Tutor/s

Dr. Vicente Albaladejo Fuentes
Dept. de Ciència dels Materials i Química Física

Dra. Irene Garcia Cano
Dept. de Ciència dels Materials i Química Física

Grau en Enginyeria Química

Treball Final de Grau

Development and evaluation of bioactive glass coatings obtained by thermal spray technology: State of the art.

Manuel Eduardo Montes Álvarez

23 (Jun. 2020)

UNIVERSITAT DE BARCELONA

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

Gracias al departamento, a Vicente y Beatriz por aceptar a un infiltrado de Ingeniería Química y a mi familia.

CONTENTS

SUMMARY

The world of implants is a necessary technological source for humans, but like all technological sources it is progressing. This progress it's related to a constant development of new materials that must comply the biomechanical and biological requirements demanded by an implant, to reduce the number of failed implants, mainly due to infections.

As a booming material, PEEK polymer properties will be described in depth in this study and different methodologies for improving and adapting this material to the needs of an implant will be reviewed.

Due to the fact that this Final Degree Project has been carried out with the support of the Thermal Spraying Center (Materials Science Department), this study will be focused on thermal spraying techniques for biomedical applications, more specifically atmospheric plasma spraying (APS) and cold gas spraying (CGS). Through these process, new materials based on bioactive glasses can be deposited as a coating to improve the bone-implant interaction of PEEK and try to be able to replace the typical commercial coatings formulated with hydroxyapatite.

In the experimental version, the main objective of this project was to prepare and characterize bioglass coatings on a PEEK substrate obtained by cold gas spray, more specifically low pressure cold gas spray (LP-CGS).

Considering that this was not possible, a bibliographic search has been made and the results of other investigations on bioactive glass and hydroxyapatite glass coatings will be compared using the spraying methods above mentioned.

Keywords: Surface engineering, biomaterials, bioglasses, thermal spray.

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

RESUMEN

El mundo de los implantes es una fuente tecnológica necesaria para los seres humanos, pero como toda fuente tecnológica va progresando. Este progreso se traduce en un desarrollo constante de nuevos materiales que han de cumplir los requerimientos biomecánicos y biológicos exigidos por un implante, para reducir el número de implantes fallidos, principalmente debido a infecciones.

Como material en auge se hablará profundamente sobre el polímero PEEK y cómo mejorarlo y adecuarlo según las necesidades del implante.

Al realizar este Proyecto de Final de Grado junto con la ayuda del Centro de Proyección Térmica (Dpto. Ciencia de Materiales) se realizará un estudio detallado de mejoras por proyección térmica, más concretamente de la proyección con plasma (APS) y de la proyección fría (CGS). Mediante estas proyecciones se emplearán, como recubrimiento, nuevos materiales basados en vidrios bioactivos para mejorar la interacción hueso-implante e intentar poder substituir los típicos recubrimientos comerciales formulados con hidroxiapatita.

Como principal objetivo de este proyecto se quería preparar y caracterizar recubrimientos de biovidrios sobre un substrato de PEEK principalmente por proyección fría, más concretamente proyección fría por baja presión (LP-CGS).

Puesto que el trabajo experimental no se ha podido llevar a cabo, el proyecto se ha reconducido hacia una búsqueda bibliográfica en la que se compararán resultados de otras investigaciones sobre recubrimientos de vidrios bioactivos y de hidroxiapatita mediante los tipos de proyección.

Palabras clave: Ingeniería de superficie, biomateriales, biovidrios, proyección térmica.

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

1. INTRODUCTION

1.1 IMPLANTS

Implants are devices or tissues that are placed inside or on the surface of the body. These devices are mainly used as prosthetics implants, when they replace a missing body part. In other cases, implants may act as medication delivers, body functions monitors, or provide support to organs and tissues.

Implants can be made from different materials; which are called biomaterials. The concept of a biomaterial has evolved over time in step with medical advances. In 1987 biomaterial was defined as ‘‘a nonviable material used in a medical device, intended to interact with biological systems’’. This definition still holds true today, but it has been modified. Thus, nowadays a biomaterial is “any substance (other than a drug) or a combination of substances, natural or synthetic, that can be used for a period of time, independently or as part of a system which treats, augments or replaces any tissue, organ or function of the body”. [1]

It is worth highlighting that any biomaterial is suitable for all the applications where they are needed and for this reason, research and development of new biomaterials is continually growing as medicine advances.

1.1.1. Classification of implants

If we pay special attention to orthopedic implants, we might observe that these are diverse and that they can be applied to different parts of the body, shown in Figure 1.

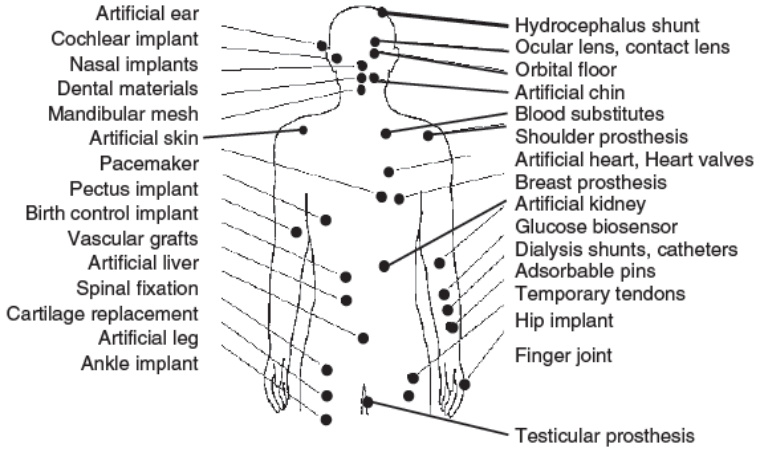

Figure 1.Implants and parts of the body where can be applied

Briefly, they can be classified in many different ways, for instance: [2]

According to their function biomaterials can be classified as follows:

- Orthopedic: artificial hips (Figure 2), knees, shoulders, wrists, intervertebral disks, fracture fixation, bone grafts.
- Cardiovascular: heart valves, pacemakers, catheters, graft, stents.
- Dental: enamels, fillings, prosthetics (Figure 2), orthodontics.
- Soft tissues: wound healing, reconstructive and augmentation, intra-ocular lens.
- Surgical materials: staples, sutures, scalpels, surgical tools.

Figure 2. Example of total hip joint replacement (left) and dental root prosthetic (right)

According to their interaction with the host tissue they can be categorized into:

- Bioactive: The bioactive materials show a specific biological response which makes possible the connections with the host tissue such as cell adhesion, proliferation, or the differentiation of a stem cell that leads to the regeneration of a damaged tissue or whole organ. An example of them are hydroxyapatite, bioglass and glass-ceramics.
- Inert: The inert materials have minimal interaction with the host tissue and stays isolated. For example: aluminum oxide, zirconium oxide.
- Resorbable: The resorbable materials resorbs gradually into the human body. This mechanism varies a lot, from dissolution to hydrolysis or even corrosion. While the implant is resorbing, a new bone tissue is forming in its place. For example: metals such as tantalum, polymers such as polylactides, and ceramics such as silicate-based glasses are accepted as resorbable materials.

According to their nature biomaterials can be classified as:

1.1.1.1. Metals

Metals used as biomaterials have excellent mechanical properties which make them an interesting option in situation when have strength is required. They show some advantages over other materials such as ceramics and polymers, since they are strong, tough and ductile (that is deformable, particularly compared to ceramics). Otherwise, they are susceptibility to corrosion and have high density and much greater stiffness than most natural materials that they try to replace (which lead to undesirable stress shielding).

Table 1 shows a summary of the main metals used for orthopedic implants and their main applications. In agreement with this classification, we can divide metals into:

- Stainless steel: The most used stainless steel implants are based in 316L, a subtype of 316 steel alloy with modified chemical composition. From a material point of view, this alloy shows reduces deleterious carbide precipitation, are inert and have excellent corrosion resistance. In addition, 316L is not magnetic, more ductile than titanium (Ti shows a hexagonal crystal structure with low ductility) and has great biocompatibility. Unfortunately, they have high percentage of nickel in its composition (10-14%), which

can provokes negative tissues response and dermatitis and its hardness may lead to the generation of stress fractures and a delay in the healing process.

- Cobalt-chromium alloys: These alloys are composed by Co, Cr, Mo, W, Ni and Fe. Its main characteristics are their extremely high hardness, thermal and corrosion resistance in body fluids and a greater wear resistance compared with the titanium implants. As disadvantages, we can find that Co-alloys have low biocompatibility due to the release of metal ions after being exposed to body fluids for a long period of time andexpensive because of processing difficulties.
- Titanium and titanium alloys: In this group we found the most used kind of metals for orthopedic implants: pure titanium, Ti6Al4V and β-titanium alloys. The advantages of theses alloys are that they have high strength, hardness and inertness joined by a very low material density. As a negative part they show low wear resistance, processing difficulties (Ti is not a very ductile material) and they do not show antibacterial activity, consequently a bacteria can easily stick to their surface.
- Nitinol: It's an alloy formed by nickel and titanium which contains 48-52% of nickel. It has high corrosion resistance and high biocompatibility in contrast with titanium alloys but is susceptible to galvanic corrosion due the high nickel content coupled to titanium, which can produce allergic and carcinogenic reactions.
- Magnesium alloys: Magnesium is characterized by unique qualities since it is the lightest of all structural metals. They have high strength, good heat and electric conductivity. They have high biocompatibility, are non-toxicity and resistant to corrosion. In comparison with other materials; Mg-alloys are stronger than polymers, more ductile than bioceramics and in addition, bioactive. By the moment reactions to the human body (like toxicity, allergies and osteointegration) are not yet examined in detail, however in preliminary results it has not been observed that the implanted magnesium alloys had any negative consequences for the patients.

Table 1. Main metals used in biomedical implants

Metal	Uses
Stainless steel	Prosthetic joints, dental implants, cranial implants, load-bearing orthopedic, pacemaker, bone fixation, heart valves, electrodes
Cobalt-chrome alloys	Orthopedic prostheses, joint replacements, bone fracture fixation, cables
Titanium and titanium alloys	Joint replacements, dental bridges and dental implants, coronary stents
Nitinol	Eyeglasses, coronary artery stents
Magnesium alloys	Biodegradable implants

1.1.1.2. Ceramics and glasses

Ceramics used as biomaterials, and in general, are characterized for being hard, brittle and insoluble in water. These properties can be related to their atomic structure. Ceramics are composed of atoms that are ion-covalently bonded into composite shapes.

Are very biocompatible (particularly with bone), are inert, have low wear rates, are resistant to microbial attack, are strong in compression, have high corrosion resistance and hardness, low friction, low thermal and electrical conductivity, do not cause allergic reactions and do not show signs of cytotoxic effect. Nevertheless, these kinds of materials have some disadvantages such as brittleness, difficulties in processing and fabrication, the potential to fail catastrophically and being difficult to machine. In Table 2 are shown some examples of ceramics (and glasses) used for medical applications and the specific uses for orthopedic implants.

Table 2. Main ceramics and glasses used in biomedical implants

Ceramics and glasses	Uses
Aluminum oxides	Hip implants, dental implants, cochlear replacement
Zirconia	Hip implants
Calcium phosphate (such hydroxyapatite)	Bone graft substitutes, surface coatings on total joint replacements, cell scaffolds
Calcium sulfate	Bone graft substitutes
Carbon	Heart valve coatings, orthopedic implants
Glass	Bone graft substitutes, fillers for dental materials
Bioglasses	Synthetic bone graft for orthopedic and periodontal

1.1.1.3. Polymers

In general, polymers are a family of materials that perfectly suit in biomedical applications because of their diverse properties. Polymers are materials with high molecular weight composed of long hydrocarbon chains, which can be flexible or rigid, can be low strength or high strength depending on their composition. Modifications of the hydrocarbon chain composition makes possible to tailor the bio-properties of the polymer: for instance, they might be resistant to protein attachment or can be modified to encourage protein attachment, biodegradable or permanent. Additionally, their low melting point allows to fabricate these materials into complex shapes by many methods. On the bad side, they deform with time, may deteriorate during sterilization, and may degrade in the body catastrophically or by release of toxic by-products. In contrast with other materials polymers have lower strengths than metals or ceramics. Despite of these disadvantages, polymers can be used widely as shown in Table 3.

Table 3. Main polymers used in biomedical implants

Polymers	Uses
Nylon	Sutgical sutures, gastrointestinal segments, tracheal tubes
Silicone rubber	Finger joints, artificial skin, breast implants, intraocular lenses, catheters
Polyester	Resorbable sutures, fracture fixation, cell sscaffolds, skin wound coverings, drug delivery devices
Polyethylene (PE)	Hip and knee implants, artificial tendons and ligaments, synthetic vascular grafts, dentures, and facial implants
Polymethylmethacrylate (PMMA)	Bone cement, intraocular lenses
Polyvinylchloride (PVC)	Tubing, facial proyheses
Poly dimethyl siloxane	Artificial heart valves
Polycaprolactone	Resorbable synthetic sutures, bolts, bone plates
Polyaryletherketone (such PEEK)	Orthopedic, trauma, and spinal implants and arthroplasty joint.

1.1.1.4. Natural materials

Natural materials are those groups of materials which are synthesized by an organism or plant. They are normally more complicated than synthetic materials. In comparison with polymers, natural polymers have high mechanical properties and high elastic modulus of synthetic polymers due the directional bonds within proteins chains. For example, the ultimate tensile strength of silk is higher than that of drawn nylon, one of the strongest synthetic polymers and the elastic modulus of silk is nearly thirteen times that of the elastic modulus of nylon. Compared to ceramics, natural ceramics are typically much tougher (resistant to fracture) than synthetic ceramics due to their highly organized microstructure which prevents crack propagation. In general, natural materials have a lower incidence of toxicity and inflammation as compared to synthetic materials. Conversely, they are expensive to produce or isolate. Their uses are shown in Table 4.

Table 4. Main natural materials used in biomedical implants

Natural materials	Uses
Collagen and gelatin	Cosmetic surgery, wound dressings, tissue engineering, cell scaffold
Cellulose	Drug delivery
Chitin	Wound dressings, cell scaffold, drug delivery
Ceramics or deminetalized ceramics	Bone graft substitute
Alginate	Drug delivery, cell encapsulation
Hyaluronic acid	Postoperative adhesion prevention, ophthalmic and orthopedic lubricant, drug delivery, cell scaffold

1.1.1.5. Composites

Composites are materials that contains at least two different constituent materials, different in their nature that are separated by a distinct interface. In composites, there is a main and continuous material, matrix, and a discontinuous phase that is typically harder and stronger than the continuous phase and is called the reinforcement. The final material performance is a combination of the constituent materials properties.

All the above-mentioned materials possess their own characteristics and combining them can lead to a decrease of their disadvantages, for these reasons, composites are becoming more widely used in biomedical applications. The properties of composites can be changed to adjust to almost any application and improve some issues related to cell adhesion and direct bone fixation, for instance. Special attention is necessary to understand feasible problems with dispersion of the second phase or weak interfacial bonds between the two phases which leads to non-expected mechanical properties and, hence, poor performance. Table 5 shows the main uses of these materials.

Table 5. Main composites used in biomedical implants

Composites	Uses
Fibre reinforced polymer composites	Bone healing, orthopedic protheses
Bioactive composite bone cements	Dental practice
Composites in general	Soft tissues replacements, medical equipment and instruments

1.1.2. Requirements of implants [4]

The requirements specified for implants are very strict, due to the fact that in the human body they are exposed to the aggressive effect of body fluids (enzymes, organic acids, etc.) and external factors.

The selection of a material for this application depends on the role that the implant will play in the body. According to this, the materials must show some specific properties. The most important to take into account are: the mechanical loading requirements (such as tensile strength, hardness, elasticity, suitable density, wear resistance, etc.), chemical and structural properties of the material and the biological requirements.

Besides, materials used for fabrication of implants should do not change after a long period of contact with the biological environment since this would lead to cause cell death, chronic inflammation or damage of the functions of the cells.

Some tips/rules that FDA say to take a good implant are [27]: The material should be strong enough so that the device does not fracture under physiologic loads. The material should have an appropriate stiffness so that the device can flex and move (or not move) as intended. If the device incorporates an articulating joint or bearing surface, the material should be able to appropriately withstand wear, so that the device does not functionally break down.

As an example of the high diversity of requirements of implant we could find out that a material used for vessel reconstruction should have high flexibility, whereas, for hip prosthesis the materials should have mechanical strength and high corrosion resistance.

All the above-mentioned considerations show that the creation of biocompatible materials and the construction of implant devices is a difficult task.

1.1.3. Failures in implants [3]

There have been dramatic changes in understanding of the level of interaction of biomaterials with the biological system. Failure is defined as an inability to fulfill a predefined set of criteria. Wear, fatigue, creep, corrosion and loosening are all pathways that failure takes. In this section is included a review of the main factors and causes that lead to failure of implants. Table 6 summarizes the most important failure mechanisms correlated with failure rate, time, and testing techniques.

Table 6. Failures in implants

Failure mechanism	Failure rate	Prosthetic parts susceptible	Time to produce failure postsurgery
Wear	8%	Any	10-15 years
Fatigue	5%	Metallic parts	10-15 years
Creep	3%	Polymeric parts	<1 year
Corrosion	2%	Metallic parts	-
Aseptic loosening	75%	Any	10-20 years
Septic loosening	7%	Parts with surface roughness	<1year

1.1.3.1. Wear

Excessive wear is a cause of failure. Wear is the mechanism by which the material particles are removed by its microscopic roughness due to contact and relative movement between two objects that are in contact. This further affects the orthopedic devices that are involved in joint replacement. In addition to leading to failure, the release of wear particles is found to contribute to the formation of pseudotumors. Some ways to detect wear are radiography, MRI, CT scans, and blood work.

1.1.3.2. Fatigue

Fatigue is a cyclic process (this cyclic process is sinusoidal between a maximum and a minimum stress) in which microscopic cracks are formed in a material as a consequence of the aplication of consecutive and cycling loads to the material. This problem appears significantly in joint replacements and drasctically decreases the lifetime of the orthopedic device. This type of failure can be characterized as very dangerous due to the difficulty for detecting it.

1.1.3.4. Creep

Creep is considered a time-dependent deformation generated even at low loads that is produced when a load is applied over a material which is kept at a temperature above 40% of its melting point (in degrees kelvin). It mainly affects polymers due they have a lower melting point than metals and ceramics, but some metallic alloys can show this kind of issue. Creep can cause shift of implants components to undesirable locations or orientations, which can lead to detrimental effects such as loosening of the orthopedic device and finally failure.

1.1.3.5. Corrosion

Corrosion is not cited at all as a kind of failure but it accelerates other processes such as wear and fatigue. It is the reaction of the surface material, how it shows Figure 3, with the environment that is sourrinding it within the human body. This mechanism occurs due to the dynamic electrochemical nature of the human body. It mainly affects metals due there are many cations and anions available to react. This can lead to undesired modifications such changes in the geometry of the device, unfavorable changes in pH and other local environment effects. The combination of these factors leads to an immune response by the host and can jeopardize the integrity of the device.

1.1.3.6. Loosening

Loosening takes place in sites where the device is not mechanically fixed. Occurs due to the loss of tight contact between the host tissue and the implant via two modes: aseptic and septic.

- Aseptic loosening occurs by either mechanical loss of fixation of the orthopedic device, biological loss of fixation, or inadequate initial fixation Figure 3 shows an example of this. It can be mechanical or biological.

- Sepsis loosening occurs due to pathogens (viruses, bacteria, etc.).

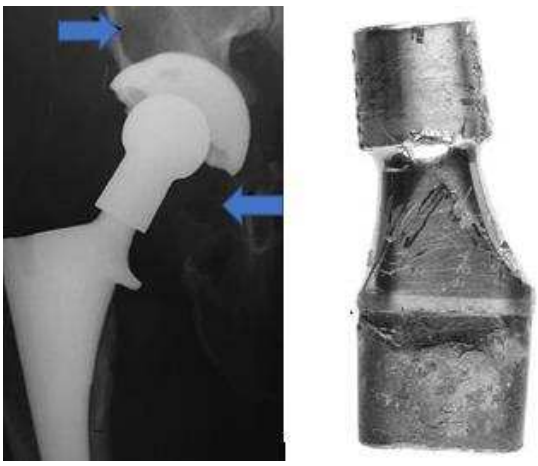

Figure 3. Example of a total hip replacement, blue arrows denote bone tissue loss (left) and a corroded implant (right)

In this introduction has been carried out a short description of orthopedic implants, materials used in this application and their requirements and feasible failures, in following sections, this work will focus on describing an specific kind of biomaterials, PEEK, and its opportunities in biomedical applications. After this, it will be shown some methodologies used for preventing the failures above-mentioned from occurring, based on physical and chemical modifications of the material surface and the benefits that ceramics like hydroxyapatite and bioglasses can bring to PEEK implants. Finally, two thermal spraying techniques will be explained and it will be made a short review of the main results found in literature regarding the use of these processes for modifying the surface activity of PEEK implants.

2. POLYARYLETHERETHERKETONE (PEEK)

Polyaryletheretherketone, commonly referred as PEEK, is a member of the polyaryletherketone polymers (PAEK's). PAEK is a family of high-performance thermoplastic polymers. PEEK is classified as a linear homopolymer. The structure of PEEK monomer is

represented in Figure 4, which consists of an aromatic backbone molecular chain, interconnected by ketone and ether functional groups.

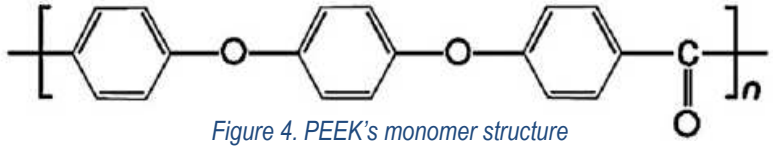

Figure 4. PEEK's monomer structure

PEEK its conformed by the model of a two-phase semi-crystalline polymer, consisting of an amorphous phase and a crystalline phase. Like many semi-crystalline polymers, the crystalline content of PEEK varies depending upon its thermal processing history (is typically processed at 390 ºC temperature flow transition (Tf)). The crystalline content varies in the range 0–40% and other properties are shown in Table 7. In this polymer there is a high relationship between mechanical properties and crystallinity grade, crystal size and orientation of the crystalline regions. PEEK with high crystallinity will result in a material with high modulus and yield stress. Polymer toughness and elongation are typically controlled by crystal size and the mobility of the amorphous phase, it is useful to characterize the crystalline content of implant components fabricated from PEEK. Thus, controlling crystallinity, crystal sizes and their orientation it will be possible to adjust PEEK properties to the final application. Despite of this, the actual size and extent of crystals in PEEK is a function of several variables during synthesis, including processing temperature, time, cooling rate and post-production annealing. [27]

Table 7. PEEK properties

Property	PEEK properties
Molecular weight [10^6 g/mol]	0.08-0.12
Poisson's ratio	0.36
Specific gravity	1.3
Young's modulus [GPa]	4
Elastic modulus [GPa]	3-4
Tensile strength [MPa]	93
Tensile elongation [%]	30-40

Testing conducted at 23ºC

The structure of PEEK confers to the polymer outstanding chemical resistance. The aryl rings are interconnected via ketone and ether groups located at opposite ends of the ring. The resonance stabilized chemical structure of PEEK results in delocalization of higher orbital electrons along the entire macromolecule, making it: extremely unreactive and inherently resistant to chemical and radiation damage. This inherent inertness of PEEK also explains its biocompatibility and compatibility with many reinforcing agents (such as glass and carbon fibers), because of its distinctive aromatic chemical structure. And due his resistance to gamma and electron beam radiation damage PEEK components can be sterilized by gamma irradiation in air.

Its stability, biocompatibility, radiolucency, mechanical properties (such ductility) and elastic properties (relatively unaffected by rate effects at body temperature, which is below the temperature glass transition (Tg) 143 ºC) make PEEK a suitable biomaterial for orthopedic and spine implants.

2.1. **SYNTHESIS OF PEEK**

In literature there are two main routes involved in the production of PAEKs. The first method involves linking aromatic ether species through ketone groups which involves an electrophilic reaction and Friedel Crafts acylation chemistry. Second method involves linking aromatic ketones by an ether bond which involves a nucleophilic displacement reaction.

The main method to the production of PEEK is the nucleophilic route and can be processed using a variety of commercial techniques, including injection molding, extrusion and compression molding.

2.2. **CLINICAL APPLICATIONS OF PEEK [6]**

By the late 1990s, PEEK had emerged as the leading high-performance thermoplastic candidate for replacing metal implant components, especially in orthopedics and trauma. Furthermore, due to the lubrication, friction and wear of PEEK composites, their use as support materials and flexible implants used for joint arthroplasty is being investigated. Finally, PEEK biomaterials research has also focused on enhancing biocompatibility of the polymer with tissues by including hydroxyapatite (HA) as bioactive component of the material, either as a composite filler or as a surface coating, in order to improve implant fixation and interaction with tissue.

Clinical applications of PEEK can be classified in:

2.2.1. Spine implants

The clinical application in which PEEK is used most is in the spine implant due their advantages over metals. PEEK radiolucency allows visualization of the critical soft tissue structures, such as the spinal cord, adjacent to the implant components. The versatility of PEEK biomaterials allows to design spinal devices with a tailored range of stiffnesses, depending on rigidity desired for a particular application.

PEEK was typically used in spine implants by cages from fusion surgery (Figure 5). This kind of surgery results in unnatural movement at adjacent levels and new implant technologies are still needed to preserve the normal movement in the spine. Consequently, a variety of new implant technologies have developed to preserve, limit, or enhance motion of the spine. Posterior dynamic stabilization devices and cervical and lumbar artificial discs are some of them.

For more mature fields, such as total joint replacements and fracture fixation implants, radiolucency is an attractive but not necessarily critical material feature.

2.2.2. Trauma implants

The first trauma implants used were metallic plates, but they present problems such corrosion and the reduction in bone quality adjacent to the plate caused to stress shielding. Thus, researchers focused their interest about high-performance, thermoplastic polymers, due to their mechanical performance, isoelasticity and thermoformability to increase the fit of the fracture fixation plates to the bone anatomy on patients in the operating room. Among thermoplastic polymers, including nylon 6-10, PBT and PS, PEEK stands out since exhibits the highest fracture toughness, bending fatigue resistance and good compatibility with the carbon fibers.

In spite of this, metallic locking plates and intramedullary nails continue to dominate the field of internal fracture fixation.

2.2.3. Femoral stems

PEEK biomaterials in orthopedics are currently in a period of consideration and conservative adoption as alternative to the traditional metal, ceramic, and polymer implants currently used for total hip and knee replacement (Figure 5).

There are still some problems associated with polymer-metals composites for orthopedics implants, being the most important the mechanical loosening of the implant.

Despite of this fact, recent studies with polymers are revealing clinical evidence of reasonably sustained fixation and reduced stress shielding when compared with traditional metallic stems. PEEK have proven to be the only polymer with the requisite combination of mechanical properties, biocompatibility, manufacturability, and consistent availability throughout this time period.

2.2.4. Arthroplasty bearing surfaces

The CFR-PEEK composite has been shown to be effective as a support material for hip replacement in the short term but not in the long term as other well-established support alternatives such as UHMWPE, MOM or COC.

However, this provides the necessary basis for considering CFR-PEEK, even in the short term, in joint replacement designs such as hip rejuvenation.

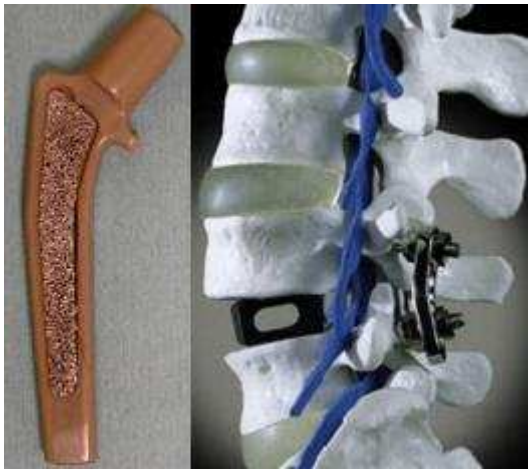

Figure 5. Example of canine hip stems (left) and CFR-PEEK lumbar fusion cage used in concert with posterior screws and rods (right)

In resume due to its structure, PEEK has perfect properties to be applied as an implant, as can be seen in Table 8 where the PEEK's modulus and density are closer than typical metal used in implants values to the natural bone. It has had the greatest clinical impact in the field of spine implant design. For more mature fields, such as total joint replacements and fracture fixation implants, it is only with the challenges of new designs, such as with isoelastic stems and hip resurfacing, that PEEK biomaterials can offer an attractive opportunity. Although PEEK's new designs are encouraging, there is still a long time before these novel approaches can be considered superior to their successful historical predecessors.

Table 8. Comparison between properties of PEEK, bone and Ti alloy Ti-6Al-4V

Property	PEEK	Bone	Ti alloy Ti-6Al-4V
Young's modulus [GPa]	4	10	80-125
Density [g/cm^3]	1.3	1.5	4.6

3. SURFACE FUNCTIONALIZATION OF IMPLANTS

Infection is one of the most serious complications from the use of implanted medical devices. For effective orthopedic procedures such as joint replacements, the average infection rate remains relatively low (<5%). For revision hip arthroplasties, infection rates can be as high as 10% and for trauma cases involving open wounds, infection rates can increase to 21%. In spinal fusions, infection is a significant risk (8.5% in primary and 12% in revisions).

Regarding this point, it is found the importance that modern biomaterials such as PEEK arouse to reduce the infection risk and control the degree of tissue reaction.

There are two main and broad categories of strategies in biomaterial designing with the goal of achieving high infection resistance materials. First strategy is based on the incorporation of agents into the biomaterial allowing elution and eradication of any contaminating bacteria in the vicinity of the implant. Agents antimicrobial such conventional antibiotics or silver, gold, and

copper, are used for its antimicrobial performance. Second one consists on the modification of surface material to minimize bacterial adhesion. It is worth indicating that this last strategy can also be applied for solving other issues related to infections. Thus, by surface modification is possible to improve the implant integration with bone which will lead to a decrease of infection possibilities [5]. This methodology is what our work consists of.

The success of any implant material is to a great extent governed by: i) the bulk properties of the implant material that controls its mechanical performance and; ii) its surface structure and chemistry that determines the biological response. When an implant is placed in the body, the first molecules to reach the surface in a biological environment is water, which is adsorbed. In case of PEEK, the orientation of the polar water molecules on the surface is influenced by the surface properties of the polymer (surface structure, chemistry, charge, and wettability). The subsequent protein interactions are consequently influenced by the orientation of these initially adsorbed water molecules. The implant will quickly come in contact with blood plasma proteins, and this adsorbed protein layer influences cellular interactions. The surface of a material is therefore integral in controlling the cell-surface interactions.

In order to improve surface wettability by body fluids, it is well established that surfaces with higher energy (surface energy should be above that of the wetting fluid) are known to promote rapid cellular adhesion and spreading, in contrast to surfaces with lower energy.

The bio-inert properties and low surface energy of PEEK in the orthopedic favor the growth of soft tissues around the PEEK implant instead of bone growth as it can be seen in the Figure 6. This low surface energy, as a result of a relatively hydrophobic surface, can limit cellular adhesion due to the orientation of cell adhesion proteins, for this fact bone is not found to form a direct chemical bond with the PEEK.

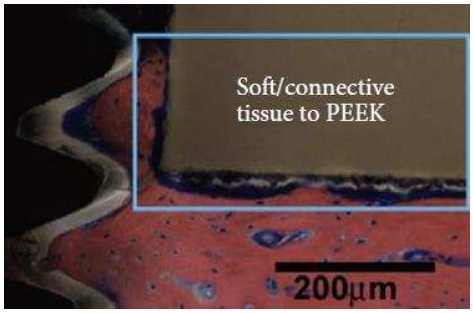

Figure 6. Growth of soft/connective tissue around PEEK

Therefore, the ultimate aim of changing the surface of a biomaterial, in orthopedic implants is to create a surface that is optimal for the application that is, promotes the bone growth, but without affecting the bulk properties of the material.

There are a wide number of methods to change the surface of a material, and these can be broadly divided into two categories: i) direct surface modification techniques and, ii) deposition techniques. Some examples for these two categories are shown in Figure 7. [10]

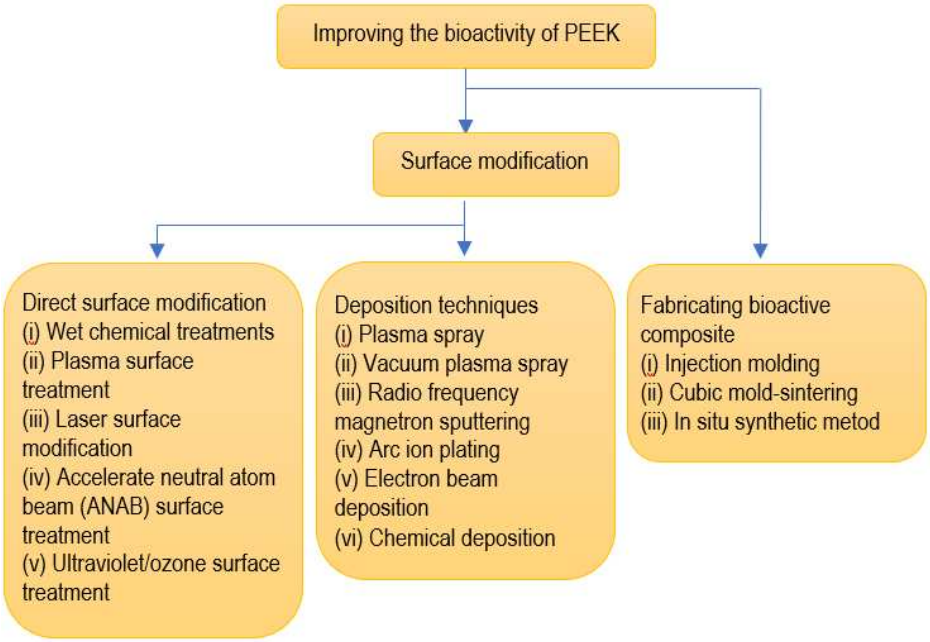

Figure 7. Methods for improve the bioactivity of PEEK

3.1. **WHAT IS USUALLY COATED ON THE IMPLANT?**

There are specific biological and chemical criteria that must be taken into consideration when modifying surfaces for biomaterials applications. Was above indicated, cell proliferation on a surface depends on surface characteristics such as wettability, surface and bulk chemistry, the ratio of hydrophobicity to hydrophilicity, surface charge and distribution, rigidity, and surface roughness. [11]

Ideally, a material for orthopedic applications has to be osteoconductive, that is, it will encourage the attachment and growth of bone cells and the formation of new bone. Coatings have been incorporated into orthopedic implants in order to modulate the surrounding biological environment of the implant as they may facilitate osseointegration and mitigate possible adverse tissue responses, including the foreign body reaction and implant infection.

Among the coating properties to pay attention to in biomedical applications, chemical purity, surface roughness, coating thickness and coating adhesion are considered the key characteristics. [7]

3.1.1. Chemical purity

Which Increases the solubility of the coating when immersed in physiological buffer solutions.

3.1.2. Surface properties

Like roughness and porosity since human osteoblasts have been shown to adhere more easily to surfaces with a roughness less than 0.5 μm than to surfaces with a roughness greater than 2 μm. However, rougher or more porous surfaces can provide more opportunities for mechanical fixation of the surrounding bone.

3.1.3. Thickness

The ideal thickness is a compromise between the coating's mechanical strength and its resorption rate.

3.1.4. Adhesion strength and mechanical properties

The adhesion strength of a coating to its substrate is important. The method of depositing a mineral coating is largely responsible for the resulting adhesion strength of the coating.

Therefore, it is also important to consider other mechanical properties that can influence the behavior of mineral coatings, such as Young's modulus in tension and compression, residual stress and hardness. These properties are also highly variable depending on the coating production method and processing parameters.

Taking these key characteristics into account, following sections have been focused on analyzing more deeply the role of mineral coatings such as bioglasses and calcium phosphate coatings in orthopedic implant, with special attention to commercial 45S5 bioglass and hydroxyapatite compounds respectively.

3.2. **HIDROXYAPATITE**

Hydroxyapatite (HA) is a natural mineral with formula $Ca_5(PO_4)_3(OH)$. This mineral has excellent biocompatibility and osseointegration ability in body environment. Hydroxyapatite coatings have great potential as they allow exploiting the mechanical properties of substrate, while utilizing the biocompatibility and bone bonding properties of the ceramic.

The inorganic component of bone is a calcium phosphate mineral closely resembling to the chemical composition of HA (hydroxyapatite), for this reason HA is shown as an osteoconductive material. However, the mechanical properties of this kind of calcium phosphates are quite poor compared to bone, as it can be seen in Table 9, and this makes them unsuitable for its use as the main implant material under load.

Table 9. Comparison of human bone, hydroxyapatite and bioglass 45S5 properties

Property	Human bone	Hidroxyapatite	Bioglass 45S5
Young's modulus [GPa]	7-30	70-120	0.035
Density [g/cm^3]	1.5-2.0	3.16	2.7
Tensile strenght [MPa]	50-150	40-100	42
Compressive strength [MPa]	100-230	100-900	500
Fracture toughness [MPa m$^{1/2}$]	2-12	0.8-1.2	0.6

The most common coating techniques for the deposition of HA coatings are: sol–gel, sputtering, pulsed laser deposition, and thermal spraying. Among them, only thermal spraying, and in particular, plasma spraying, is a commercially accepted method by Food and Drug Administration (FDA).

As expected, deposition of HA on PEEK implants surfaces has been investigated in order to improve the poor polymer osteointegration previously described. In Table 10 are shown some of the studied areas where HA has been coated on PEEK and besides, a brief summary of the results and/or conclusions obtained.

Table 10. Conclusions of the studies of the composite HA/PEEK for orthopedic implants

Composite material	Studied areas	Results
HA	Biocompatibility and bioactivity study of the produced composite via in situ synthetic method	Produced composite showed nontoxic and the bioactive properties.
	In vitro bioactivity study of HA/PEEK composite produced by selective laser sintering method	Improvement in bioactivity of the composite and higher content of HA exhibited higher bioactivity rate

3.3. **BIOGLASSES**

This family of materials, bioglasses (BG), was found out as the first material to form a bond with bone. The atomic structure is everything to a glass, since it determines all its properties, and for this application especially its bioactivity and degradation rate. A glass i's an amorphous material with tetrahedral silicate coordination units linked in all the three-dimensional space. The amorphous “structure” is a consequence of the defects generated due to the incorporation of cations (for instance sodium or calcium) in the lattice which break the tetrahedral silicate bonds. The structure of a glass can be represented as a mixture of oxides, for instance Na_2O–CaO–P_2O_5·SiO_2 (in mol% 24.35 Na_2O, 26.9 CaO, 2.57 P_2O_5, and 46.1 SiO_2). [8]

In agreement with HA, deposition of BG onto PEEK surfaces has been also evaluated in order to and in Table 11 are shown the results and the studied areas where BG has been coated onto PEEK implants.

Table 11. Results of the studies of the composite BG/PEEK

Composite material	Studied areas	Results
BG	Biocompatibility and bioactivity study of the produced composite via laser sintering method	Produced composite via laser sintering method was nontoxic. PEEK/carbon/bioglass composite showed improvement in the bioactive property.

3.3.1. Bioactive glass surface mechanism

The mechanism for dissolution and bone bonding of a bioactive glass proposed by Larry Hench is a multi-stage process involving the following steps showed in Figure 8. When a bioglass

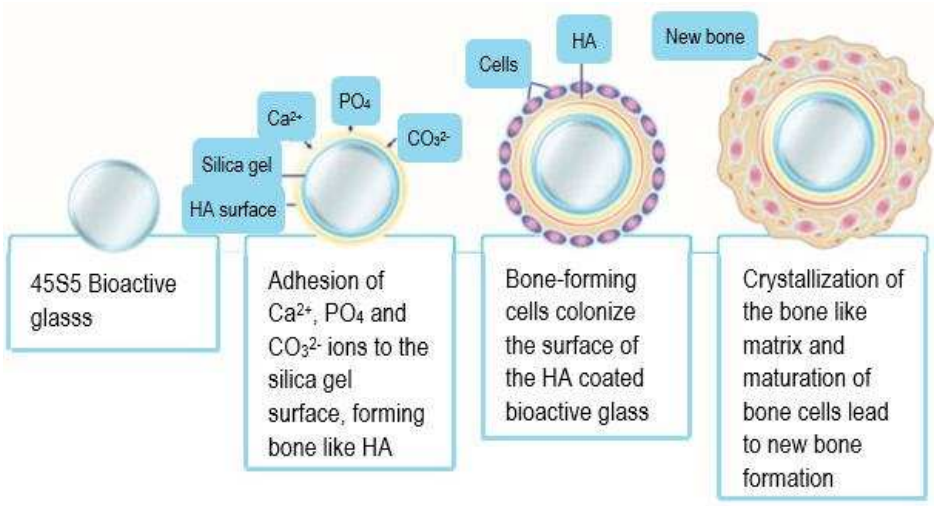

Figure 8. Bioactive glass surface reaction

is implanted (introduced into the human), the glass degrades slowly and the dissolution products stimulate progenitor cells to start a pathway that leads to bone cell (osteoblast) generation, that is, they increase the growth of bone cells. This phenomenon is called osteoinduction. The BG (bioglass) bonds to existing bone (osseintegrates) and encourages new bone growth along its surface (osteoconductive). Bone bonding is due to the formation of a calcium phosphate (hydroxyapatite, HA) layer on the glass surface, which happens in the first few hours after implantation.

BG have poor mechanical properties (as shown in Table 9) which means that they cannot be implanted into load-bearing bone defects as main material. For these reasons, they are more often used for repairing defects that are surrounded by host bone.

The crucial requirement to assure a chemical bond with the surrounding tissues is related to the ability of the coating to form a biologically active hydroxyapatite layer on its surface. A glass or glass-ceramic coating gives several interesting advantages with respect to the uncoated substrate:

(i) It avoids substrate corrosion and degradation.

(ii) It protects the surrounding tissues from adverse interactions with the degradations products of the substrate.

(iii) It promotes the bioactive fixation of the implant to the living bone, inducing its osteointegration.

(iv) It is easier to modify a glass coating rather than a metal implant to deliver ions such as antibacterial silver or to functionalize the glass surface with drugs or growth factors.

Several methods can be used to coat a substrate with a glass or glass-ceramic layer: enameling, glazing, plasma spraying, spin casting, sputtering, electrophoresis, and pulsed laser ablation. Each of them has several advantages and disadvantages, beside different features, in terms of compositional homogeneity, coating thickness, ease of application, and tailoring of properties.

4. SURFACE FUNCTIONALIZATION BY THERMAL SPRAYING

There are several different methods of producing mineral coatings, all of them with their advantages and disadvantages. Furthermore, by changing the processing parameters used in each method, it is possible to produce a wide array of coatings. In the following table (Table 12) is shown a summary of the existing deposition methods/materials for improving PEEK bioactivity.

Table 12. Deposition methods/materials for improve PEEK bioactivity

Deposited material	Deposition method	Area of studies	Findings
HA	Plasma spraying	Crystallographic compositions, adhesions and microstructures of HA coating on different PEEK specimens were studied and compared with HA coating on Ti-6Al-4V	Almost the same structure of HA coatings for both substrates. Plasma spraying method does not have negative effect on mechanical properties of PEEK
TiO_2	Arc ion plating	In vitro study via osteoblast	Improvement in cell adhesion, proliferation and differentiation
Ti	Plasma spray	In vivo study	Enhancement bone-to-implant contact ratio
DLC	Plasma immersion ion implantation and deposition	In vitro study via osteoblast	Enhancement of attachment, proliferation and differentiation of osteoblast
BG	LP-CGS	This TFG project.	Unexplored.

The goal of this project, in the experimental version, was to explore the opportunities of thermal spraying, and specifically, Low Pressure Cold Gas Spray (LP-CGS) for preparing bioglass coatings onto PEEK surface. Taking this into account, in the following sections is carried out a description of the main aspects of the thermal spraying techniques used for these applications and in addition, a short review of the studies found in bibliography related to this topic.

4.1. **ATMOSPHERIC PLASMA SPRAY (APS)**

The atmospheric plasma spray process uses a high voltage that causes the gas ionization which provokes the formation of a direct current electric arc to generate a high temperature ionized plasma gas. This high temperature ionized plasma gas, which acts as the spraying source of heat, expands and escapes through the open end of the gun to form a very hot, high-velocity plasma jet [9].

In a plasma spraying gun, for creating this plasma, gases such as Ar, H_2, He, N_2 or mixtures of them, are injected into the "chamber" space between two cylindrical electrodes (Cu anode and W cathode, both are water cooled) where a high intensity discharge creates de plasma. The end of the gun which is shaped as a constricting nozzle join by the high gas flow is responsible of the formation of a high temperature jet. A schematic diagram of plasma spraying equipment is shown in Figure 9.

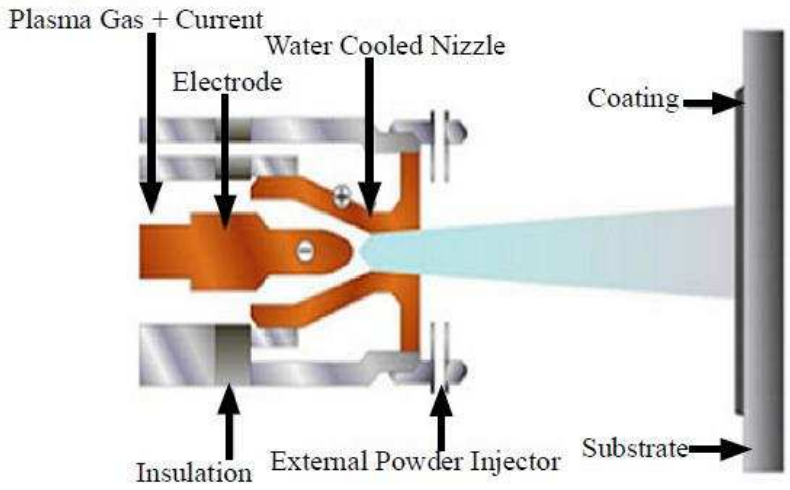

Figure 9. Atmospheric plasma spray process

The coating material, in powder form, is carried into the plasma jet using an inert gas stream where it is heated and propelled towards the substrate. The position of the powder injector can vary; it can be placed inside the spraying gun or at its end outside the plasma jet. The high dissociation and ionization energies confer to the plasma jet a lot of energy; this way, plasma torch can produce temperatures in the range between 7000 and 20000 °C although the exit plasma temperature range goes from 5000 to 6000 °C. These high temperatures and velocities are responsible of the powder particle adhesion onto the substrate. As a result of the particle impact, the particle shape is deformed, and lamellae coating is formed. This technique allows preparing coatings with different microstructures which properties are strongly dependent on:[12]

- Spraying equipment (type of torch, gun configuration, process gases, pressure);
- Type, density and viscosity of the material;
- Chemistry, morphology, particle size distribution of the feedstock material;
- Temperature and thermal energy;
- Kinetic energy (particle impact speed);
- Powder injector position, powder injection angle, powder impact angle;
- Coating spraying parameters (flow rates, voltage, amperage, plasma and carrier gas flows,);
- Processing variables (spraying distance, spraying trajectory, cooling system);
- Substrate surface activation and cleaning;
- Surface area;
- Chemical-physical properties (solidification speed) of both coating material and substrate.

Table 13. Atmospheric Plasma Spraying parameters

Parameters	APS parameters
Net energy [kW]	Up to 650
Materials	Powder (ceramics, metals, polymers)
Jet Temperature [ºC]	Up to 20000
Spraying rate [kg/h]	up to 8
Powder feeding angle [º]	75-105

An example of the most common plasma spraying parameters for plasma spraying are given in the Table 13.

Plasma spraying has the advantage that due to the high energy values reach into the jet, this technique is capable to melt every existing material. This is a cost-effective technique capable to rapidly coat large areas with high deposition efficiency. APS coatings are considered porous coatings; however, the presence of formed porosity can represent a disadvantage or an advantage depending on the mechanical, chemical, thermal or bioactivity properties desired for the layer.

It is worth indicating that for the topic under study in this work, the main weakness of this technique is the generation of amorphous calcium phosphate (ACP) which is not a bioactive calcium phosphate phase due to the high temperature reached for the powder particle into the plasma jet. The presence of large amounts of ACP is undesirable since its strong in vivo resorption may cause mechanical and adhesive instabilities of the coating. Figure 10 represents an example of Ti coating by APS.

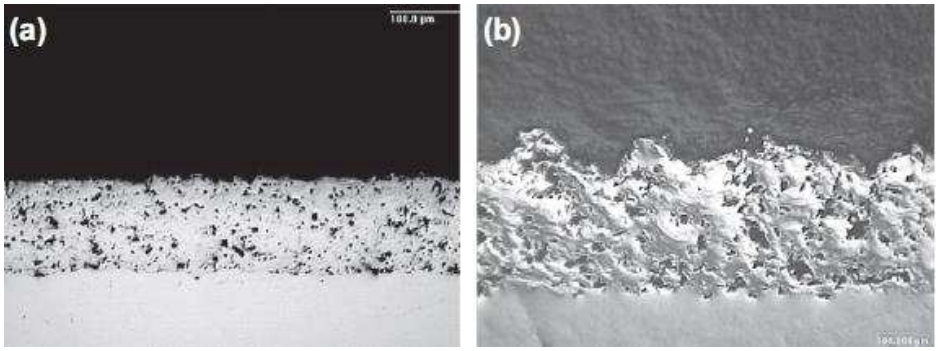

Figure 10. Example of a) low-roughness APS; b) high-roughness APS coating

4.2. **LOW PRESSURE COLD GAS SPRAY (LP-CGS)**

Cold Gas Spray is a solid-state technique that is capable to form coatings or solid components through the impacts of particles onto a target substrate at very high speeds. It is possible to deposit a wide range of materials onto different substrates by CGS without the use of high temperatures, that is, without melting or semi-melting the spraying raw material like in conventional thermal spray process. CGS process only uses kinetic energy in order to build-up splattering deposits layers.[12]

The particles are accelerated in a stream of pre-heated and compressed nitrogen or helium gas (although air may be also used) through a converging-diverging De Laval nozzle. The gas after the minimum section of the nozzle expands to supersonic velocities, while pressure and temperature begin to decrease. Powder particle are injected in this high velocity jet and the high kinetic energy that they reached causes particle deformation when impinging the substrate. For this reason, CGS is considered as a solid-state process. In Figure 11 is shown a diagram that describes this cold gas spray process.

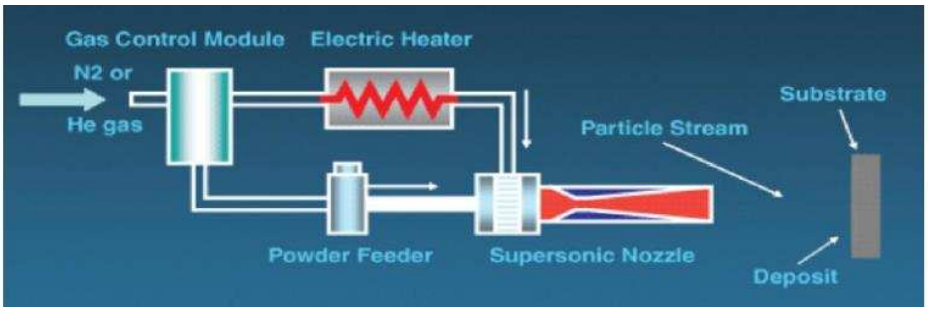

Figure 11. Cold gas spray process

In order to make clearer the process the diagram of a commercial LP-CGS equipment and nozzle is represented in Figure 12 and is described below. This equipment uses compressed air and nitrogen, among others, as propellant gases (1). The nozzle is a stainless steel converging-diverging De Laval type (2), with a round exit and an expansion ratio of about 1.56 (3). The convergent-divergent design of the nozzle is able to accelerate powder particles to supersonic velocities. The powder is injected into the gas jet from radial direction at the diverging part (4) of the nozzle. The gas can be heated up to 632 °C with a resistance (5) inside the spraying gun before the powder injector. The pressure represents a key parameter because it provides high kinetic energy to the in-flight particles at the outlet in order to reach a proper bonding onto the substrate.

During LP-CGS spraying process, spraying parameters are well stablished, however they can be modified dictated values as it can be seen in Table 14. The main spraying parameters for this technique are:

• Gas heating temperature (the higher is the temperature, the higher is the gas acceleration to supersonic regime. Low temperatures help to improve coatings quality, while high temperatures can enhance the deposition efficiency);

• Critical particle velocity, which depends on gas pressure and temperature.

• Substrate temperature (it can enhance coating deposition, reduce internal stresses and minimize the oxidation processes).

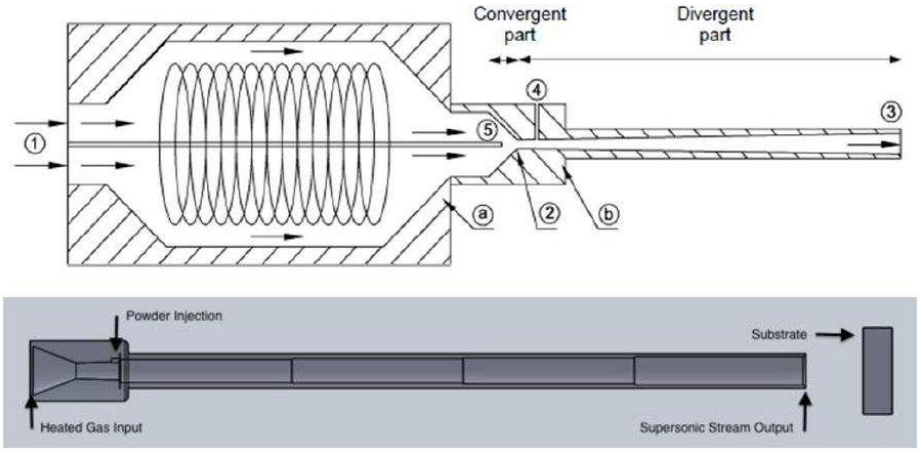

Figure 12. Commercial low-pressure cold gas spray equipment and nozzle SK-20

Low Pressure Cold Gas Spray technology is a competitive, cost-effective and fast process. Technically, LP-CGS possesses a lower particle velocity in comparison to HP-CGS, as a consequence of low pressure, and does not utilize high temperatures, so any high temperature phase transformation of the materials is avoided. Moreover, this new type of technology uses compressed air or nitrogen as propellant gas, so LP-CGS is also environmentally friendly because no dangerous gases and no chemically aggressive wastes are released during the deposition procedure. Another great advantage of LP-CGS is that the equipment is compact and portable. This fact represents an important and practical characteristic for industrial enterprises since it allows in situ spraying onto surfaces.

Table 14. Low pressure cold gas parameters

Parameters	LP-CGS parameters
Operation pressure [bars]	5-10
Powder feeding rate [g/min]	<30
Spraying distance [mm]	5-15
Spraying angle [º]	45-105
Thickness [mm]	0.005-10
Porosity [%]	1-5

As a disadvantage, with this technology it is not possible to directly spray nano powders mainly because of powder flowability problems or because static agglomeration of the extremely fine particles. Figure 13 represents an example of Ti coating by CGS

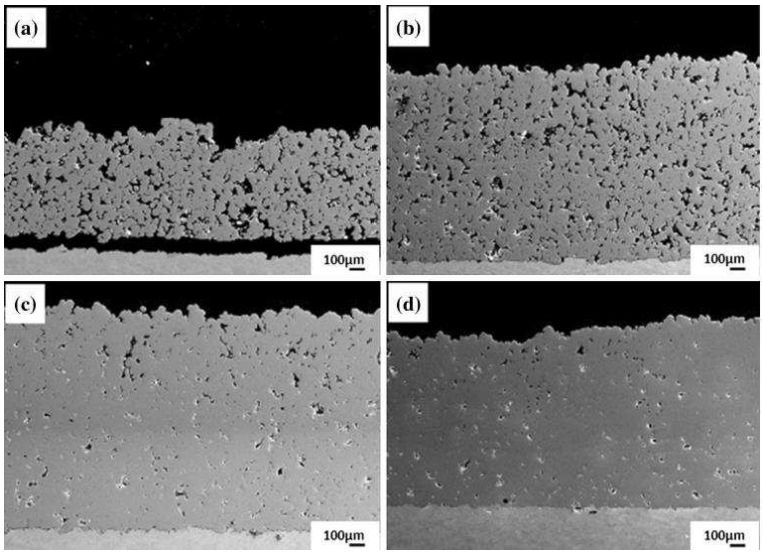

Figure 13. Example of less to high energetic conditions (a–d) CGS coating

4.3. THERMAL PROJECTION IN THE FUNCTIONALIZATION OF IMPLANTS

In this last section, some examples and results of hydroxyapatite and bioglass coated onto PEEK by atmospheric plasma spray and low-pressure cold gas spray will be explained below, and the results obtained will be discussed.

4.3.1. HA by APS

In Table 15 are shown the values of the chemical composition, crystallographic composition, adhesion and the microstructure for two HA coatings deposited onto different substrates, a Ti alloy and PEEK . Experiment made by S. Beauvais et. al.

Data in this table allow observing that the HA coatings obtained by APS on both substrates are semicristallyne, however the crystallinity ratio of HA/PEEK is relatively low (74%) compared with HA/Ti-6Al-4V (87%). In both cases Ca/P ratio is close to the Ca/P ratio of pure hydroxyapatite (Ca/P = 1.667) and the morphology (porosity and roughness) of the HA coating on PEEK, and on Ti-6Al-4V samples were appreciably equivalent. This result allows concluding that the material substrate did not affect significantly the properties of the HA coating.

Table 15. Comparison of chemical composition, crystallographic composition, adhesion and the microstructure between HA on Ti-6Al-4V and HA on PEEK

Parameters	HA on Ti-6Al-4V	HA on PEEK
Ca/P	1.695	1.694
Crystallinity [%]	87	74
Adherence [MPa]	18	7.5
Substrate roughness [µm]:		
Ra	5.2	5.2
Rt	46	36
Thickness [µm]	164	158
Porosity [±1%]	5	5

Taken into account data in Table 15, it might be thought that the main difference between HA/PEEK and HA/Ti-6Al-4V coatings obtained by APS are related to their adherence values. As it can be seen, HA coatings onto PEEK are weakly adhered to the substrate and this can be a serious problem for implants applications.

A common strategy for solving this issue in thermal spraying is to add an interlayer between the coating and the substrate (bond coating) which improves the adhesion between materials. In the images presented in Figure 14 are shown the HA coatings obtained onto PEEK by APS with and without a TiO2 bonding layer, obtained by Laura Barillas et. al.[13]. In general, better and more uniform depositions were delivered with an intermediate TiO_2 as a bonding layer for the HA coating (Figure 14 - case b) in comparation without intermediate TiO_2 as a bonding (Figure 14 - case a). One of the reasons for better adhesion of HA with TiO_2 is the increase in surface roughness given by the interface layer.

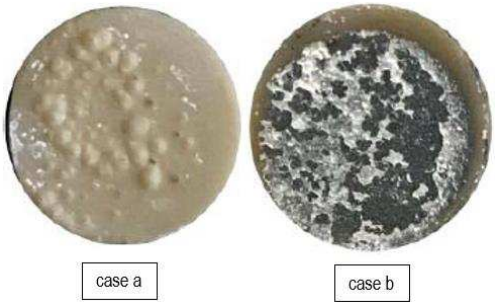

Figure 14. Comparison of the adherence between HA/PEEK and HA/TiO_2/PEEK

Looking at the PEEK substrate in Figure 14- case b, it can be observed that after APS process there is partial thermal degradation of the polymer. This issue is the main problem that APS technology shows for the deposition of HA onto a polymer due to the high temperatures of the plasma jet. For this reason, it is important to carefully set the spraying parameters in order to avoid this effect.

Xiao-mei Liu et. al. [20] studied the formation conditions of columnar grains by coating HA with same microstructure deposition on Ti-6Al-4 V, at different spray parameters and substrate temperatures (both showed at the Table 16).

Table 16. Experimental spraying parameters of Xiao-mei Liu

Spray parameters	HA coated on 25ºC substrate	HA coated on 300ºC substrate	HA coated on 600ºC substrate
Current [A]	330	330	330
Voltage [V]	50	50	50
Flow rate of Ar [L/min]	40	23	23
Stand-off distance [mm]	60	60	110
Gun traverse speed [m/s]	150	150	150
Powder feed rate [g/min]	6.5	6.5	6.5
Carrier gas flow rate [L/min]	5.2	5.2	5.2

Slow cooling rate and completely molten in-flight particles are necessary requirements for deposition of HA coatings with strong crystallographic texture. The results show HA coatings with strong crystallographic texture were obtained at preheating temperature of 600 ºC who exhibited a columnar structure.

Liu concludes that columnar grain growth could be achieved by APS controlling the spraying parameter and substrate temperature. Crystalline structure, composition, porosity and surface morphology can be controlled to a certain extent by simply adjusting APS spray parameters and substrate temperature.

4.3.2. HA by LP-CGS

Different studies have been developed to come upon optimal conditions for cold spraying of spraying HA. Singh et al [19] to optimize HA conditions in CS; they calculated the percentage contribution of all factors on exit particle velocity of HA powder, being as follows in descending order: gas type>particle diameter>gas inlet pressure>particle temperature>gas inlet temperature.

The study of Jae Hyup Lee et. al [22] showed (by LP-CGS) what was being commented on this work of the HA / PEEK composite: HA coating layer modified the surface of PEEK to be rough (which improves the fixation strength), hydrophilic and biocompatible (which affects positively the

osteointegration) and making it a suitable environment for cells to grow on as it can see in the Figure 15 and in the Tables 17 and 18.

Table 17. Results of tensile force and bone-implant contact ratio of Jae Hyup Lee experiment

Parameters	PEEK-4 weeks	HA on PEEK-4 weeks	PEEK-8 weeks	HA on PEEK-8 weeks
Mean tensile force [N]	8.7±5.3	90.2±46.5	18.5±14.1	193.2±94.5
Bone-implant contact ratio	0.229±0.173	0.399±0.160	0.262±0.121	0.363±0.080

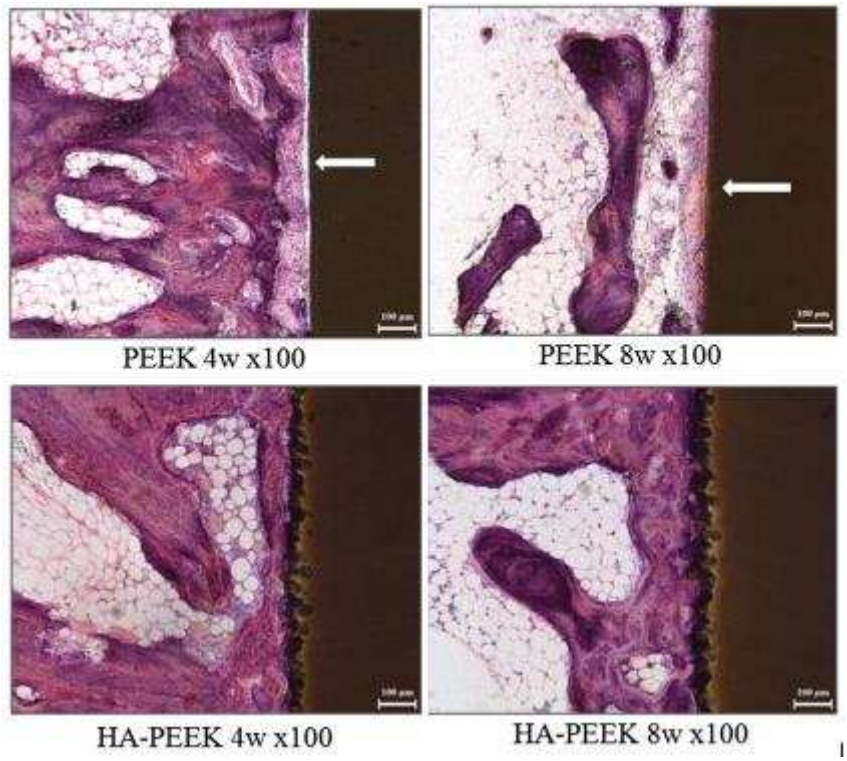

Figure 15. Comparison of bone tissue improvement for PEEK with HA-coated and non-coated in different weeks

Table 18. Results of adhesion and mean cell number at different times of Jae Hyup Lee experiment

Parameters	Bare PEEK	HA-coated PEEK
Adhesion [MPa]	5.71	7.16
Mean cell number:		
10 [min]	3.5±1.3	4.0±1.3
30 [min]	13.8±6.8	21.0±13.1
60 [min]	196.8±68.6	314.5±68.4
120 [min]	779.0±121.8	819.8±72.9

Even though HA is recognized as a bioactive material, there is a great interest in the incorporation of additives to the coating composition:

i) For enhancing its anti-microbial resistance. Such silver (Ag) which is an outstanding antibacterial material. The combination of the bioactivity of HA and the antibacterial properties of Ag has been studied by Sanpo N et. al. [17], and the results indicated that the antibacterial activity increased with increasing HA–Ag nano powder concentrations. Figure 16 shows the effect of killing rate of the bacteria E. coli with increasing HA-Ag nano powder concentration by cold gas-sprayed samples.

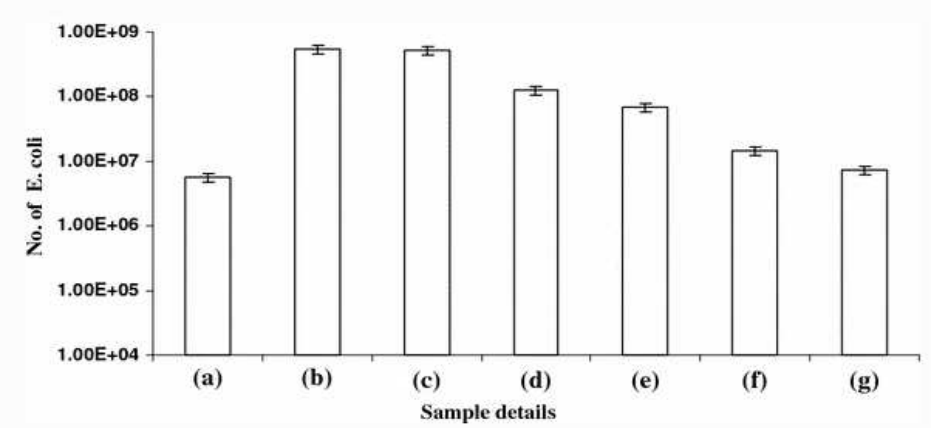

Figure 16. Antibacterial properties quantitative analysis of HA-Ag/PEEK coatings corresponding (a) E coli at 0 hours (b) E coli at 24 hours (c) pure HA (d) HA-Ag 20/PEEK 80 (e) HA-Ag 40/PEEK 60 (f) HA-Ag 60/PEEK 40 (g) HA-Ag 80/PEEK 20

ii) For avoid the concerns related to its long-term performance, graphene has been added to HA coatings. Liu Y, et. al. [23] studies the addition of graphene to HA coatings markedly enhanced attachment and proliferation of the osteoblast cells. It is showed at Figure 17.

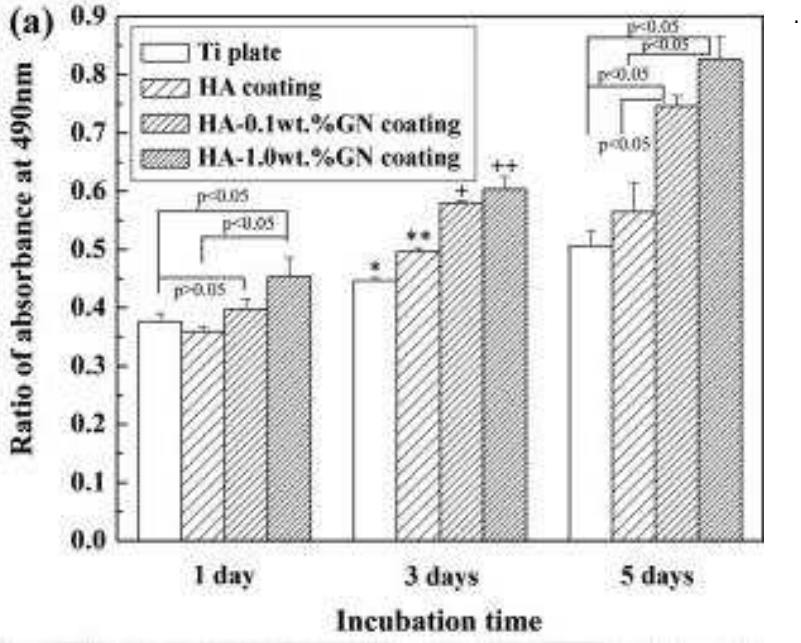

Figure 17. Representation of the results for the cells proliferated on the surfaces of the coating samples

4.3.3. BG by APS

A plasma spray process requires a great number of parameters to be optimized as it has been commented for the HA case. Some of them will be shown:

Powder morphology is a variable that influences the heat rate exchange, flowability of the raw materials employed, kinetic energy and hence the final properties of coatings. Cañas et al.[18] studied the effect of powder fractions with different particle size and morphology of bioactive glass coatings prepared by APS. Table 19 and Figure 18 represents these results. The results conclude that the particle size of the bioglass powder was directly related to the efficiency of the APS process and should be in the range from 63 to 200 μm, while ideal morphology is often spherical, since flowability tends to improve with respect to that observed for irregular shape particles.

Table 19. Results of Caña's experiment

Parameters	BG-1	BG-2	BG-3	BG-4
Particle size distribution [µm]	400–200	200–100	150–63	<63
Coating	No coating was obtained	No coating was obtained	No coating was obtained	No coating was obtained
Observation	Particles cannot adhere	Peak and valley, cracked and porous surface	Similar to BG-2	No powder flowability

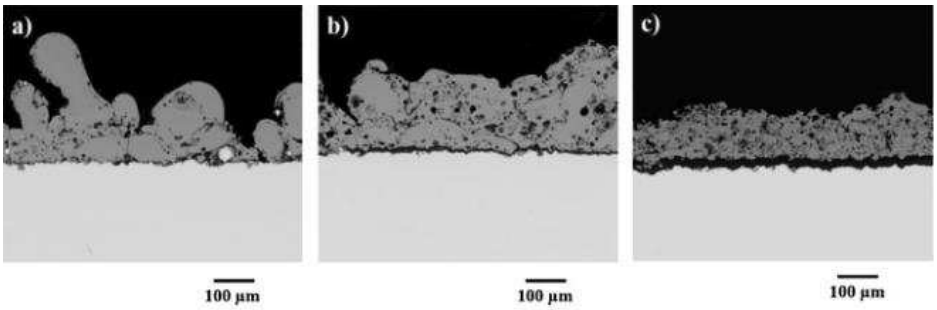

Figure 18. Obtained coatings with (a) BG-2, (b) BG-3 and (c) BG-4 (with 1 wt% fluidizer) powder fractions.

Regarding to bioactive glass composition its important (depending on the use) to maintain the typical amorphous phase of bio-glasses, due the fact that crystallization of bioactive glasses could modify their mechanical and chemical behavior since new phases appear on the coatings.

His fast cooling processed by APS can favor an increase in the amount of amorphous phase content in those systems due de fact that this fast cooling reduces the mobility of the atoms before they can pack into a more thermodynamically favorable crystalline state. This partial crystallization is also a function of the chemical composition of the bioactive glass system, since each system has a specific glass forming ability (GFA). The GFA represents the capacity of a liquid material to form an amorphous phase upon cooling. The degree of amorphous phases in the final coatings

by APS due that fact, the initial feedstock powder is totally or partially molten, will depend on the GFA of bioactive glass particles and temperature.

This phenomenon was observed by Monsalve et al. [24] using two different bioactive glass compositions with practically the same projection parameters. As it is show in Table 20, M3 and M4 are slightly more crystallized than M1 and M2, which can be explained by the lower stability of the P2 powder against crystallization.

Table 20. Results of Monsalve's experiment

Parameters	M1	M2	M3	M4
Particle composition [%]	31SiO_2-56CaO-2MgO-11P_2O_5	31SiO2-56CaO-2MgO-11P2O5	31SiO_2-58CaO-11P_2O_5	31SiO2-58CaO-11P2O5
Spray time [min]	1.3	0.4	1.4	0.5
Results [wt.%]:				
SiO_2	0.9±0.3	1.6±0.4	1.8±0.4	0.8±0.2
$Ca_3(PO_4)_2$	6.0±0.4	2.8±0.2	3.1±0.2	3.9±0.2
HA	5.9±0.4	9.4±0.6	10.6±0.7	10.8±0.8
Ca_2SiO_4	2.2±0.5	1.2±0.5	1.3±0.4	1.9±0.5
Amorphous phase	85.0	85.0	83.2	82.6

Another important spraying parameter is the standoff distance. This value is associated with the kinetic energy and final thermal of the particles. Helsen et al. [26] studied the effect of standoff distance on the formation of bioactive glass coatings and how much influences other spraying parameters (Table 21). They reported that the standoff distance influences the degree of crystallinity. They conclude that if the standoff distance increased, the crystallinity increased, this is attributed to the excess of thermal energy in the particles due to the longer residence times in

the plasma plume. In general, this standoff distances by APS is compressed in the range from 60 to 140 mm.

Table 21. Ratios and favoured factor levels for four parameters

	Current [A]	Arc gas flow [l/min]	Carrier gas flow [l/min]	Spray distance [cm]
Ratio effect	1.9	0.92	0.84	2.54
Favoured level	700	40	4	10

It is worth mentioning that there are other techniques to produce bioactive glasses such as new suspension-based techniques (SPS, SPPS and HVSFS). These techniques achieve lower processing temperatures than conventional thermal spray processes and can be used to process thinner coatings with controlled amounts of crystalline or amorphous phases which it has been demonstrated that is an important parameter. This is discussed in the study of John Henao et. al. [15] which concludes that the content of the glassy phase is determined by the technique used. Depending on whether you want: high density and good bond strength (corresponding on high processing temperatures such APS) or, conversely, high porosity and low bond strength (corresponding on low processing temperatures such the above-mentioned) you will choose one technique or another.

4.3.4. BG by LP-CGS

As it has been mentioned at the beginning of this section, there is a very short number of studies focused on the deposition of BG coatings by CGS. Due to the lack of information in this area, it has been decided to review the effect of spraying parameters on the properties of metals (which are the main materials used in CGS) and mineral coatings (because there are some studies of they and have similar properties with BG).

In the studies about metals it has been found how different properties vary: i)Porosity levels, which can vary by the effect of heat treatment on coating microstructure or the addition of materials such as magnesium or aluminum. Presented the microstructure of cold-sprayed Ti and Ti6Al4V

coatings onto Ti6Al4V substrates and evaluates the effect of heat treatment on coating microstructure. They achieved an average porosity from 5.4 ± 2.4 and 22.3 ± 4.7 % to 21.6 ± 4.6 and 29.7 ± 5.1 % respectively for each coating probably by the healing of the incomplete interfaces through the atom diffusion during annealing treatment. The addition of materials such as magnesium or aluminum to produce porosity was studied who produced porous titanium coatings by spraying Mg+Ti powders onto titanium, where the magnesium behaved as a space holder and is eliminated by vacuum sintering.

ii)The density, which can be influenced by the tamping effect; explains that the successive impact of following particles, therefore leading to less density structures on the top rather than near the interface with the substrate.

On the other part, for mineral coatings M.Robotti et al [21] studied the anchoring mechanism between polymer microparticles (Halar® 6014) and ceramic nanoparticles (TiO_2) during two different mixing processes such as Attrition and Cryogenic Milling.

It was found that the mechanical anchoring of Attrition Milling was more efficient due to the low plastic compacting and deformation of the surface of the polymeric particles. The reason of this difference which shows Table 22, is related to the higher deformation and compacting of the material during the milling process. Denser and compacted starting particles give lower thickness and less porosity.

Table 22. Coatings parameters of Robotti's experiment

Parameters	**Sieved 60-80 µm + TiO_2 AM 1h**	**Sieved 60-80 µm + TiO_2 CM 1h**
Thickness [µm]	957.1 ± 20.8	768.6 ± 19.3
Porosity [%]	12.0 ± 2.2	9.8 ± 2.2
Substrate roughness [µm]:		
Ra	17.0 ± 1.4	14.0 ± 2.6

Alternatively, to HA-Ag, zinc oxide (ZnO), calcium oxide (CaO), and magnesium oxide (MgO) has found antibacterial activity. Sanpo N et. al.[28] again studied combinations of ZnO/Ti powders with different ratios to produce composite-coated implants; the results show that the viability of cells on ZnO20/Ti80 was higher than that on ZnO50/Ti50 and ZnO80/Ti20 samples, thus proving that the cell viability decreased with increasing ZnO concentration in the coating composition. This conclusion is similar to the one with HA-Ag.

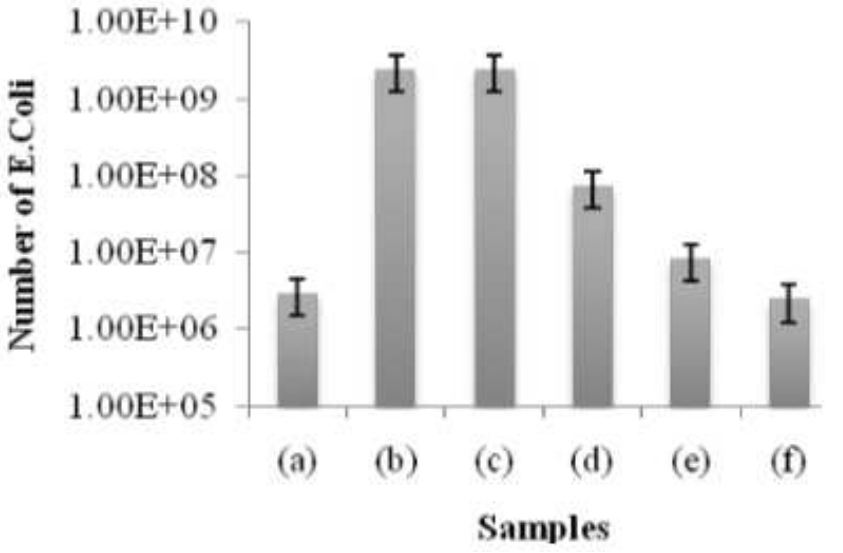

Figure 19. Antibacterial properties quantitative analysis of ZnO/Ti coatings (a) E. coli at 0 hours, (b) E. coli at 24 hours, (c) Al 6061 substrate, (d) ZnO 20/ Ti 80, (e) ZnO 50/ Ti 50 and (f) ZnO 80/ Ti 20

According to the literature, ceramic powder preparation and pressure of the working gas are the most important parameters. One of the problems of LP-CGS is his low tensile bond strength coating/substrate. So, it's important to find binders which mixed with the powder coating or pre-coated on the substrate can improve those. K.Spencer [25] produced on AZ91E substrates pure Al with Al_2O_3 particle-reinforced composite coatings using cold spray (Figure 20). In other words, they modified the ceramic powder preparation with different compositions of Al_2O_3.

The strength interface of the coating/substrate was getting stronger with the increment of Al_2O_3 than the coating itself and causes a little increase of the coating hardness. And also shows that wear rate of the coatings is lower than bulk Al alloys but corrosion resistance is similar to that of bulk pure Al.

Figure 20. Results of LP-CGS at different mixtures (a) 6061Al coating on AZ91, (b) 6061Al–25% Al2O3 coating on AZ91 (c) 6061Al–75% Al2O3 coating on AZ91

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

5. CONCLUSIONS

The objective of this project was to prepare and characterize bioglass coatings on a PEEK substrate, mainly by low pressure cold spray (LP-CGS). As above indicated, this project was finally modified from an experimental version to a literature revision. From the data reviewed it can be concluded that:

- Despite the fact that metals are the most widely used materials as implants, PEEK has been found to have interesting properties even better than metals in some areas such as: i) radiolucency, ii) extremely unreactive which make it biocompatibility and compatibility, iii) inherently resistant to chemical and radiation damage. However, PEEK is a biocompatible but inert material, and this makes necessary some kind of surface modification for enhancing implant integration into the body.

- CGS is a technology frequently used in biomedical implants when a porous coatings are necessary onto the surface of an implant and when the implant and coating materials show low tolerance to high temperatures; either for damaging the substrate or for compositional issues.

- From the results of experiments that have been reviewed regarding to coat the PEEK for improving the bone-implant interaction with BG, it can be concluded that adjusting the spraying parameters and playing with the composition of the powder, good coatings and with high bioactivity can be obtained onto PEEK by different thermal spraying techniques. The main problem found for this kind of coatings is a possible failure related to the low coating-substrate adhesion shown for them.

Considering the short information found about the use of LP-CGS for coating PEEK with BG, it can be concluded that it might be very interesting to carry out the experimental study planned in this project to fill this lack of information.

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

REFERENCES AND NOTES

[1] L. T. Kuhn, “BIOMATERIALS,” in Introduction to Biomedical Engineering, Elsevier, 2005, pp. 255–312.

[2] M. A. Fernandez-Yague, S. A. Abbah, L. McNamara, D. I. Zeugolis, A. Pandit, and M. J. Biggs, “Biomimetic approaches in bone tissue engineering: Integrating biological and physicomechanical strategies,” Adv. Drug Deliv. Rev., vol. 84, pp. 1–29, 2015, doi: 10.1016/j.addr.2014.09.005.

[3] A. C. Marsh, N. P. Chamorro, and X. Chatzistavrou, Long-term performance and failure of orthopedic devices, Second Edi. Elsevier Ltd, 2019.

[4] D. D. Kiradzhiyska and R. D. Mantcheva, “Overview of Biocompatible Materials and Their Use in Medicine,” Folia Med. (Plovdiv)., vol. 61, no. 1, pp. 34–40, 2019, doi: 10.2478/folmed-2018-0038.

[5] N. J. Hickok, E. T. J. Rochford, D. J. Jaekel, R. Geoff Richards, T. Fintan Moriarty, and A. H. C. Poulsson, Bacterial Interactions With PEEK, 2nd ed. Elsevier Inc., 2019.

[6] S. M. Kurtz and J. N. Devine, “PEEK biomaterials in trauma, orthopedic, and spinal implants,” Biomaterials, vol. 28, no. 32, pp. 4845–4869, 2007, doi: 10.1016/j.biomaterials.2007.07.013.

[7] J. J. R. and C. A. G., Bio-Glasses Edited by. .

[8] J. R. Jones, “Review of bioactive glass: From Hench to hybrids,” Acta Biomater., vol. 9, no. 1, pp. 4457–4486, 2013, doi: 10.1016/j.actbio.2012.08.023.

[9] A. S. Kang, G. Singh, and V. Chawla, “Some Problems Associated With Thermal Sprayed Ha Coatings : a Review,” Int. J. Surf. Eng. Mater. Technol., vol. 144601, no. 1, pp. 10–14, 2013.

[10] D. Almasi, N. Iqbal, M. Sadeghi, I. Sudin, M. R. Abdul Kadir, and T. Kamarul, “Preparation Methods for Improving PEEK’s Bioactivity for Orthopedic and Dental Application: A Review,” Int. J. Biomater., vol. 2016, 2016, doi: 10.1155/2016/8202653.

[11] M. Driver, Coatings for biomedical applications. 2012.

[12] M. Robotti, “Functional surfaces obtained by thermal spray techniques,” p. 126, 2016.

[13] L. Barillas, J. M. Cubero-Sesin, and I. Vargas-Blanco, “Hydroxyapatite Coatings on Polymers Using a Custom Low-Energy Plasma Spray System,” IEEE Trans. Plasma Sci., vol. 46, no. 7, pp. 2420–2424, 2018, doi: 10.1109/TPS.2018.2810639.

[14] S. Beauvais and O. Decaux, “Plasma sprayed biocompatible coatings on PEEK implants,” Therm. Spray 2007 Glob. Coat. Solut., no. June, pp. 371–377, 2007, doi: 10.1361/cp2007itsc0371.

[15] J. Henao, C. Poblano-Salas, M. Monsalve, J. Corona-Castuera, and O. Barceinas-Sanchez, “Bio-active glass coatings manufactured by thermal spray: A status report,” J. Mater. Res. Technol., vol. 8, no. 5, pp. 4965–4984, 2019, doi: 10.1016/j.jmrt.2019.07.011.

[16] A. M. Vilardell, N. Cinca, A. Concustell, S. Dosta, I. G. Cano, and J. M. Guilemany, “Cold spray as an emerging technology for biocompatible and antibacterial coatings: state of art,” J. Mater. Sci., vol. 50, no. 13, pp. 4441–4462, 2015, doi: 10.1007/s10853-015-9013-1.

[17] N. Sanpo, M. L. Tan, P. Cheang, and K. A. Khor, “Antibacterial property of cold-sprayed HA-Ag/PEEK coating,” J. Therm. Spray Technol., vol. 18, no. 1, pp. 10–15, 2009, doi: 10.1007/s11666-008-9283-0.

[18] E. Cañas, M. Vicent, E. Bannier, P. Carpio, M. J. Orts, and E. Sánchez, “Effect of particle size on processing of bioactive glass powder for atmospheric plasma spraying,” J. Eur. Ceram. Soc., vol. 36, no. 3, pp. 837–845, 2016, doi: 10.1016/j.jeurceramsoc.2015.09.039.

[19] R. P. Singh and U. Batra, “Effect of cold spraying parameters and their interaction an hydroxyapatite deposition,” J. Appl. Fluid Mech., vol. 6, no. 4, pp. 555–561, 2013, doi: 10.36884/jafm.6.04.21277.

[20] X. mei Liu et al., “Atmospheric Plasma-Sprayed Hydroxyapatite Coatings with (002) Texture,” J. Therm. Spray Technol., vol. 27, no. 8, pp. 1291–1301, 2018, doi: 10.1007/s11666-018-0768-1.

[21] M. Robotti, S. Dosta, I. G. Cano, A. Concustell, N. Cinca, and J. M. Guilemany, “Attrition and Cryogenic milling powder production for Low Pressure Cold Gas Spray and composite coatings characterization,” Adv. Powder Technol., vol. 27, no. 4, pp. 1257–1264, 2016, doi: 10.1016/j.apt.2016.04.014.

[22] J. H. Lee et al., “In vitro and in vivo evaluation of the bioactivity of hydroxyapatite-coated polyetheretherketone biocomposites created by cold spray technology,” Acta Biomater., vol. 9, no. 4, pp. 6177–6187, 2013, doi: 10.1016/j.actbio.2012.11.030.

[23] Y. Liu, Z. Dang, Y. Wang, J. Huang, and H. Li, "Hydroxyapatite/graphene-nanosheet composite coatings deposited by vacuum cold spraying for biomedical applications: Inherited nanostructures and enhanced properties," Carbon N. Y., vol. 67, pp. 250–259, 2014, doi: 10.1016/j.carbon.2013.09.088.

[24] M. Monsalve, H. Ageorges, E. Lopez, F. Vargas, and F. Bolivar, "Bioactivity and mechanical properties of plasma-sprayed coatings of bioglass powders," Surf. Coatings Technol., vol. 220, pp. 60–66, 2013, doi: 10.1016/j.surfcoat.2012.11.075.

[25] K. Spencer, D. M. Fabijanic, and M. X. Zhang, "The use of Al-Al2O3 cold spray coatings to improve the surface properties of magnesium alloys," Surf. Coatings Technol., vol. 204, no. 3, pp. 336–344, 2009, doi: 10.1016/j.surfcoat.2009.07.032.

[26] J. A. Helsen, J. Proost, J. Schrooten, G. Timmermans, E. Brauns, and J. Vanderstraeten, "Glasses and Bioglasses: Synthesis and Coatings," J. Eur. Ceram. Soc., vol. 17, no. 2–3, pp. 147–152, 1997, doi: 10.1016/s0955-2219(96)00176-8.

[27] Steven M. Kurtz, "PEEK BIOMATERIALS HANDBOOK" First edition 2012.

[28] Noppakun Sanpo, Kelvin Loke, Hailan Chen, Pak Keng Koh, "Biocompatibility and Antibacterial property of Cold Sprayed ZnO/Titanium Composite Coating" November 2010.

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

6. ACRONYMS

- Ti6Al4V: Titanium alloys with 6% of Al and 4% of V
- FDA: U.S. Food and Drug Administration
- MRI: Magnetic resonance Imaging
- PEEK: Polyetheretherketone
- PE: Polyethylene
- PMMA: Polymethylmethacrylate
- PVC: Polyvinylchloride
- HA: Hydroxyapatite
- BG: Bioglass
- CFR-PEEK: Carbon fiber reinforced PEEK
- UHMWPE: Ultra-high-molecular-weight polyethylene
- MOM: Metal on metal
- COC: Ceramic on ceramic
- $Ca_5(PO_4)_3(OH)$: Hydroxicalciumphosphate
- DLC: Diamond-like carbon
- LP-CGS: low pressure cold gas spray
- HP-CGS: high pressure cold gas spray
- CGS: cold gas spray
- CS: cold spray
- APS: atmospheric plasma spray
- SPS: Spark plasma sintering
- SPPS: Peptide synthesis
- HVSFS: High velocity suspension flame spraying
- Ra: Roughness Average
- Rt: Maximum Height of the Profile
- AM: Attrition Milling
- MC: Cryogenic Milling
- AZ91E: Magnesium alloy

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ

Document signat digitalment per: MANUEL EDUARDO MONTES ALVREZ