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REVIEW

Radiation Grafting for the Functionalization and Development of Smart Polymeric Materials

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Abstract Gamma radiation has been shown particularly useful for the functionalization of surfaces with stimuli-responsive polymers. This method involves the formation of active sites (free radicals) onto the polymeric backbone as a result of the high-energy radiation exposition over the polymeric material. Thus, a microenvironment suitable for the reaction among monomer and/or polymer and the active sites is formed and then leading to propagation to form side-chain grafts. The modification of polymers using high-energy irradiation can be performed by the following methods: direct or simultaneous, pre-irradiation oxidative, and pre-irradiation. The most frequently used ones correspond to the pre-irradiation oxidative method as well as the direct one. Radiation-grafting has many advantages over other conventional methods because it does not require the use of catalyst nor additives to initiate the reaction and usually no changes on the mechanical properties with respect to the pristine polymeric matrix are observed. This chapter is focused on the synthesis of smart polymers and coatings obtained by the use of gamma radiation. In addition, the diverse applications of these materials in the biomedical area are also reported, with focus in drug delivery, sutures, and biosensors.

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1 Introduction

Since the synthesis of PVC obtained by Henri Victor Regnault in 1838, a large number of polymeric synthetic materials with chemical–mechanical–thermal properties of the most diverse have been developed [1]. There are a high number of degrees of freedom for the synthesis conditions; and consequently, the properties of the resulting material can be as varied. Polymer chemistry has advanced to the point where it is often possible to tailor-make a variety of different types of polymers with specified molecular weights and structures [2]. However, sometimes a small change in the synthesis conditions or concentrations of reagents generates undesirable changes in the final properties of the material. Surface modification of polymeric materials has come to represent an interesting and useful alternative for generation of polymers with specific physical–chemical properties, coupled with the properties conferred by surface modifications.

There are several means to modify polymers properties, viz. blending, grafting, and curing. 'Blending' is the physical mixture of two (or more) polymers to obtain the requisite properties. 'Grafting' is a method wherein monomers are covalently bonded (modified) onto the polymer chain, whereas in curing, the polymerization of an oligomer mixture forms a coating which adheres to the substrate by physical forces [3].

Among the methods for polymer modification, "grafting" is a promising technique for the introduction of special functional groups in order to modify their original properties and broad its applications [4].

2 Grafting Techniques

A graft copolymer is a polymer that is composed of two or more chemically different polymeric parts [5]. Generally, graft copolymers are polymers composed of a main polymer chain (backbone) to which one or more side chains (branches) are chemically connected through covalent bonds [6]. On a random, statistical, or alternate copolymerization processes, the different monomers compete with each other to add to propagating centers (radical or ionic), unlike grafting processes wherein synthesis is carried out not simultaneously; instead, a sequence of separate noncompetitive polymerizations is used to incorporate the different monomers into one polymer chain [7].

Graft copolymers have very different properties to raw materials and that has gained great interest in recent years because it is possible to obtain new materials from already available ones. The main purposes of a surface modification are improving the wettability, biocompatibility, and mechanical properties, etc., of a surface polymer. Grafting copolymers can be obtained mainly by two mechanisms known as grafting from and grafting to [8]. There are several parameters that control

the brush properties, such as grafting density, chain length, and chemical composition of the chains [9].

The processes of "grafting to" and "grafting from" are two different ways to change the chemical and physical properties of a polymeric surface (Fig. 1). "Grafting to" allows a preformed polymer to adhere to either polymeric surface through covalent bonds. Due to the larger volume of the coiled polymer to graft and the steric hindrance this causes, the grafting density obtained by this technique is low [10]. On the other hand, the "grafting from" process requires the activation of a backbone polymer previously, which can be carried out by chemical (chemical initiators) or physics methods (ionizing radiations), initiating the polymerization process with monomer units around it. With the "grafting from" mechanism, it is possible to obtain high grafting densities, since there is more access to the chain ends [11].

Grafting a polymer can be achieved by several techniques, such as chemical, radiation, photochemical, plasma-induced, and enzymatic means. The different types of initiators give their name to each grafting technique. Chemical grafting involves free-radical or ionic initiators; radiation induces graft copolymerization that uses high-energy radiation (generally gamma, UV, and electrons); photochemical techniques include photo-sensitive reagents as initiators [12] and plasma-induced grafting implies electron-induced excitation, ionization, and dissociation attained by slow discharge conditions. Then the accelerated electrons from the plasma have sufficient energy to induce cleavage of the chemical bonds in the polymeric structure to form macromolecule radicals, which subsequently initiate graft copolymerization [3].

Among the grafting techniques, radiation processing is presented as an alternative with interesting features over other conventional synthesis and

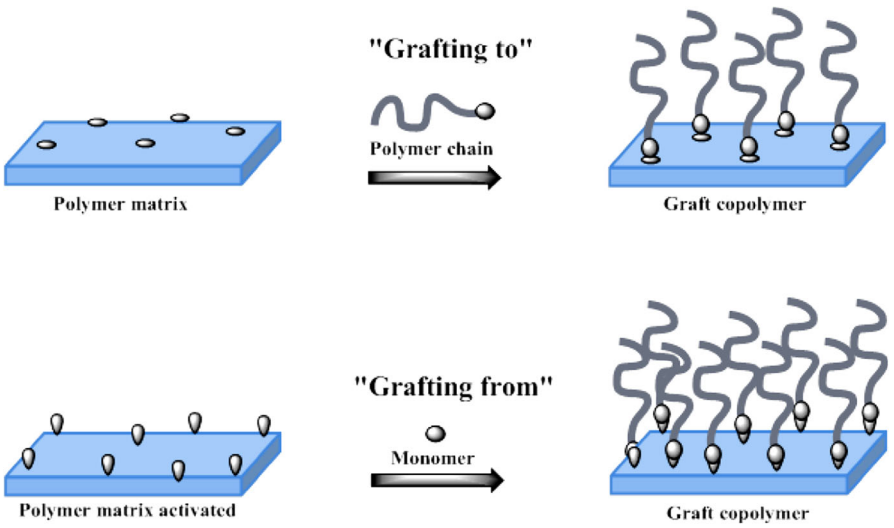

Fig. 1 Synthesis of polymer brushes using "grafting to" and "grafting from" approaches

modification of polymer matrices methods. The lack of catalysts or additives in order to initiate the reaction as well as its simplicity are issues to consider [13]. Polymer modification by radiation grafting techniques has been extensively applied to prepare novel materials (including adsorbents for environmental and industrial applications) and it is of particular interest to achieve specific chemical properties as well as excellent mechanical properties [14].

3 Radiation-Induced Grafting

The process of radiation-induced grafting is based on the deposition of energy from the radiation in the material to be modified. From this energy, highly reactive free radicals, which give rise to secondary reactions with molecules present in the medium, will be generated. These radicals easily react with appropriate functional monomers to form covalent bonds and, as a consequence, growth of macromolecular chains [15], and all of this without the use of chemical initiators.

Each type of ionizing radiation produces the same effect by interacting with matter (ionization and excitation) [16], but according to their specific nature (charge, penetrating power (range), linear energy transfer (LET) and stopping power of the material), highly concentrated free radical areas or homogeneous radical production along the material can be produced. In the case of electrons, ions, and protons; due to its high LET, charge and particle size; each particle delivers its entire energy in a few millimeters and almost without path deviations). For gamma radiation, an homogeneous delivery of energy will occur, both surface and bulk due to the high penetration of gamma rays [17]. In some cases, the types of radiation are combined to generate uniform changes in the material [18], so the type and energy of ionizing radiation used will determine the changes in structure of the resulting material.

Due to the inclusion of "new" molecules in the material, the polymer properties change. Graft copolymerization has been commonly used to modify properties in polymer structures like poly(ethylene terephthalate) (PET), cellulose, polypropylene (PP), and polyethylene (PE), with a wide variety of monomers [19].

Another advantage presented by radiation-induced graft copolymerization is that it enables imparting tailored modifications ranging from surface to bulk of backbone polymers unlike photo- and plasma initiation, which impart surface modification only [20].

The degree of grafting in the copolymer may be adjusted by selection of irradiation and reaction parameters to develop specially designed selective copolymers for specific applications. Radiation-induced graft copolymerization may also be initiated over a wide range of temperatures, including sub-ambient temperatures for monomers available in bulk, solution, or emulsion [20].

There are two basic methods for radiation-induced grafting; including the pre-irradiation, as well as the mutual or the simultaneous method; with an energy source being either gamma ray, UV, or electrons [21–23].

3.1 Methods of Synthesis

Since graft copolymers result from the chemical combination of two macromolecules of different chemical nature, and since radiation is known to create "active sites" in polymeric matrix, it is logical to think that various chemical routes can be followed for the combination of these macromolecules. Among the various methods that can be envisaged for this purpose, four have received special attention; these include direct radiation grafting and grafting on radiation-peroxidized polymers. When polymers are exposed to ionizing radiation under aerated conditions, trapped radicals and peroxides (or hydroperoxides) are formed and remain ready to initiate grafting copolymerization reactions [24].

3.1.1 Direct Radiation Grafting Method

In the direct or simultaneous method (Fig. 2), the simple radiation-chemical method for producing graft copolymers is directly derived from the study of radiation polymerizations. Most radiation-initiated polymerizations proceed via free-radical mechanisms, initiated by the free radicals produced from the radiolysis of the monomer. Nevertheless, since the action of ionizing radiation on matter is unselective, any substance that is added to the monomer also undergoes radiolysis and consequently contributes to the initiation of polymerization [5].

In this method, the polymer substrate is immersed in a monomer-solvent mixture, which may be liquid or vapor and may contain additives. Irradiation produces active sites in the polymer matrix, mainly macroradicals, which can initiate the graft polymerization but also the interaction of radiation with monomer can generate homopolymerization. The latter is an untoward side reaction. As polymer degradation requires higher absorbed doses than the grafting process, it is possible to perform direct grafting under controlled conditions without significant damage to the substrate [21].

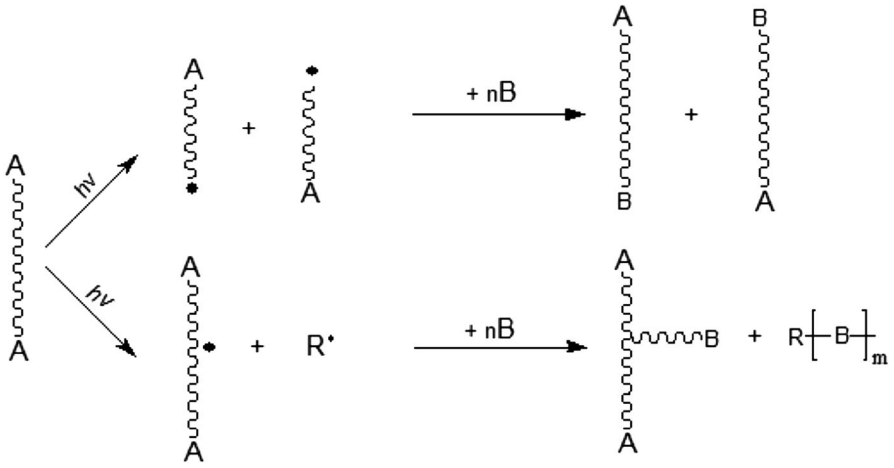

Fig. 2 Grafting by γ-irradiation applying a direct method

3.1.2 Pre-Irradiation Grafting Method

The polymer matrix is irradiated in the absence of air (in vacuo or under an inert atmosphere). Grafting is initiated by macroradicals trapped in the irradiated polymer and homopolymerization is avoided. A disadvantage of this method is the possible degradation of the polymer matrix due to the need of higher doses than the direct method. Besides, there's a significant dependence on the reaction temperature and crystallinity of the polymer because the concentration of trapped macroradicals is higher in a crystalline than in an amorphous polymer, and a comparatively low degree of grafting is obtained [5, 21].

3.1.3 Pre-Irradiation Oxidative Grafting Method

This method involves pre-irradiation of the polymer, but in the presence of air or oxygen. In this way, the macroradicals formed are converted to peroxides and/or hydroperoxides, and when the irradiated polymer is heated in the presence of monomer (in the absence of air), the peroxides decompose to give the macroradicals, which are the active sites for graft polymerization (Fig. 3).

An advantage of the peroxide method is the possibility of storing the irradiated polymer some time before grafting. Some disadvantages are that the hydroxyl radical (OH·) produced by the homolytic cleavage of the hydroperoxide group

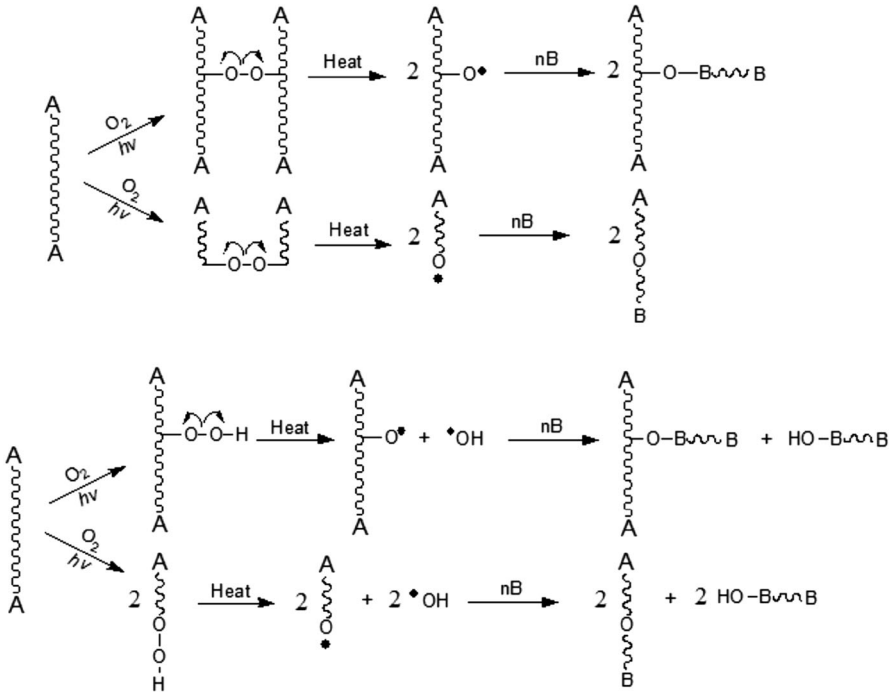

Fig. 3 Grafting by γ-irradiation applying a pre-irradiation method

induces homopolymerization and the pre-irradiation method requires a higher dose of radiation than the direct method [5, 21].

The pre-irradiation technique is a clean and effective method for modification of PP, PE, poly(tetrafluorethylene) (PTFE), etc. Some reports on grafting polar monomers onto pre-irradiated films have been published [25].

3.2 Modifying Properties by Grafting

Irradiation produces active sites in the polymer matrix, mainly macroradicals, which can initiate the graft polymerization and homopolymerization of the monomer. If the polymer has the tendency to crosslinking [e.g., PP, PE, polystyrene (PS), poly(vinyl chloride) (PVC), etc.] a grafted copolymer is formed. On the other hand, when a polymer has the tendency to chain cleavage [e.g., PTFE, poly(isobutylene), cellulose, poly(methyl methacrylate) (PMMA), and polymers containing tetrasubstituted carbon atoms in the main chain] the process can result in a block copolymer formation. Because degradation of polymers requires higher absorbed doses than the grafting process, it is possible to perform grafting on these polymers [5, 26].

As mentioned before, the type of monomer grafted into the polymer matrix will determine the resulting properties, and of course, the properties of the monomers are dictated by the functional groups' content. Grafting hydrophilic or hydrophobic monomers can improve the hydrophilicity or hydrophobicity of the material respectively; with pH-sensitive monomers we can electrically charge the surface of a material, or modify its swelling properties at different pH's; grafting self-repairing materials can improve the mechanical resistance to scratches, etc. Thermosensitive polymers are a special category of polymers which have in their structure a hydrophobic and a hydrophilic functional groups [e.g., poly(N-isopropylacrylamide), PNIPAAm] [27]; pH-sensitive polymers has ionizable functional groups [e.g., poly(acrylic acid), PAAc]. Monomers with amines affect the swelling behavior of the polymer, because amine protonation results in swelling under acid conditions due to the formation of the ammonium polyelectrolyte, similarly carboxylic acid substituents form ionized salts at basic pH resulting in increased network swelling [28]. Polymers that form complexes may associate due to Van der Waals interactions, ionic bonds, hydrogen bonds, coordination interactions, or salt bridges formed by polyvalent metal ions [29].

3.3 Grafting Quantification and Characterization Techniques

Innumerous techniques are currently available for polymer characterization in terms of the assessment of polymer properties. Of those, thermal [30], mechanical [31], optical [32], and rheological [33] approaches might be determined and used for further comparison with the grafted material.

Characterization methods used to confirm or track down the grafting process include Fourier transform infrared spectroscopy (FTIR) [34], nuclear magnetic resonance (NMR) [35], and X-ray diffraction analysis (XRD) [36]. Considering that these analyses may detail with precision the grafting process as well as the novel chemical linkages, such techniques are currently in the spotlight.

In addition to the above-mentioned techniques, surface studies may also play a key role in the characterization of grafted copolymers due to their ability to reveal important information in terms of microstructure and overall morphology of the grafted polymer [32, 37]. For instance, scanning electron microscopy corresponds to a very usual technique of choice [38]. Other approaches may be used to evidence the graft copolymerization, including differential scanning calorimetry [30, 39] and water contact angle [40, 41], among other techniques.

On the other hand, regarding approaches to quantify grafting, the determination of grafting yields and grafting efficiency are perhaps the most representative ones. Both estimations can be performed based on weight of the samples, as represented in Eqs. (1) and (2) for grafting yields and grafting efficiency, respectively, whereas W_a stands as the initial weight of the sample, W_b corresponds to the dried weight of the grafted sample before the extraction, and W_c represents the dried weight of the grafted sample after extraction [42–44].

$$\text{Grafting yield } (\%) = \frac{W_c - W_a}{W_a} \times 100 \tag{1}$$

$$\text{Grafting efficiency } (\%) = \frac{W_c - W_a}{W_b - W_a} \times 100. \tag{2}$$

When it comes to functionalized materials aside from the careful and precise characterization to assure and provide experimental evidence of the functionalization itself, the tailored function or modification shall be assessed in order to demonstrate and detail the acquired properties, e.g., thermo-responsiveness is well demonstrated by LCST measurements [45, 46], while pH-responsivity is commonly evaluated by determining the pH critical point [47]. In practical means, the characterization and experimental evaluation of the functionality should be carefully designed and performed on a responsiveness or "functionality"-based approach.

4 Smart Polymers

Stimuli-responsive polymers are polymers that respond sharply to small changes in physical or chemical conditions with relatively large phase or property changes [48]. The stimuli in which smart polymers respond to are commonly classified into three categories: physical, chemical, or biological [49]. Temperature and pH stimuli-responsive macromolecular materials have attracted great attention due to their obvious applications in biomedicine and biotechnology [50].

4.1 Smart Polymeric Materials Obtained by Ionizing Radiation

Responsive behavior of polymeric materials could be formally considered as a combination or sequence of several events: (a) reception of an external signal (physical or chemical), (b) chemical change of the material and/or changes in the material properties, and finally (c) transduction of the changes into a macro/

microscopically significant event such as aggregation-deaggregation (commonly referred to as *response*). For example, microgel particles from a crosslinked weak polyelectrolyte (polybase) dispersed in water are sensitive to variations in pH of the medium. Changes (decreases) in pH cause changes in the ionization degree of the polyelectrolyte, and with the change in the ionization degree of the polyelectrolyte comes a molecular conformational modification [51, 52]. One of the smart polymers most studied is probably PNIPAAm, which exhibits a lower critical solution temperature (LCST) between 30 and 35 °C [53]. Acrylic acid (AAc) is one of the important monomers grafted on the matrix of different polymers, where their chains act as reaction sites to introduce various functions through carboxyl groups, and because of its pH-sensitive response [54].

4.1.1 Temperature-Responsive Polymers

Temperature-sensitive polymers exhibit LCST behavior where phase separation is induced at a certain temperature threshold. Polymers of this type undergo thermally induced reversible phase transition. They are soluble in aqueous solutions at low temperatures but become insoluble as the temperature rises above the LCST. It is possible to increase the functionality of microgel particles by finding the right balance of hydrophobic and hydrophilic co-monomers or by tuning to a desired temperature range by copolymerization using more hydrophilic (which raises the LCST) or more hydrophobic (which lowers the LCST) co-monomers [55, 56].

Heskins and Gillet were the first to report an endotherm observed at the LCST upon heating an aqueous solution of PNIPAAm [57]. Grinberg [58] have studied the volume phase transition in responsive polymers using high-sensitivity differential scanning calorimetry (DSC) and as well as the swelling behavior of the polymers at different scanning rates. It was possible to measure the dependence of the transition parameters on the heating rate. The DSC measurements, by heating at different rates (from 1 to 10 °C/min), provided results nearly approximating equilibrium and LCST or UCST. The transition temperature, enthalpy, and entropy of this thermosensitive behavior as well as the transition LCST are parameters that may be estimated.

4.1.2 pH-Responsive Polymers

pH-responsive polymers consist of ionizable pendants capable of accepting and donating protons in response to environmental changes in pH such as carboxylic acids and basic amino alkyl moieties [59]. The change in the charge of pendant groups causes an alteration of the hydrodynamic volume of the polymer chains [60]. Then, the transition from collapsed state to swollen state is caused by the osmotic pressure generated by mobile counterions which neutralize the charges [61]. The phase transition of pH-sensitive polymers is nominated critical pH. In the human body, pH variations are present along the gastrointestinal tract and in problematic sectors like tumor areas and surrounding tissues [62]. Drug delivery in these specific areas make relevant the need for the development of pH-sensitive systems with fast response to changes in environmental stimuli. A fast response of a polymer and a repetitive function of another polymer may be combined using different

functionalization techniques such as γ-irradiation. Most grafting reactions, which take place on the surface or in the bulk polymeric matrix, allow the design of clinically effective controlled drug-delivery systems, supported by the concept of achieving optimized combinations between monomer and the polymer itself.

5 Applications

Applications of functionalized materials by grafting abound in the literature, as such modifications brought to light novel applications and perspectives in terms of their usage, considering the possibility to tailor the materials as desired or required [63]. Examples of materials based on functionalized polymers include smart membranes for separation science [3], conducing polymers [63] for energy and wire technology, responsive materials, including pH- [4], thermo-responsive polymers [64], as well as light- [65] and magnetic-responsive polymers [66], for a wide variety of biomedical and technological applications.

In terms of biomedical applications, functionalized polymers are currently applied for tissue engineering and cell cultivation, biotechnology, biomedicine, and pharmaceutical technology, among others areas that may directly benefit from the advancement of material sciences. A highlighted application is related to cell and tissue cultivation as the grafting of biological substances or other bioactive ones onto polymer substrates has been proven effective towards controlling important parameters for cell growth and tissue development, which may somehow modulate cell affinity, and therefore provide control over the process. However, this work debates the biomedical applications of grafted functionalized polymers by means of sensors, drug delivery, and sutures specifically.

As reviewed earlier, grafting different functional groups in polymer matrices allows us to modify the original properties of the irradiated material, but if we graft molecules with stimuli-responsive properties, we can obtain materials with unique properties that change their behavior according to the environment in which they are. Researchers around the world have found various application fields of intelligent polymers grafted on polymeric surfaces in the areas of development of medical devices for drug delivery, biosensors, and implant development.

5.1 Surface Modification Polymers for Medical Purposes

Gamma-ray irradiation enables the grafting of medical devices with polymers containing functional groups capable of interacting with drug molecules. Depending on the chemical structure of the substrate and the monomers to be grafted, different levels of performance can be achieved [67].

The synthesis of new polymeric materials for biomedical applications are of great interest. However, they should pass exhaustive testing to demonstrate their non-toxicity, biocompatibility, and industrial feasibility; so a lot of time will pass before these kinds of materials have real application and then most of them will be discarded [68]. Instead of synthesis of new materials, biomaterial modifications seem to be the short-term solution for improvement of medical devices to some

extent, as biological safety will have to be determined as a brand new system. Applying surface modification on materials already approved for medical use, we could enhance their properties as biocompatibility, resistance to degradation, mechanical properties, and thermal stability providing perhaps a shorter way for novel alternatives for most.

Device-related infections are among the most serious complications in medical procedures. Its importance arises from the high occurrence and the consequences that it implies in terms of morbidity and mortality. As a result, the presence of these two factors increases hospital costs significantly. If scientists get to synthesize drug-coated biomaterials, it will be possible to reduce device-related infections contracted at surgery during the early post-insertion period, and most infections identified in patients that have been treated with polymeric implants should be delayed, even infections caused by microorganisms from the skin flora and nosocomial environment.

Surface modification of materials used on medical device manufacturing to obtain drug impregnated polymers takes relevance when we talk about microbial resistance to antibiotics. Research has recently been published that accounts for the existence of antimicrobial-resistant strains. Many of them indicate the existence of methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomona aeruginosa*, and *Escherichia coli* cells. The direct treatment of microbial infections with drug-impregnated medical devices suggests a simple method that releases the drug at a specific site, decreases costs [69], avoids or reduces invasive dosage forms, and minimizes the antimicrobial-resistance effect by not unnecessarily exposing other bacteria to antibiotics [70, 71]. Another area of opportunity for surface modification includes body-contacting materials [72]. Surgical devices and biomedical materials could incorporate drug-delivery systems through insertion of hydrophilic groups with hosting drugs capability through ionic interactions, van de Waals, and hydrogen bond.

The effort should focus mainly on three aspects. First of all, improving the treatment of the complication (treatment and administration routes); secondly, enhancing the hydrophilicity (obtaining lubricity) of biomedical devices, improving biocompatibility [73], and reducing protein adhesion [74]; and finally, increasing preventive measures. This latter point may be the most interesting of all because it focuses on prevention [68].

Medical devices used in vivo should satisfy requirements for performance, bio-interaction, and biocompatibility. The understanding of structure–properties relationships in polymers is advanced, so the desired mechanical properties, durability, and functionality can be achieved [75]. Bio-integration is the ideal outcome expected of an artificial implant. This implies that the phenomena that occur at the interface between the implant and host tissues do not induce any deleterious effects such as chronic inflammatory response or formation of unusual tissues [76].

The most interesting methods to modify a polymer for biomedical purposes are plasma and high energies, (Fig. 4) due to simultaneous sterilization of the material provided by the method [75] and no need of chemical initiators that could represent a biocompatibility problem. It is possible to change many properties with this kind of method (Table 1). Surface treatments can be broadly categorized as functionalization, derivatization, polymerization, and mechanical or surface architecture modification.

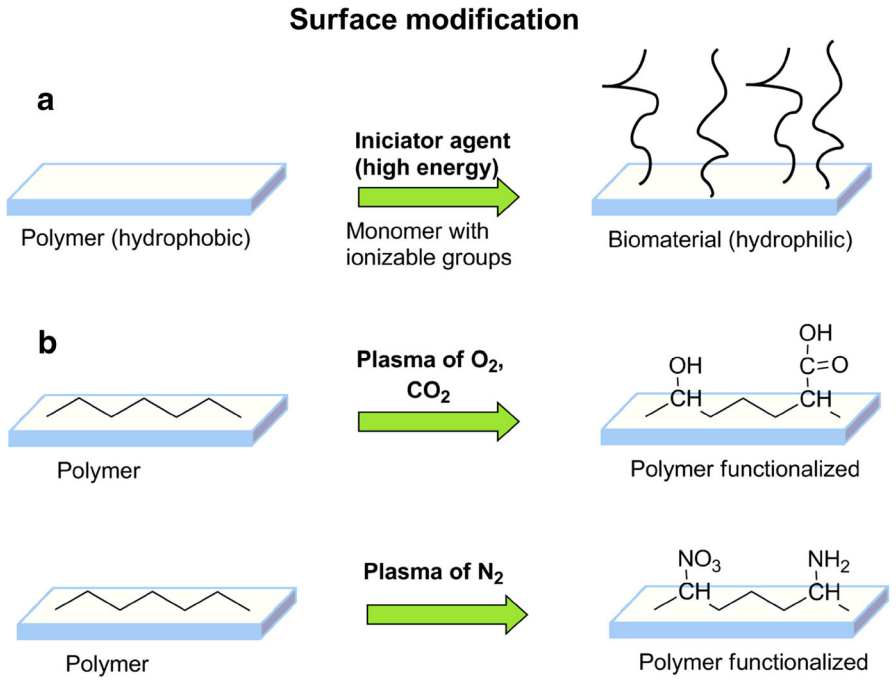

Fig. 4 Surface modification of polymers using ionizing radiation: gamma rays, UV, and electrons (**a**). Functionalization using plasma with different agents (**b**)

Table 1 Surface modification of polymer materials

Physically	Physical adsorption; Langmuir–Blodgett films
Chemically	Alkaline or acid-etching oxidation, e.g., through ozone; other chemical transformations
Physico-chemically	Photo activation (UV); corona treatment; treatment with electron or ion irradiation; laser treatment, gamma irradiation; plasma treatment

Dozens of review articles have been reported about surface-modified materials trying to provide a possible solution to biocompatibility and drug release [77]. Materials such as poly (acrylonitrile butadiene styrene) (ABS), silicone rubber (SR), PE [78], PP, and polyurethanes (PU) [79, 80] have been functionalized grafting organic compounds with ionizable groups [e.g., poly(carboxylic acids), poly(*N*,*N*-diakyl aminoethyl methacrylate) [81], chitosan, etc.] in order to host anti-inflammatory drugs or antimicrobials such as ibuprofen, sodium diclofenac (bacteriostatic), naproxen, vancomycin, or for biomolecule immobilization (enzymes) [82, 83]. Several reports mention that inclusion of poly(ethylene oxide) or poly(ethylene oxide)-acrylic acid mix on catheters surface [84] present a reduction in bacterial adhesion caused for negatively charged surface [85]. On the other hand, fabrication of surfaces with positive charge results in broad-spectrum antimicrobial

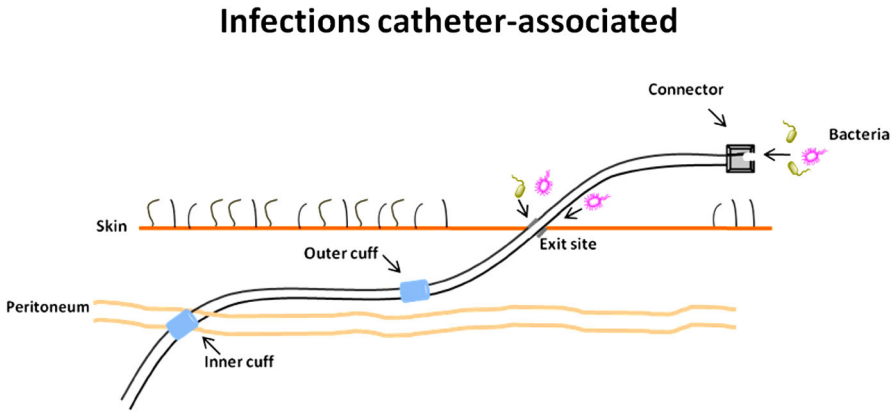

Fig. 5 Infection sites in an implanted urinary catheter. Bacteria can gain access to the peritoneal cavity either by contaminating the connector and the catheter lumen, or by migration from the skin exit site down the catheter track through the tissue

activity [86, 87]. Although the mechanism of action is still subject of debate, the general consensus is that the positive charge disrupts the lipid membrane of microbes. Polysaccharides such as chitosan and poly(4-viylpyridine) show this activity due to the high nitrogen content of the polymer creating a cationic surface.

5.1.1 Catheters

A polymeric implant is another type of application (probes, prosthetic valves, and catheters). The infection process starts in the implant site; there, the bacteria slowly grow and the antimicrobial hardly gets there, mainly when drugs are intravenously administered or by pills. The cell-adhesion profiles depend of surface architecture and roughness of implants [88]. There are studies that indicate the existence between cell adhesion and polymer surface; the bacteria adhesion occurs mainly when the polymer has a hydrophobic surface [89, 90]. Complications associated with catheters are very common around the world (450,000 cases per year in the USA alone) and the direct costs amount to over a billion dollars [91]. The main reason for the infection is due to adhesion of (Fig. 5) *Escherichia coli*, *Candida spp*., *Enterococcus spp*., *Pseudomona aeruginosa*, *Enterobacter spp*., *Staphylococcus epidermidis*, *Bacillus subtilis*, and *Staphylococcus aureus* [92, 93]. Avoiding and solving this problem when it occurs is very important in preventing complications that could cause a patient's death.

5.1.2 Coating with Shape-Memory Polymers

Temperature-sensitive polymers, and more specifically shape-memory polymers, have been used in the preparation of minimally invasive surgery medical devices. The unique properties of these materials allow the introduction of the medical device in a compressed form followed by expansion once it is located in the desired place by minimally invasive surgery procedures [68]. Materials such as guidewires,

stents, and others biomedical metallic materials have been surface-modified using an exterior coating method with poly(tetrafluoroethylene) (PTFE) or a hydrophilic polymer to reduce friction and simultaneously provide the necessary properties for a guidewire to negotiate a tortuous ureter path [94].

The chemical and physical characterization of biomaterials generally focus on the structure and properties of the polymer matrix, however, in the case of surface-modification polymers, the characterization techniques focuses mainly on surface functional groups, functional layer thickness, roughness, etc. Roughness is a very important factor to analyze in biomaterials because it is intrinsically related to bacterial adhesion [88].

The three most commonly used surface composition characterization techniques are ATR-FTIR, XPS, and SEM (Table 2); each with different penetration depths. Cell adhesion and toxicity tests with some cell (biocompatibility) are necessary to know if materials have toxic effects [95].

5.1.3 Graft Sutures

Suture is a fiber or fibrous structure attached to a metallic needle [96], mainly employed in surgery procedures as biomaterial device, used to ligate blood vessels and hold tissues together [97]. They can be classified according to the origin of the materials which they are made of (natural or synthetic), the permanence of the material in the body (absorbable or non-absorbable) and the construction process (braided, monofilament) [98, 99]. Suture materials should satisfy specific requirements: easy to handle, elicit minimal tissue reaction, do not support bacterial growth, possess high tensile strength, easy to sterilize, hypoallergenic properties, and do not induce carcinogenic action [97].

Table 2 Biomedical-related surface properties with corresponding measuring methods

Surface characteristics	Methods
Geometry: roughness, topography, specific surface, layer thickness	Profilometry, field emission, REM, AFM, interface microscopy-adsorption isotherms, BET surface area, pore radius distribution
Surface energy: wettability (specially; hydrophilicity)	Contact angle geometry; for biomaterials, mainly the captive bubble method is used
Physical characteristics: adsorption, scratch resistance, other mechanical, electric and optical characteristics, adhesion	Adhesion test after cross-hatch cut, and/or thermo test, permeation measurements, elastic characteristics; for diagnostic purposes; refractive index and fluorescence background radiation
Chemical composition: surfaces and thin layer, chemical functionality of surfaces	FTIR-ATR, IR microscopy and spectroscopy, ESCA-imaging, AES/SAM, fluorescence spectrometry, MALDI-TOF–SIMS
Biological characteristics: biocompatibility, cell adhesion, specific/non-specific, protein adsorption	Growth and toxicity tests with various cells, protein adsorption with IR and fluorescence labeling

In general terms the most important requirements of sutures materials are physical and mechanical properties, biocompatibility and antimicrobial nature [96]; in this sense, some materials currently marketed may become fallible and, as a result, multiple side-infections related to suturing procedures occur in a certain percentage of the patients [100]. This raises the need to develop or modify the existing suture devices in order to make them able to acquire antimicrobial activity analogous to the drug design, either by coating [101] or grafting pristine sutures with antimicrobial polymers and/or containing functional groups capable to load or adhere antimicrobial drugs onto the surface of the modified suture (Fig. 6).

Most commonly, reports for grafting sutures employs ^{60}Co as γ-radiation source (Fig. 7). Radiation grafting has proved to be a very effective technique to get desirable properties onto a polymeric material without any consideration of the shape of the material [102].

The irradiated materials may retain most of their original characteristics and also acquire additional properties of the grafted moiety; the structure, in some cases, changes during the modification process, depending on the nature and the amount of monomer grafted [103, 104]. It is true that the radiation-grafting technique may have limitations to generate biomedical devices because it produces changes not only in the biomaterial surface but throughout the polymer matrix, which can lead to undesirable changes in the structure and properties of the device [105]. In other cases, the use of ionizing radiation provides the energy required for activation of molecules in the material that under other conditions cannot be achieved by the lack of reactive groups.

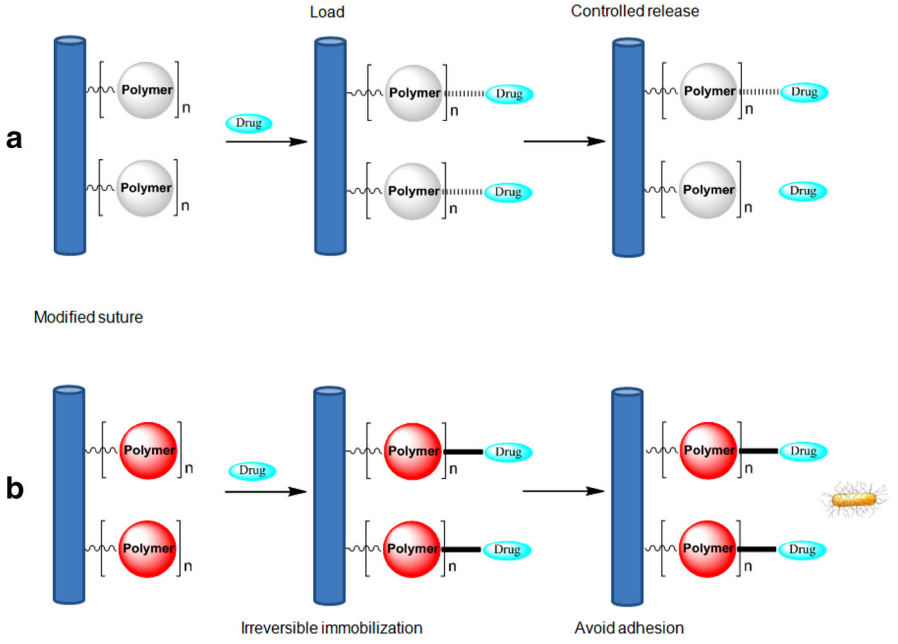

Fig. 6 Electrostatic load-release (**a**) and covalent immobilization (**b**) of drugs on modified sutures

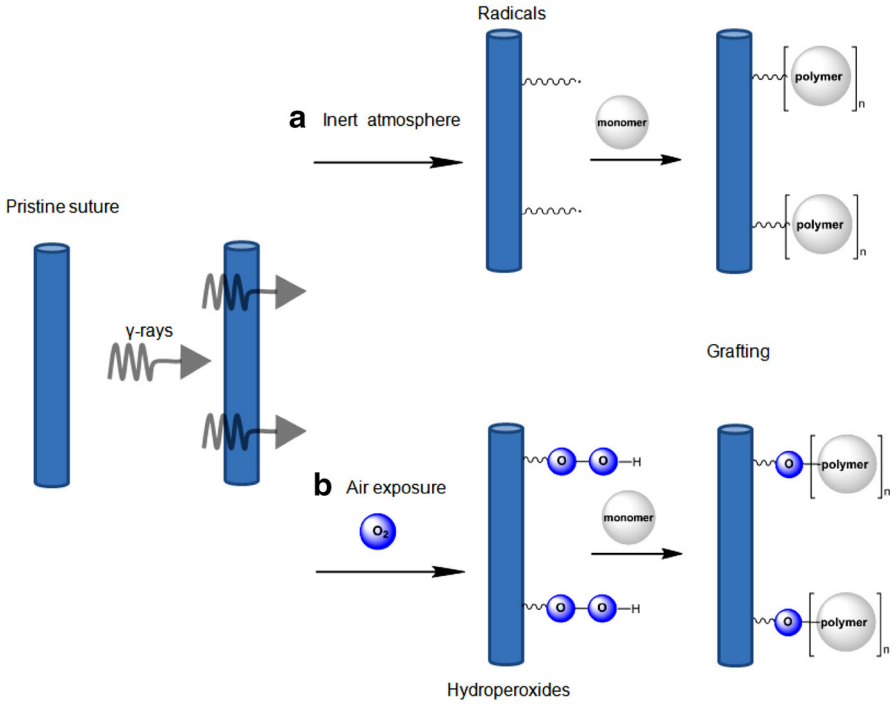

Fig. 7 Suture γ-radiation grafting: **a** direct irradiation and **b** pre-irradiation grafting method

Some examples of PP grafting matrix are described below [102, 104, 106]:

PP-*g*-PAN and PP-*g*-PAAc: Acrylic acid is one of the most popular monomers that have been grafted onto different polymeric matrices and its polymer or copolymers with pH-sensitive response have the capability to undergo further chemical reaction to produce new functional groups [4]. The grafting percentage of AAc onto PP films by pre-irradiation method was increased as a function of reaction time and reaction temperature [14].

Due to the inherent reactivity of the acrylic acid, homopolymer formation is the main polymerization reaction when radiation-grafting technique is used. Efforts have been made to obtain carboxylic acids' high-content surfaces without compromising the sutures' physical properties.

The grafting polymerization using pre-irradiation technique of acrylonitrile (AN) onto PP monofilament leads to an increase in tenacity up to a graft level of 5 % [104]. Subsequent hydrolysis is an effective way to introduce carboxylic groups into the monofilament. The transformation of nitrile groups into carboxylic groups proceeds under sodium hydroxide conditions to achieve PP-*g*-AAc, as this reaction is necessary for loading the drug; the hydrolysis leads to a considerable loss of mechanical strength in the grafted suture. This approach produces a suture with carboxyl functionality PP-*g*-AAc of 62 % or about 0.25 mmol/g, which is enough for subsequent antimicrobial drug immobilization [102, 106].

PP-*g*-PVIm: Here, sutures were prepared by the simultaneous radiation grafting of 1-vinylimidazole (VIm) onto PP monofilament with results around 5–20 %. The tenacity slightly decreases, whereas the elongation augments with the increment in the degree of grafting.

The grafted suture has reasonably good water uptake. The PP-*g*-PVIm grafting was immobilized with an antimicrobial drug, ciprofloxacin. The modified suture releases the drug over a period of 4–5 days, the same period of time that the material showed antimicrobial activity in vitro against *Escherichia coli* [107].

PP-*g*-PAAc and PP-*g*-PGMA: Recently, our investigation group developed separately grafting AAc and glycidyl methacrylate, GMA onto PP sutures applying γ-ray pre-irradiation oxidative method under various experimental conditions, therefore a different range of grafting was obtained (GMA: 25–800 %, AAc: 9–454 %). Synthesis and antimicrobial activity from this study was: (a) with PP-*g*-AAc load and release of vancomycin drug, here only ionic interactions are involved and (b) the irreversible covalent immobilization of the drug onto PP-*g*-GMA via the opening ring of the epoxy groups, then, the alcohol oxidation to the aldehyde, which reacts with the amino groups of the vancomycin and finally to the reductive amination of the copolymer. In both cases, antimicrobial activity against *Staphylococcus aureus* was corroborated [103].

5.2 Biosensors

Sensors are transducers that detect changes or events in the environment to produce an outcome, i.e., have the feature to convert one sort of energy (signal) to another, generally into an electrical signal. The advantage of sensors against chemical analysis techniques results from the fact that they are specialized, small size, portable, and inexpensive devices that are suitable for in situ analysis and real-time monitoring of chemical and physical parameters [108].

Within the different types of sensors used today, biosensors have gained importance and interest in the scientific community due to their performance and application possibilities for knowledge and monitoring of biological processes. Biomedical sensors acquire signals thanks to a bioreceptor (biological recognition element), representing biomedical variables or phenomena and transform them into electrical signals. These kinds of sensors have an interface between a biologic part and an electronic system; thus both parts must function in such a way that do not change or affect adversely the systems. Table 3 shows different types of sensors according to its interface. In the last years, these sort of sensors have been defined as biosensors.

A variety of sensors can be applied for biomedical purposes; it is possible to classify them into two wide groups according to the transduction principles involved. Table 4 shows the two groups of sensors.

The sensors with physical structure can measure the changes in electrical and optical phenomena inside the human body, e.g., quantify pressure, blood flow, corporal temperature, muscular stretching, and bone growth [108]. On the other hand, although chemical sensors can be applied to measure these changes too, they are particularly useful for detecting, quantifying, and monitoring the presence of

Table 3 Types of sensors (interface)

Non-contacting (non-invasive)
Skin surface (contacting)
Indwelling (minimally invasive)
Implantable (invasive)

Table 4 General classification of sensors (biomedical application)

Physical structure	Chemical structure
Mechanical	Electrochemical
Electric	Photometric
Thermal	Bioanalytic
Optical	Gas
Geometric	Physical chemical methods
Hydraulic	

different elements or compounds in specific concentrations, as well as for determining the activity and interaction with other elements inside a determined biological process to generate a possible diagnosis and therapy [109].

The materials to design and develop biosensors have been changing over time. One of the main problems faced by the biosensor technology is the rejection of the device by biological systems [110]. Thus, efforts have been focused to provide different materials that permit the correct integration between systems (biocompatibility). Moreover, it is well known that sensor performance can be modified by the interaction with biological systems. The degradation due to the exposition to biological matter is related to the type of sensor. In the case of internal sensors (inside the body) degradation degree is faster and, as a consequence, the performance would be decreased and the structure-design will be compromised. Biomedical sensors should have a flexible base structure capable of deforming and adapting to body form. The latest research has been testing and developing biocompatible polymers with excellent mechanical properties. The principal biomedical applications are generating wound-relief membranes with drug delivery [111], adhesives for biological implants, sensor skin support [112], cartilage and artificial meniscus [113], and eye-drop lubricant and fibers [114].

Radiation-induced grafting is presented as an alternative method for functionalization of polymer surfaces to improve biocompatibility of biosensors. Not only can they improve biocompatibility, molecules or polymers sensitive to electrical, magnetic, or chemical changes can be grafted, meaning a higher sensitivity, resistance, and specificity to certain biological processes. Poly(vinyl alcohol) (PVA) is one of the polymers used for this purpose. It is both water-soluble and flexible, characteristics that increase biocompatibility and mechanical resistance, respectively. Another polymer is PS, which excellent biocompatibility, low permeability, non toxicity, has good adsorption, mechanical, and chemical resistance. All of these features make polystyrene a candidate for use as a base for immobilizing enzymes [115] and drug delivery [116]. PMMA is another biomedical material that is

resistant to inorganic solvents, has good optical capacity (92 % transparency), a high rate of refraction and biocompatibility. A common application is for intraocular lenses, dental prosthesis [114], thin films, electronic skin devices, and support [112].

Other materials with the possibility of being grafted for sensor applications are conductive polymers (CP). Unless the knowledge about the amorphous structure on polymers and classified like electrical isolators, the CP have conducting properties achieved by incorporation of small concentrations of conducting materials (doping) or by inclusion of conjugated π electrons systems [117]. In some cases, CP let a good flow of electrons closing to conductivity values of some metals ($>10^3$ S/cm). Polymeric materials with conductive properties gather structural physical–chemical characteristics inherent to polymers with electrical conductivity of metals [118]. One of the most used conductive polymers is polypyrrole (PPy) due to its characteristics of high conductivity, biocompatibility, oxide-reduction activity, ductility, possibility of surface modification [119], capability to form thin films [120], and corrosion protection [121]. Grafting polypyrrole molecules onto different substrates generates materials with applications in organic electronic devices [121], rechargeable batteries, light emission diodes (LED) [118], electrochemical sensors [121], thin films [119], synthetic fibers, and protection shields on semiconductors [120]. Another CP is the polyaniline (PANI). Chemical and thermal stability, controllable conductivity, high conductivity in terms of frequency, electromagnetic shield interference and microwave absorption [122] are their common characteristics, and are usually used to fabricate low-cost photovoltaic panels, high-performance batteries [119], organic volatile compound detectors [123], and organic electronic circuits [124]. Another material is the polythiophene (PT), with properties like biocompatibility, possibility of chemical modification, high conductivity, and stability, being one of the early organic materials used in the electronic industry, like FET transistors [125] and semiconductor films [126]. All of these materials modify their conductive properties through increasing or decreasing the electrical resistance based upon reactions of oxide-reduction.

5.3 Grafting Polymer Matrixes for Cell and Tissue Cultivation

Another important application for radiation grafting technique is the modification of biomaterials to enhance or lighten-up interactions with living tissues. The surface of the biomaterial comes in contact with the living tissues, thus the initial response of the body towards a biomaterial depends on its characteristics. Hence, proper designing and/or modification of the surface is of considerable importance for enhanced compatibility of the biomaterial. In the tissue compatibility case, two types of reactions can occur: inflammation and immunogenicity, but in the blood compatibility the fastest reaction is often thrombogenicity. The inevitable inflammation in the tissue compatibility occurs around the implanted material and its function is to allow elimination of dead cell debris and further tissue repair. A material of optimal biocompatibility should not increase the intensity and duration to the basic response, nor prevent the tissue repair. The interactions between blood and a polymer surface depend on various parameters determined by the structure

(e.g., crystallinity, molecular conformation, roughness, rigidity, and degradation), composition (e.g., chemical group associated with the hydrophilic/hydrophobic balance, type of electrical charge, ionizable groups, and micro-domains), and dimensions (e.g., surface area and size) of the material. Grafting several molecules on the biomaterial surface allows us to modify these parameters and characteristics in order to promote tissue growth and, as a consequence, the acceptance of the polymeric material by living tissue and biocompatibility. These reactions are generally different for each material, but at the design and synthesis of a polymer for biomedical use, these parameters must be taken into account [127, 128].

Current approaches are giving considerable efforts in providing niche theories and solid bases considering a pore-size perspective ranging from nano to micrometer range, trying to establish a direct connection with cell growth. In this context, several works are being carried out considering the development of scaffolds with well-defined pore size and distribution [129, 130]. Apart from a size perspective, grafting of biomolecules of biomedical interest may also be directed towards functionalization of surfaces and polymers that were seek for site specific delivery, provide biological affinity, among other properties. From a developmental point of view, several modifications may be carried out on a surface or backbone level for improving biological affinity [131–133]. Within this perspective, several potential biomolecules may be grafted onto polymeric matrixes, also along polymer structure, including proteins [131–134], growth factors [135], among other biomolecules of interest.

A highlighted and renowned application for grafted polymer and grafted polymer matrices is related to cell and tissue cultivation, whereas grafting of biological substances or other bioactive compounds onto polymer substrates has been proven effective towards controlling important parameters for cell growth and tissue development, which may somehow modulate cell affinity and therefore provide control over the process. Thus, when it comes to tissue engineering or cell cultivation, lots of attention has been driven towards the development of smart matrices capable of promoting cell attachment and adhesion and cell growth [136–139].

Advanced systems comprise stimuli-responsive materials, e.g., thermoresponsive matrices [135], which may modulate cell affinity as a function of temperature. In practical terms, these systems allow cell cultivation with adequate adherence by providing a suitable microenvironment for cell and tissue growth, and when appropriate, changes in temperature lead to complete cell detachment, which is adequate for quick tissue removal, without requiring direct handling.

6 Conclusions and Remarks

In terms of relevance, the contribution of polymer grafting to the advancement of materials science is well established, as it unraveled novel applications for conventional materials as a result of the responsive or tunable properties added to the products through the grafting process. Within this context, this chapter detailed the state of the art of polymer grafting, by means of high-energy irradiation,

including fundamental aspects of synthesis and characterization, with focus on the functionalization of surfaces for biomedical applications.

Three techniques are currently available for the development of grafted polymers or functionalization of surfaces with stimuli-responsive polymers by the use of high-energy irradiation, known as the pre-irradiation method, pre-irradiation oxidative method, and the direct method. Such techniques lead to distinct grafting and homopolymer formation yields and require different experimental parameters or conditions to be applied. Thus, the selection of the method should rely on the characteristics of the monomer or functional group, and the polymer itself, as well as the desired properties to be achieved.

Radiation-grafting has advantages over conventional methods, including the lack of a needed catalyst or additives to initiate the reaction, and usually, no changes of the mechanical properties with respect to the pristine polymeric matrix are observed. In addition to these characteristics, irradiation may allow simultaneous sterilization of the systems, depending upon the irradiation dose.

Finally, some applications of grafted polymers and grafted polymer-based materials were described including the development of graft biomaterials for drug delivery, graft sutures, and for use as biosensors. The main advancement provided by the technique towards biomaterial development concerns the possibility to originate materials capable of responding to biological or microenvironmental changes, without the need for an external interference. In terms of drug delivery as an example, the benefits arise as low doses of medicines may be administered in longer periods of time with less toxicity as a consequence. On this account, future perspectives abound as novel possibilities and functionalized materials are created continuously in the search to solve issues regarding drawbacks of polymers or polymer-based materials.

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