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Blood compatibility of diamond-like carbon (DLC) coatings

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Abstract: Diamond-like carbon (DLC) films offer numerous functional characteristics that make them particularly attractive as potential wear resistant coatings for biomedical applications. This chapter first discusses the blood compatibility of various forms of plain and doped DLCs, and evaluates possible correlations with film structure and surface properties. The chapter then considers the application of DLC coatings to different typologies of implants and medical devices, with special regard to cardiovascular prostheses.

Key words: diamond-like carbon, coatings, blood compatibility, cardiovascular applications.

4.1 Introduction

Carbon is a highly versatile element. Various allotropes originate from the multiple possible hybridization states of its orbitals, including graphite, diamond and fullerene, and each of these materials offers different properties dependent on its particular structure.

Development of a special class of carbon-based materials called diamond-like carbon (DLC) began during the 1970s and has rapidly gained the interest of the scientific community due to the outstanding qualities and performance exhibited.

The term DLC is used to define a large family of amorphous carbon-based materials containing both sp^3 and sp^2 carbon bonds in variable amounts, and potentially including hydrogen or other alloying elements, such as nitrogen, fluorine, silicon or phosphorous. DLC forms isotropic disordered thin films, which exhibit some extreme properties similar to those of diamond, including hardness, elastic modulus and chemical inertness (Robertson, 2002).

Different deposition techniques have been proposed that give origin to a large selection of amorphous carbons with varying sp^3 and hydrogen content. The fraction of sp^3 bonds and the hydrogen content significantly contribute to determining the structure and, consequently, the final properties of DLC films.

DLC coatings are characterized by a high level of hardness, low friction coefficient, high resistance to corrosion and smooth surface finishing. These properties make them attractive as potential wear resistant coatings for several interesting applications, including optical, mechanical, microelectronic and

biomedical applications. Another big advantage of DLC coatings is that they can be produced at low deposition temperatures on various substrates and can therefore be used in coating heat-sensitive materials such as polymers.

Since its discovery, DLC has been the object of intensive research studies, leading to greater knowledge of its properties and facilitating the development of different deposition techniques that can be used to tailor its characteristics.

DLC was first produced in 1953 by Schmellenmeier using C_2H_2 gas in glow-discharge plasma (Donnet and Erdemir, 2008). This was followed in the early 1970s by Aisenberg and Chabot, who used an ion beam deposition system to produce amorphous carbon films with remarkable mechanical properties (Aisenberg and Chabot, 1971; Donnet and Erdemir, 2008). However, it was not until the early 1990s that interest in DLCs really began to increase. Their properties and processing techniques started to be studied and improved, and a variety of possible applications began to be identified (Boehm *et al.*, 2011; Donnet and Erdemir, 2008).

Due to their unique properties, DLC coatings have been used for various industrial applications, including optics and microelectronics, manufacturing and transportation, and have been employed in the production of items ranging from razor blades and eyeglasses to magnetic storage media, fuel injectors and critical engine components (Table 4.1).

Alongside their other key characteristics, DLCs demonstrate superior bio- and blood-compatibility properties, and are therefore being used as coatings for a wide range of biomedical implants, devices and tools (Roy and Lee, 2007; Lackner and Waldhauser, 2010; Donnet and Erdemir, 2008; Dearnaley and Arps, 2005;

Table 4.1 Applications of diamond-like carbon coatings

Biomedical	Other
Hip, knee and shoulder joints	Magnetic recording systems
Coronary stents and guidewires	Optical storage devices
Vascular prostheses	Sliding/friction parts
Heart valves, blood pumps for ventricular assistance and artificial hearts	Engine components (e.g. cylinders and pistons, fuel injectors, etc.)
Sutures	Drill bits
Catheters	Precision gauges
Breast implants	Razor blades
Orthodontic archwires	Antireflective and wear protective coating for infrared optics and windows
Cochlear implants	Microelectronics
Surgical instruments (e.g. laparoscopic instruments and needles for corneal surgery)	Thin film cathodes for field emission displays
Orthopaedic screws	

Arps and Dearnaley, 2004). The deposition of a thin DLC layer on the surface of medical device components can considerably increase their biocompatibility, improving materials interaction with the biological environment. Their use decreases, for example, the probability of thrombus formation in the case of blood environment, and stimulates cell adhesion and proliferation.

Moreover, a hard and wear resistant coating like DLC can act as a protective barrier contributing to a reduction in corrosion, formation of wear debris and release of toxic elements (e.g. Ni, Co, Cr, Al and V), thus preventing possible allergic, inflammatory or carcinogenic reactions.

The first tentative application of DLC coatings to blood-contacting devices originated from the knowledge of the excellent blood compatibility properties demonstrated by pyrolytic carbon, which can in some ways be considered the antenate of DLC. Pyrolytic carbon, a turbostratic form of isotropic carbon, is currently used for mechanical heart valves and other implantable prosthetic devices due to its blood compatibility, first largely investigated by Bokros, Gott *et al.* in the 1970s.

Bio- and blood-compatibility of various forms of DLC have been investigated by *in vitro* and *in vivo* analysis, and the influence of deposition parameters on the properties of the coatings has been studied. In particular, several studies have demonstrated that DLC coatings can improve the thromboresistance of cardiovascular implants by reducing platelet adhesion and activation (Fedel *et al.*, 2009; Jones *et al.*, 2000), whereas hydrogenated DLC films showed a tendency to prolong clotting time and suppress the platelet and complement convertase activation (Nurdin *et al.*, 2003). Moreover, DLC do not seem to induce haemolytic effects in whole blood (Jones *et al.*, 1999), nor provoke macrophage activation or inflammatory signals from monocytic cells (Linder *et al.*, 2002).

Tentative descriptions of DLC blood compatibility as a function of material properties (for example sp^3/sp^2 fraction, wettability and surface energy) have been formulated with some contrasting results.

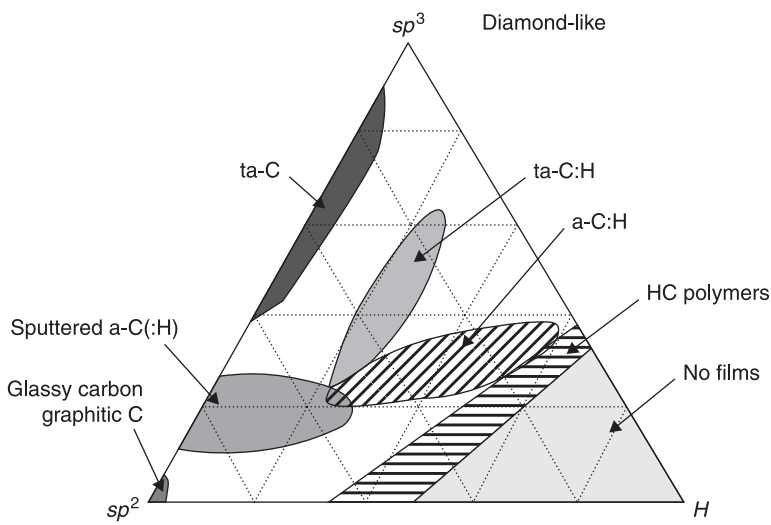
At present, DLC coatings are applied to devices for total joint replacement, orthopaedic screws, dental prostheses and surgical needles for corneal surgery, as well as to medical and surgical instrumentation. Application in the field of cardiovascular devices is of particular interest, and DLC coatings have been employed for vascular prostheses, heart valves, rotary pumps for ventricular assistance, dialysis membranes, stents and guidewires (Table 4.1).

In the following paragraphs DLC structure, properties and production technologies are examined, and the great influence that these features can have on the biological response of materials considered. Extensive analysis of the scientific literature related to the response of DLCs to the biological environment follows, discussing in detail DLC blood compatibility properties and considering both *in vitro* and *in vivo* performance. The influence of doping elements on the properties and haemocompatibility of DLC is explored, and current applications of DLCs as coatings for implants and medical devices are described.

4.2 Diamond-like carbon (DLC) structure, properties and applications

The term 'diamond-like carbon' commonly describes a family of metastable amorphous carbon films obtained via different deposition processes and characterized by a variable but significant fraction of sp^3 type C-C bonds along with an absence of long-range order in a dense amorphous structure (Robertson, 2002).

To clarify the terminology used for different forms of amorphous carbons as a function of their content of sp^2 and sp^3 bonding and of their hydrogenation degree, we can refer to the ternary phase diagram reported in Fig. 4.1. The type, structure and final properties of the amorphous carbon film depend on both the deposition method and the hydrogen content. We can, therefore, have amorphous carbon (a-C), hydrogenated amorphous carbon (a-C:H), tetrahedral amorphous carbon (ta-C) or hydrogenated tetrahedral amorphous carbon (ta-C:H), depending on the fraction of sp^3 bonding and on the presence of H in the carbon film. Hydrogen free ta-C has a C-C sp^3 content higher than 60–80%, whereas ta-C:H features a hydrogen content of around 25–30 at.% with a very high percentage of sp^3 bonding (up to 70% or higher if deposited at high ion energies) (Chhowalla *et al.*, 1997). Hydrogenated and non-hydrogenated a-C films have a lower sp^3 content with respect to tetrahedral amorphous carbons, and a variable amount of H ranging from less than 1% for a-C up to 50 at.% for a-C:H (Robertson, 2002; Grill, 1999; Lifshitz, 1999; Dongping and Baoxiang, 2006; Casiraghi *et al.*, 2007).



4.1 Amorphous carbon regions in a ternary phase diagram of bonding in carbon-hydrogen alloys. Reprinted from *Materials Science and Engineering: R: Reports*, 37(4–6), Robertson J, 'Diamond-like amorphous carbon', pages 129–281. Copyright (2002), used with permission from Elsevier.

The use of the term 'diamond-like' is justified by the high presence of tetrahedral sp^3-hybridized carbon atoms. This high presence contributes to several interesting properties of the film similar to the properties of diamond, including high hardness and elastic modulus, excellent wear resistance and chemical inertness. As shown in Table 4.2, DLC films offer a range of very attractive characteristics, including exceptional mechanical, tribological, chemical, electronic, optical and biological properties, making them suitable candidates for several applications. In Table 4.3 the main structural and mechanical properties of different types of DLCs are presented and compared to the properties of diamond and graphite, as well as to pyrolytic carbon.

Mechanical properties and density of DLC depend mainly on the presence of C-C sp^3 bonds. In general, DLC films are characterized by high hardness and high

Table 4.2 Main properties of DLC films

High density
High hardness and elastic modulus
Smoothness
Low friction coefficient and high wear resistance
Chemical inertness and corrosion resistance
Optical transparency (mainly infrared)
Good thermal conductivity
Wide band gap semiconductor
Low dielectric constant
Possible deposition at low temperature
Biocompatibility and blood compatibility

Table 4.3 Structural and mechanical properties of different diamond-like carbon (DLC) films compared to crystalline carbon allotropes (diamond and graphite), and to pyrolytic carbon

	sp^3 content	H content	Density (g cm^{-3})	Young's modulus	Hardness
Diamond	100%	0%	3.52	1000–1200 GPa	100 GPa
ta-C	>80%	0%	3.1–3.5	800 GPa	80 GPa
ta-C:H	70%	30%	2.4	n.a.	50 GPa
a-C:H soft	60%	40–50%	1.2–1.6	n.a.	<10 GPa
a-C:H hard	40%	30–40%	1.6–2.2	n.a.	10–20 GPa
Graphite	0%	0%	2.3	686 GPa (//a) low (⊥a)	–
Pyrolytic carbon	–	–	1.5–2.1	28 GPa	>230 (DPH 500 g)

Source: Data obtained from Grill, 1999; Koidl *et al.*, 1990; Lifshitz, 1999; More *et al.*, 2004.

elastic modulus. Typical hardness values of a-C:H films are in the range of 10–30 GPa (Grill, 1999) and can increase up to 40–80 GPa in the case of hydrogen-free ta-C. As expected, increasing hardness and elastic modulus correlate with an increasing sp^3 percentage and a decreasing hydrogen content. Furthermore, the properties of DLC films can be varied over a wide range by changing the deposition conditions. Mechanical characteristics, in particular, depend on the substrate temperature and usually improve with increasing ion energy per condensing carbon atom.

Thanks to their special properties, DLCs have manifold applications in different areas, including, the automotive and transportation industry, optics and electronics fields. They are often used for data storage (hard discs and heads, tape-recording heads and guides, for example), or as wear protective coatings on components requiring superior mechanical and tribological qualities, as in the case of engines or sliding parts.

Moreover, due to the combination of their physico-chemical and mechanical properties with specific bio- and blood-compatibility properties, DLCs present a valuable success in the biomedical field, and particular importance can be attributed to the properties of DLC films that can be exploited for the improvement of medical implants and devices. Hardness and wear resistance are particular requirements for several implant components, for example orthopaedic joints, mechanical heart valves and other devices which are subjected to fatigue and repetitive cyclical stresses. The presence of a biocompatible carbon-based coating on the surface of a metallic component (Co-Cr alloys, Ti-6Al-4V, NiTi, etc.) can protect the organism from contact with toxic or potentially allergenic, inflammatory or carcinogenic elements. It can also help prevent the release of metal ions and the detachment from polymeric (e.g. HDPE) or metallic components of dangerous debris with the potential to cause an adverse response of the host organism through foreign body reaction.

Chemical inertness and corrosion resistance are also especially important characteristics. The human body presents a range of very aggressive, hostile environments, and body fluids could easily trigger corrosion, etching or oxidation phenomena. DLC films therefore represent ideal coatings for metallic or polymeric bulk materials for the avoidance of corrosion, degradation or oxidation phenomena on the surface of devices inserted in the human body.

Besides a great number of advantageous properties, DLC films feature a small number of critical characteristics. In particular, they are subject to high internal compressive stresses, mainly resulting from the quenching of the impinging species during film growth (Donnet and Erdemir, 2008). This reduces their adhesion to the substrate and prevents the growth of thick coatings, limiting film thickness to less than 1 μm (Grill, 1999).

DLCs have been reported to adhere well on substrates containing carbide-forming elements (for example silicon or titanium), but often intermediate layers need to be deposited on different substrates to improve the deposition

and adhesion of DLC films (Donnet and Erdemir, 2008). Critical adhesion and delamination properties represent one of the main limitations related to DLC films and to their industrial applications, especially for biomedical applications.

4.3 Deposition techniques for DLC films

Diamond-like carbon coatings can be deposited using a number of different techniques. These techniques can generally be divided in two categories: chemical vapour deposition (CVD) and physical vapour deposition (PVD).

In general, a carbonaceous precursor and an energy source are required. The carbon source may be an ionized carbon-containing gas or a solid carbon target that can be activated by, for example, thermal evaporation, ion sputtering or laser ablation. Most of the processes upon which DLC deposition is based are physical in nature, as the sp^3 bonds are produced by the impact of carbon (or hydrocarbon) ions on the growing film. The physical processes that have been proposed to deposit DLC thin films include direct ion beam (IB) and ion beam assisted deposition (IBAD), filtered cathodic vacuum arc (FCVA), DC and RF sputtering, pulsed laser deposition (PLD), and plasma immersion ion implantation (PIII). Other techniques involving chemical processes include plasma enhanced chemical vapour deposition (PECVD) and electron cyclotron resonance plasma chemical vapour deposition (ECR-CVD).

The first DLC films produced by Aisenberg and Chabot were obtained by direct IB deposition. In this method, the target surface is bombarded under vacuum conditions by energetic carbon ions, produced by plasma activation from a graphite cathode or from a hydrocarbon gas such as methane. Mass selected ion beam (MSIB) represents a more controllable deposition technique, which allows the flux ratio of ions to be increased to neutral species, and permits the fine adjustment of DLC properties, despite holding a low deposition rate. In this case, carbon ions C^+ are produced with a very sharp ion energy distribution (1–10 eV), accelerated to a high voltage (20–30 kV) and passed through a magnetic filter, which removes from the beam neutral unionized particles and/or contaminants. The ion beam, which diverges due to Coulomb repulsion, is then focused and decelerated by an electrostatic lens so that it impacts the substrate surface with a controlled energy, typically in the range from 5 eV to 20 keV (Lifshitz, 1999; Robertson, 2002).

Cathodic arc deposition involves generation of an electric discharge between a graphite cathode and an anode. This produces highly energetic plasma, with very high carbon fluxes and high deposition rates. As the plasma can contain, besides carbon ions, neutral carbon and particulate, these films may present a variable amount of graphitic bonding. In FCVA, a toroidal magnetic filter is used, helping to remove micro- and macro-particles and thereby increasing the purity of cathodic arc deposited DLC films. The films obtained by FCVA deposition, which can be

virtually hydrogen-free, offer particularly beneficial properties, including high smoothness and hardness (Arps and Dearnaley, 2004). Cathodic arc and FCVA are frequently used on an industrial scale. The advantages of these systems include high deposition rates and the potential use as coating for insulating materials, thanks to the neutral nature of the plasma.

In pulsed laser ablation, an excimer laser (ArF) is used to vaporize carbon species from a carbon target using very short, intense laser pulses. Depending on the source (e.g. graphite or polycarbonate), ta-C or a-C:H can be produced (Robertson, 2002; Arps and Dearnaley, 2004).

Sputtering is a very typical method used for the production of DLC films and, as a very versatile and controllable process, is frequently exploited at the industrial level. Non-hydrogenated DLC films are produced by DC or RF sputtering of pure graphite targets using an Ar plasma. In magnetron sputtering, magnets are placed behind the target and used to increase the ionization degree of the plasma, thus increasing the deposition rate of DLC film on the substrate by PVD. In some cases, dual ion beam sputtering (also called IBAD) is used to produce relatively pure DLC films. This involves the simultaneous use of two ion guns: one Ar gun is used to sputter carbon from a graphite target, and a second gun is used to bombard the substrate, encouraging sp^3 bond formation in the growing film.

In PIII, the substrate is immersed in plasma and periodic high-voltage pulses are applied to form an electric sheath between the substrate and the plasma. Carbon ions from the plasma are thus accelerated to the substrate by the expanding sheath's electric field (Anders, 2000). PIII deposited carbon films typically present high hardness and low friction coefficients, occasionally with high compressive stress values (Arps and Dearnaley, 2004).

A different method frequently used for the laboratory production of DLC films is PECVD. Based on a CVD process, PECVD involves the decomposition of a selected precursor (such as methane, ethane, ethylene, acetylene, etc.) at high temperature and low pressure to maximize the ion radical fraction. In PECVD the energy for the chemical reaction is supplied by plasma, generally created by RF frequency or DC discharge between two electrodes in a chamber filled with the reacting gases. Several process parameters can be varied, including composition, pressure and flow rate of the source gas, or frequency and intensity of the RF power source. These modifications can influence such film characteristics as adhesion, hydrogen content, density and mechanical properties. By using PECVD, hydrogenated DLC films can be obtained, as the presence of hydrogen (10–50%) is required to passivate the dangling bonds in the amorphous structures (Grill, 1999). Doped films can also be produced using opportune gas mixtures. PECVD is particularly interesting as it allows the deposition of thin films at a much lower temperature than that commonly used in conventional CVD reactors. With this technique, good film adhesion and high growth rates can be achieved.

As reported, a number of different methods have been proposed to fabricate DLC coatings, and the composition (sp^3-to-sp^2 fraction and H content), microstructure and related properties can vary significantly depending on the technique, deposition parameters, substrate temperature and carbon precursor used (Cho *et al.*, 1992).

Recent advances in DLC film deposition and characterization facilitate the production of materials with controlled properties, tailored to suit specific requirements. In some cases, further film modifications (gas plasma treatments or laser irradiation, for example) can be introduced following deposition, in order to improve some characteristics of the coating and obtain the desired performance for specific applications.

4.4 DLC blood compatibility

Implants, prostheses and some medical devices are engineered to enter the human body and work in particular physiological environments, dependent on the specific function they are required to fulfil. In the case of cardiovascular implants, in particular, the specific biological environment is represented by the complex blood system. When a biomaterial is placed in contact with blood, it is recognized as a foreign element by the host, and key reactions such as thrombosis, inflammation and fibrosis can take place (Gorbet and Sefton, 2004). Thrombosis is the major and most frequent complication related to devices for cardiovascular applications. This can take place when blood contacts a foreign surface, triggering platelet adhesion and activation of the coagulation cascade through the intrinsic pathway.

Protein adsorption assumes a particularly critical role in blood compatibility, as it is the first event that rapidly occurs on all surfaces exposed to blood, and is finally responsible for the haemocompatibility of a material. Within seconds of contact between the material and the blood, the surface is covered by a layer of proteins whose composition, relative concentration and conformation guide the subsequent host response, therefore playing a key role in determining the fate of the material. Blood plasma contains various molecular species and hundreds of proteins in a wide range of molecular weights, charges, structures, and concentrations. About a dozen proteins, 'the big twelve,' are considered to dominate plasma protein adsorption. These include albumin (HSA), immunoglobulins (IgG, IgA, IgM), C3 complement component, fibrinogen (Fng), haptoglobin, α1-antitrypsin and α2-macroglobulin, as well as low and high density lipoproteins (Andrade and Hlady, 1987). In particular albumin, fibrinogen and, to a lesser extent, fibronectin, assume a prominent role in leading blood–material interactions.

A series of biological reactions, such as platelet adhesion/activation, triggering of coagulation and complement systems, and activation of leucocytes, are strongly dependent on protein adsorption. Thus the adsorption of contact phase proteins, for example, may be responsible for the activation of the intrinsic coagulation

system (Gorbet and Sefton, 2004), whereas platelet adhesion is likely to take place thanks to the role of adsorbed adhesive plasma proteins, including fibrinogen, von Willebrand factor, fibronectin and vitronectin.

Due to the complexity of the blood system and of possible blood–material interaction mechanisms, various aspects have to be considered for a complete assessment of DLC haemocompatibility, including protein adsorption, platelet adhesion/activation, triggering of coagulation and complement systems, activation of leucocytes and haemolysis. As such, several studies have been presented in the literature analyzing diverse aspects of the blood compatibility of different types of DLC coatings.

In our previous work, we studied the properties of commercially available DLC films deposited at low temperature by PVD on different substrata, including a Co-Cr alloy used for heart valve components and silicon chips (Fedel *et al.*, 2009; Fedel *et al.*, 2010). DLC films were compared to uncoated substrata and to pyrolytic carbon, an isotropic carbon coating used for biomedical applications (More *et al.*, 2004). Protein adsorption kinetics and binding strength, as well as platelet adhesion/activation on the sample surfaces were analyzed *in vitro*.

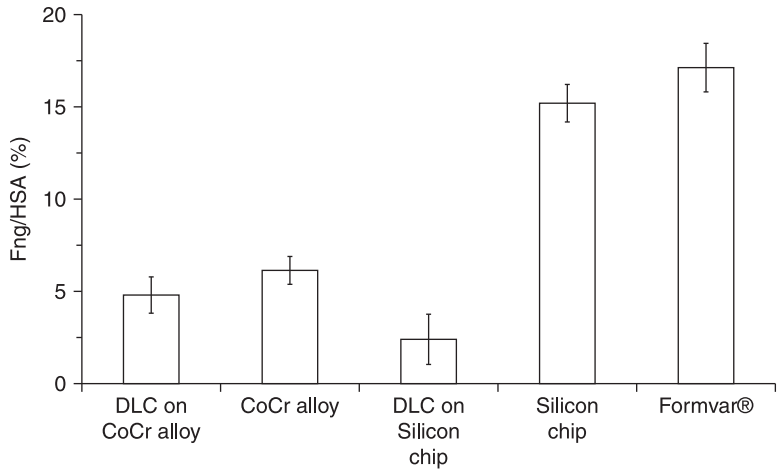
As a general rule, the results showed that the protein mainly adsorbed on the carbon-coated surfaces was albumin, whereas the control materials presented more rich and complex protein adsorption profiles. DLC surfaces revealed a weak and reversible interaction with a small amount of mid- and high-MW plasma proteins, whereas a preferential and tenacious albumin adsorption was enhanced.

The fibrinogen-to-albumin adsorption ratio was studied as a measure of the blood compatibility of a material, as surface competition between these two plasma proteins can contribute to defining the thrombogenic/non-thrombogenic behaviour of artificial blood-contacting materials (Cui and Li, 2000). Human serum albumin (HSA, 66 kDa) and fibrinogen (Fng, 340 kDa) are two of the most abundant plasma proteins, and present opposite haemocompatibility potential, as Fng is a pro-adhesive protein (Grunkemeier *et al.*, 2000; Wu *et al.*, 2005) which stimulates platelet activation, whereas HSA seems to inhibit the initial blood platelet adhesion (Young *et al.*, 1982).

A low fibrinogen-to-albumin ratio was observed for DLC deposited on Co-Cr alloy and silicon at all the residence intervals tested, in particular at high incubation times (Fig. 4.2). This was a result of lower Fng adsorption for these samples in relation to control materials.

Platelet activation on the sample surfaces has been assessed by analyzing the morphology of adherent platelets, as the activation process is characterized by platelet change from the typical resting discoid shape to varying degrees of spreading (Goodman *et al.*, 1996).

According to our findings, all of the carbon-coated materials presented a significantly lower level of platelet adhesion and activation after 15 and 25 minute incubation periods with platelet-poor plasma and a lower propensity to form



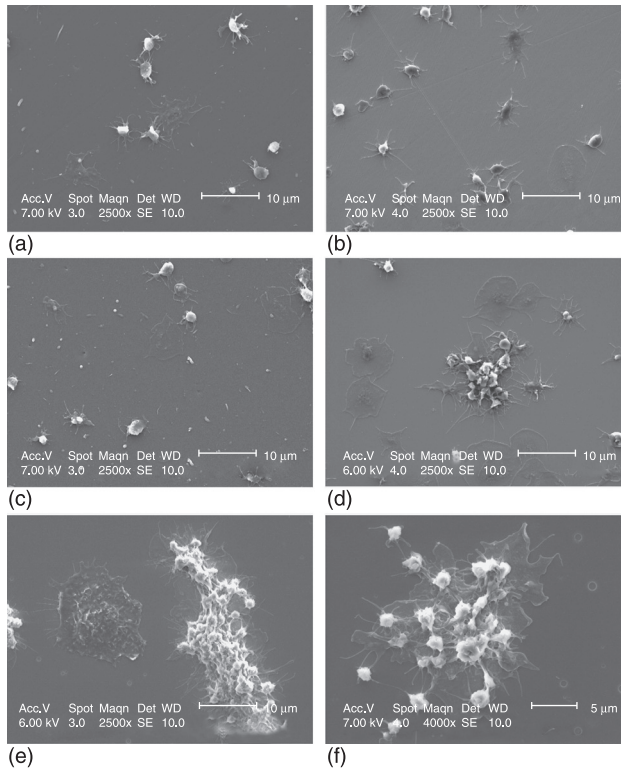
4.2 Protein adsorption on DLC-coated and uncoated samples and on Formvar positive control. Fibrinogen-to-albumin surface adsorption ratio after 25 minutes incubation with platelet-poor plasma (Fedel *et al.*, 2009).

three-dimensional (3-D) platelet aggregates in comparison to the respective non-coated substrata and control materials (Fig. 4.3). A specific relationship was found between the degree of platelet activation and the amount of Fng-to-HSA adsorbed on the tested surfaces. Minimum platelet spreading was evident on the surfaces presenting lower Fng-to-HSA adsorption ratios from plasma, whereas the highest degree of platelet spreading was reported in the case of higher Fng/HSA adsorption (Fedel *et al.*, 2009).

According to our work, DLC blood compatibility seems to be related to surface chemical heterogeneity more than to the absolute hydrophilicity/hydrophobicity degree of materials. Blood compatibility may be guided by a favourable disposition of the acid/base and dispersive sites on the amorphous carbon film surface (Fedel *et al.*, 2009). Moreover, the smooth topography of DLC films may contribute to inhibit the adsorption and retention of mid- and high-MW proteins (Fedel *et al.*, 2010).

Our studies support the hypothesis that rapid and tenacious binding of albumin globular molecules to carbon-based materials through 'domain-match' mechanisms contributes to passivation of the surfaces. The tightly bound albumin layer prevents the adsorption of Fng and higher MW proteins on DLC surfaces, thus rendering the coating more thromboresistant and less adhesive and activating for platelets.

In agreement with our studies, various authors reported a typical propensity of DLC films produced by several different deposition technologies to limit platelet adhesion and activation. DLC films have been compared to numerous materials,



4.3 Platelet adhesion and spreading on DLC-coated (a, c) and uncoated substrata after 25 minutes incubation with platelet-rich plasma. DLC on CoCr alloy (a), uncoated CoCr alloy (b), DLC on silicon chip (c), silicon chip (d), Formvar® positive control (e, f). Adapted from Fedel *et al.* (2009).

including polymers, metals, oxides and thin layers, demonstrating, in most cases, superior properties in terms of thromboresistance (Nurdin *et al.*, 2003; Alanazi *et al.*, 2000; Jones *et al.*, 2000; Dion *et al.*, 1993; Cui and Li, 2000; Sui *et al.*, 2006) (Table 4.4).

Alanazi *et al.* evaluated the blood compatibility of DLC deposited on polycarbonate in comparison with polycarbonate substrata (PC), PC coated with heparin (Heparin-PC) and 2-hydroxyethylmethacrylathe/styrene (HEMA/St), with a different level of platelet adhesion observed on the various materials (HEMA/St < DLC < Heparin-PC < PC) (Alanazi *et al.*, 2000).

A quantitative study using I-125 labelled platelets under dynamic conditions reported a considerably reduced platelet adhesion on PECVD-deposited DLC coatings with respect to titanium samples (Krishnan *et al.*, 2002), and showed the dependence of platelet adhesion on the shear rate exerted by blood fluids on the

Table 4.4 Blood compatibility of DLC films discussed for different deposition techniques and physico-chemical characteristics and compared to different control materials

Material	Deposition technique	Main characteristics	Control materials	Blood compatibility with respect to control materials	References
a-C:H	PECVD	Smooth coating Water contact angle 56° ca	Ti TiN TiC	Good haemocompatibility Higher HSA/Fng ratio Low platelet spreading	Jones *et al.*, 1999 Jones *et al.*, 2000
DLC	IBAD?		CN PMMA	Higher HSA/Fng ratio Lower platelet adhesion	Cui *et al.*, 2000
a-C:H	Magnetron sputtering	Smooth surface Intermediate hydrophobicity	SiC MS PDMS LDPE PMMA SiR	Delay of clotting time Inhibition of platelet adhesion, activation and aggregation Absence of activated complement factor adsorption	Nurdin *et al.*, 2003
a-C:H @ different deposition conditions	PIII-D + annealing		SS LTIC	Platelet adhesion and activation on a-C:H is affected by annealing Platelets are strongly activated by –C:H deposited at high bias, and the situation worsens after annealing	Yang *et al.*, 2004
a-C a-C:H ta-C @ different deposition conditions	RF magnetron sputtering FCVA			Haemocompatibility improves with sp^3 content on sputtered a-C films a-C:H films exhibit better haemocompatibility than a-C Platelets activate and aggregate on biased a-C:H films Higher HSA/Fng ratio and round platelets on floating a-C:H films	Logothetidis *et al.*, 2007

(*Continued*)

Table 4.4 Continued

Material	Deposition technique	Main characteristics	Control materials	Blood compatibility with respect to control materials	References
a-C:H @ different deposition conditions	RF magnetron sputtering	Film density increases by the increase of sp^3 and decreases by the incorporation of hydrogen		a-C:H films grown with floating substrates and with 10 at.% H_2 showed the highest HSA/Fng ratio Rougher protein layers are formed on films deposited under floating conditions	Lousinian *et al.*, 2007
a-C:H(CH_4) a-C:H(C_2H_2) ta-C	PECVD FCVA	sp^3 fraction: a-C:H(CH_4) < a-C:H(C_2H_2)<ta-C H content: ta-C< a-C:H(C_2H_2)<a-C:H(CH_4) Surface energy:a-C:H(CH_4)< a-C:H(C_2H_2)<ta-C Surface roughness: a-C:H(CH_4)< a-C:H(C_2H_2)<ta-C	Si Thermanox	DLC suppressed macrophage attachment Macrophage viability: Thermanox <a-C:H(CH_4)< a-C:H(C_2H_2)<ta-C<Si HSA/Fng ratio: a-C:H(CH_4)< a-C:H(C_2H_2)<ta-C The higher the H content, the lower the HSA/Fng adsorption ratio	Ma *et al.*, 2007
Carbofilm™ on different substrata	PVD	Low surface roughness Moderate hydrophilicity High hysteresis between advancing and receding contact angle	Stellite Si PET Formvar ®	Tenacious HSA binding Low Fng/HSA adsorption Low platelet adhesion and activation	Fedel *et al.*, 2009
DLC	PVD	Equilibrium contact angle: DLC ≤ PyC < F < S	PyC Formvar ®	Rapid and tight binding of HSA globular molecules passivate DLC surfaces, inducing low platelet adhesion and activation	Fedel *et al.*, 2010

Note: FCVA: filtered cathodic vacuum arc; IBAD: ion beam assisted deposition; PIII-D: plasma immersion ion implantation and deposition; PVD: physical vapour deposition; PECVD: plasma enhanced chemical vapour deposition; CN: carbon nitride; HEMA/St: 2-hydroxyethylmethacrylathe/styrene; Heparin-PC: polycarbonate coated with heparin; LDPE: low density polyethylene; LTIC: low temperature isotropic carbon; MS: medical steel; PDMS: polydimethylsiloxane; PET: polyethylene terephthalate; PMMA: polymethyl methacrylate; PyC: pyrolytic carbon; Si: silicon; SiC: silicon carbide; SiR: silicone rubber; SS: stainless steel; Ti: titanium; TiC: titanium carbide; TiN: titanium nitride; Fng: fibrinogen; HSA: human serum albumin.

material surface. In many cases, a low degree of platelet adhesion or activation was related to a high albumin-to-fibrinogen adsorption ratio on DLC films in comparison to different materials commonly used for biomedical applications, such as medical grade silicone elastomer (Dion *et al.*, 1993), carbon nitride (CN) or poly(methyl methacrylate) (PMMA) (Cui and Li, 2000).

Jones *et al.* (2000) analyzed the HSA/Fng ratio as a possible marker of haemocompatibility, and reported a favourable blood compatibility of DLC coatings with respect to Ti substrate, TiN and TiC layers. Although the authors could not find a direct correlation between material surface energy and protein adsorption, they suggested that the high HSA/Fng ratio on DLC coatings contributed to reduce platelet activation and spreading, even in cases where platelet attachment was not reduced.

In a previous work, Jones *et al.* reported the absence of a DLC-induced haemolytic effect when compared to a medical-grade polystyrene control, and related the lower platelet degree of spreading to the hydrophobic nature of DLC surfaces (Jones *et al.*, 1999). The hydrophobic character of DLC coatings, as well as low surface energy and low surface roughness, were formerly defined by McLaughlin *et al.* as possible causes of DLC haemocompatibility (McLaughlin *et al.*, 1996).

In a comprehensive work, Nurdin *et al.* (2003) evaluated the haemocompatibility of DLC and SiC films deposited by the PECVD technique through the analysis of coagulation, platelets and complement activation. The authors demonstrated that clotting was delayed on DLC surfaces, and complement convertases adsorbed on DLC surfaces were inactive as a result. Moreover, DLC-coated materials presented strongly reduced platelet adhesion and activation, while generally showing good *in vitro* blood compatibility when compared to other materials like PMMA, LDPE, PDMS and medical steel. According to Nurdin and co-authors, the chemically inert nature and smoothness of the DLC coating appears to control protein adsorption and blood compatibility (Nurdin *et al.*, 2003).

Haemolysis has also been tested as one of the factors concurring to DLC blood compatibility. A lower tendency to induce haemolysis was found in the case of DLC films with respect to LTI-carbon (Yu *et al.*, 2000). This result, combined with low platelet density on ta-C films produced by FCVA deposition, was ascribed to material work function (Yu *et al.*, 2000).

It is reasonable to think that deposition techniques and parameters used for DLC film preparation can influence the surface physico-chemical properties, and, consequently, the biological response of the coatings belonging to the large DLC family. Among various parameters, sp^3 and sp^2 bonding fractions and hydrogen content may be important factors influencing the biological response of DLC films. Various authors have tried to investigate the dependence of blood compatibility on the intrinsic properties of DLC films, providing a set of variable results. In particular, the dependence of HSA/Fng protein adsorption and of

platelet adhesion/activation on DLC structural and compositional properties has been studied. However, a univocal response has not been determined.

Better blood compatibility of a-C:H and ta-C films deposited by PIII (Chen *et al.*, 2002; Cheng and Zheng, 2006) or by PECVD (Huang *et al.*, 2004) has been reported at minimum I_D/I_G ratio in the Raman spectra, that is to say for films with lower sp^3 content (Leng *et al.*, 2003). Some authors have shown the opposite behaviour, claiming higher haemocompatibility for DLC films with higher sp^3/sp^2, as in the case of DLC deposited on NiTi alloys by PIII (Sui *et al.*, 2006) or in the case of magnetron sputtered DLC films (Logothetidis *et al.*, 2005). Lousinian *et al.* (Lousinian *et al.*, 2008) described a lower possibility of thrombus formation for a-C:H films with 40–45% sp^3 content, whereas, according to Vinnichenko *et al.*, sp^3 content does not correlate to the amount of adsorbed albumin, but more likely to surface wetting properties (Vinnichenko *et al.*, 2004).

According to Logothetidis *et al.*, the higher HSA/Fng ratio was related to higher hydrogen content in the amorphous carbon film, as well as to positive bias of the substrate (Logothetidis *et al.*, 2005), resulting in better haemocompatibility for films with a higher polymeric component. The same authors, in a more recent work, performed a careful characterization and comparison of carbon based thin films (Logothetidis, 2007). a-C and a-C:H films were deposited by RF magnetron sputtering at room temperature, varying the substrate bias, whereas ta-C films were produced by FCVA deposition. In this study, the authors analyzed the dependence of deposition conditions and H content on the blood compatibility of DLC films, concluding that the haemocompatibility increased with sp^3 content on magnetron sputtered a-C films, even if a-C:H exhibited better haemocompatibility properties. On the whole, biased a-C:H films induced small values of HSA/Fng ratio as well as platelet spreading and aggregation. In contrast, a-C:H films grown under floating conditions presented round resting platelets and a higher albumin-to-fibrinogen ratio, demonstrating an overall higher blood compatibility.

Other DLC surface characteristics have been analyzed, such as wettability, surface energy, roughness and bias, in order to evaluate possible effects on blood compatibility. Hasebe studied the effects of surface roughness on platelets, demonstrating that platelet surface coverage on DLC and F-DLC was not affected by coating roughness at the nanoscale (Hasebe *et al.*, 2007). Deposition conditions have also been analyzed, generally showing that platelet activation increases with high bias and annealing temperature (Yang *et al.*, 2004; Karagkiozaki *et al.*, 2008).

Last but not least, the structure and composition of DLC coatings also appear to influence the inflammatory response. In fact, *in vitro* studies showed a different response to the attachment and viability of macrophages depending on film sp^3 fraction and hydrogen content. In general, DLC coatings showed the ability to suppress the inflammatory response, generating lower monocyte/macrophage attachment in relation to uncoated Si surfaces (Ma *et al.*, 2007), as well as presenting reduced hydrogen peroxide production compared to stainless steel,

thermanox and polyurethane-coated stainless steel (Ball *et al.*, 2004). Ma *et al.* tested different types of DLC films. Besides having a low HSA/Fng ratio, a-C:H with the highest H content, lower sp^3 fraction, lowest surface roughness and surface energy revealed a lower propensity towards macrophage adhesion and viability (Ma *et al.*, 2007).

In general, some dominant trends guiding DLC haemocompatibility have been identified. But the description of material blood compatibility is highly complex as many factors concur to determine the behaviour of a material. Moreover, the various interlinked aspects related to blood compatibility, including platelet activation, protein adsorption and coagulation and leucocyte activation, have to be considered.

As a general rule, good blood compatibility properties can be claimed for DLC films. However, specific materials must be tested on a case-by-case basis, as deposition techniques and parameters used, as well as source material and possible surface treatments, could significantly affect the final haemocompatibility of the films.

4.5 Modified DLC films

Since the early 1990s, DLC coatings have become increasingly attractive to both industry and the scientific community. In the meantime, novel types of DLC films have been formulated in an attempt to improve the properties of these promising materials and to widen their fields of application, tailoring DLCs to produce specific responses and to meet specific requirements.

Recently, several new carbon-based films have been synthesized and tested, including hydrogenated or non-hydrogenated forms of DLC films doped with nitrogen, silicon, phosphorous, fluorine, calcium, boron, as well as metal ions such as tungsten, chromium or titanium. Such modifications have been introduced to modulate the mechanical, tribological, electrical and biological properties of films. As an example, N, Si or metal incorporation has been introduced to reduce the typically high internal compressive stresses of DLCs, whereas F or Si–O have been used to decrease surface energy and friction coefficients. The doped DLC films are deposited by the same techniques as carbon films (see Section 4.3), adding the doping-carrier species to the deposition environment (Grill, 1999). Other types of surface modification, such as gas plasma treatments, infrared or ultraviolet irradiation by nanosecond laser, have also been used to change the surface properties of DLC films (Mochizuki *et al.*, 2011; Grigonis *et al.*, 2011).

Systematic studies have been carried out to characterize the new modified DLC coatings, providing detailed information about their chemistry, mechanical and tribological properties, as well as bio- and blood-compatibility (Table 4.5). The effects of fluorine doping on DLC properties have been investigated, showing reduced film surface energy and Young's modulus, as well as increased flexibility.

Table 4.5 Blood compatibility of modified DLC films discussed for different deposition techniques and physico-chemical characteristics in comparison with DLC and different control materials

Material	Deposition technique	Main properties	Control materials	Blood compatibility with respect to control materials	References
a-C:N	PIII-D	Graphitization induced degradation of the wettability properties	a-C LTIC	The amount of N is critical to the haemocompatibility of the materials The blood compatibility of hydrogen-free a-C films is better than that of LTIC and it can be further improved by the addition of nitrogen	Kwok *et al.*, 2004
F-DLC	RF-PECVD	Contact angle: Si < DLC < F-DLC	DLC Si	Low platelet adhesion and activation: F-DLC < DLC < Si	Saito *et al.*, 2005
Ca-DLC CaP-DLC P-DLC	PIII-D	Contact angle: P-DLC< CaP-DLC<LTIC<Ca-DLC	LTIC	P-DLC and Ca-DLC exhibited lower platelet adhesion and activation P-DLC and Ca-DLC high interfacial energy seems to inhibit albumin adhesion and cause Fng conformational changes	Kwok *et al.*, 2006
F-DLC	RF-PECVD	Contact angle: SUS316L <DLC<F-DLC	DLC SUS316L PC	F-DLC low thrombogenicity *in vitro* Absence of inflammatory response HSA/Fng ratio: PC < DLC < F-DLC Reduction of platelet activation and coagulation biomarkers Greater suppression of platelet adhesion and activation with increasing F doping in the F-DLC films	Hasebe *et al.*, 2006 Hasebe *et al.*, 2007
a-C(Si)	Magnetron sputtering	Si doping decreases the fraction of sp^2 carbon bonds	a-C	The number of adherent platelets diminished with increasing Si concentration	Ong *et al.*, 2007

ta-C:P	FCVA	Contact angle: ta-C:P < ta-C γ_S: ta-C < ta-C:P γ^p_S/γ^d_S: ta-C < ta-C:P	ta-C	Low platelet adhesion and activation Phosphorus incorporation improved the wettability and blood compatibility of ta-C film	Liu *et al.*, 2008
Plasma-treated (CF_4, N_2, O_2) Si-DLC	RF-PECVD	Contact angle: Si-DLC(O_2) < Si ≤ Si-DLC(N_2) < Si-DLC < Si-DLC(CF_4)	Si NiTi	Improved haemocompatibility (protein adsorption, activated partial thromboplastin time, platelet adhesion) of N_2- or O_2-plasma treated surfaces	Roy *et al.*, 2009
F-DLC	RF-PECVD	C-F bonds increased with increasing CF_4/CH_4	DLC PTFE	Adsorbed BSA decreased with increasing CF_4 ratio Fng and γ-globulin adsorption increased with the CF_4 ratio	Ozeki *et al.*, 2010

Note: FCVA: filtered cathodic vacuum arc; PIII-D: plasma immersion ion implantation and deposition; RF-PECVD: radio frequency plasma enhanced chemical vapour deposition; LTIC: low temperature isotropic carbon; NiTi: nickel-titanium; PC: polycarbonate; PTFE: polytetrafluoroethylene; Si: silicon; BSA: bovine serum albumin; Fng: fibrinogen; HSA: human serum albumin.

These characteristics permit significant improvements to the films as candidate coatings for biomedical devices. Saito *et al.* demonstrated improved antithrombogenicity of F-DLC in relation to DLC films showing significantly lower platelet adhesion and activation compared to more hydrophilic silicon substrata (Saito *et al.*, 2005).

Hasebe *et al.* compared the properties of fluorinated and conventional DLC films prepared by RF-CVD. They demonstrated that the more hydrophobic F-DLC surface was less thrombogenic if compared to conventional DLC or stainless steel (SUS316L) (Hasebe *et al.*, 2006a). A higher HSA/Fng adsorption ratio was observed on F-DLC in comparison to DLC and polycarbonate films, while the increase of F doping in the F-DLC films induced greater suppression of platelet adhesion and activation (Hasebe *et al.*, 2007).

In the work of Ozeki *et al.*, F-DLC coatings have been deposited on polytetrafluoroetilene (PTFE) using RF plasma enhanced CVD (Ozeki *et al.*, 2010). In contrast to other authors, Ozeki and colleagues showed that the amount of adsorbed albumin on the F-DLC films decreased with increasing F/C ratio, whereas the amount of adsorbed fibrinogen and γ-globulin increased. From these results the authors hypothesized that the non-doped films had higher antithrombogenicity with respect to the fluorinated carbon coatings.

Phosphorus incorporation was shown to improve the wettability and blood compatibility of tetrahedral amorphous carbon films (Liu *et al.*, 2008). Kwok *et al.* analyzed calcium and phosphorous-doped a-C:H films synthesized by PIII, assessing that both P-DLC and Ca-DLC films presented a smaller number of adhered and unactivated platelets in relation to LTIC, whereas, in contrast, a higher number of platelets was found on DLC doped with a combination of Ca and P (Kwok *et al.*, 2005; Kwok *et al.*, 2006). The same authors demonstrated that the amount of nitrogen is critical for the haemocompatibility of N-DLC films (Kwok *et al.*, 2004). Comparing a-C:N with varying nitrogen content, they showed variable adhesion and activation of platelets, depending on the fraction of sp^2 bonding. Other *in vitro* tests on nitrogen-doped hydrogenated amorphous carbon (a-C:H:N) films fabricated by PIII showed no cytotoxicity on human micro-vascular endothelial cells (HMEC), and better antithrombotic properties with respect to a-C:H films (Yang *et al.*, 2006).

Silicon incorporation in amorphous carbon coatings has been performed by various authors (Okpalugo *et al.*, 2004; Ong *et al.*, 2007; Roy *et al.*, 2009). Okpalugo *et al.* showed that a modification of microstructure, surface energy and electron conduction was induced by Si incorporation in DLC films (Okpalugo *et al.*, 2004). A lower level of platelet aggregation on Si-doped a-C:H synthesized by PE-CVD was revealed when compared to undoped DLC.

A recent study investigated the haemocompatibility of Si-incorporated DLC films, surface-modified by gas plasma treatments (O_2, N_2 and CF_4). The authors demonstrated that plasma treatments mostly affected the polar component of surface energy, and argued that the negatively charged polarity

induced on Si-DLC by N_2 and O_2 plasma treatments improved the haemocompatibility of the films, suppressing fibrinogen adsorption and platelet adhesion (Roy *et al.*, 2009). Similarly, the decrease of platelet adhesion with Si concentration onto Si-DLC films was reported as a consequence of decreased sp^2 carbon bonding fraction, and of an increased polar component of the surface energy (Ong *et al.*, 2007).

DLC films treated by different gas plasmas (O_2, Ar, C_2H_2 and NH_3) under either low- or high-vacuum conditions showed excellent compatibility with blood platelets (low adhesion) regardless of the gas plasma used in comparison to polyethylene terephthalate (PET), stainless steel or untreated DLC (Mochizuki *et al.*, 2011). The films treated with ammonia plasma showed better performance with regard to the generation of thrombin-antithrombin complex (TAT) and kallikrein-like plasma activity. Alternatively, the surfaces treated with oxygen plasma presented higher surface concentration of carboxyl groups and activated the coagulation system via the intrinsic pathway.

Besides improved haemocompatibility, some modified DLC films presented promising antifouling properties and showed a significant inhibition of bacterial adhesion, as in the case of Si, N or F-doped DLC coatings (Shao *et al.*, 2010; Zhao *et al.*, 2009; Su *et al.*, 2010).

The work of Choi *et al.* showed that modifications at different levels are introduced by the incorporation of Ag into DLC films, suggesting possible use of Ag-DLCs for biomedical applications to exploit Ag antibacterial properties. The same authors showed changes of microstructure (increase of sp^2 C bonds in the amorphous carbon) and wetting, gradual decrease of surface energy, and an intensification of the HSA/Fng protein adsorption ratio with increasing Ag concentration (from 0.1 to 9.7 at.%) (Choi *et al.*, 2008).

4.6 Biomedical applications of DLC coatings

A high percentage of the implants and medical devices currently used in clinical practice exhibit specific characteristics and advanced qualities. In the development of these highly demanding medical products, scientists and medical engineers must consider numerous parameters that can concur to ensure the success or failure of the device. The use of materials for applications in the human body must, in fact, take into account various aspects, such as the suitability of mechanical, tribological and chemical properties of the materials with respect to their specific application, as well as their biocompatibility (Ruckenstein and Gourisankar, 1986).

In particular, surface properties are very important as biomaterials cross-talk with the surrounding biological environment through their surface. Biomaterials interact with different tissues and organs in the living organism, coming into contact with body fluids containing ions, proteins and other biomolecules, as well as with cells from different tissues. The performance and fate of a medical device are highly dependent on its interaction with the specific biological environment it is intended

to work in. Various adverse events can cause the failure of medical implants, including mechanical failure (wear, tear, cracking or fatigue), degradation, corrosion or oxidation. Other possible problems could include thrombosis, infection, formation of a fibrotic capsule, release of debris and sensitization reactions.

Surface modification of biomaterials can appropriately contribute to the limitation of such adverse events and significantly improve the performance and probability of success of numerous implants and medical devices.

Due to their singular properties, DLC coatings are exploited in a wide range of highly demanding biomedical applications (Fig. 4.4), for example where high hardness, low friction, or resistance to wear and corrosion are required. One of the advantages of DLCs is that they can be deposited at low temperature, thus allowing the coating of heat-sensitive and insulating materials. DLCs are applied to metallic (stainless steel, Al, Co-Cr, NiTi or Ti-6Al-4V alloys), polymeric (PET, PTFE, silicone, polyurethanes) or ceramic materials for medical devices. Amorphous carbon films are often used to protect implants against bio-deterioration and corrosion, and to serve as diffusion barriers, significantly decreasing the probability of toxic element release (Ni, Cr, V, Co, for example) or wear particulate into the tissues (Santavirta, 2003). In addition, coatings can reduce the effects of body fluids on implants, protecting them from corrosion and potential structural failure (Sheeja *et al.*, 2001; Tiainen, 2001).

DLC are exploited to coat orthopaedic prostheses for total joint replacement, such as hip (both femoral heads and/or acetabular cups), knee and shoulder, as well as transcutaneous prostheses and orthopaedic screws. Because of their

4.4 DLC-coated implants and medical devices.

ultralow roughness and chemical resistance to saliva, carbon coatings are also used for dental prostheses and orthodontic NiTi wires, showing limited Ni ion release and low bacterial biofilm adhesion (Kobayashi *et al.*, 2005).

The deposition of DLC coatings on cutting tools was reported to improve performance and energy efficiency (Zolgharni *et al.*, 2008). DLCs are also used on surgical instruments where, alongside biocompatibility, criteria such as functional performance, sterility and cleanability, structural integrity and fatigue resistance must be satisfied (for example in arthroscopic instrumentation and scissors). They can be employed in devices for urological dialysis, surgical needles for corneal surgery and in coating intraocular lenses. Their excellent smoothness and low friction make DLCs suitable candidates for coating urinary catheters. Moreover, their recognized antiadhesive properties can help decreasing the probability of microbial biofilm adhesion on catheter surfaces.

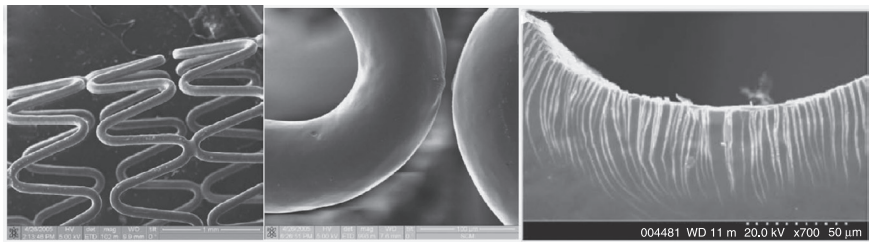
DLCs are particularly utilized in the case of cardiovascular devices. They have been employed for coating vascular prostheses, vascular stents and guidewires, heart valves, rotary blood pumps for ventricular assistance, artificial hearts and dialysis membranes.

The major requirements for materials used for cardiovascular applications are good surface mechanical properties and blood compatibility. DLCs can assure excellent mechanical and tribological properties, like wear and fatigue resistance (which are fundamental for high-demand implants such as heart valves), or smoothness and stability (required for vascular stents).

The main complication related to the use of cardiovascular devices is thrombosis, a crucial event that can consequently induce thromboembolism in the case of heart valves or occlusion and restenosis at the site of stent implantation. Both thromboembolism and thrombotic occlusion are related to platelet activation and aggregation on contact with the foreign surface of an implant. The use of carbon-based coatings has been adopted to decrease the risk of thrombosis, stenosis and thromboembolism.

Since the 1970s, pyrolytic carbon (PyC) has been used to improve the haemocompatibility of graphite occluders in mechanical heart valves (HV). The subsequent development, in the mid-1980s, of new deposition technologies allowed the coating of many different types of substrates with thin carbon films, overcoming intrinsic PyC manufacturing limits (such as process temperature). Because of their excellent structural characteristics, good biocompatibility and haemocompatibility, these carbon films were suitable for cardiovascular implantable devices. The use of low temperature deposition techniques encouraged the deposition on metallic and polymeric materials, and was then applied to stents (Fig. 4.5) and vascular prostheses, as well as to the polymeric fibres (PTFE, PET) of heart valve sewing rings.

As reported in the previous paragraphs, the blood compatibility of conventional and modified DLC films has been extensively demonstrated by *in vitro* tests. *In vivo* studies on DLC-coated implants are, in contrast, quite scarce. However, the research conducted so far has revealed no adverse reactions to DLC films.



(a) (b) (c)

4.5 (a) DLC-coated stent, (b) smooth integral expanded film, (c) film microcracking. Elaborated from *Diamond and Related Materials*, 17(4c5), McLaughlin J A and Maguire P D, 'Advances on the use of carbon based materials at the biological and surface interface for applications in medical implants', pages 873–877. Copyright (2008), used with permission from Elsevier.

Tran *et al.* showed that DLC coating of mechanical heart valve components may render the surfaces of mechanical HV more thromboresistant in the vascular system, due to various effects, including surface cleaning of organic and inorganic debris, generation of reactive and functional groups, improved adhesion of endothelial cells and albumin, and decreased platelet adhesion (Tran *et al.*, 1999).

Carbofilm™-coated cylinders (Sorin Biomedica Cardio S.p.A.) implanted in the cubital bone of sheep were histologically evaluated at 3 and 12 months. Coated cylinders showed a better biological response (lower osteoclastic erosion and connective-tissue formation) in comparison to uncoated samples (Vallana *et al.*, 1993).

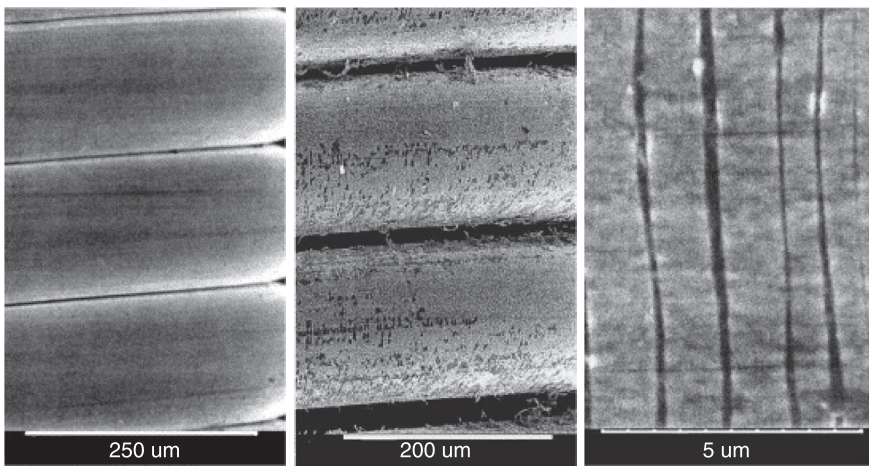
Thrombosis can be triggered by the activation of platelets as a consequence of shear stress, contact with foreign materials or release of metal ions. The effects of metallic stent coating by DLC were investigated by Gutensohn and colleagues (2000). During a thorough *in vitro* study the authors compared ion release and platelet activation on carbon-coated and stainless steel uncoated stents. The results of the study showed that coating intracoronary stents with DLC significantly reduced thrombogenicity. In particular, the release of metal ions (Cr, Ni, Mo and Mn) was significantly higher for stainless steel uncoated stents, and corresponded to a lower level of platelet activation in the case of DLC-coated stents. The authors thus concluded that DLC coatings improve the blood compatibility of vascular stents (Gutensohn *et al.*, 2000).

Analyzing the mechanical stability, corrosion resistance and bioresponse of DLC coatings for stents and guidewires, Maguire and colleagues showed that Si doping and use of an a-Si:H interlayer can help minimize the risk of adhesion failure or film cracking (Maguire *et al.*, 2005) (Fig. 4.6). Moreover, Si doping improved barrier properties (McLaughlin and Maguire, 2008) and reduced platelet adhesion, while increasing the attachment of human microvascular endothelial cells in comparison to undoped a-C.

Korkmaz and colleagues evaluated the consequences of stent carbon coating on inflammatory response, comparing carbon-coated and uncoated MAC stents (AMG®, Raesfeld-Erle, Germany) (Korkmaz *et al.*, 2002). They analyzed the plasma concentration of C-reactive protein (CRP), fibrinogen and several cytokines (TNF, IL-1b, IL-6, IL-8) as well as leukocyte counts. These showed no significant differences when compared to patients treated with carbon-coated or stainless steel uncoated stents. According to this study, coating stainless steel stents with carbon film does not affect the inflammatory response.

The biocompatibility of two diamond-like stent coatings (Dylyn, Bekaert, Belgium) was tested in a porcine coronary stent model, demonstrating that the films contributed to decrease thrombogenicity and neointimal hyperplasia (De Scheerder *et al.*, 2000).

Although the antithrombogenic properties of DLCs seem to be well established, some clinical trials report conflicting results for carbon-coated stent performance with regard to neointimal formation and in-stent restenosis. For example, in a study on 112 patients, Antoniucci *et al.* proved very low 6-month restenosis (11%) and reintervention (10%) rates with a Carbofilm™-coated stent (Sorin Biomedica Cardio, Saluggia, Italy) (Antoniucci *et al.*, 2000). With a randomized trial including 196 patients, Salahas and colleagues provided clinical evidence that DLC-coated



4.6 (a) Conformal DLC coating with minimal cracking after winding, (b) DLC-coated guidewire showing adhesion and cracking failure after winding, (c) transverse cracking of DLC after winding. Elaborated from *Diamond and Related Materials*, Vol 14, Issue 8, Maguire P D, McLaughlin J A, Okpalugo T I T, Lemoine P, Papakonstantinou P, McAdams E T, Needham M, Ogwu A A, Ball M and Abbas G A, 'Mechanical stability, corrosion performance and bioresponse of amorphous diamond-like carbon for medical stents and guidewires', Pages 1277–1288, Copyright (2005), used with permission from Elsevier.

stent implantation correlated with high success rates, safety and efficacy both in the hospital and six months after the interventional procedure (Salahas *et al.*, 2007). In contrast, other studies showed no significant improvements of DLC-coated versus uncoated stents as regards restenosis rate, major adverse cardiac events (Haase *et al.*, 2003; Airoldi *et al.*, 2004) or angiographic results (Sick *et al.*, 2004).

Thanks to their lubricating properties, DLC films are promising candidates for the coating of intravascular guidewires and catheters (Hasebe, *et al.*, 2006b). Good adherence, good friction coefficient and better haemocompatibility were reported in the case of DLC-coated stainless steel guidewires in relation to other coatings, such as PTFE (McLaughlin *et al.*, 1996). Moreover, it has been reported that DLC and heparin based coatings are the coatings most commonly used for ventricular assistance devices (VAD), owing to their elevated haemocompatibility, durability and technical maturity (Sin *et al.*, 2009).

Since its discovery, researchers have made great efforts to better understand DLC properties, as well as to evaluate and develop possible medical applications. The high number of patents involving DLC coatings is a testament to this intensive research (Table 4.6). At present, DLCs represent an important class of materials

Table 4.6 Some of the patents involving carbon coatings for medical applications

US patent #	Description	Authors	Original assegnee	Issue date
3952334	Biocompatible carbon prosthetic devices	Bokros J.C., Horsley J.B.	General Atomic Company	Apr 27, 1976
4537791	Carbon coating of grafts or catheters	Tarjan P.P.	Cordis Corporation	Aug 27, 1985
5370684	Prosthesis of polymeric material coated with biocompatible carbon	Vallana F. *et al.*	Sorin Biomedica S.p.A.	Dec 6, 1994
5387247	Prosthetic device having a biocompatible carbon film thereon and a method of and apparatus for forming such device	Vallana F., Arru P.	Sorin Biomedica S.p.A.	Feb 7, 1995
5423886	Cyclically deformable haemocompatible and biocompatible devices coated with biocompatible carbonaceous material	Arru P. *et al.*	Sorin Biomedica S.p.A.	Jun 13, 1995
5725573	Medical implants made of metal alloys bearing cohesive diamond like carbon coatings	Dearnaley G., Lankford, J.	Southwest Research Institute	Mar 10, 1998
6761736	Medical article with a diamond-like carbon coated polymer	Woo Y. *et al.*	St. Jude Medical, Inc.	Jul 13, 2004

with exceptionally attractive properties, which are already exploited for numerous biomedical products commercially available on the market, and hold the potential to be used in many more.

4.7 Conclusion and future trends

DLC films exhibit several exceptional characteristics, such as elevated hardness, low friction, high wear resistance and chemical inertness, making them particularly attractive for various high-demand applications in different fields.

Although DLC films have been developed relatively recently, the scientific literature about the blood compatibility of this class of materials is quite extensive. Several studies have investigated the degree of haemocompatibility of DLC films produced by different deposition techniques in different working conditions in relation to their specific structural and surface characteristics. *In vitro* and *in vivo* tests have been used to evaluate the feasibility of employing these materials in the biomedical field, finding in general a good response of DLCs in the blood environment.

Despite belonging to the same family, the large variety of materials and wide range of different properties they display means that it is not possible to generalize in describing the bioresponse of DLCs. Thus, each specific material must be considered and tested individually. Nevertheless, it is well established that, in general, this class of materials presents extraordinary properties with regard to their mechanical, tribological and chemical performances, as well as a superior blood compatibility in comparison to many other materials. For this reason, pure or doped DLC coatings represent ideal materials for coating prostheses components and medical devices in the cardiovascular, orthopaedic, ophthalmic and orthodontic fields.

One of the key issues that may limit the usefulness of DLCs in biomedical applications is the low degree of adhesion of this material to common biomedical alloys. This problem may be overcome in a number of ways, including reducing high internal stress by introducing doping elements in the DLC films.

Research should continue to further optimize DLC films, trying to improve critical aspects like interfacial adhesion, uniformity and integrity of DLC coatings on medical devices, especially in the case of complex geometric substrates.

4.8 References

Airoldi F, Colombo A, Tavano D, *et al.* (2004), 'Comparison of diamond-like carbon-coated stents versus uncoated stainless steel stents in coronary artery disease', *The American Journal of Cardiology*, 93(4), 474–477.

Aisenberg S and Chabot R (1971), 'Ion Beam Deposition of Thin Films of Diamondlike Carbon', *Journal of Applied Physics*, 42(7), 2953–2958.

Alanazi A, Nojiri C, Kido T, *et al.* (2000), 'Engineering analysis of diamond-like carbon coated polymeric materials for biomedical applications', *Artificial Organs*, 24(8), 624–627.

Anders A (2000), *Handbook of plasma immersion ion implantation and deposition* Anders A, New York/Chichester/Weinheim/Brisbane/Singapore/Toronto, John Wiley & Sons.

Andrade J and Hlady V (1987), 'Plasma Protein Adsorption: The Big Twelve', *Annals Of The New York Academy Of Sciences*, 516(1), 158–172.

Antoniucci D, Bartorelli A, Valenti R, *et al.* (2000), 'Clinical and angiographic outcome after coronary arterial stenting with the carbostent', *The American Journal of Cardiology*, 85(7), 821–5.

Arps J H and Dearnaley G (2004), 'Diamond and Diamond-Like Carbons', *Encyclopedia of Biomaterials and Biomedical Engineering*, 446–455.

Ball M, O'Brien A, Dolan F, *et al.* (2004), 'Macrophage responses to vascular stent coatings', *Journal of Biomedical Materials Research Part A*, 70A(3), 380–390.

Boehm R D, Jin C and Narayan R J (2011), 'Carbon and Diamond', in Ducheyne P, Healy K, Hutmacher D, Grainger D and Kirkpatrick C, *Comprehensive biomaterials*, Amsterdam, Oxford, Waltham, Elsevier Ltd., 115–119.

Casiraghi C, Robertson J and Ferrari A C (2007), 'Diamond-like carbon for data and beer storage', *Materials Today*, 10(1–2), 44–53.

Chen J Y, Wang L P, Fu K Y, *et al.* (2002), 'Blood compatibility and sp3/sp2 contents of diamond-like carbon (DLC) synthesized by plasma immersion ion implantation-deposition', *Surface and Coatings Technology*, 156, 289–294.

Cheng Y and Zheng Y F (2006), 'The corrosion behavior and hemocompatibility of TiNi alloys coated with DLC by plasma based ion implantation', *Surface and Coatings Technology*, 200(14–15), 4543–4548.

Chhowalla M, Robertson J, Chen C W, *et al.* (1997), 'Influence of ion energy and substrate temperature on the optical and electronic properties of tetrahedral amorphous carbon (ta-C) films', *Journal of Applied Physics*, 81(1), 139–145.

Cho N H, Veirs D K, Ager J W, *et al.* (1992), 'Effects of substrate temperature on chemical structure of amorphous carbon films', *Journal of Applied Physics*, 71(5), 2243.

Choi H, Dauskardt R, Lee S, *et al.* (2008), 'Characteristic of silver doped DLC films on surface properties and protein adsorption', *Diamond and Related Materials*, 17(3), 252–257.

Cui F and Li D (2000), 'A review of investigations on biocompatibility of diamond-like carbon and carbon nitride films', *Surface and Coatings Technology*, 131(1–3), 481–487.

Dearnaley G and Arps J (2005), 'Biomedical applications of diamond-like carbon (DLC) coatings: A review', *Surface and Coatings Technology*, 200(7), 2518–2524.

Dion I, Roques X, Baquey C, *et al.* (1993), 'Hemocompatibility of diamond-like carbon coating', *Biomedical Materials Engineering*, 3, 51–55.

Dongping L and Baoxiang C (2006), 'Structures of Diamond-Like Carbon Films', *Plasma Science and Technology*, 8(3), 285–291.

Donnet C and Erdemir A (2008), 'Diamond-like Carbon Films: A Historical Overview', in Donnet C and Erdemir A, *Tribology of diamond-like carbon films: fundamentals and applications*, New York, Springer.

Fedel M, Motta A, Maniglio D and Migliaresi C (2010), 'Carbon Coatings for Cardiovascular Applications: Physico-Chemical Properties and Blood Compatibility', *Journal of Biomaterials Applications*, 25, 57–74.

Fedel M, Motta A, Maniglio D and Migliaresi C (2009), 'Surface properties and blood compatibility of commercially available diamond-like carbon coatings for cardiovascular devices', *Journal of Biomedical Materials Research. Part B, Applied Biomaterials*, 90(1), 338–349.

Goodman S L, Tweden K S and Albrecht R M (1996), 'Platelet interaction with pyrolytic carbon heart-valve leaflets', *Journal of Biomedical Materials Research*, 32(2), 249–258.

Gorbet M B and Sefton M V (2004), 'Biomaterial-associated thrombosis: roles of coagulation factors, complement, platelets and leukocytes', *Biomaterials*, 25(26), 5681–703.

Gott V L and Furuse A (1973), 'The current status of in vivo screening of carbon for use in bioengineering', *Medical Instrumentation*, 7, 121–129.

Grigonis A, Marcinauskas L, Vinciunaite V and Raciukaitis G (2011), 'Modification of the amorphous carbon films by the ns-laser irradiation', *Central European Journal of Physics*, 9(5), 1344–1350.

Grill A (1999), 'Diamond-like carbon: state of the art', *Diamond and Related Materials*, 8 (July 1998), 428–434.

Grunkemeier J M, Tsai W B, McFarland C D and Horbett T A (2000), 'The effect of adsorbed fibrinogen, fibronectin, von Willebrand factor and vitronectin on the procoagulant state of adherent platelets', *Biomaterials*, 21(22), 2243–2252.

Gutensohn K, Beythien C, Bau J, *et al.* (2000), 'In vitro analyses of diamond-like carbon coated stents. Reduction of metal ion release, platelet activation, and thrombogenicity', *Thrombosis Research*, 99(6), 577–85.

Haase J, Storger H, Hofmann M, *et al.* (2003), 'Comparison of stainless steel stents coated with turbostratic carbon and uncoated stents for percutaneous coronary interventions', *The Journal of Invasive Cardiology*, 15(10), 562–565.

Hasebe T, Ishimaru T, Kamijo A, *et al.* (2007), 'Effects of surface roughness on anti-thrombogenicity of diamond-like carbon films', *Diamond and Related Materials*, 16(4–7), 1343–1348.

Hasebe T, Matsuoka Y., Kodama H, *et al.* (2006a), 'Lubrication performance of diamond-like carbon and fluorinated diamond-like carbon coatings for intravascular guidewires', *Diamond and Related Materials*, 15(1), 129–132.

Hasebe T, Shimada A, Suzuki Tetsuya, *et al.* (2006b), 'Fluorinated diamond-like carbon as antithrombogenic coating for blood-contacting devices', *Journal of Biomedical Materials Research. Part A*, 76(1), 86–94.

Huang N, Yang P, Leng YX, *et al.* (2004), 'Surface Modification for Controlling the Blood-Materials Interface', *Key Engineering Materials*, 288–289, 295–298.

Jones M I, McColl I R, Grant D M, *et al.* (1999), 'Haemocompatibility of DLC and TiC–TiN interlayers on titanium', *Diamond and Related Materials*, 8(2–5), 457–462.

Jones M I, McColl I R, Grant D M, *et al.* (2000), 'Protein adsorption and platelet attachment and activation, on TiN, TiC, and DLC coatings on titanium for cardiovascular applications', *Journal of Biomedical Materials Research*, 52(2), 413–421.

Karagkiozaki V, Logothetidis S, Laskarakis A, *et al.* (2008), 'AFM study of the thrombogenicity of carbon-based coatings for cardiovascular applications', *Materials Science and Engineering: B*, 152(1–3), 16–21.

Kobayashi S, Ohgoe Y, Ozeki K, *et al.* (2005), 'Diamond-like carbon coatings on orthodontic archwires', *Diamond and Related Materials*, 14(3–7), 1094–1097.

Koidl P, Wild C, Dischler B, *et al.* (1990), 'Plasma deposition, properties and structure of amorphous hydrogenated carbon films', *Materials Science Forum*, 52–53, 41–70.

Korkmaz M E, Tayfun E, Muderrisoglu H, *et al.* (2002), 'Carbon Coating of Stents Has No Effect on Inflammatory Response to Primary Stent Deployment', *Angiology*, 53(5), 563–568.

Krishnan L K, Varghese N, Muraleedharan C V, *et al.* (2002), 'Quantitation of platelet adhesion to Ti and DLC-coated Ti in vitro using (125)I-labeled platelets', *Biomolecular Engineering*, 19(2–6), 251–253.

Kwok S C H, Ha P C T, McKenzie D R, *et al.* (2006), 'Biocompatibility of calcium and phosphorus doped diamond-like carbon thin films synthesized by plasma immersion ion implantation and deposition', *Diamond and Related Materials*, 15(4–8), 893–897.

Kwok S C H, Yang P, Wang J, *et al.* (2004), 'Hemocompatibility of nitrogen-doped, hydrogen-free diamond-like carbon prepared by nitrogen plasma immersion ion implantation-deposition', *Journal of Biomedical Materials Research. Part A*, 70(1), 107–114.

Kwok S, Wang J and Chu P (2005), 'Surface energy, wettability, and blood compatibility phosphorus doped diamond-like carbon films', *Diamond and Related Materials*, 14(1), 78–85.

Lackner J M and Waldhauser W (2010), 'Diamond and Diamond-like Carbon Coated Surfaces as Biomaterials', *BHM*, 155(11), 528–533.

Leng YX, Chen JY, Yang P, *et al.* (2003), 'Mechanical properties and platelet adhesion behavior of diamond-like carbon films synthesized by pulsed vacuum arc plasma deposition', *Surface Science*, 531(2), 177–184.

Lifshitz Y (1999), 'Diamond-like carbon – present status', *Diamond and Related Materials*, 8, 1659–1676.

Linder S, Pinkowski W and Aepfelbacher M (2002), 'Adhesion, cytoskeletal architecture and activation status of primary human macrophages on a diamond-like carbon coated surface', *Biomaterials*, 23(3), 767–773.

Liu Aiping, Zhu J, Liu M, *et al.* (2008), 'Platelet adhesion on phosphorus-incorporated tetrahedral amorphous carbon films', *Applied Surface Science*, 255(2), 279–281.

Logothetidis S (2007), 'Haemocompatibility of carbon based thin films', *Diamond and Related Materials*, 16(10), 1847–1857.

Logothetidis S, Gioti M, Lousinian S and Fotiadou S (2005), 'Haemocompatibility studies on carbon-based thin films by ellipsometry', *Thin Solid Films*, 482(1–2), 126–132.

Lousinian S, Kalfagiannis N and Logothetidis S (2008), 'Albumin and fibrinogen adsorption on boron nitride and carbon-based thin films', *Materials Science and Engineering: B*, 152(1–3), 12–15.

Ma W J, Ruys A J, Mason R S, *et al.* (2007), 'DLC coatings: effects of physical and chemical properties on biological response', *Biomaterials*, 28(9), 1620–1628.

Maguire P D, McLaughlin J A, Okpalugo T I T, *et al.* (2005), 'Mechanical stability, corrosion performance and bioresponse of amorphous diamond-like carbon for medical stents and guidewires', *Diamond and Related Materials*, 14(8), 1277–1288.

McLaughlin JA, Meenan B, Maguire P and Jamieson N (1996), 'Properties of diamond like carbon thin film coatings on stainless steel medical guidewires', *Diamond and Related Materials*, 5, 486–491.

McLaughlin JA and Maguire PD (2008), 'Advances on the use of carbon based materials at the biological and surface interface for applications in medical implants', *Diamond and Related Materials*, 17(4–5), 873–877.

Mochizuki A, Ogawa T, Okamoto K, *et al.* (2011), 'Blood compatibility of gas plasma-treated diamond-like carbon surface—Effect of physicochemical properties of DLC surface on blood compatibility', *Materials Science and Engineering: C*, 31(3), 567–573.

More R B, Sines G, Ma L and Bokros J C (2004), 'Pyrolytic Carbon', *Encyclopedia of Biomaterials and Biomedical Engineering*, 1308–1319.

Nurdin N, François P, Mugnier Y, *et al.* (2003), 'Haemocompatibility evaluation of DLC- and SiC-coated surfaces', *European Cells Materials*, 5(6328), 17–26; discussion 26–28.

Okpalugo TIT, Ogwu AA, Maguire PD and McLaughlin JAD (2004), 'Platelet adhesion on silicon modified hydrogenated amorphous carbon films', *Biomaterials*, 25(2), 239–245.

Ong S-E, Zhang S, Du H, *et al.* (2007), 'Influence of silicon concentration on the haemocompatibility of amorphous carbon', *Biomaterials*, 28(28), 4033–4038.

Ozeki K, Nagashima I, Hirakuri K K and Masuzawa T (2010), 'Adsorptive properties of albumin, fibrinogen, and gamma-globulin on fluorinated diamond-like carbon films coated on PTFE', *Journal of Materials Science. Materials in Medicine*, 21(5), 1641–1648.

Robertson J (2002), 'Diamond-like amorphous carbon', *Materials Science and Engineering: R: Reports*, 37(4–6), 129–281.

Roy R K, Choi H W, Yi J W, *et al.* (2009), 'Hemocompatibility of surface-modified, silicon-incorporated, diamond-like carbon films', *Acta Biomaterialia*, 5(1), 249–256.

Roy RK and Lee K-R (2007), 'Biomedical Applications of Diamond-Like Carbon Coatings: A Review', *Journal of Biomedical Materials Research Part B: Appl Biomater*, 83B, 72–84.

Ruckenstein E and Gourisankar S V (1986), 'Preparation and characterization of thin film surface coatings for biological environments', *Biomaterials*, 7(6), 403–422.

Saito T, Hasebe T, Yohena S, *et al.* (2005), 'Antithrombogenicity of fluorinated diamond-like carbon films', *Diamond and Related Materials*, 14(3–7), 1116–1119.

Salahas A, Vrahatis A, Karabinos I, *et al.* (2007), 'Success, safety, and efficacy of implantation of diamond-like carbon-coated stents', *Angiology*, 58(2), 203–210.

Santavirta S (2003), 'Compatibility of the totally replaced hip – Reduction of wear by amorphous diamond coating', *Acta Orthopaedica Scandinavica Supplementum*, 74(310), 1–19.

De Scheerder I, Szilard M, Yanming H, *et al.* (2000), 'Evaluation of the biocompatibility of two new diamond-like stent coatings (Dylyn) in a porcine coronary stent model', *Journal of Invasive Cardiology*, 12(8), 389–394.

Shao W, Zhao Q, Abel E W and Bendavid A (2010), 'Influence of interaction energy between Si-doped diamond-like carbon films and bacteria on bacterial adhesion under flow conditions', *Journal of Biomedical Materials Research. Part A*, 93(1), 133–139.

Sheeja D, Tay B K, Lau S P and Nung L N (2001), 'Tribological characterisation of diamond-like carbon coatings on Co–Cr–Mo alloy for orthopaedic applications', *Surface and Coatings Technology*, 146–147(0), 410–416.

Sick P B, Gelbrich G, Kalnins U, *et al.* (2004), 'Comparison of early and late results of a Carbofilm-coated stent versus a pure high-grade stainless steel stent (the Carbostent-Trial)', *The American Journal of Cardiology*, 93(11), 1351–1356, A5.

Sin D-C, Kei H-L and Miao X (2009), 'Surface coatings for ventricular assist devices', *Expert Review of Medical Devices*, 6(1), 51–60.

Su X J, Zhao Q, Wang S and Bendavid A (2010), 'Modification of diamond-like carbon coatings with fluorine to reduce biofouling adhesion', *Surface and Coatings Technology*, 204(15), 2454–2458.

Sui J, Cai W, Liu Ailian, *et al.* (2006), 'Surface characterization and blood compatibility of diamond-like carbon (DLC) films on the NiTi alloys', *Materials Transactions*, 47(3), 691–693.

Tiainen V (2001), 'Amorphous carbon as a bio-mechanical coating – mechanical properties and biological applications', *Diamond and Related Materials*, 10, 153–160.

Tran H S, Puc M M, Hewitt C W, *et al.* (1999), 'Diamond-Like Carbon Coating and Plasma or Glow Discharge Treatment of Mechanical Heart Valves', *Journal of Investigative Surgery*, 12(3), 133–140.

Vallana F, Pasquino E, Rinaldi S, *et al.* (1993), 'Carbofilm™: Present and future applications in biomedical devices', *Ceramics International*, 19(3), 169–179.

Vinnichenko M, Gago R, Huang N, *et al.* (2004), 'Spectroscopic ellipsometry investigation of amorphous carbon films with different sp3 content: relation with protein adsorption', *Thin Solid Films*, 455–456, 530–534.

Wu Y, Simonovsky F I, Ratner B D and Horbett Thomas A (2005), 'The role of adsorbed fibrinogen in platelet adhesion to polyurethane surfaces: A comparison of surface hydrophobicity, protein adsorption, monoclonal antibody binding, and platelet adhesion', *Journal of Biomedical Materials Research Part A*, 74A(4), 722–738.

Yang P, Chen JY, Leng YX, *et al.* (2004), 'Effect of annealing on structure and biomedical properties of amorphous hydrogenated carbon films', *Surface and Coatings Technology*, 186(1–2), 125–130.

Yang P, Huang N, Leng YX, *et al.* (2006), 'Wettability and biocompatibility of nitrogen-doped hydrogenated amorphous carbon films: Effect of nitrogen', *Nuclear Instruments and Methods in Physics Research Section B*, 242(1–2), 22–25.

Young B, Lambrecht L, Cooper S and Mosher D (1982), 'Biomaterials, interfacial phenomena and applications', in Cooper SL and Peppas NA, *Biomaterials, interfacial phenomena and applications*, Washington DC, ACS, 317.

Yu L, Wang X, Wang X and Liu X (2000), 'Haemocompatibility of tetrahedral amorphous carbon films', *Surface and Coatings Technology*, 128–129, 484–488.

Zhao Q, Su X, Wang S, *et al.* (2009), 'Bacterial attachment and removal properties of silicon- and nitrogen-doped diamond-like carbon coatings', *Biofouling*, 25(5), 377–385.

Zolgharni M, Jones B J, Bulpett R, *et al.* (2008), 'Energy efficiency improvements in dry drilling with optimised diamond-like carbon coatings', *Diamond and Related Materials*, 17(7–10), 1733–1737.