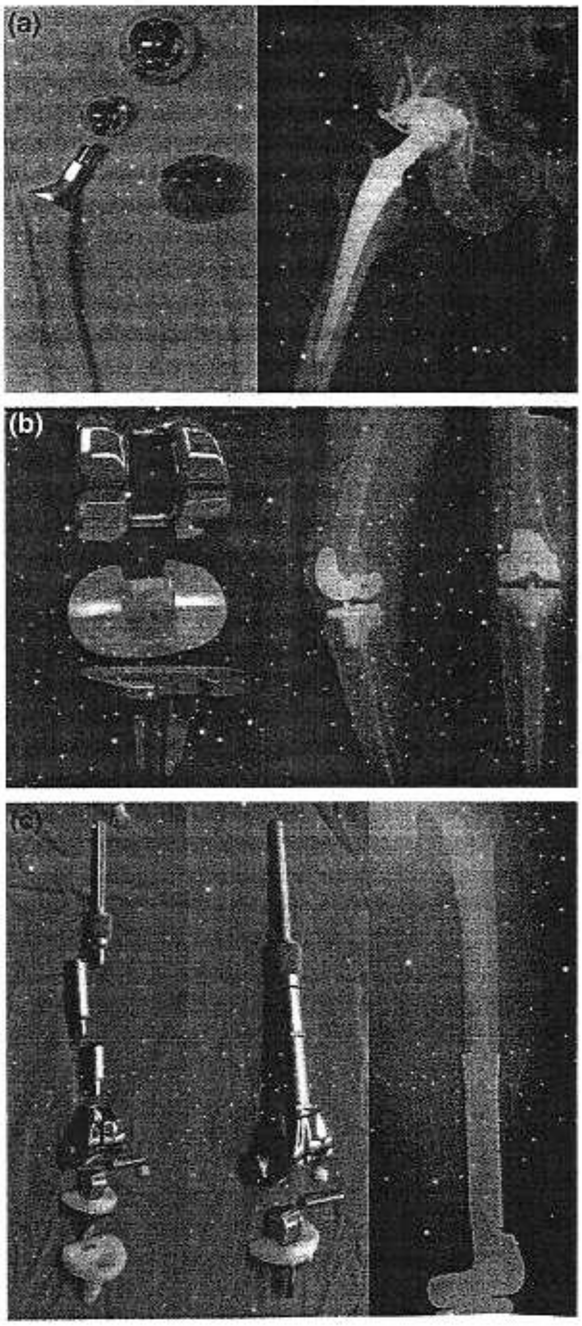

Fig. 8 Various prostheses used in reconstructive surgery: **a** total hip arthroplasty; **b** total knee arthroplasty; **c** mega prostheses for distal femur (Courtesy of Dr. Soetomo General Hospital, Surabaya)

to improve fixation. In around 1950s, Charnley introduced the used of dental cement although in later time, the failure of cement shifted the favor of cemented implants (Khanuja et al. 2011). Comparing the durability of both fixation techniques, cemented one has lower durability after 10 years compared to the cementless one, thus causes a higher rate of revision surgery due to aseptic loosening. However, without counting the revision surgery, cemented stem performs slightly better than cementless one (Mäkelä et al. 2008).

Wear and osteolysis following total joint arthroplasty occur as a result of a complex interaction of many variables. These variables include: patient-specific characteristics (e.g. weight, activity level and age) which affect the magnitude and direction of loads across the joint as well as joint kinematics; and implant design and material factors that control how the implant components respond to the mechanical burden placed upon them (Gillespie and Porteous 2007; Foran et al. 2004). Equally important, surgical factors (e.g. component position and orientation) can also affect joint loads and kinematics. When surgical technique is optimized, the ideal implant position is realized and the best possible wear performance of the total joint arthroplasty can be achieved. However, when malposition, damaged, or misassembled occurred, a specific prosthesis may experience greatly increased wear. Osteolysis can occur as a response to peri-prosthetic particulate debris that results from and is dependent on material type as well as particle size, shape, and amount. In overall, the multiple factors influencing clinical wear performance of hip and knee arthroplasty can be separated into patient specific, implant-specific, and surgical factors that contribute to wear directly or indirectly (Tsao et al. 2008).

4 Recent Development of Orthopaedic Implants in Indonesia

4.1 *The Rise of Local Implant Industry*

Until the era of 1990s, all orthopedic implants required for surgeries in Indonesia are imported from overseas. There was no local implant industry. Imported implants are relatively expensive for Indonesian people as most of the population is not covered by adequate health insurance. Moreover, as the products were mostly imported from Europe and USA, their size is often too big to fit Indonesian people anatomy. These factors has caused orthopaedic service was not optimally delivered and many patients then looked for alternative therapies such as the service of bone setter that offers lower price. This condition has been causing a high number of disability on orthopaedic patients. Nowadays, in line with the improvement of Indonesian economic, education and lifestyle, alternative medicine has been becoming less popular that hospital (modern) medicine. On the other side, traumatic fracture incidences also increases following the increasing number of motor vehicle accidents, especially motorcycle. Therefore, the need for implants in Indonesia especially the traumatic type is very real.

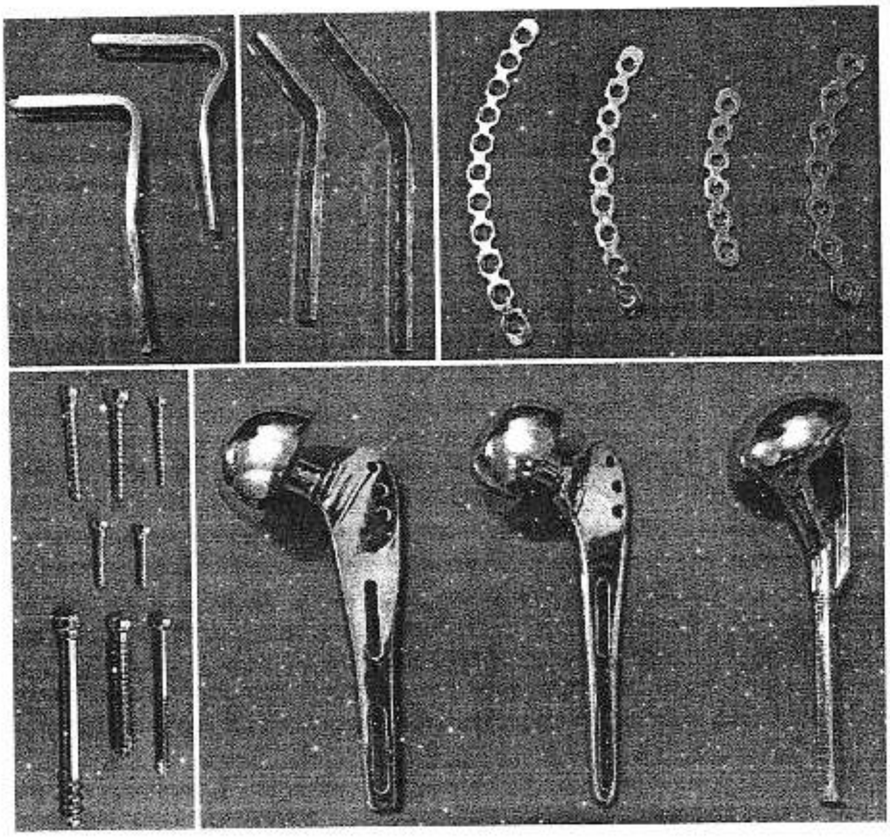

Fig. 9 Locally made orthopaedic implants: various plates, screws and arthroplasty implants (Courtesy Dr. Soetomo General Hospital, Surabaya)

This situation has become a trigger for many orthopaedic surgeons at Dr. Soetomo General Hospital, affiliated with the Faculty of Medicine, Airlangga University in Surabaya, to become the pioneer in producing local implants. In 1993, the first implant manufacturer company was established with the main products focused on plates and screws and arthoplasty implants (Fig. 9). The material used for producing the implants was mostly type 316L stainless steel sheets, rods and ingots imported from the overseas. The manufacturing process involved machining and casting processes. For fabricating bone plates, the stainless steel sheet was cut and drilled according to the predetermined size (patient specific) and number of holes, and then finished by polishing. Since the implants are made locally and near to the hospital, they offer competitive price and deliverability. Beside more reasonable price, the implants offer many advantages including adjustable size that fits to Indonesian people posture, and can be custom-made for specific patient's need

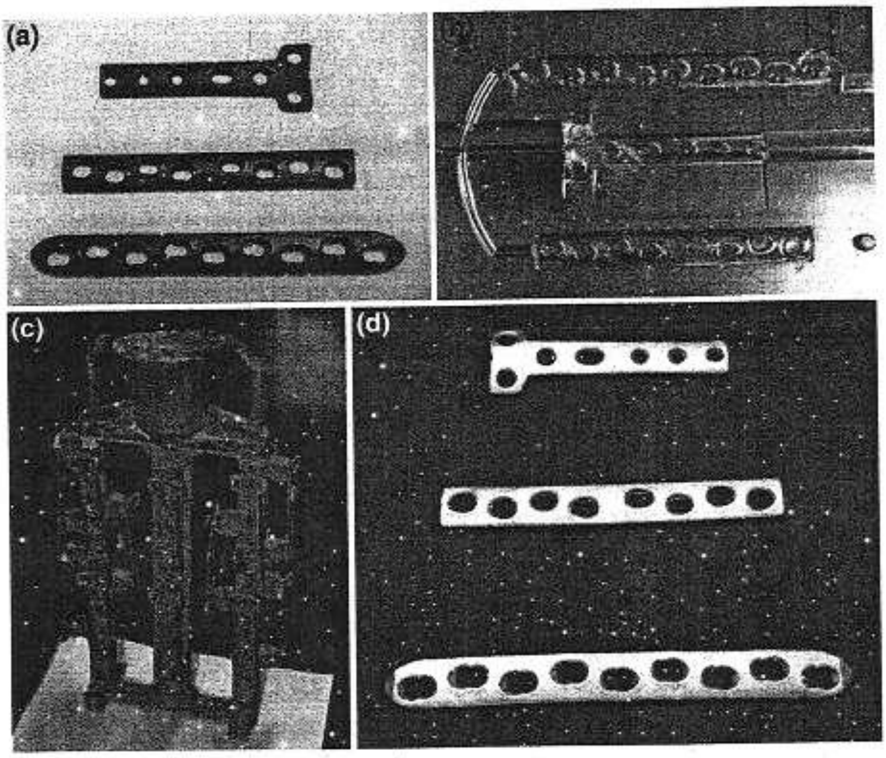

Fig. 10 Investment casting process of bone plates: **a** implant model; **b** waxed model; **c** cast product with casting system; **d** pre-finished implants (Courtesy of Dr. Soetomo General Hospital, Surabaya)

and disorder. This local implant industry has received a lot of appreciation from many users in the country and the implants have been distributed not only in East Java but started to reach every corner of Indonesia.

4.2 *The Challenge and Collaboration*

Nowadays there are several implant factories that produce local implants, but still they could not fulfill the high demand of implants in Indonesia. Moreover, the technology used by local manufacturers still has many limitations including low production capacity and limited product variety (mainly for complex shaped implants such as arthroplasty). The type of raw materials being used is still limited to stainless steels as the price for other metals (e.g. Ti and Co-Cr alloys) are still considerably too expensive.

The orthopaedists at Dr. Soetomo General Hospital have been collaborating with metallurgical scientists and engineers to address the above challenges. They have been conducting R&D activities on orthopaedic implants manufacturing technology with the main purpose to produce high quality implants in large quality at low or reasonable price. Since 2001, the Department of Orthopaedics and Traumatology, Faculty of Medicine, Airlangga University has been collaborating with the Centre of Material Technology, Indonesian Agency for the Assessment and Application of Technology (better known as BPPT) in making bone graft from synthetic hydroxyapatite. Since 2005, this collaboration has been focusing on developing investment casting technology for orthopaedic implants (Fig. 10). This collaboration receives a full support from the Indonesia Government as it aligns with the national programme on supporting local products and the new general health insurance programme which covers every citizen of Indonesia.

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