# Recent advances in biopolymeric composite materials: Future sustainability of bone-implant

**Bankole I. Oladapo [a, *], S. Abolfazl Zahedi[b], Sikiru O. Ismail [b], Aderinsola M.Olawumi, David B.Olawade, Francis T.Omigbodun, Aderogba V.Adebiyi**

[a] *Engineering Department, Heart of Worcestershire College, Worcester, UK*

[b]*School of Engineering and Sustainable Development, De Montfort University, Leicester, UK*
[c]*School of Physics, Engineering and Computer Science, University of Hertfordshire, AL10 9AB, England, UK*
[d]*Wolfson School of Mechanical, Electrical and Manufacturing Engineering, Loughborough University, UK*
[e]*Department of Environmental Health Sciences, University of Ibadan, Nigeria*
[f]*Faculty of Engineering, Environment and Computing, Coventry University, Coventry, UK*
*Corresponding author: E-mail:

**Abstract**

Direct structural and purposeful relation between bone and implant is known as osteointegration. When an implant is inserted into the bone, a bone-implant interface is created, a critical area between the surface implanted biomaterial and the surrounding bone. This research aimed to summarise the outcome of a crucial review conducted on poly-ether-ether-ketone (PEEK) and its composite materials, such as cellular calcium hydroxyapatite (cHAp) for medical applications. The prospective medical implant interface of PEEK is studied. Also, critical analysis and review on 3D printing of PEEK, its composites and natural macromolecular behaviour interface healing process for a bone implant are highlighted. Scopus database was used for electronic and Google search, and peer-reviewed papers in the last twelve years are studied. The study further includes a novel classification of polymer PEEK, the mechanical strength involved during the regeneration process of bone tissues. Due to the extraordinary power of the PEEK and its composites and their excellent natural behaviour, critical PEEK 3D printability research is reported for various biomedical applications and its natural health sustainable behaviours. In addition, the effectiveness and efficiency of the implant interface of PEEK depend on the natural conditions of the bone, design characteristics of implant and distribution of loads between bone and implant. Also explained are the ideal options to boost PEEK composites' 3D printability and scientific mechanisms. This detailed review would benefit the Scientific and medical community to enhance sustainability. Lastly, the description of the bone-implant interface reported within this compendious review can be used to determine the most relevant characteristics to consider in formulating a model of osteointegration of bone implants.

**Keywords:** Poly-ether-ether-ketone; cellular calcium hydroxyapatite (cHAp); bone-implant interface; bio-functionality; 3D printing; bone growth, cellular composite.

## 1. Introduction

Osteointegration is the firm, stable and lasting connection between a loaded implant and the surrounding bone. The success of the bone-implant connection interface depends on the natural and systemic factors of the patient and the characteristics of implant and surface, among other factors [1-3]. Proper osteointegration is subject to acceptance of the implant by living tissues without the formation of fibrous tissue in the bone-implant interface and the presence of symptoms of severe inflammation [4-6]. For its part, the bone-implant bone interface is characterised by the properties that are favourable to the growth and formation of new bone that the implant possesses on its surface and by the design of the implant, allowing it to distribute the mechanical loads exerted

during chewing adequately [6-8]. Therefore, this interface should be considered for the interaction of a set of factors that modulate the natural response and determine the success of osteointegration, among which are the patient's immune response [8-10].

In general, bone is a type of connective tissue characterised by its mineralised extracellular matrix. This matrix consists of collagen fibres, calcium and phosphate ions, and proteoglycans that are deposited in the form of hydroxyapatite (HAp) and glycoproteins [10-12]. Its composition allows the bone to support loads, protects against external loads against sensitive organs, such as the brain and spinal cord and provides the reserved body minerals involved in homeostatic processes [12-14]. Due to these mineral reserves and external loads, the bone experiences constantly dynamic growth, resorption and deposition. This dynamic allows the bone to possess a recovery conditioned to the direction of the external loads to which it is subjected after an injury, thus reaching its complete anatomical and functional adaptation [13-15]. The recovery process after an injury is known as the bone healing process, while the law governing the adjustment of the bone to external loads is known as Wolf's Law.

Furthermore, an injury triggers bone healing to the mineralised matrix of the bone, such as the insertion of a bone implant. When this matrix is exposed to extracellular fluids, a series of proteins, enzymes, cytokines and growth factors are released [15-17]. To activate bone formation, chemically attracted bone marrow and surrounding bone cells invade the site of injury by proliferating and differentiating into cells that anatomically and functionally recover injured tissues. This recovery is stimulated and controlled by the loading effects caused by internal and external loads and the interaction between cells, healing tissues and the implant surface [17-19]. The sum of the natural factors associated with the recovery of natural tissues and the series of mechanical events that modulate their biophysical formation and adaptation are mechanobiology [19-21].

Some materials show up as plastic strings or filaments during printing, released from a twist and dealt with through an ejection ramble. The spout melts and pushes the strands on the base, sometimes called the stage or table of the structure [22-24]. Both the fixture and base are obliged by a personal computer, which discipline components of an article in x, y and z directions. In a typical FDM structure, the ejection winding machine moves through the assembly stage on a plane of a level and vertically 'draws' a cross-section of a part to the location. This modest plastic layer cools and quickly places authority on the layer below it. The base is usually cut down by about one-seventeen inches when an imprint layer is printed to ready for the corresponding plastic layer [24-26]. The 3D printer head or extruder is a bit of a material removal system that requires a predictable profile for producing substances for rough materials and surrounding materials. Many fibre materials are removed, including thermoplastics, such as polylactic acid (PLA), thermoplastic polyurethane (TPU) and high impact polystyrene sheet (HIPS) [26-28]. 3D printing, in like manner, insinuated as included substance manufacturing and incorporates delivering an area by putting away material layer by layer. Many additive manufacturing (AM) progressions, including material ejection, material flying and facilitated imperativeness sworn statement. These techniques support extruders and remove different materials for better performance [27-29].

The production of 3D printing process which uses an incessant fibre of a thermoplastic material, often known as FDM and a freestyle fibre manufacture under the reserved term. An annotated statement shows FDM as a process of material expulsion using thermoplastic polymers to produce objects in an additional substance method [29-31]. This provides new design and manufacturing options, which makes 3D printing innovation generally relevant. Printing machines based on this innovation are also called FFF, or commonly-named 3D printers. The printer stage, just like the printer head, includes 3D printers fired on FDM innovation [32,34]. The fibre crude material is the same. The platform or bed is constantly manufactured out of a particular metal, steel or plastic. The

output of the FDM presses is connected to a mechanical case with a belt and screw-moving system. The entire extrusion can be moved in x, y and z dimensions through a motorised system.

A fourth motor drives the thermoplastic material to the fuel, and PC restricts all head and crude material developments [34-36]. The raw material is usually thermoplastics of creative quality. Sometimes, metal is also used. When presented to warming and set up again when the warmth is pulled back, the thermoplastic material is equipped for more than one softness. The thermoplastic fibre or metal wires are twisted [36-38]. The improved 3D printer class makes it possible to keep the spout temperature up close to the progress temperature of the material being expelled. This makes it possible to dispose of the material in a semi-fluid state, but it immediately returns to a vital state. This result has more excellent dimensional accuracy [38-40].

Moving forward, every thermoplastic can be used as raw material on a fundamental level for FDM printers. Financially, nylon, ABS and its composites, PLA and TPU, form a number of the mainstream decisions on raw material. The crude material is expelled through the warmed bottom as fibre when the FDM printer begins to print. It is stored at the bottom of the printer stage [41-43]. The following layer is ejected, and the object is built up layer by layer from the bottom up. On a fundamental basis, any thermoplastic can be used as a raw material for FDM printers. It is stored and cements at the bottom of the printer point. The subsequent layer is expelled, and the object is built up layer by layer from the ground up [43-45]. In the first instance, most FDM printers immediately print the internal and external edges, with inner layers as either a string or an input frame. There are sensitive 'overhangs' in specific items/models that hang unless they are helped. A component consolidated by the FDM printers is printed alongside the article in these aided structures [46-48]. After the manufacture is completed, they are evacuated. The swaggers are usually of a material similar to the item. Several printers have a second extruder to store explicit swaggers of dissolvable thermoplastics when the shades need to be stopped. These swaggers may be an unexpected component of the 3D modelled thermoplastic [48-50].

This review paper explains the natural processes of bone formation, healing and the various internal and external mechanical stimuli that regulate tissue recovery. The mechanical-biology analysis enables a simplified abstraction of the bone-implant interface to offer a mathematical model of bone osseointegration. In the subsequent section, the natural and biochemical sequences are described, which allow new bone formation at the interface of the bone implant. Then, throughout the entire healing time of the interface, there is a new classification of the mechanical phenomena, and their effect on implant osseointegration is elucidated. Finally, several mathematical models in the literature are examined, describing specific tissue-recovery mechanisms, typical healing of bone-bone implants and formulation of a simplified mathematical model of implant integration and its mechanical-natural reality. Fig. 1 represent a **c**lassification lowchart of composite materials and manufacturing Methods use in additive manuacturing

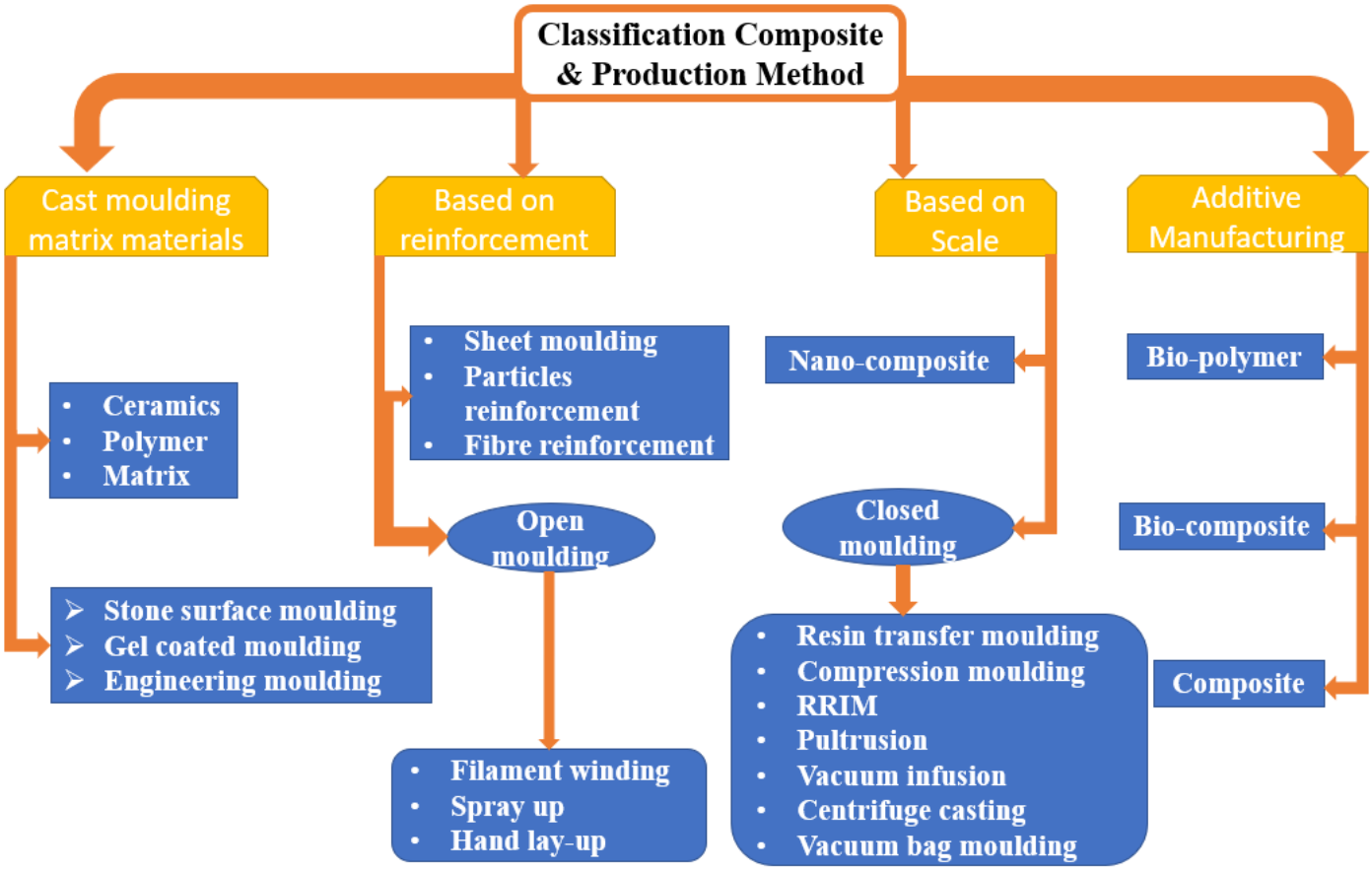


**Fig. 1.** Classification of composite materials and manufacturing Methods

## 2. Implantation

An orthopaedic embed is a clinical gadget fabricated to displace a missing joint or bone and help a harmed bone. The clinical embed is predominantly created, utilising preserved steel and PEEK combinations for superiority. The plastic layer is done as a fake ligament. Interior obsession is an activity in orthopaedics that includes careful inserts to fix a bone [51-53]. During the medical procedure of broken bones through inward obsession, the bone sections are first diminished into their typical arrangement. They are held along with the assistance of internal fixators. For example, plates, screws, nails, pins and wires are used. Good knee tendons help the joint. Current embed structures perceive the multifaceted nature of the common and intently impersonate the movement of a typical knee [54-56]. For example, the joints stabilise the joint in a good knee. Common structures of the knee, where the femur, tibia, and fibula meet close to the tibia, are some embedded planes that protect the patient's tendons, some placed by others. In the anterior part of the knee, the Kneecap patella lies against the femur [56–58]. These bones are associated with tendons, muscles and ligaments that help structure the joint axis and provide joint adaptability. **Fig. 2.** Shows an implantation process of PEEK composites for medical applications. Although there are four bones around the knee joint, only the femur, tibia, and patella are affected by an implant. As artificial knee joints consist of three parts, several tooling organisations design and manufacture knee joints that can be made with various metals, plastic and ceramic [59-61].

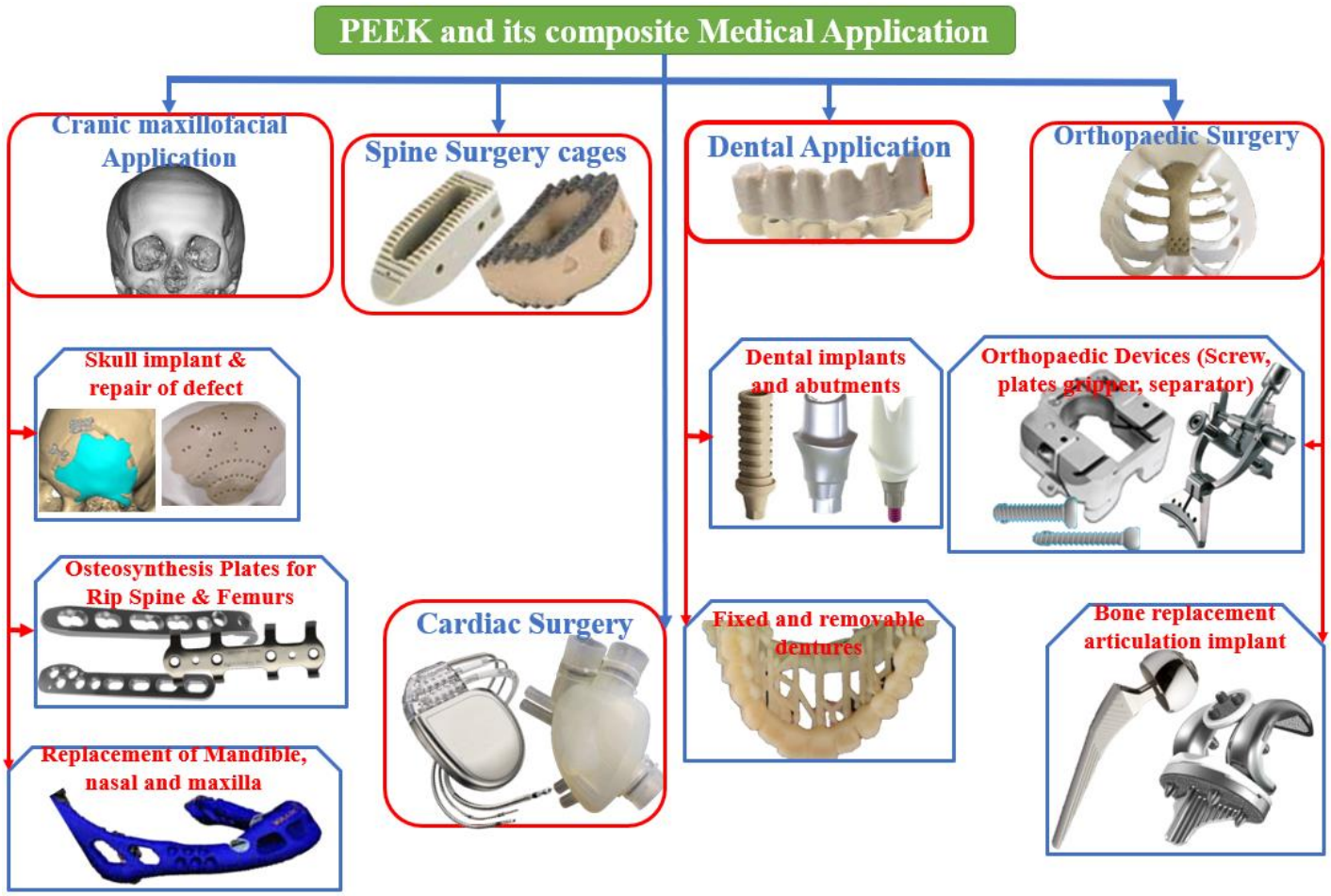


**Fig. 2.** Implantation of PEEK composites for medical applications.

*2.1. PEEK for implantation*

Fake new parts can be made of solid plastic, metal, or ceramic. All knee replacements in between or all the way through will claim a few different materials, possibly metals and plastic. As a general rule, each segment is machined from PEEK, cobalt-chromium amalgams, or metal mixed with PEEK and cobalt. The chosen materials must be resistant, allow some adaptability during development and be biocompatible. That is, they will not be rejected, corroded or react with the body. Chromium amalgams are one of the most used materials in inlays. This metal is biocompatible, dense, malleable and does not separate in the body. This material is commonly used for femoral inlay as it is extremely durable. The femoral pad is heavily supported against the plastic spacer during development [61-64]. Some particles of this metal can enter the bloodstream of sensitive people to nickel and cause a reaction. The ideal is to notify the specialist if there is hypersensitivity because there are options. Original PEEK is not used, but mainly cobalt is used as PEEK. Cobalt PEEK is used as much as cobalt-chromium blends in gasket replacement segments. PEEK compounds are biocompatible and do not corrode or alter the body. Cobalt PEEK is more flexible and positive for a joint bone that embedding involves. Because this metal is softer, it usually forms the replacement shin that the plastic inserts attach. The metal decision is less important in the shin segment, as there is little adherence or friction during development [64-66].

## 3. Strengths of composites

Good false bone inlay requires large pores to improve reinforcement transport, small pores to allow seeding of

cells, and bone-like mechanical properties to maintain a strategic distance from pressure protection. Herein, newly developed gyroid cross-sections with millimetre-scale gyroid splitter separations and additional micrometre-scale pores in the splitters are reported. The structures are efficiently produced by electron column liquefaction using PEEK to achieve high part properties while exhibiting bone-like mechanical properties under Young's modulus of 15-22 GPa. The improved design also allows for stable flexion of the structure, eliminating fragile frustrations [67-69]. Using a systematic screening method, five types of gyroid structures were efficiently generated, with cell divider thicknesses, "range" between 1200 and 2000 µm, additional pores in gyroid dividers, and sizes of approximately 640 to 750 µm. Properties of the part are considered [69-71]. Fig. 3. Represent summary of a method of PEEK, its implants and their applications in the medical field. The huge gap allows reinforcement tools to enter the inlay, while small-scale pores seed bone cells. At the beginning of functionalisation, the sections also have Young's modulus coverage of 3-4 GPa, and compression quality of 150 to 250 MPa under the characteristics of the common human problem that remains unsolved. The presentation of multiple pores also improved the stability of transverse distortion. Tension fasteners evenly distributed around the pores allow for a method of dampened torsional plus bending [71-73].

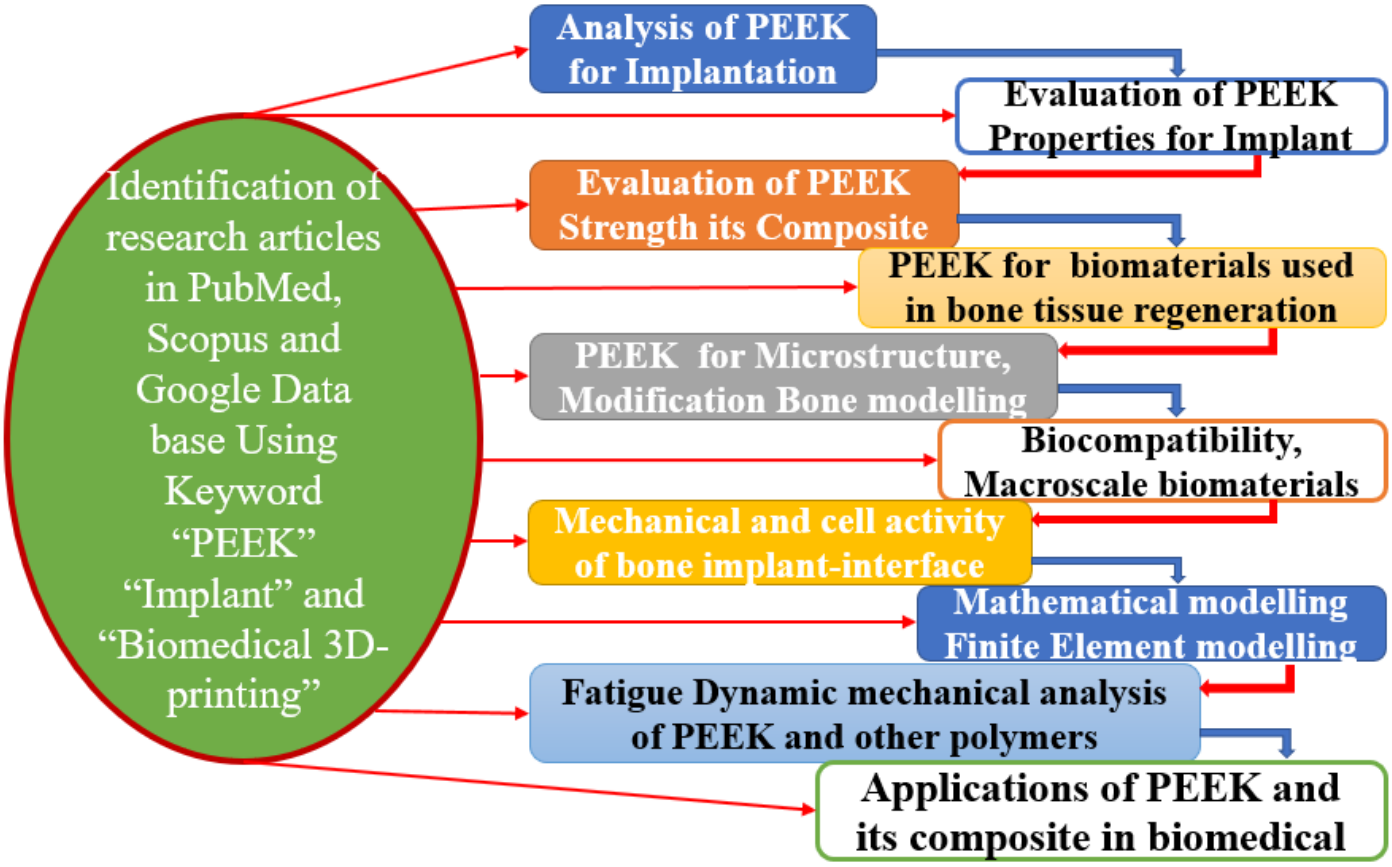


Fig. 3. Summary of a method of PEEK, its implants and their applications in the medical field.

In addition to assembling substances and heading plan strategies, the progress of meta-biomaterials has been enabled with exceptional mechanical and organic properties mingling in general metamaterials. These are arranged and designed topology by repeating multiple common unit cells in various forms to create a transverse structure. Establishing the precise association of geographical features is fundamental to these materials. This article focuses on Application-oriented AM metal metabiomaterials, such as bone substitutes and orthopaedic fillers. It examines the currently available evidence for mechanical presentation under cyclic and semi-static stacking conditions. Geographic feature connections are verified. This includes relationships based on coaxial

cross-sectional structures. Plate grid structure slightly uneven surface and the plane assessed [73-75]. The prestigious models, including expository and computational models, used to develop geographic property connections are also secured. The impacts of AM forms on sensational mechanical characteristics and exhaustive performance of meta-Biomaterials are further described below, as are tissue engineering, biodegrading, surface biofunctionalisation and stacking profiles. Meta-biomaterials with AM display abnormal mechanical characteristics, including negative proportions of Poisson to auxetic meta-bios, memory behaviour, superelasticity, and the common usage of such irregular, practice. The study concludes with specific recommendations [76-78].

## 4. Bleeding and clotting of bone-implant interface

The natural process of forming the bone-bone implant interface is related to the healing process of a fracture. After an injury produced by inserting a bone implant, the mineralised bone matrix is recovered following four stages, each associated with a characteristic natural event of formation of hematoma bleeding and coagulation. The degradation of the clot and cleaning of the wound, granular tissue formation, fibroplasia, angiogenesis and formation of new bone matrix [77-79].

It is common during the surgical procedure to insert a bone implant. Bleeding occurs due to the injury caused to the soft tissues, such as gums and hard tissues, including alveolar bone. This bleeding is the starting point of the series of natural events that conclude with the osseointegration of the bone-implant interface. Initial reacción to the injury and finish with hematoma or coagulation [79-81] is summarised by bleeding and coagulation. Following the degradation of this coagulation, vascular structures are recovered and the fibrillary primary connective tissue network called the granular tissue is constructed. The migration of the cells of the osteoprogenitor begins with this fine tissue, which ultimately restore the mineralised bone matrix. Subsequently, each of these natural events is explained in detail.

Moreover, during implant insertion, blood conducted through the broken blood vessels infiltrates the implantation site. The blood contains red blood cells, white and platelet blood cells. While red blood cells are geared more to transport oxygen, the healing process begins with leucocytes and plates. White blood cells are responsible for initiating the immune response, while platelets are responsible for stopping blood flow from the injury. Platelets are made up of many glycoproteins, a dense tubular system, and two granular types: dense granules and alpha granules. Dense grains contain adenosine, serotonin and histamine nucleotides.[81-84]. For its part, fibrinogen is actively involved in the cell adhesion mechanisms of platelets and constitutes 10% of the content of granules. Fibrinogen is also present in the blood and plays an important role throughout the clotting process. Bleeding begins with natural events that culminate in wound healing. The first part of this healing begins with constricting the broken blood vessels and forming a platelet plug that stops blood flow. Platelets normally do not attach to the endothelium that lines the blood vessels [84-86]. However, blood vessels are exposed to the subendothelial environment rich in collagen and microfibres when blood vessels are broken. The released platelets use the glycoproteins present in their cytoplasm to adhere to their new environment through junction bridges with the factor of safety and fibrinogen. It has been found that on the surface of an implant, this platelet adhesion mechanism is a function of the microtexture on that surface, suggesting that implants with a rough surface topography have greater adhesion than implants with smooth surface topography. Fabrication, Mechanical properties and characterisation of highly porous PEEK nanocomposites incorporated with an electrostatically bonded hydroxyapatite is show in Fig. 4.

In addition, blood contact with the implant surface creates on the implant surface a layer of proteins that

modulates the connection of cells that arrive from surrounding tissue. The presence of adhesion proteins called integrins in this layer allows cells to join, move on, proliferate and differentiate [86-89]. After adhesion, platelets are activated to release their granular content in the extracellular environment, change shape, and extend cytoplasmic extensions that increase their interaction. This temporary platelet plug is the start of a cascade of events that ends with blood clotting and the formation of a hemostatic.

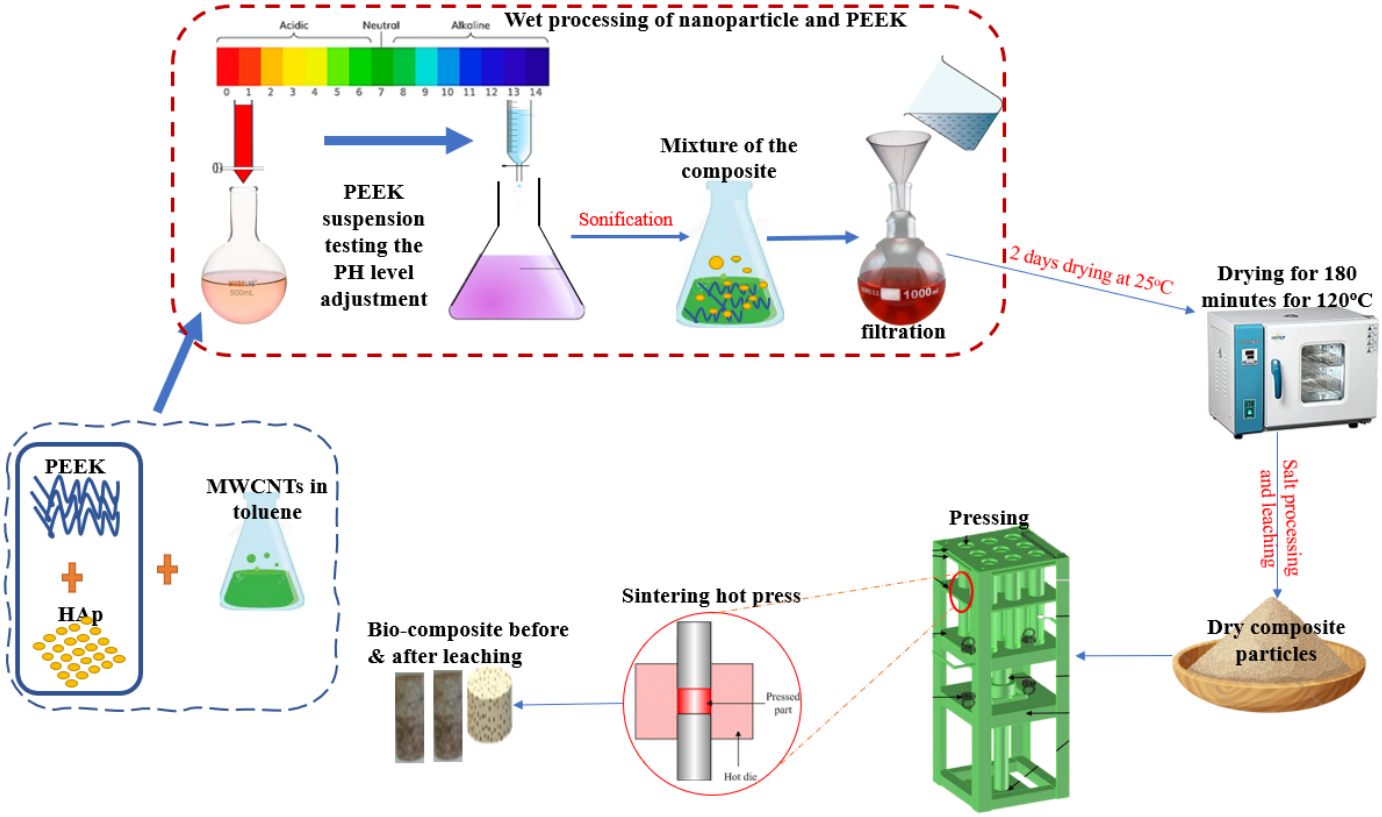


Fig. 4. Fabrication, Mechanical properties and characterisation of highly porous PEEK nanocomposites incorporated with an electrostatically bonded hydroxyapatite

## 5. Biomaterials used in bone tissue regeneration

Metallic materials, especially alloys derived from titanium, such as Ti6Al4V have been used widely in dental and bone prostheses. However, PEEK implants and their primary alloys have too high mechanical properties that cause a lag with the surrounding tissue for application in the treatment of bone lesions. This lag negatively influences the integration of titanium-based prostheses, leading to a mismatch process known as the stress shielding effect [90-92]. AM techniques with this type of material allow obtaining porous structures that reduce the elastic modulus, and parameters similar to the bone can be obtained. In this sense, the most widely used technologies for obtaining porous structure-based titanium are those based on sintering processes, such as electron beam melting or selective laser melting [93-96]. Recently, the introduction of nano-HAp as an additive of these alloys has been proposed to obtain potentially more bioactive structures than the usual titanium-based metal alloys. For example, the effects of ceramic particles on the internal system of the metallic material during the sintering process have been studied. Despite its usefulness as a manufacturing material for dental and bone prostheses, metal structures are not biodegradable. They have a surface that does not favour tissue development since they are bioinert materials [96-98].

For this reason, various surface modifications have been proposed on titanium surfaces, such as the use of coatings with HAp or chitosan, among other bioactive substances capable of improving cell proliferation on the surface of metal structures. HAp coatings are achieved through electrochemical procedures, such as electrophoretic deposition [98-100]. On the other hand, a pre-activation of the titanium surface is carried out by obtaining polymer coverings, such as chitosan or alginate, with oxidation using acids and oxidising substances. That form oxidised groups of titanium on the surface that serve as anchor points for covering them with polymeric substances, which have a greater affinity than metallic material. Also, the use of metal structures presents an additional drawback for pediatric cases, in which the musculoskeletal system is still growing. The summary of manufacturing methods and applications Composite of PEEK is represented in table 1. In these situations, the use of subsequent surgical phases is mandatory to remove the supports that, with time, are no longer adequate to the anatomy of the patients. The use of resorbable implants is especially interesting for these cases [100-102].

**Table 1**

Summary of manufacturing methods and applications Composite of PEEK.

| Materials | Methods | Results/findings | Application | Ref. |
|---|---|---|---|---|
| Graphene/PEEK of nano, film composite | Composite moulding. | The powder blend of graphene-modified in ethanol with polyester (PES) and PEEK powder. The film was made using the hot pressing process using dry composite powder for a half-hour elevation. | Composite with high electrical conductivity. | [66-68] |
| | | Microwave heating. | Adhesive. | [68,69] |
| | Graphene with PES modified thermally reduced. | Enhanced thermal and electric conductivity with homogeneous graph dispersion. | | [70-72] |
| | | Ultrasound of the powder scattered through ethanol with a twin extruder melting. | | [73-75] |
| | | Powder sonification in ethanol, solvent evaporation, method for the doctor blade. | Medical implant. | [76-79] |
| | | Machine for dry mixing injections with a new screw design. | | [80-82] |
| Different HAp/PEEK | Vacuum and plasma spray. | Good connectivity and prevention of substrate damage between PEEK substrate and intermediate titanium layer. The coating layer has low adhesion to the substratum. *In vitro*, mesenchymal stem cells and *in vivo*, in human bone marrow studies. Cell differentiation and proliferation enhanced with improved viability. They are encouraging bone development. | PEEK intermediate coating layer for orthopaedic. | [83-85] |
| | Spin coating. | *In vivo* study (histomorphometry) of osseointegration improved contact area between bone and implant. | Osseointegration | [86-88] |
| | Aerosol deposition. | *In vivo* and *in vitro* studies of microstructure, dense pores free and cracked microstructure—bioactivity improvement in cell proliferation, differentiation, morphological adhesion and bone-implant contact ratios. | Bone tissue engineering. | [88-90] |
| | Chemical deposition. | The proposed method did not employ high temperatures and improved the weather resistance to the $SO_3H$ functional group by sulfonation. | Dentals and spine implant. | [90-92] |
| | Selective laser sintering method. | The *in vitro* HAp/PEEK composite bioactivity study improves composite bioactivity and higher HAp contents show higher bioactivity levels. | Hip implant. | [92-94] |
| | Simulated body fluid (SBF) immersion. | The best bioactivity compared with other sampled nanocomposites with 30 volume percent (vol.%) of NHA content effect of NHA volume fraction on bioactivity through cell adherence and proliferation | Biocompatibility of implant. | [95-97] |

| | | | | |
|---|---|---|---|---|
| | | *in vitro*. | | |
| | Fused deposition modeling. | Study of biocompatibility and bioactivity of the composite product *in situ* nontoxic and bioactive properties have been presented in produced composites. Confirmed enhancement of composite bioactivity by the presence of fibroblast cells, osteoid formation and osteocyte formation within lamellars. | | [97-100] |
| Carbon fiber/PEEK | Polyethleneimine composite fabrication. | The environmentally friendly way to boost PEEK crystalline interface. | | [100-102] |
| | Purification, oxidative and non oxidative treatment based on silicone. | Enhanced matrix adherence of fibre increase cord strength and bending strength in interlaminar. | | [102-104] |
| | Compression moulding. | It provides bipolar plates with a vacuum bag for polymer electrolyte membrane (PEM) fuel cells, abrasive wear thermal ageing, normal strength of 5 $kgm/s^2$, rotating sample on rotating drum with sandpaper. | | [104-107] |
| | --- | Ring plate high conditions for load and speed. | Automobiles and aeroplanes. | [107,108] |
| Multi-walled carbon nanotube (MWCNT)/ PEEK | Functionalised with aminated polyethersulfone /ethanolamine. | Impact strength, increase in tensile strength: low wear rate and performance of the stress at failure and friction coefficient. Extremely good fibre and matrix adhesion with carbon nanotube (CNT) can be easily dispersed. | | [109-111] |
| | Melt blending. | It works—sulfone of polyethers sonication. Composite film moulding solution made up of a glass pane Polymer solution. | | [111-113] |

## 6. PEEK microstructure and modification

In PEEK structure, the soft segment provides the elastomeric properties. To achieve these properties in the PEEK, delicate components have a high molecular weight since increasing the molecular weight improves the elongation to the rupture. When the length of soft segment chains is increased, greater interaction is created between the polymer chains. While decreasing the polarity of the chains will decrease the polarity of the functional group of the chains of the soft polymer segment, favouring the interaction between rigid PEEK segments [102-104]. The delicate features of the PEEK are amorphous and elastomeric at body temperature since the glass transition temperature (Tg) presented is below ambient temperature. The rigid segments formed by the union of the chain extender and the diisocyanate give rise to hydrogen bonds between the urethane functional groups. Stacking of π-type interactions between the aromatic rings of the adjacent chains that form microdomains of rigid segments [105-107]. These microdomains reinforce the matrix and provide rigidity to the PEEK, since they create small cross-linking points. These small cross-links fix the smooth segments at their two ends, preventing the chains from flowing, as they are deformed under a certainly applied tension, since without creep, the details can return to their original shape, releasing the applied tension [108-110]. Different types of PEEK have been observed depending on the method and reagents used for their elaboration, thus giving other uses in various medical applications. Fig. 5 show a schematic current strategies for PEEK modification and bioactivity state in osseointegration and future perspective. The basic classification of PEEK is presented as PEEK based on polyesters. When implanted into the human body, they undergo rapid hydrolyses; therefore, medical applications are limited. Polyether-based PEEK is preferred for medical use because it is less susceptible to hydrolysis. They are also very stable, based on polycaprolactam in the physiological environment. This feature allows rapid

crystallisation as adhesives, medical solvents and pressures on sensitive adhesives. [111-114]. The PEEK based composite can be used as compounds for encapsulation. However, due to their low tear resistance, it is difficult to find their use in medical applications.

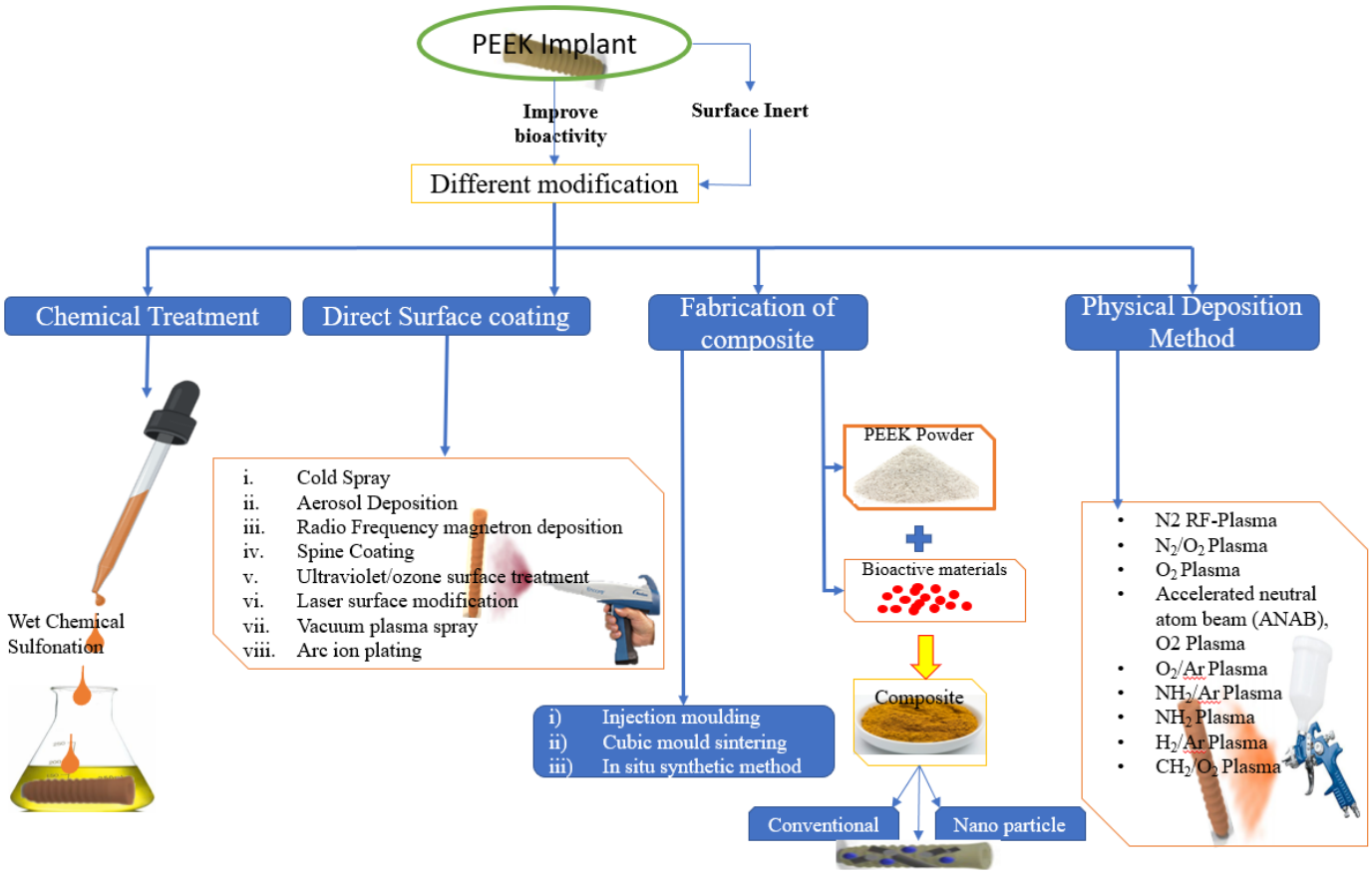


**Fig. 5.** Schematic current strategies for PEEK modification and bioactivity state in osseointegration and future perspective.

## 7. Bone modelling

Once the recovery of the blood supply ends, replacing the provisional connective tissue matrix synthesised by the osteoprogenitor cells begins, culminating in the formation of new bone. This process is known as bone modelling [16]. Although bone tissue recovery along the new vascular structure begins about 21 days after injury, osteoprogenitor cells start to appear as early as the third day. Their appearance is associated with hematopoietic differentiation of stem cells activated by bone morphogenic proteins produced by mesenchymal cells and fibroblasts [115-119]. The subsequent activation of the protein complex responsible for transmitting the signal to the nuclei of these cells and their expressions support the activation of the osteogenic genotype. This leads to the final differentiation of osteoblasts, cells responsible for secreting the compounds of the new bone matrix and regulating its mineralisation [119-121].

The matrix comprises 90% collagen proteins, especially type I collagen and 10% of non-collagen proteins, osteocalcin, osteonectin, bone sialoprotein and osteopontin. Other osteoblast secretion products are proteoglycans I and II, related to the growth and change in the diameter of collagen fibres and alkaline phosphatase. A molecule that promotes the formation of mineral crystals in the extracellular matrix and that, together with collagen synthesis, characterise the osteogenic lineage [121-123].

In addition, during the differentiation process of osteoblasts, four cell types can be distinguished

preosteoblasts, covering cells, osteoblasts and osteocytes. Preosteoblasts, as osteoblastic precursors, share some characteristics of the phenotype with osteoblasts, such as the enzymatic activity of alkaline phosphatase, but do not express the secretion products of mature osteoblasts. The covering cells are more inactive than osteoblasts, and with their thin and elongated shape, they cover the bone surface [123-125]. Osteocytes are the type of bone cells that are more abundant, approximately in a ratio 1:9 concerning osteoblasts. They come from mature osteoblasts that are immersed in the mineralised extracellular matrix. In the differentiation process, osteocytes lose the ability to synthesise bone matrix but acquire others, among which blood calcium homeostasis and the control of functional adaptation of the bone. The osteocytes adopt a stellate shape with dendritic cytoplasmic extensions [125-127]. The osteocytes connect through these extensions, and the osteoblasts surround the bone in its covering cell form. These connections create communicating junctions or gap junctions between the cytoplasm of osteocytes and the cytoplasm of osteoblasts. The function of these junctions is to form a network of cells within the mineralised matrix that allows the conversion of external mechanical stimuli into biochemical signals, which control bone deposition and resorption [127-129].

Bone formation, better known as osteogenesis, begins from the vascular structures. Osteoprogenitor cells migrate and gather in the vicinity of a capillary, where they start to differentiate into osteoblasts and secrete the first collagen fibres. These initial fibres are small, have a disordered distribution, and leave ample spaces around the capillary. As this happens, some osteoblasts become osteocytes that begin to secrete inhibitory factors that decrease the rate of bone formation. When the deposition reaches a height of nearly 2 cm, mineralisation begins [129-131]. The mineralisation of this new matrix, known as osteoid, occurs between one and three days after its formation. It is characterised by the nucleation of calcium phosphate crystals and their conversion to HAp, the main mineral of the bone. The release of these first crystals activates a chain reaction that aims to nucleate each collagen molecule present in the new osteoid. Finally, subsequent processes of bone deposition and apposition cause the remodelling of the mineralised matrix that converts the primary matrix into a rigid matrix that complies with the physiological conditions of the bone. Due to this, the complete process of osteogenesis and bone recovery can take between two and six months [130-132].

In case of bone implants, both the synthesis of new osteoid and its mineralisation are related to the surface topography of the implant. Bone implants on their surface must have the ability to withstand the stresses exerted by the cells that migrate over the fibrin and collagen network and restore the injured tissues. It has been identified that this surface must have a micro and nano scale topography that resembles the natural character of the bone. A surface treatment that creates. Such a topography increases the surface area of contact between the bone implant and the tissues in formation. It intensifies the absorption of proteins that stimulate the activation and degranulation of platelets. The fibrin network formation and the migration of osteoprogenitor cells towards the implant surface occur [132-135].

Furthermore, the formation of osteoid on the surface of the implant begins with the deposition of a cementation line that matches a non-collagenous matrix and smoothes the raw surface. This line of cementation intersperses the implant's surface and enables collagen osteoid formation. The differentiated osteoblasts still form the new matrix of the cement line that is mineralised. Implants with smooth surfaces have been observed to have fewer capacities than implants with superficial treatments to retain the new osteoid. Fig. 6 represent a natural life cycle sustainability development of PEEK and its composites, as biomedical materials. The cement line is the bord between the biomaterial and the living tissue that ensures osseointegration [135-138]. The natural healing process ends with the modelling of the interface between the bone and bone. However, the mechanical reaction of the interface is linked with factors such as cell migration and proliferation of the surrounding tissue, cell adhesion and

internal and external action loads. The following section describes each of these factors and highlights the mechanonatural reality of the bone-bone implant interface [138-140].

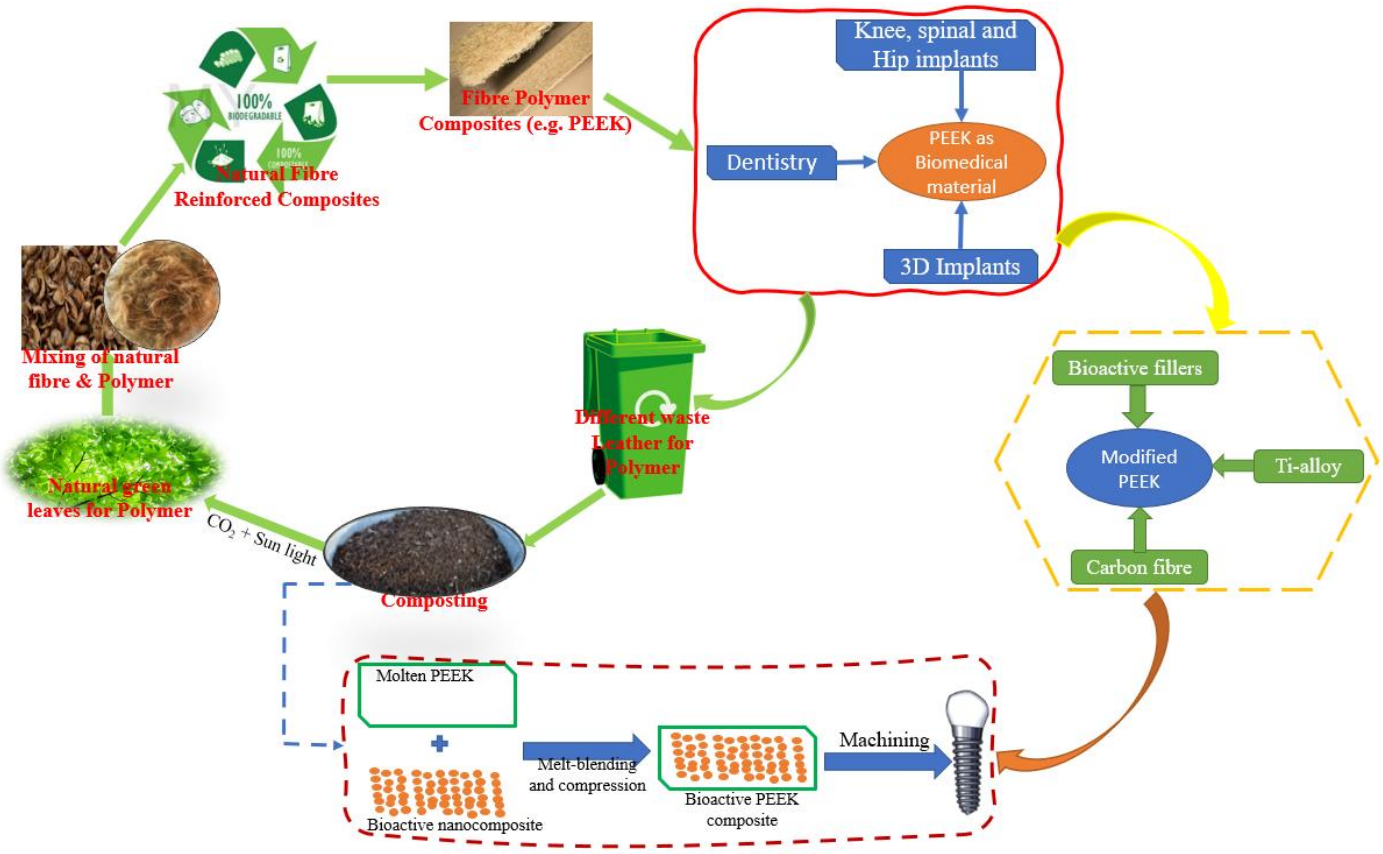


**Fig. 6.** Natural life cycle sustainability development of PEEK and its composites, as biomedical materials.

## 8. Biocompatibility: Macroscale biomaterials

Macrobiomaterials carry out frames that can be implanted and delicate injectable materials. There are unbelievable cooperative energies with hostile immunotherapies for malignant growth. Immunotherapy has helps transporting characteristics, all by itself and usually requires a regularly rehabilitated high-speed infusion, which has real off-tumor effects and limited adequacy. Planned biomaterials normally take into consideration a discreet containment and controlled arrival of immunotherapists. They have been present in a huge number of uses to improve the results of immunotherapy treatment for tumours [140-142]. Macro-scale frameworks for biomaterial transport between different methodologies can appear strong, similar to platforms precisely incorporated in a resection site to discharge modified immune cells.

On the other hand, they can form a delicate gel-like material grafted onto muscle tumours or surgical targets to induce antagonists and tumour-insensitive reactions. Integrated biomaterials of components such as polymers and peptides can participate in any immunotherapy. In a field of state-of-the-art instruments [142-144], from checkpoint inhibitors and stimulant additives to fiercely growing antigen receptor cells. They provided unique cooperation and enhanced repair capabilities. The field has rapidly evolved with written distributions and as biomaterials-based immunotherapy enters clinical trials and human patients. It can be an exciting time for cancer biomaterials and immunotherapy analysts. Other studies seek to understand the more fundamental structural design of the next generation and the future of biomaterials immunotherapy [144-146]. These reports review the latest advances in the transition from limited biomaterials immunotherapy macro level

The expansion of implantable biomedical devices also reveals the potential to reward illnesses and problems in bone lesions Orthopedic surgery. The number of individuals has increased recently, including irritability or deterioration due to bacterial contamination [145-147]. Implantable devices can promote microbes because these microscopic organisms can implant, grow and create biofilms. They facilitate the understanding and mitigation of these phenomena. Biomaterials with antimicrobial specialists that can be drained or introduced into the nearby microenvironment have become the main focus of discovery. This review focuses on the main factors that govern antimicrobial therapy for bone disease sites, such as critical molecular considerations and transport procedures and chains and chains in the body model advancing tides and flows in the field [147-149].

In terms of tissue structure, biocompatibility can be characterised as the coordination of a biomaterial embedded in the host's tissues. Promote tissue healing without provoking an essential hostile neighbour: the exchange between embedded biomaterials and the non-sensitive nature of the host. The effect of the safe host structure on the embedded biomaterial and vice versa is one of the most important factors in the biocompatibility of the implanted material and designs, a premise of the work described [149-151]. Empty spots in this area are two floors. The first is to hide the omnidirectional resistive reaction to prevent safe ignition and direct the host insensitive reaction to a beneficial and good phenotype. PEEK, and its amalgams are a promising material for bone burial due to their high weight ratio, solidity and excellent biocompatibility. Several scientists investigated several PEEK amalgams with good properties with various bones combining various components. Low and non-destructive flex modulus and biosimilarity are some important limits investigated in writing Magnesium (Mg) stands out for its biodegradability. Fig. 7 show analysis of biodegradable synthetic polymer-ceramic composites as well as cHAp and their sustainability. Titanium magnesium (Ti-Mg) compound developed as an excellent competitor for bone implantation due to its low flexibility, consistency, high weight stability and great similarity. The biodegradability of Mg is based on an unprecedented decision to mix with Ti, which provides a solution for tissue growth. However, the weakening of the filler strength after Mg degradation limits Mg to Ti-Mg compounds. Powder metallurgy is emerging as a viable assembly strategy for Ti-Mg compounds. Further end-to-end exploration of the limits of the powder metallurgy process is needed to improve Ti-Mg's properties. In addition, the study of the cracking behaviour of inserts under weak loading is also at an early stage, and there is an extension to explore the future of inserts [48-152].

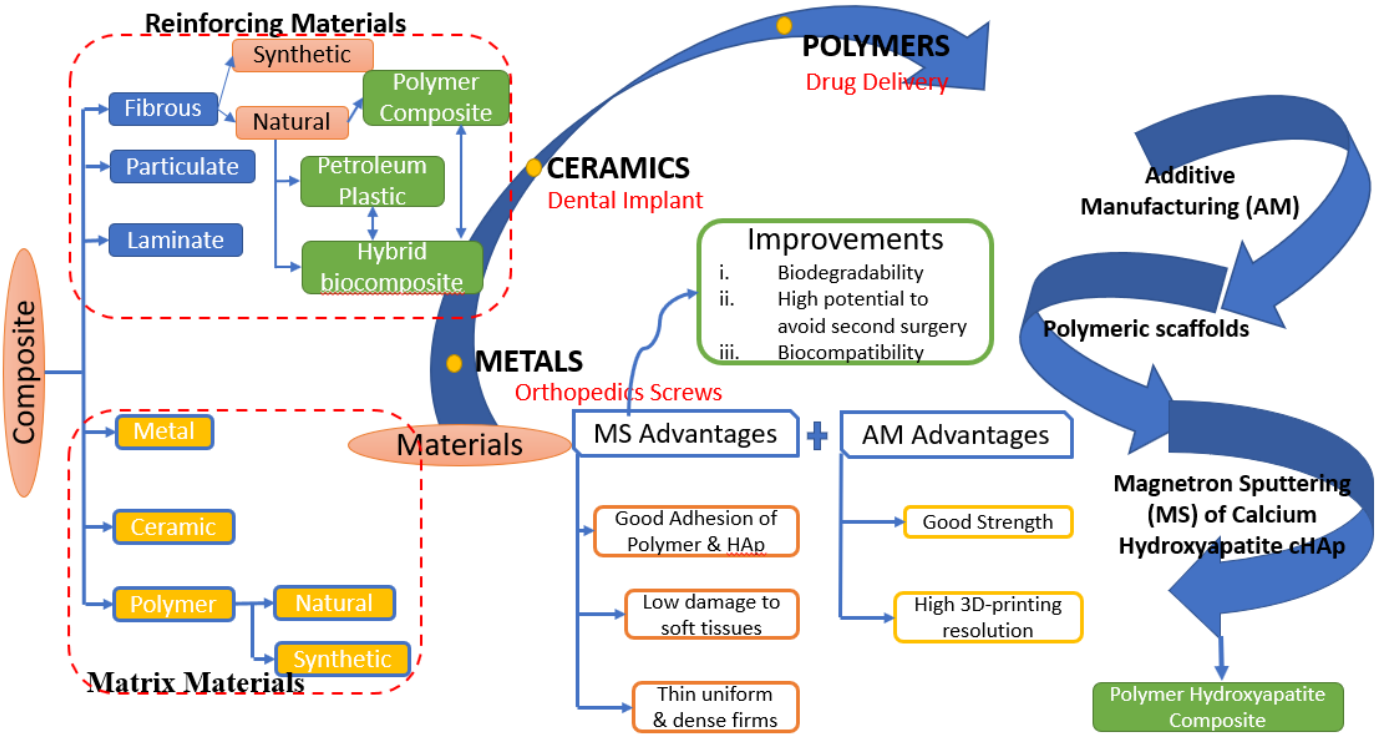


**Fig. 7.** Analysis of biodegradable synthetic polymer-ceramic composites as well as cHAp and their sustainability.

*8.1. Mechanical and cell activity of bone-implant interface*

From a natural perspective, the formation of the implant interface includes a series of tissue and cellular responses, which allow the recovery of injured tissues and the construction of new bone around the implant. However, these natural events are related to mechanical phenomena caused by the activity of cells and dissolved proteins in the extracellular environment and the transmission of external loads necessary for tissue engineering. At the bone-implant interface, the mechanical phenomena can be classified according to their nature, activation, contraction and adhesion mechanisms. Adhesion phenomena are those produced by fixing the cells to a substrate [150-152]. During the healing of the interface, the substrate can be the surface of an implant, the existing tissues or the tissues in formation. Adhesion phenomena are characterised by tensions between the cytoplasm of the substrate of a cell they adhere. This cellular adhesion is divided into two phases: the first approach phase. In a matter of minutes, the ionic and Van der Waals forces govern the physical-chemical interaction between cells and the surface. The second adhesion phase that lasts for several hours involves protein interaction between the cell and the substrate [152-154]. The adhesion process takes place on specific substrates, where the integrins enable the connection between the cytoskeleton of the cell and the extracellular matrix. At these sites, called focal contacts, the integrins clump together and act on the actin chains present in the cell cytoplasm, reducing the distance between the cell and the substrate to around 10-15 nanometers. This new distance creates an adhesion tension with an order of magnitude, which regulates cell capacity for migration, proliferation and differentiation.

In general, the tensile forces created by adhesion phenomena are the first type of mechanical control that exists throughout the healing process of the bone-implant interface. In this first control, the binding action of the integrins acts as the first mechanism that is sensitive to external charges and capable of converting a physical stimulus into a natural response, a process known as mechanotransduction. After adhesion, cells begin to develop changes in their cytoplasm, expanding and increasing the area of contact with the substrate. This expansion activates cell migration and proliferation that create additional stresses. These new stresses are part of the second classification

of mechanical phenomena: contraction phenomena. Contraction is a mechanical phenomenon produced by cells moving around on a substrate. During the bone-implant interface healing, contraction results from cell migration during fibroplasia, angiogenesis and modelling [153-155]. Fibroplastics and modelling adhere to the fibrin network and start moving in an attempt to colonise the implant surface by fibroblasts and osteoprogenitor cells. During this displacement, stresses are exerted on the fibres that may eventually contract the network and separate it from the implant. These stresses have approximately three nN and are associated with the contraction activity created by fibroblasts when differentiating into myoblasts. The contraction phenomena are the cellular movement of products made by concentration gradients in the chemoattractants specific for a cell contingent [154-156]. When there is a chemoattractant gradient, the activated cells exert tensile forces that induce the appearance of multiple focal contacts, which contract the cellular cytoskeleton of actin and finally displace the cell. However, cellular movement is favoured by these concentration gradients, the rigidity topography substrate on which the displacement is carried out. Therefore, any attempt at cell migration on the fibrin network is unsuccessful if there is not adequate cell adhesion. This implies that cell adhesion is a necessary condition for cell migration to exist on a substrate. According to the surface of the substrate, three types of adhesion are considered. In the first type, the surface is not very adhesive, and the cells are not fixed. In the second type, in which the substrate is highly adhesive, the cells lose their ability to move when set. The third type, which has a balance between the adhesion forces, allows cell mobility. This balance is obtained of troops, and there must be a compromise between cell adhesion phenomena and the substrate surface to allow cell migration by the contraction phenomena [156-158]. Recently, the term mechanosensing has been used to refer to the process by which cells, after adhesion to the substrate, exert contraction forces to explore their environment. Integrins are believed to be responsible for regulating mechanisms due to their ability to transmit mechanical stimuli to and from the cell. The appearance of these forces gives rise to the concept of cellular tensegrity. Each cell is in equilibrium regarding the contraction forces generated in the actin cytoskeleton and the compression or reaction forces produced in the focal contacts with the substrate. This fact explains why it is necessary to suture a deep wound to achieve its healing [157-159]. Both tensegrity and mechanosensing are the bases of mechanical action in cell movement processes and help explain mechanotransduction. Fig. 8. represent an example of biocompatibility of PEEK composite in bone-implant

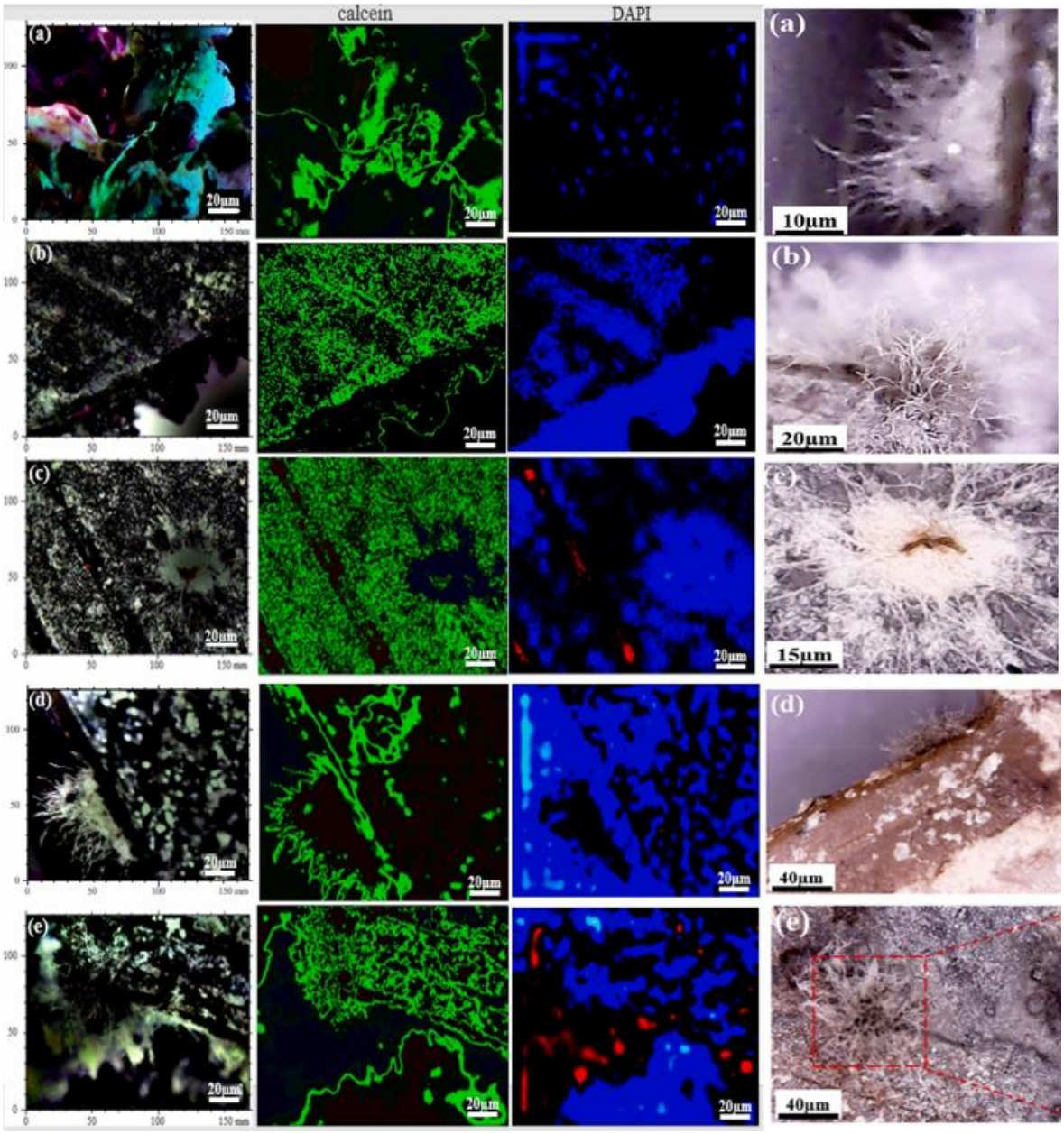


**Fig. 8.** Example of biocompatibility of PEEK composite in bone-implant (a) PEEK tested with Dulbecco's modified eagle medium (DMEM), (b) poly-ether-ether-ketone/reduced graphene oxide/cellular calcium hydroxyapatite (PEEK/rGO/cHAp) tested with DMEM, (c) Nutrient Agar solution tested in PEEK and (d-e) PEEK/rGO/cHAp tested for various days in the nutrient Agar solution. Live/dead colouring of FDM 3D PEEK composite sample surfaces following cultivation of nutrient agar solution: (a) 10 µm PEEK/rGO/cHAp showing cell live growth after 24 hour(s), (b) cell phosphatase expansion and alkalin cells activity for 3rd day PEEK/rGO/cHAp 20 µm, (c) 10 µm PEEK cell dispensing for the 7th day PEEK/rGO/cHAp with minute dead cells (d) the 14th day of PEEK cell propagation and the 14th day of (e-f) the dead cell PEEK/rGO/cHAp [13].

In an external charge, mechanical activation phenomena induce the metabolic activity necessary to bring about structural changes in the extracellular matrix. In the final phase of cure, the bone-implant interface activation phenomena are usually present and constitute bone mechanotransduction. The interaction between the natural function and external loads forms mechanotransduction and explains the functional adaptation to the loads that bone exhibits. Bone mechanotransduction occurs when cells of the bone matrix census external mechanical stimuli produced in response to a series of natural signals that stimulate the production or degradation of the matrix [159-

161]. The cells responsible for controlling this signalling are osteocytes. The interconnection network generated between them provides the cellular structure necessary for the census of mechanical stimuli. Although, the calcified bone matrix surrounds osteocytes, the osteoid mineralisation leaves a space without calcifying in the vicinity of the cytoplasm of each cell and the cytoplasmic extensions through which they interconnect canaliculi. This set of structures make up the osteocyte syncytium, the rationale behind the mechanotransduction mechanism. Through the additional connections that osteocytes have with the capillaries and through a transudation mechanism by pressure gradients. The syncytium of osteocytes is filled with a pericellular fluid that produces a natural hydrostatic pressure [160-162]. The production of biochemical signals similar to those produced by endothelial cells when blood flow increases allow blood vessels to dilate. These biochemical signals include prostaglandins and nitric oxide. Particularly inducing proliferation and differentiation of osteoclasts, cells are responsible for adapting the mineralised bone matrix, while nitric oxide stimulates osteoblastic proliferation [160-163].

Osteocytes remain stable under normal loading conditions due to the continuous exchange of nutrients and waste. Under these conditions, the osteocyte network is tough, and the communicating junctions are functional. In the presence of an overload, the change in fluid pressure stimulates osteocytes to induce osteoblast recruitment and produce new osteoid that recovers mechanical balance. Conversely, when the loading stimulus decreases, for example, during long periods of rest or in states of weightlessness, osteocytes lose the mechanical stimulation produced by the fluid. This causes the viability of the osteocytes to be reduced, and they enter a state of apoptosis. In this case, the need to recover the mechanical stimulus causes the osteocytes to induce osteoclast recruitment and bone resorption to restore balance in the fluid pressure [162-164]. Fig. 9 represent an implantation, showing injection at bone tissue defect and biodegradable polymer nanocomposites for ligament and tendon tissue engineering. A second resorption mechanism is related to repetitive loading stimuli that produces microfractures in the mineralised matrix. These microfractures can damage the interconnections between osteocytes, inducing osteoclast recruitment, bone resorption and subsequent apposition against osteoid to remove damage.

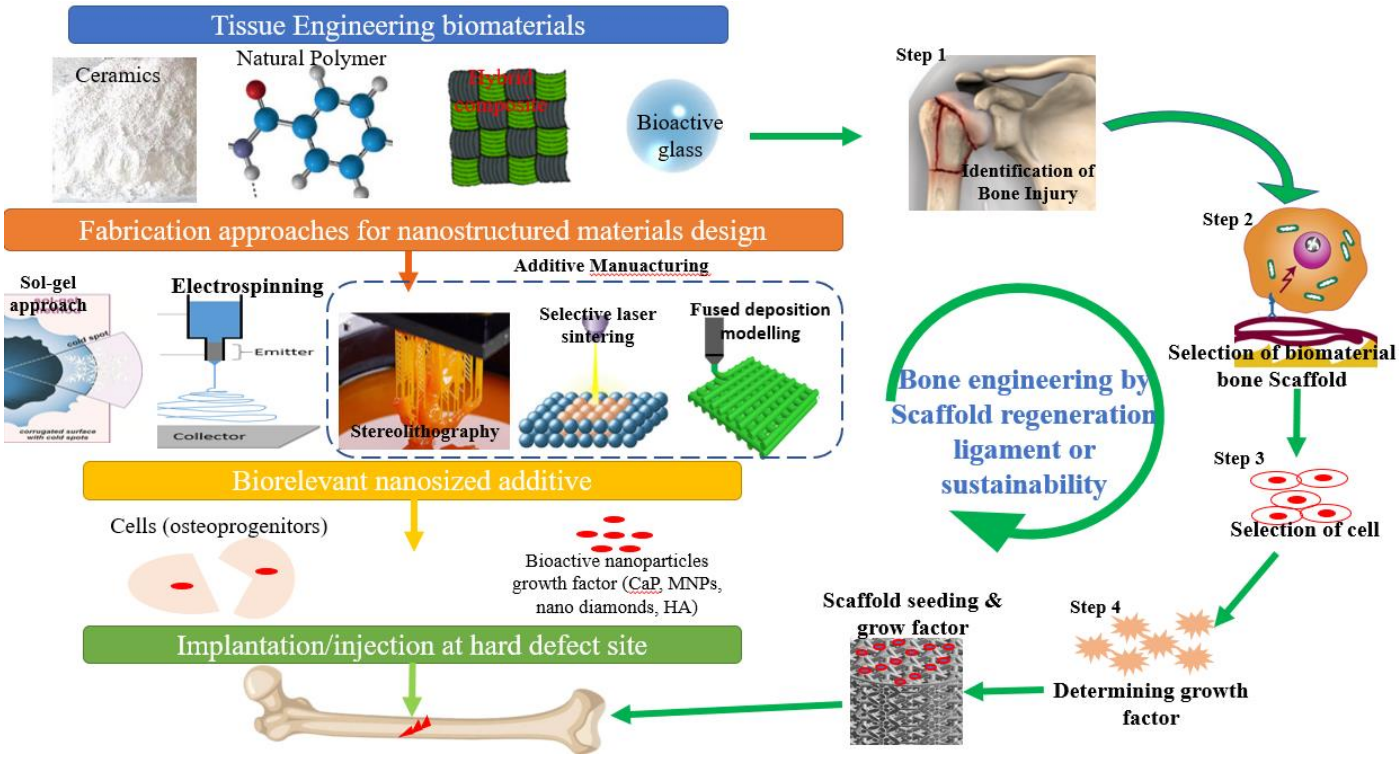

**Fig. 9.** Implantation, showing injection at bone tissue defect and biodegradable polymer nanocomposites for ligament and tendon tissue engineering.

Besides, mechanical stimulation changes the volume and syncytium of the bone matrix from the microstructural point of view, thus altering the hydrostatic pressure that produces the aforementioned biochemical response. This change in the importance of the matrix is controlled by the viscoelastic type response that bone exhibits in response to an external load. Accordingly, the bone acts viscously under low magnitude loads and behaves as a material elastic when it is subjected to loads of great magnitude. This viscoelastic property is due to the maturity of the collagen network and the mineralisation of the HAp. It explains why bone formation depends on mechanical stimulation and is greater when the load is dynamic and less when the load is static [165-167].

Dynamic loads are characterised by their frequencies, which can be in the range of 10 to 100 Hz, because they have an osteogenic effect independent of their magnitude. However, the levels of load magnitude regulate the apposition and resorption of bone and define their functional adaptation. In the case of the bone-implant interface, these loads adjust the viscoelastic property of the new bone and, together with the surface of the implant, increase its biomechanical properties. It is believed that the application of loads that generate stresses between 260 and 410 psi produces maximum bone growth at the interface. In comparison, an effort greater than 710 psi makes pathological resorption of the bone, and an effort less than 220psi induces its atrophy [167-169]. Additionally, the functional adaptation of the bone-implant interface depends on the stability of the implant, determined by the micromovements of the implant. This gives rise to fibrous tissue formation and leads to the loss of stability at the interface and absence of osseointegration, and by the presence of high shear loads magnitude.

Due to the continued existence of mechanical stimuli, the new bone tissue is consolidated, and the bone-implant interface is properly cured. Mechanical stimulation and natural process balance is the anatomical and functional reality that supports mechanobiology as a science that studies the natural action of mechanical stimuli and how tissue architecture impacts [168-170]. Although, much of the knowledge on the subject comes from experimental work. The development of mathematical computational models that analyse numerically natural processes and mechanical phenomena have produced quantitative results over the last years. A proper balance between experimental and computational mechanobiology makes it possible to understand experimental results better and to supply data for mathematical models. Hence, some useful mathematical models are used to formulate a model that expands knowledge of the bone-implant interface and its osseointegration, as subsequently elucidated.

### *8.2. Mathematical modelling*

Both natural and mechanical factors converge at the bone-implant interface; still, most reported mathematical models consider only mechanical factors and conclude the long-term viability of implants, bone load distribution and behaviour. Mechanical aspects of the materials they are manufactured in these models and the formation of the bone-implant interface are neglected. It is assumed that the implants are stable and completely bone-integrated. Some models try to approach the natural phenomenon of healing of the interface, describing the formation of fibrous tissue as a consequence of mechanical variables or from the phenomenological behaviour of the mechanics involved. Fig. 10 showa a parameter values of PEEK/rGo/HAp, showing: i(a) curve extracted the profile of length 144-159 mm, (b) filtered extracted waviness profile of Gaussian filter settings, cut-off of 2.50 mm, (c) extracted profile of length 84.1 mm (upper) as well ii(a) volumetric parameter KL transformed and (b) peak count distribution of KL transformation (lower). Natural-based model descriptions are based on interface phase changes,

changes in cell concentration and density. These include special terms used to describe mitosis, proliferation, differentiation, and apoptosis cellular processes and natural matrix development, transformation and degradation events. [169-171].

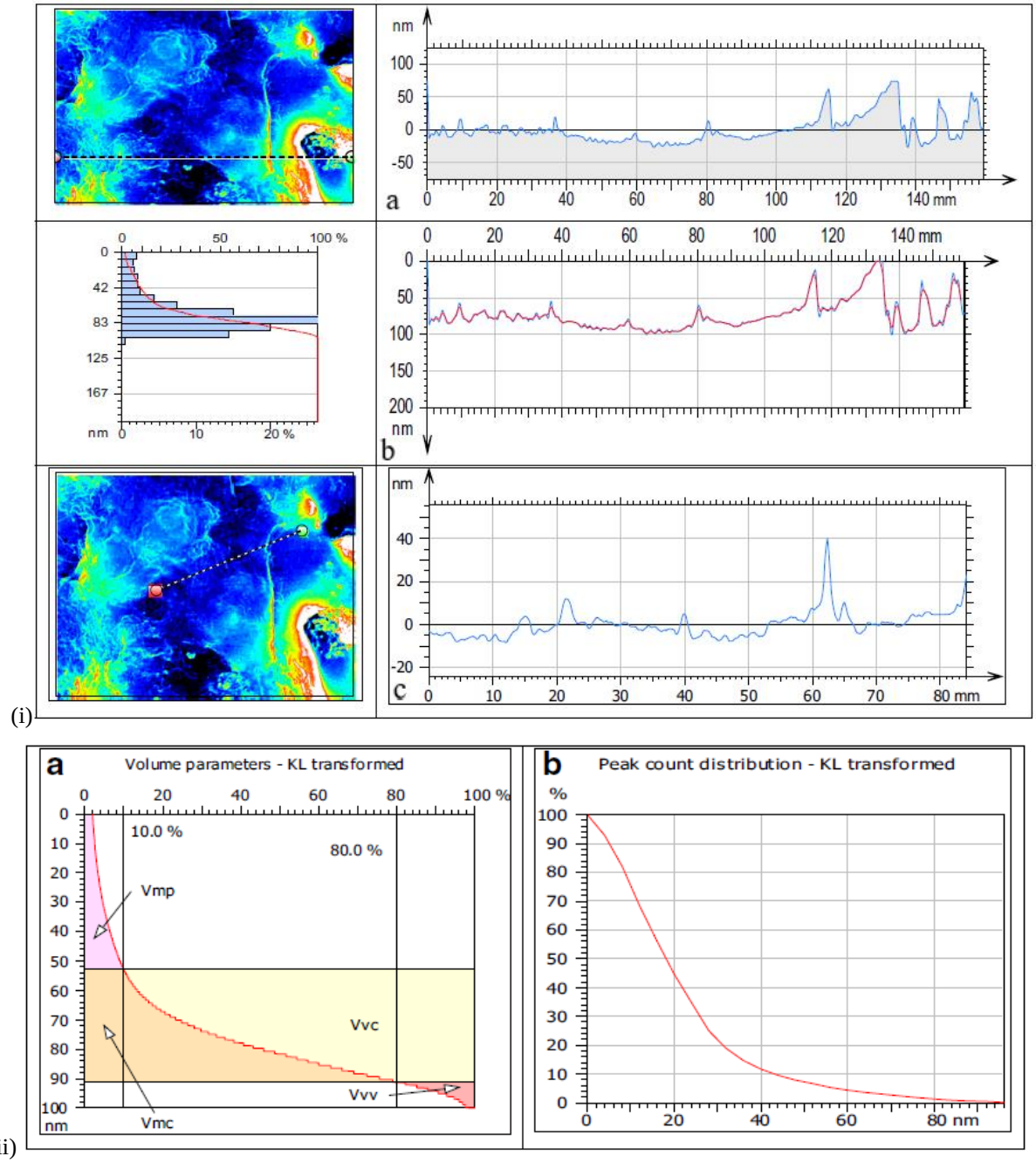


**Fig. 10.** Parameter values of PEEK/rGo/HAp, showing: i(a) curve extracted the profile of length 144-159 mm, (b) filtered extracted waviness profile of Gaussian filter settings, cut-off of 2.50 mm, (c) extracted profile of length 84.1 mm (upper) as well ii(a) volumetric parameter KL transformed and (b) peak count distribution of KL transformation (lower).

The mechanonatural model of the formation and healing of the bone-implant interface is not known. Several authors have reported success in formulating mathematical models that describe some of the interface stages, including the associated natural and mechanical factors. This is the case of cell adhesion and proliferation models, coagulation models, models of cellular angiogenesis and contraction, and models of bone formation. The

following characteristics can be taken into account in forming a complete mechanonatal bone-implant interface model from the reality of natural and mechanical processes of creating and healing the bone-implant interface and the results provided by the above mentioned mathematical models [170-172]. The natural phases of interface healing are to be understood as sequence events of minutes to months on a time scale. Due to combined thrombin and fibrinogen, the bleeding stage is simplified as fibrin clot formation  phase of fibrinolysis could be considered a natural degradation period for clot. In a particular case which leads to a synthesis of a new collagen matrix, fibroplasia and angiogenesis can be simplified at the same time. The formation and substitution of the new osteoid in the collagen matrix are linked to the existence of a specific concentrated osteogenic cell and the presence of a chemical attractant that controls the migration and proliferation of cells [172-174]. The proper bone formation around the implant depends on its topography and the creation of the cementation line. The mechanical phenomena of adhesion can be neglected, considering that cell differentiation and tissue formation directly affect cell adhesion. Fig. 11 represent a **s**teps of development of PEEK, as a biomedical material and bioinspired modifications of PEEK implants for bone tissue engineering and applications of general polymeric. At the macrostructural level the mechanical contraction and activation factors are similar and can be simplified with the viscoelastic behaviour of the fibrin matrix and new osteoid. The loading effects on the implant are negligible when considering a recommended initial healing of 3 to 6 months. These characteristics and the theoretical contribution from a review of the previous research [174-179] allow the formulation of a preliminary model of the formation and healing processes of the polymeric implant interface with body tissue.

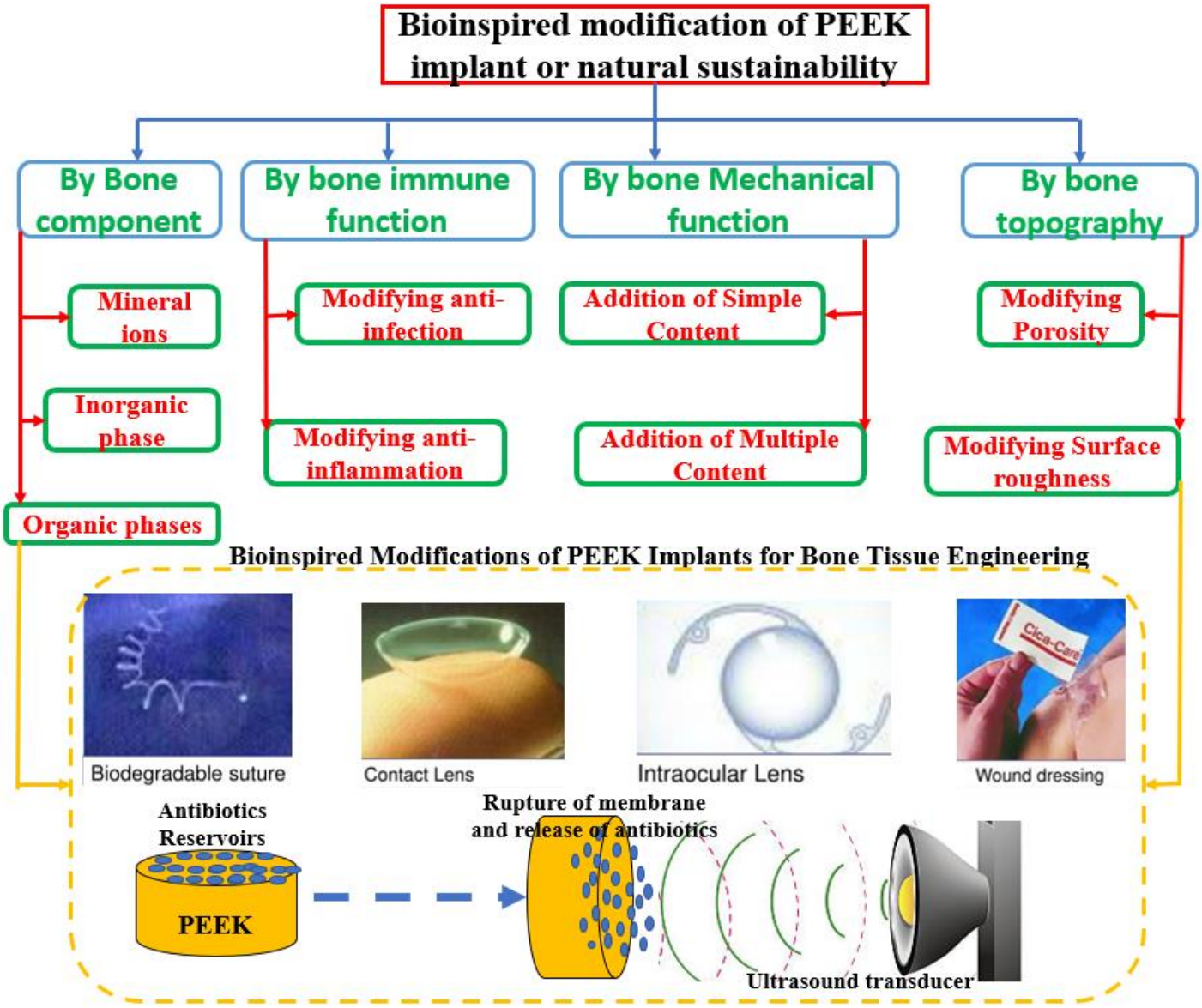


**Fig. 11.** Steps of development of PEEK, as a biomedical material and bioinspired modifications of PEEK implants for bone tissue engineering and applications of general polymeric.

More importantly, as a sequence of stages associate with a number of events, the model simplifies the natural healing process. Bleeding and coagulation steps are therefore simplified as the formation of fibrin-clot by the action of thrombin and fibrinogen conversion reactions. The migration of osteoprogenitor cells begins during fibroplasia, with the action of chemo-attracting substances, while plasmin degrades the fibrin clot. In a single granular tissue stage, a new collagen matrix formation by osteoprogenitor cells simplifies fibroplasia and angiogenesis [179-183]. Fig. 12 show a schematic examples of the applications of PEEK implants in medical orthopaedics. The displacement of osteoprogenitor cells on this matrix causes their contraction, conditioned by a viscoelastic mechanical response and controlled by the properties of collagen. This contraction constitutes the interaction that is made in the model between the natural process and mechanical phenomena. Finally, the synthesis of new osteoid, conditioned by the topography of the implant and the adequate formation of the cementation line, results in the initial osseointegration of implant.

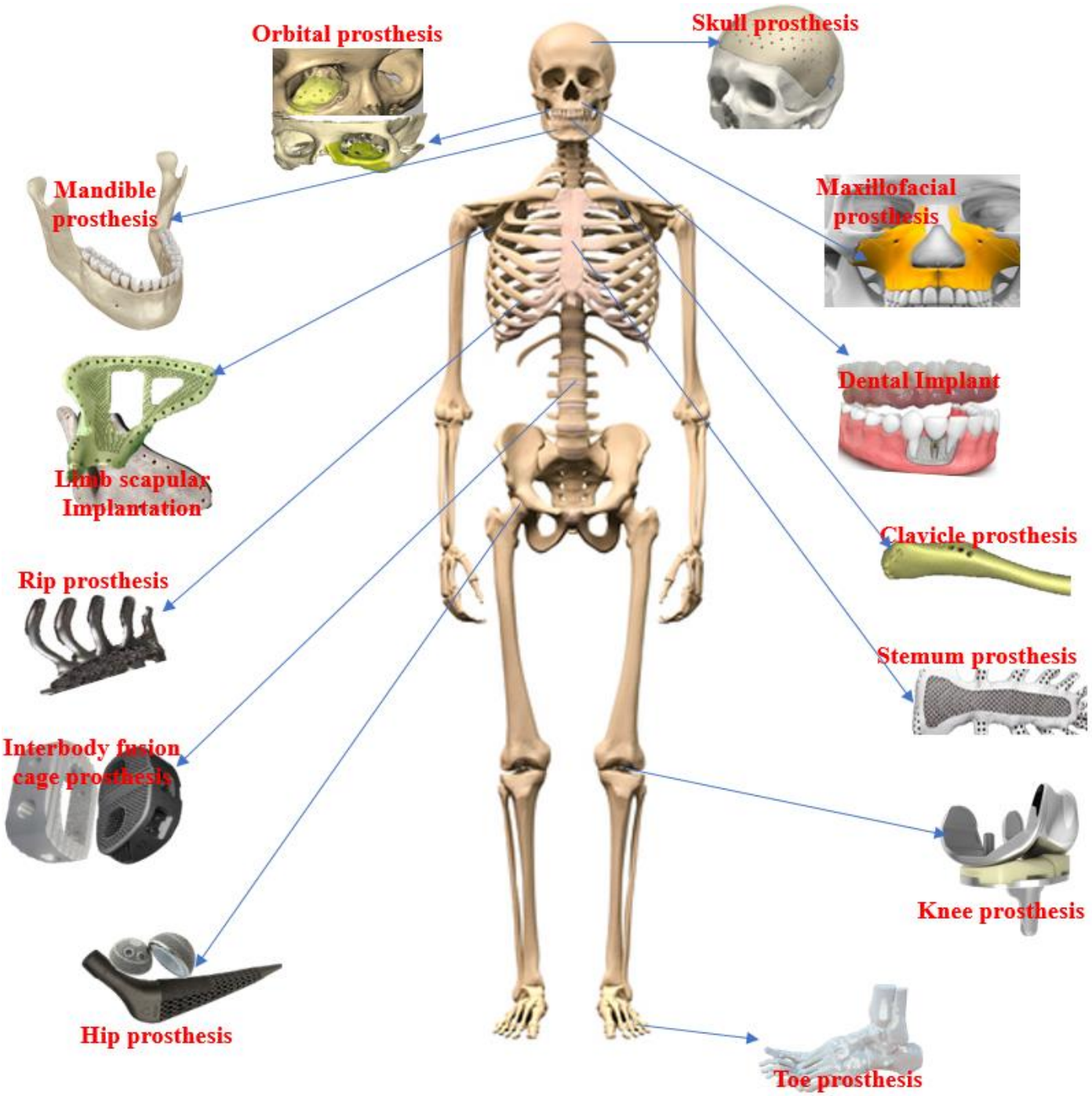


Fig. 12. Schematic examples of the applications of PEEK implants in medical orthopaedics

## 9. Conclusions

PEEK is a high-performance semi-crystalline polymer. It can replace metallic biomaterials, and hence, it has received full attention from the biomedical industry. It exhibits excellent bioactive, mechanical, chemical and structural properties. Also, it is often used for biomedical applications without surface pre-treatment. Therefore, different strategies have been proposed over the years to adapt to the modification of PEEK composites biomedical development for the human body basic needs. The process of formation and healing of the bone-implant interface is highly complex. It involves a wide range of cell types, growth factors, other molecules and a set of mechanical phenomena resulting from internal and external events. Although mathematical models of the complete process are unknown, several works on separate modelling of several natural and mechanical mechanisms related to the bone-implant interface mechanobiology. Therefore, the results and theoretical review presented in this current

study are relevant to all the stakeholders interested in or working on a bone-implant interface to obtain a set of general characteristics required to formulate a mathematical model of the osseointegration of bone implants.

Considering the natural, mechanical and physical properties of PEEK with a combination of some natural, sustainable composite, such as rGO and cHAp similar to bone, PEEK can be used in many biomedical applications. Improving the bioactivity of PEEK composite for implants without compromising their mechanical bioactive properties has a breakthrough in the present research compared with past years of complicated challenges. Further modifications and improving the material properties increase PEEK applications in biomedical engineering. Moving forward, it can be concluded in this research that incorporation of nano-sized particles, such as nano-cHAp using extrusion, melt mixing and coating methods improved the properties of PEEK. The continuous processing method of extrusion can be analysed by modifying the strength configuration and incorporating mixing elements without decreasing the molecular weight of the thermoplastic PEEK significantly. The antimicrobial capacity, mechanical durability, cell compatibility, abrasion resistance and wettability of PEEK and its composites have been similarly elucidated. It was evident that different modification approaches, such as coating and extrusion, are promising methods of manufacturing PEEK composites and 3D printing techniques. To this end, it was discovered that new designs and production of rGO/cHAp reinforced PEEK matrix-supported different bone implants.

It is hereby recommended as a future work that continuous studies on the development of PEEK nanocomposite systems with cHAp, rGO and silver (nAg) powder, among other nanoparticles in different ratios or proportions should be carried out, hoping for an improvement in the physicomechanical and antimicrobial properties of the PEEK composites. Summarily, this present article has reviewed the practical applications of PEEK and its composites, especially in terms of natural and surface modifications. It also highlighted potential approaches to promote scientific interest and future developments in PEEK for biomedical engineering applications.

**References**


[1] Vaezi M, Black C, Gibbs DM, et al. Characterisation of New PEEK/HA Composites with 3D HA Network Fabricated by Extrusion Freeforming. *Molecules*. 2016;21(6):687. Published 2016 May 26.

[2] Kurtz SM, Devine JN. PEEK biomaterials in trauma, orthopedic, and spinal implants. *Biomaterials*. 2007;28(32):4845-4869. doi:10.1016/j.biomaterials.2007.07.013

[3] Peek ME, Cargill A, Huang ES. Diabetes systematic review of health care interventions. *Med Care Res Rev*. 2007;64(5 Suppl):101S-56S.

[4] Gonçalves J, Lima P, Krause B, et al. Electrically Conductive PEEK Nanocomposite Filaments: From Production to Fused Deposition Modeling. *Polymers (Basel)*. 2018;10(8):925. Published 2018 Aug 18.

[5] Lodhia V, Karanja S, Lees S, Bastawrous A. Acceptability, PEEK Mobile Phone mHealth Intervention for Eye Care in Kenya: Qualitative Study. *JMIR Mhealth Uhealth*. 2016;4(2):e30. Published 2016 May 9.

[6] M. Tafaoli-Masoule, M. Shakeri, S.A. Zahedi, H. Seitz, M. Vaezi, 3D printing of PEEK-based medical devices Transactions on Additive Manufacturing Meets Medicine 1 (1) (2019).

[7] Wickramasinghe S, Do T, Tran P. FDM-Based 3D Printing of Polymer and Associated Composite: A Review on Mechanical Properties. *Polymers (Basel)*. 2020;12(7):1529. Published 2020 Jul 10.

[8] Bankole I. Oladapo, S. Abolfazl Zahedi, Sikiru O. Ismail, Francis T. Omigbodun, 3D printing of PEEK and its composite to increase biointerfaces as a biomedical material- A review, Colloids Surf. B: Biointerf., 203 (2021), Article 111726

[9] *Panayotov IV, Orti V, Cuisinier F, Yachouh J. J Mater Sci Mater Med. 2016 Jul; 27(7):118. Epub 2016 Jun 3.*

[10] *Ma R, Tang T. Int J Mol Sci. 2014 Mar 28; 15(4):5426-45. Epub 2014 Mar 28.*

[11] *Abu Bakar MS, Cheng MH, Tang SM, Yu SC, Liao K, Tan CT, Khor KA, Cheang P. Biomaterials. 2003 Jun; 24(13):2245-50.*

[12] B.I. Oladapo, S.O. Ismail, T.D. Afolalu, D.B. Olawade, M. Zahedi, Review on 3D printing: Fight against COVID-19, Mater. Chem. Phys., 258, 123943.

[13] *Ma R, Yu Z, Tang S, Pan Y, Wei J, Tang T. Int J Nanomedicine. 2016; 11:6023-6033. Epub 2016 Nov 14.*

[14] Bankole I. Oladapo, S. Abolfazl Zahedi, Sikiru O. Ismail, Mechanical performances of hip implant design and fabrication with PEEK composite, Polymer19 May 2021

[15] *Morales X, Cortés-Domínguez I, Ortiz-de-Solorzano C. Gels. 2021 Feb 12; 7(1): 17*

[16] *Rodzeń K, Sharma PK, McIlhagger A, Mokhtari M, Dave F, Tormey D, Sherlock R, Meenan BJ, Boyd A. Polymers. 2021 Feb 12; 13(4): 545*

[17] *Cidonio G, Cooke M, Glinka M, Dawson JI, Grover L, Oreffo RO. Materials Today Bio. 2019 Sep 16; 4: 100028*

[18] Gregor A, Filová E, Novák M, et al. Designing of PLA scaffolds for bone tissue replacement fabricated by ordinary commercial 3D printer. *J Biol Eng*. 2017;11:31. Published 2017 Oct 16.

[19] *Zhong G, Vaezi M, Mei X, Liu P, Yang S. ACS Omega. 2019 Nov 5; 4(21): 19238-19245*

[20] Fellmann C, Hoffmann T, Sridhar V, Hopfgartner B, Muhar M, Roth M, Lai DY, Barbosa IA, Kwon JS, Guan Y, Sinha N, Zuber J. Cell Rep. 2013 Dec 26;5(6):1704-13.

[21] O.K Bowoto, B.I. Oladapo, S.A. Zahedi, F.T. Omigbodun, O.P. Emenuvwe, Analytical modelling of in situ layer-wise defect detection in 3D-printed parts: additive manufacturing, Int. J. Adv. Manuf. Technol., 111 (7), 2311.

[22] Khalil HPSA, Jummaat F, Yahya EB, et al. A Review on Tissue Engineering Applications. *Polymers (Basel)*. 2020;12(9):2043.

[23] Han F, Wang J, Ding L, et al. Tissue Engineering. *Front Bioeng Biotechnol*. 2020;8:83.

[24] Peng S, Feng P, Wu P, et al. Graphene oxide as PEEK/HAP tissue engineering scaffolds. *Sci Rep*. 2017;7:46604.

[25] Liao C, Li Y, Tjong SC. Polyetheretherketone. *Polymers (Basel)*. 2020;12(12):2858.

[26] Guillot R, Pignot-Paintrand I, Lavaud J, et al PEEK implants in the rabbit femoral condyle. *Acta Biomater*. 2016;36:310-322.

[27] Bankole I. Oladapo, S. Abolfazl Zahedi, Francis T. Omigbodun, A systematic review of polymer composite in biomedical engineering,European Polymer Journal23 May 2021.

[28] Tite T, Popa AC, Balescu LM, et al. Cationic Substitutions in Hydroxyapatite. *Materials (Basel)*. 2018;11(11):2081

[29] Kersten RF, van Gaalen SM, Arts MP, et al. The SNAP trial. *BMC Musculoskelet Disord*. 2014;15:57.

[30] Ishihama H, Ishii K, Nagai S, et al. An antibacterial coated polymer. *Sci Rep*. 2021;11(1):3602.

[31] Shuai C, Shuai C, Wu P, et al. PEEK/Polyglycolicacid)-HAP. *Materials (Basel)*. 2016;9(11):934.

[32] Kawasaki S, Inagaki Y, Akahane M, Furukawa A, Shigematsu H, Tanaka Y. In PEEK. *BMC Musculoskelet Disord*. 2020;21(1):692.

[33] Bankole I.Oladapo, S. Abolfazl Zahedi, Vincent A.Balogun, Sikiru O.Ismail, Yarjan A.Samad, Overview of Additive Manufacturing Biopolymer Composites, Reference Module in Materials Science and Materials Engineering, 23 March 2021. https://doi.org/10.1016/B978-0-12-819724-0.00035-5.

[34] Uddin MN, Dhanasekaran PS, Asmatulu R. PEEK. *Prog Biomater*. 2019;8(3):211-221.

[35] Rahmitasari F, Ishida Y, Kurahashi K, Matsuda T, Watanabe M, Ichikawa T. PEEK with Reinforced. *Dent J (Basel)*. 2017;5(4):35.

[36] Swaminathan PD, Uddin MN, Wooley P, Asmatulu R. Highly Porous PEEK Bionanocomposites. *Molecules*. 2020;25(16):3572.

[37] Cao L, Chen Q, Jiang LB, et al.. *Int J Nanomedicine*. 2017;12:7197-7205.

[38] B.I. Oladapo, S.O. Ismail, O.K. Bowoto, F.T. Omigbodun, M.A. Olawumi, Lattice design and 3D-printing of PEEK with Ca10 (OH)(PO4) 3 and in-vitro bio-composite for bone implant, Int. J. Biol. Macromol., 165, 50–62.

[39] Shang L, Ma B, Wang F, et al.. *Cell Prolif*. 2020;53(11):e12917.

[40] Dudek K, Dulski M, Łosiewicz B. Functionalization on $SiO_2$-$TiO_2$ Glass Interlayer. *Materials (Basel)*. 2020;13(7):1648.

[41] Vinicius Beserra Dos Santos M, Bastos Nogueira Rocha L, Gomes Vieira E, et al. *Materials (Basel)*. 2019;12(15):2389.

[42] Shirazi SF, Gharehkhani S, Mehrali M, et al. 3D printing. *Sci Technol Adv Mater*. 2015;16(3):033502.

[43] Kadavil H, Zagho M, Elzatahry A, Altahtamouni T.. *Nanomaterials (Basel)*. 2019;9(1):77.

[44] B.I. Oladapo, A.O.M. Adeoye, M. Ismail, Analytical optimisation of a nanoparticle of microstructural fused deposition of resins for additive manufacturing, Compos. Part B Eng., 150 (2018), pp. 248-254

[45] Huang HY, Manga YB, Huang WN, et al. Effect of Hydroxyapatite. *Materials (Basel)*. 2018;11(10):1897.

[46] Dulski M, Gawecki R, Sułowicz S, et al. *Int J Mol Sci*. 2021;22(2):507.

[47] *Graziani G, Bianchi M, Sassoni E, Russo A, Marcacci M. Mater Sci Eng C Mater Biol Appl. 2017 May 1; 74:219-229. Epub 2016 Dec 8.*

[48] *Qadir M, Li Y, Wen C. Acta Biomater. 2019 Apr 15; 89:14-32. Epub 2019 Mar 6.*

[49] *Laskus A, Kolmas J. Int J Mol Sci. 2017 Nov 27; 18(12). Epub 2017 Nov 27.*

[50] B.I. Oladapo, E.A. Oshin, A.M. Olawumi. Nanostructural computation of 4D printing carboxymethylcellulose (CMC) composite, Nano-Struct. Nano-Objects, 21, 100423.

[51] Baykal D, Siskey RS, Underwood RJ, Briscoe A, Kurtz SM. The Biotribology of PEEK. *Clin Orthop Relat Res*. 2016;474(11):2384-2393.

[52] *Turlybekuly A, Pogrebnjak AD, Sukhodub LF, et al. Mater Sci Eng C Mater Biol Appl. 2019 Nov; 104:109965.*

[53] *Mumith A, Cheong VS, Fromme P, Coathup MJ, Blunn GW. PLoS One. 2020; 15(1):e0227232. Epub 2020 Jan 10.*

[54] *Rewak-Soroczynska J, Sobierajska P, Targonska S, Piecuch A, Grosman L, Rachuna J, Wasik S, Arabski M, Ogorek R, Wiglusz RJ. Int. J. of Mol Sc. 2021 Mar 18; 22(6): 3112*

[55] B.I. Oladapo, I.A. Daniyan, O.M. Ikumapayi, O.B. Malachi, I.O. Malachi, Microanalysis of hybrid characterisation of PLA/cHA polymer scaffolds for bone regeneration, Polym. Test., 83, 106341.

[56] Yang HW, Tang XS, Tian ZW, et, al,. Effects of Nano-Hydroxyapatite/Polyetheretherketone-Coated, *Med Sci Monit*. 2017;23:4601-4611.

[57] *Mocanu A, Cadar O, Frangopol PT, Petean I, Tomoaia G, Paltinean GA, Racz CP, Horovitz O, Tomoaia-Cotisel M. Royal Society Open Science. 2021 Jan 13; 8(1): 201785*

[58] *Aslam Khan MU, Abd Razak SI, Al Arjan WS, Nazir S, Sahaya Anand TJ, Mehboob H, Amin R. Molecules. 2021 Jan 25; 26(3): 619*

[59] *Ma R, Tang T. Int J Mol Sci. 2014 Mar 28; 15(4):5426-45. Epub 2014 Mar 28.*

[60] *B.I. Oladapo, S.A. Zahedi, A.O.M. Adeoye, 3D printing of bone scaffolds with hybrid biomaterials, Compos. Part B Eng., 158 (2019), pp. 428-436*

[61] B.I. Oladapo, S.A. Zahedi, F. Vahidnia, O.M. Ikumapayi, M.U. Farooq, Three-dimensional finite element analysis of a porcelain crowned tooth, Beni-Suef Univ. J. Basic Appl. Sci., 7 (2019), pp. 461-464

[62] *Miculescu F, Luță C, Constantinescu AE, Maidaniuc A, Mocanu AC, Miculescu M, Voicu ȘI, Ciocan LT. Journal of Functional Biomaterials. 2020 Nov 15; 11(4): 82*

[63] *Komarova EG, Sharkeev YP, Sedelnikova MB,et. Al,. Materials. 2020 Sep 30; 13(19): 4366*

[64] *Mao AS, Mooney DJ. Proc Natl Acad Sci. 2015 Nov 24; 112(47):14452-9.*

[65] B.I. Oladapo, A.V. Adebiyi, E.I. Elemure, Microstructural 4D printing investigation of ultra-sonication biocomposite polymer, J. King Saud University-Eng. Sci.

[66] *Wubneh A, Tsekoura EK, Ayranci C, Uludağ H. Acta Biomater. 2018 Oct 15; 80:1-30. Epub 2018 Sep 22.*

[67] Becker M, Lorenz S, Strand D, Vahl CF,. *ScientificWorldJournal*. 2013;2013:616535.

[68] *Frith JE, Hudson JE, Cooper-White JJ. Regen Med. 2011 Mar; 6(2):167-70.*

[69] B.I. Oladapo, O.I. Sikiru, Z. Mohsen, K. Affan, U. Hazrat, 3D printing and morphological characterisation of polymeric composite scaffolds, Eng. Struct., Article 110752.

[70] *Olson JL, Atala A, Yoo JJ. Chonnam Med J. 2011 Apr; 47(1):1-13. Epub 2011 Apr 26.*

[71] *Tang X, Qin H, Gu X, Fu X. Biomaterials. 2017 Apr; 124:78-94. Epub 2017 Feb 3.*

[72] Torstrick FB, Evans NT, Stevens HY, Gall K, Guldberg RE. Do Surface Porosity and Pore Size Influence Mechanical Properties and Cellular Response to PEEK. *Clin Orthop Relat Res*. 2016;474(11):2373-2383. doi:10.1007/s11999-016-4833-0

[73] *James EC, Tomaskovic-Crook E, Crook JM. International*

[74] Ma R, Tang T. improve the bioactivity of PEEK. *Int J Mol Sci*. 2014;15(4):5426-5445.

[75] V.A. Balogun, B.I. Oladapo, Electrical energy demand modeling of 3D printing technology for sustainable manufacture, Inter. J. Eng., 29 (2019), pp. 1-8

[76] *Yang DH, Lee DW, Kwon YD, Tissue Eng Regen Med. 2015 Sep; 9(9):1067-77. Epub 2014 Dec 19.*

[77] *Strąkowska P, Beutner R, Gnyba M, Zielinski A, Scharnweber D. Mater Sci Eng C Mater Biol Appl. 2016 Feb; 59:624-635. Epub 2015 Oct 22.*

[78] Ma R, Guo D. Evaluating the bioactivity of a hydroxyapatite-incorporated polyetheretherketone biocomposite. *J Orthop Surg Res*. 2019;14(1):32.

[79] *Pan J, Prabakaran S, Rajan M. Biomed Pharmacother. 2019 Nov; 119:109404. Epub 2019 Sep 14.*

[80] *Panayotov IV, Orti V, Cuisinier F, Yachouh J. J Mater Sci Mater Med. 2016 Jul; 27(7):118. Epub 2016 Jun 3.*

[81] O.P. Bodunde, O.M. Ikumapayi, E.T. Akinlabi, B.I. Oladapo, A.O.M. Adeoye, A futuristic insight into a "nano-doctor": A clinical review on medical diagnosis and devices using nanotechnology, Mater. Today: Proc.

[82] *Letic-Gavrilovic A, Scandurra R, Abe K. Dent Mater J. 2000 Jun; 19(2):99-132.*

[83] Stratton-Powell AA, Pasko KM, Brockett CL, Tipper JL. A Systematic Review. *Clin Orthop Relat Res*. 2016;474(11):2394-2404.

[84] *Rodzeń K, Sharma PK, McIlhagger A, Mokhtari M, Dave F, Tormey D, Sherlock R, Meenan BJ, Boyd A. Polymers. 2021 Feb 12; 13(4): 545*

[85] *Qadir M, Li Y, Wen C. Acta Biomater. 2019 Apr 15; 89:14-32. Epub 2019 Mar 6.*

[86] Selim A, Mercer S, Tang F. Polyetheretherketone (PEEK). *Int J Spine Surg*. 2018;12(2):190-200.

[87] Pang Z, Pan Z, Ma M, et al.. *Int J Nanomedicine*. 2021;16:725-740.

[88] Dai Y, Guo H, Chu L, et al. polyetheretherketone. *J Orthop Translat*. 2019;24:198-208. Published 2019 Nov 21.

[89] *Asensio G, Vázquez-Lasa B, Rojo L. Journal of Clinical Medicine. 2019 Nov 14; 8(11): 1982*

[90] Stratton-Powell AA, Pasko KM, Brockett CL, Tipper JL. A Systematic Review. *Clin Orthop Relat Res*. 2016;474(11):2394-2404.

[91] *Cidonio G, Cooke M, Glinka M, Dawson JI, Grover L, Oreffo RO. Materials Today Bio. 2019 Sep 16; 4: 100028*

[92] Oyane A, Nakamura M, Sakamaki et. Al., surface-functionalisation of PEEK. *PLoS One*. 2018;13(10):e0206524.

[93] Ouellette ES, Gilbert JL. Composite PEEK. *Clin Orthop Relat Res*. 2016;474(11):2414-2427.

[94] *Abu Bakar MS, Cheng MH, Tang SM, Yu SC, Liao K, Tan CT, Khor KA, Cheang P. Biomaterials. 2003 Jun; 24(13):2245-50.*

[95] Bankole, I. Oladapo, Abolfazl S. Zahedi, Improving bioactivity and strength of PEEK composite polymer for bone application, Mater. Chem. Phys. (2021), 10.1016/j.matchemphys.2021.124485

[96] Lee HC, Chen CH, Wu CY, Guo JH, Chen YS. PEEK cage-plate fusion system. *Medicine (Baltimore)*. 2019;98(5):e14277.

[97] Peng S, Feng P, Wu P, et al. Graphene oxide tissue engineering scaffolds. *Sci Rep*. 2017;7:46604. Published 2017 Apr 20.

[98] Guo H, Wang Y, Zhao Y, Liu H.. *BMC Oral Health*. 2020;20(1):201. Published 2020 Jul 10. doi:10.1186/s12903-020-01184-6

[99] Yang J, Sun T, Yuan Y, Li X, Yu H, Guan J. A prospective, multicenter, non-randomised controlled trial. *Medicine (Baltimore)*. 2020;99(30):e21251.

[100] Niu Y, Guo L, Hu F, et al. Activity and Inducing Cell Responses. *Int J Nanomedicine*. 2020;15:2403-2417.

[101] Gao X, Tang K, Xia Y, et al. PEEK Rods for Giant Lumbar Disc Herniation:. *Pain Res Manag*. 2020;2020:3401605.

[102] Kao TH, Wu CH, Chou YC, et. al, PEEK cages: a review of 82 cases and 182 levels. *Arch Orthop Trauma Surg*. 2014;134(10):1343-1351.

[103] Brockett CL, Carbone S, Abdelgaied A, Fisher J, Jennings LM. CFR-PEEK for orthopaedic applications. *J Mech Behav Biomed Mater*. 2016;63:10-16.

[104] Liao C, Li Y, Tjong SC. Polyetheretherketone. *Polymers (Basel)*. 2020;12(12):2858.

[105] Chong E, Mobbs RJ, Pelletier MH, Walsh WR. Early Clinical Outcomes and Fusion Rates. *Orthop Surg*. 2016;8(1):19-26.

[106] Chen Y, Wang X, Lu X, et al. *Eur Spine J*. 2013;22(7):1539-1546.

[107] Liao JC, Niu CC, Chen WJ, Chen LH. Polyetheretherketone (PEEK). *Int Orthop*. 2008;32(5):643-648.

[108] Makino T, Kaito T, Sakai Y, et. al, polyetheretherketone cage in vivo: A pilot study. *Medicine (Baltimore)*. 2018;97(37):e12379.

[109] Yang S, Yu Y, Liu X, et al. *Medicine (Baltimore)*. 2019;98(45):e17935.

[110] B.I. Oladapo, S.A. Zahedi, S.O. Ismail, F.T. Omigbodun, O.K. Bowoto, 3D printing of PEEK–cHAp scaffold for medical bone implant, Bio-Des. Manuf., 1–16.

[111] Qin L, Yao S, Zhao J, et al. Review on Development and Dental Applications of Polyetheretherketone-. *Materials (Basel)*. 2021;14(2):408.

[112] Li ZJ, Wang Y, Xu GJ, Tian P. Is PEEK cage better than titanium cage in anterior cervical discectomy and fusion surgery? A meta-analysis. *BMC Musculoskelet Disord*. 2016;17(1):379. Published 2016 Sep 1. doi:10.1186/s12891-016-1234-1

[113] Cabraja M, Oezdemir S, Koeppen D, et, al,. *BMC Musculoskelet Disord*. 2012;13:172.

[114] Nevelsky A, Borzov E, Daniel S,. *J Appl Clin Med Phys*. 2017;18(2):62-68. doi:10.1002/acm2.12046

[115] de Ruiter L, Janssen D, Briscoe A, Verdonschot N. *Proc Inst Mech Eng H*. 2017;231(12):1204-1212.

[116] Rao PJ, Pelletier MH, Walsh WR, et, al,. *Orthop Surg*. 2014;6(2):81-89. doi:10.1111/os.12098

[117] Cowie RM, Briscoe A, Fisher J, Jennings LM. Wear and Friction of UHMWPE-on-PEEK OPTIMA™. *J Mech Behav Biomed Mater*. 2019;89:65-71.

[118] Delaney LJ, MacDonald D, Leung J, et al.. *Acta Biomater*. 2019;93:12-24.

[119] Rankin KE, Dickinson AS, Briscoe A, Browne M. Does a PEEK Femoral. *Clin Orthop Relat Res*. 2016;474(11):2405-2413.

[120] Carpenter RD, Klosterhoff BS, Torstrick FB, et al. A finite element analysis comparing titanium and PEEK. *J Mech Behav Biomed Mater*. 2018;80:68-76.

[121] Cowie RM, Briscoe A, Fisher J, Jennings LM. PEEK-OPTIMA™ . *Proc Inst Mech Eng H*. 2016;230(11):1008-1015.

[122] Evans NT, Torstrick FB, Lee CS, et al.. *Acta Biomater*. 2015;13:159-167.

[123] Yu H, Chen Y, Mao M, Liu D, Ai J, Leng W. PEEK-biphasic. *Mol Med Rep*. 2018;17(6):8221-8227.

[124] Guo L, Smeets R, Kluwe L, et al.. *Int J Mol Sci*. 2019;20(22):5596.

[125] Paulus AC, Haßelt S, Jansson V, et al. Histopathological Analysis of PEEK. *Biomed Res Int*. 2016;2016:2198914.

[126] Wu X, Liu X, Wei J, Ma J, Deng F, Wei S. Nano-TiO2/PEEK. *Int J Nanomedicine*. 2012;7:1215-1225.

[127] Kurtz SM, Lanman TH, Higgs G, et al. Retrieval analysis of PEEK. *Eur Spine J*. 2013;22(12):2752-2759.

[128] Selim A, Mercer S, Tang F. Polyetheretherketone (PEEK). *Int J Spine Surg*. 2018;12(2):190-200.

[129] Elizabeth Anne Gallagher, Steven Lamorinière, J. of the Mech Beh of Bio Materials, 17 March 2018.

[130] N. Bonnheim, F. Ansari, M. Regis, P. Bracco, L. Pruitt, PEEK,J. Mech. Behav. Biomed. Mater., 90 (2019), pp. 484-492,

[131] J. Day, S.M. Kurtz, K. Ong, Isoelastic PEEK Implants for Total Joint Replacement, (second ed.), Elsevier Inc. (2019),

[132] C.L. Brockett, S. Carbone, J. Fisher, L.M. Jennings, PEEK and CFR-PEEK as alternative bearing materials to UHMWPE in a fixed bearing total knee replacement: an experimental wear study, Wear, 374–375 (2017), pp. 86-91,

[133] A. DAmore, A. Pompo, L. Nicolais, Viscoelastic effects in poly(ether ether ketone) (PEEK) and PEEK-based composites, Compos. Sci. Technol., 41 (1991), pp. 303-325,

[134] S.M. Kurtz, J. Nevelos, PEEK Bearing Materials for Total Joint Replacement, (second ed.), Elsevier Inc. (2019)

[135] M. Regis, A. Lanzutti, P. Bracco, L. Fedrizzi, Wear behavior of medical grade PEEK and CFR PEEK under dry and bovine serum conditions, Wear (2018),

[136] S.C. Scholes, A. Unsworth, Wear studies on the likely performance of CFR-PEEK/CoCrMo for use as artificial joint bearing materials, J. Mater. Sci. Mater. Med., 20 (2009), pp. 163-170

[137] A. Schwitalla, W.D. Müller, PEEK dental implants: a review of the literature, J. Oral Implantol., 39 (2013), pp. 743-749,

[138] A.D. Schwitalla, T. Spintig, I. Kallage, W.D. Müller, Flexural behavior of PEEK materials for dental application, Dent. Mater., 31 (2015), pp. 1377-1384,

[139] A.A. Stratton-Powell, K.M. Pasko, C.L. Brockett, J.L. Tipper The biologic response to polyetheretherketone (PEEK) wear particles in total joint replacement: a systematic review

[140] S. Utzschneider, F. Becker, T.M. Grupp, B. Sievers, A. Paulus, O. Gottschalk, V. Jansson, Inflammatory response against different carbon fiber-reinforced PEEK wear particles compared with UHMWPE in vivo, Acta Biomater., 6 (2010), pp. 4296-4304

[141] F. Chen, H. Ou, B. Lu, H. Long, A constitutive model of polyether-ether-ketone (PEEK), J. Mech. Behav. Biomed. Mater., 53 (2016), pp. 427-433,

[142] F. El Halabi, J.F. Rodriguez, L. Rebolledo, E. Hurtós, M. Doblaré, Mechanical characterisation and numerical simulation of polyether-ether-ketone (PEEK) cranial implants, J. Mech. Behav. Biomed. Mater., 4 (8) (2011), pp. 1819-1832,

[143] L. Hallmann, A. Mehl, N. Sereno, C.H. Hämmerle, The improvement of adhesive properties of PEEK through different pre-treatments, Appl. Surf. Sci., 258 (18) (2012), pp. 7213-7218,

[144] G.Z. Voyiadjis, A. Samadi-Dooki, L. Malekmotiei, Nanoindentation of high performance semi-crystalline polymers: a case study on PEEK, Polym. Test. (2017),

[145] Davood Almasi, Nida Iqbal, Maliheh Sadeghi, et al., Int. J. Biomater. (2016)

[146] R.B. Durairaj, P. Borah, Y. Thuvaragees, Characterization of PEEK coated S.S316 l for biomedical application, ARPN J. Eng. Appl. Sci., 10 (11) (2015), pp. 4794-4798

[147] John W. Durham III, Sergio A. Montelongo, Joo L. Ong, Teja Guda, Matthew J. Allen, Afsaneh Rabiei, Hydroxyapatite coating on PEEK implants: biomechanical and histological study in a rabbit model, Mater. Sci. Eng. C, 68 (2016), pp. 723-731

[148] D. Almasi, S. Izman, M. Assadian, M. Ghanbari, M.R. Abdul Kadir, Crystalline ha coating on PEEK via chemical deposition, Appl. Surf. Sci., 314 (2014), pp. 1034-1040

[149] F.E. Başţana, M.A. Rehmanb, Y.Y. Avcub, E. Avcub, F. Ustela, A.R. Boccaccini, Electrophoretic Co-deposition of PEEK-Hydroxyapatite composite coatings for biomedical applications, Colloids Surf. B Biointerfaces, 169 (2018), pp. 176-182

[150] P.C. Gerszten, E. Paschel, H. Mashaly, H. Sabry, H. Jalalod'din, K. Saoud, Cureus, 8 (9) (2016), p. e775

[151] QQ. Wang, J.J. Wu, A. Unsworth, A. Briscoe, M. Jarman-Smith, C. Lowry, D. Simpson, S. Collins, Biotribological study of, J. Mater. Sci. Mater. Med., 23 (2012), pp. 1533-1542,

[152] P.J. Rae, E.N. Brown, E.B. Orler, The mechanical PEEK with emphasis on the large compressive strain response, polymer, 48 (2007), pp. 598-615

[153] Rupinder Singh, Jaskaran Singh, Ranvijay Kumar, Experimental Investigations for Joining of 3D Printed PEEK Substrates for Biomedical Applications, Ency of Ren and Suste Mat 20 January 2020.

[154] Nishant Ranjan, Rupinder Singh, Inderpreet S. Ahuja, Biocompatible Thermoplastic Composite Blended With HAp and CS for 3D Printing, Encyclopedia of Renewable and Sustainable Materials20 January 2020...

[155] A. J. Ashwin, J. M. Jafferson, State of the art direct ink writing (DIW) and experimental trial on DIW of HAp bio-ceramics, Materials Today: Proceedings, Available online 8 March 2021.

[156] M. M. COSTA, T. A. DANTAS, F. TOPTAN, Corrosion behaviour of PEEK or β-TCP-impregnated Ti6Al4V SLM structures targeting biomedical applications, Transactions of Nonferrous Metals Society of China30 December 2019.

[157] S.M. Kurtz, J.N. Devine, PEEK biomaterials in trauma, orthopedic, and spinal implants, Biomaterials, 28 (2007), pp. 4845-4869

[158] E.M. Feerick, J. Kennedy, H. Mullett, D. FitzPatrick, P. McGarry, Investigation of metallic and carbon fibre PEEK fracture fixation devices for three-part proximal humeral fractures, Med. Eng. Phys., 35 (2013), pp. 712-722,

[159] Sunpreet Singh, Chander Prakash, Seeram Ramakrishna, Plasma treatment of polyether-ether-ketone: A means of obtaining desirable biomedical characteristics, European Polymer Journal21 June 2019

[160] M. Tafaoli-Masoule, M. Shakeri, S.A. Zahedi, H. Seitz, M. Vaezi, 3D printing of PEEK-based medical devices, Trans. Addit. Manuf. Meets Med., 1 (1) (2019)

[161] R.K. Goyal, A.N. Tiwari, U.P. Mulik, Y.S. Negi, Dynamic mechanical properties of Al2O3/poly (ether ether ketone) composites, J. Appl. Polym. Sci., 104 (1) (2007), pp. 568-575

[162] Daniel J. HickeyBess, LormanIra L. Fedder. Improved response of osteoprogenitor cells to titanium plasma-sprayed PEEK surfaces, Colloids Surf. B: Biointerf., 13 December 2018.

[163] J. Bijwe, S. Sen, A. Ghosh, Influence of PTFE content in PEEK–PTFE blends on mechanical properties and tribo-performance in various wear modes, Wear, 258 (10) (2005), pp. 1536-1542

[164] L. Petrovic, D. Pohle, H. Münstedt, T. Rechtenwald, K.A. Schlegel, S. Rupprecht, Effect of βTCP filled polyetheretherketone on osteoblast cell proliferation in vitro, J. Biomed. Sci., 13 (1) (2006), pp. 41-46

[165] Xinke Lv, Xuehong Wang, Jie Wei, Incorporation of molybdenum disulfide into polyetheretherketone creating biocomposites with improved mechanical, tribological performances and cytocompatibility for artificial joints applications, Colloids Surf. B: Biointerf., 21 January 2020.

[166] L. Wang, L. Weng, S. Song, Q. Sun, Mechanical properties, and microstructure of polyetheretherketone–hydroxyapatite nanocomposite materials, Mater. Lett., 64 (20) (2010), pp. 2201-2204

[167] Jiuping Wu, Linlong Li, Peibiao Zhang, Micro-porous PEEK cell adhesion and osteogenic differentiation, Colloids Surf. B: Biointerf., 15 May 2018.

[168] Tao Lu, Shi Qian, Xuanyong Liu, Enhanced osteogenic activity of poly ether ether ketone using calcium plasma immersion ion implantation, Colloids Surf. B: Biointerf., 1 June 2016.

[169] Wanqi Yu, Haibo Zhang, Zhenhua Jiang, Enhanced bioactivity and osteogenic property of carbon fiber reinforced polyetheretherketone composites modified with amino groups, Colloids Surf. B: Biointerf., 7 May 2020.

[170] Lijun Deng, Yi Deng, Kenan Xie, AgNPs-decorated 3D printed PEEK implant for infection control and bone repair, Colloids Surf. B: Biointerf., 2 October 2017.

[171] P. Feng, J. Jia, S. Peng, W. Yang, S. Bin, C. Shuai, Graphene oxide-driven interfacial coupling in laser 3D printed PEEK/PVA scaffolds for bone regeneration. Virtual Phys Prototy, 15 (2020), pp. 211-226

[172] M.M. Hanasono, N. Goel, F. DeMonte, Calvarial reconstruction with polyetheretherketone implants, Ann. Plastic Surg., 62 (2009), pp. 653-655

[173] J.M. Toth, M. Wang, B.T. Estes, J.L. Scifert, H.B. Seim III, A.S. Turner, Polyetheretherketone as a biomaterial for spinal applications, Biomaterials, 27 (3) (2006), pp. 324-334

[174] J.W. Tseng, C.Y. Liu, Y.K. Yen, J. Belkner, T. Bremicker, B.H. Liu, T.J. Sun, A.B. Wang, Screw extrusion-based additive manufacturing of PEEK, Mater. Des., 140 (2018), pp. 209-221

[175] J.M. Toth, M. Wang, B.T. Estes, J.L. Scifert, I.I.I.H.B. Seim, A.S. Turner, Polyetheretherketone as a biomaterial for spinal applications, Biomater, 27 (3) (2006), pp. 324-334

[176] P. Xing, G.P. Robertson, M.D. Guiver, S.D. Mikhailenko, K. Wang, S. Kaliaguine, Synthesis and characterisation of sulfonated PEEK for proton exchange membranes. J. Memb. Sci., 229 (2004), pp. 95-106

[177] C.M. Han, E.J. Lee, H.E. Kim, Y.H. Koh, K.N. Kim, Y. Ha, S.U. Kuh, The electron beam deposition of titanium on polyetheretherketone (PEEK) and the resulting enhanced natural properties, Biomater, 31 (2010), pp. 3465-3470

[178] C. Zhang, G. Zhang, J.L. Vincent, H. Liao, S. Costil, C. Coddet, Microstructure and mechanical properties of flame-sprayed PEEK coating remelted by laser process, Prog. Org Coat, 66 (2009), pp. 248-253

[179] M.M. Kim, K.D. Boahene, P.J. Byrne, Use of customised polyetheretherketone (PEEK) implants in the reconstruction of complex maxillofacial defects, Arch. Fac. Plast. Surg., 11 (2009), pp. 53-57

[180] S. Ramakrishna, J. Mayer, E. Wintermantel, K.W. Leong, Biomedical applications of polymer-composite materials: a review, Compos. Sci. Technol., 61 (2001), pp. 1189-1224

[181] M.R. Abdullah, A. Goharian, M.R. Abdul-Kadir, M.U. Wahit, Biomechanical and bioactivity concepts of polyetheretherketone composites for use in orthopedic implants—a review

[182] C.H. Rivard, S. Rhalmi, C. Coillard, In vivo biocompatibility testing of peek polymer for a spinal implant system: a study in rabbits, J. Biomed. Mater. Res.: Offic. J. Soc. Biomater., Jpn. Soc. Biomater., Austr. Soc. Biomater. Kor. Soc. Biomater., 62 (2002), pp. 488-498

[183] N. Ranjan, R. Singh, I.S. Ahuja, Biocompatible thermoplastic composite blended with cHAp and CS for 3D printing, S. Hashmi, L.A. Choudhury (Eds.), Ref Mod Mater Sci Mater Eng Encycl Ren Sust Mater, 4 (2020), pp. 379-388