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Deposition of Thin Films by Plasma Polymerization for Biomedical Application

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Abstract. This study represents a review of deposition of polyethylene oxide-like thin films by means of low pressure plasma discharges. Current state-of-the-art is discussed and novel approach based on plasma assisted vacuum thermal degradation is introduced together with the first experimental results reached using this technique.

Introduction

When a material is exposed to a biological environment such as human body fluids, a thin layer of biomolecules (proteins, lipids, polysaccharides, and others) rapidly covers the surface. This adsorbed layer subsequently mediates the interactions of the material with the environment. In particular, it can enhance the uptake of bacteria, which could organize in complex community structures called biofilms.

There are many techniques currently used for controlling bacterial uptake and biofilm formation involving either their mechanical removal, brushing or ultrasound cleaning, treatments with biocidal substances such as organometallic-based paints, water chlorination or antibiotic therapies in patients with medical implants. Nevertheless, the biocidal methods pose certain drawbacks such as pollution hazards, problems associated with long-lasting antibiotic therapies and with the impossibility of administering drugs to some patients.

The alternative approach is to fabricate surface limiting biomolecules adhesion. Regarding this strategy, one of the suggested methods is based on a deposition of polyethylene oxide (PEO) coatings using plasma polymerization. The interest in PEO is given mainly by its advantageous properties: it belongs to a class of compounds with fouling-resistant properties arising from their hydrophilic character, from their capability of binding water molecules in aqueous solutions, and, in case of grafted PEO chains, from their mobility [1].

On the other side, PEO itself is well soluble in water, which complicates its use as an interfacial layer between the surface of a medical instrument or implant and biological medium. Solubility of PEO-like plasma polymers can be, however, controlled by adjusting the extent of cross-linking within the films. Related to this effect it has been observed that the higher power of discharge enhances cross-linking and results in deposition of non-soluble films, which is however at expense of poor retention of PEO structure and to the loss of non-fouling properties of the coating.

The aim of this study is to introduce a novel method of PEO-like thin films deposition based on plasma assisted vacuum thermal degradation of PEO and to demonstrate that under appropriate operational condition this method can lead to fabrication of thin films, which will resist protein adsorption and be stable in aqueous environment.

State-of-the-art

Several research groups have focused their attention on deposition of PEO-like plasma polymers. Table 1 summarizes the deposition parameters used together with the maximal concentration of ether (C-O-C) groups being the marker of retention of PEO character in plasma polymers. The results reached using different monomers related to the chemical composition and non-fouling properties of resulting deposits are briefly summarized in following text.

Organic coatings deposited by means of radio-frequency glow discharges fed with 2,5,8,11-tetraoxa-dodecane (triglyme) vapours have been investigated in [1] in order to explore the feasibility of this process for deposition of thin films with polyethylene oxide-like features. The operational pressure in this study was 400 mTorr and RF power input in the range 2–50W was applied. Carbon and oxygen were the only atoms present in the deposited film, as revealed by the XPS analysis; however, due to the monomer fragmentation in the plasma phase, the chemical composition of the films was different from that of the triglyme. Hydrogen atoms are not detectable by this diagnostics method. Therefore they were not included. As shown in Figure 1, the C1s signal shows 4 peak components. Whereas the peak C_1 can be ascribed to carbon present in an ether form typical of polyethylene oxide and representing thus PEO-like character of the material[1], three remaining peak components (C_0, C_2, C_3) cannot be assigned to chemical groups present in the monomer molecule.

According to the fitting attributions reported in Table II, the peak C_0 can be uniquely ascribed to hydrocarbons, while some uncertainty could arise in properly assigning the other two peaks. In fact, C_2 and C_3 peaks refer to carbon doubly and triply bonded to oxygen atoms, as carbonyl and carboxylic carbon, respectively [1].

In another study [2], the attachment of fibrinogen, bovine serum albumin, and immunoglobulin on continuous wave (CW) and pulsed plasma polymerized di(ethylene glycol) monovinyl ether was investigated using Surface Plasmon Resonance (SPR) spectroscopy and waveguide mode spectroscopy (WaMS). Of particular practical importance was the dramatic difference in the behaviour of these films after their immersion in to aqueous protein solutions. Films generated under CW conditions retained their inherent thickness and refractive index even after prolonged immersions. Films deposited under CW or higher duty cycle conditions exhibited relatively strong affinity for protein adsorption, along with an unexpected increased protein affinity with increasing film thickness. On the contrary, the films deposited at low DC had strongly reduced affinity for protein adsorption.

Table 1. Parameters of PEO-like plasma polymer deposition.

Monomers	Pressure, mTorr	Type of discharge	Power, W	% C-O-C	References
2,5,8,11-tetraoxa-dedocane (Triglyme)	400	CW and Pulsed	2–50	75	[1]
Diethylene glycol monovinyl ether EO2		CW and Pulsed	25–100	—	[2]
Diethylene glycol vinyl ether(EO2V) $[CH_2{=}CH(OCH_2CH_2)_2OH]$	30–40	CW and Pulsed	6–50	—	[3]
Tetraethylene glycol dimethyl ether (Tetraglyme) $(CH_3–O–(CH_2–CH_2–O)_4–CH_3)$	5–340	CW	5–80	80–83	[4, 5]
Diethylglycol dimethyl ether (DEGDME),$CH_3O(CH_2CH_2O)_2CH_3$	50–400	CW	5–100	73–80	[6, 7, 8, 9]
Triethylene glycol monoallyl ether (EO3A)	200	CW and Pulsed	5–50	—	[10]
Oligoglyme, dioxane and crown ether	200–250	CW	5–80	80-85	[11]

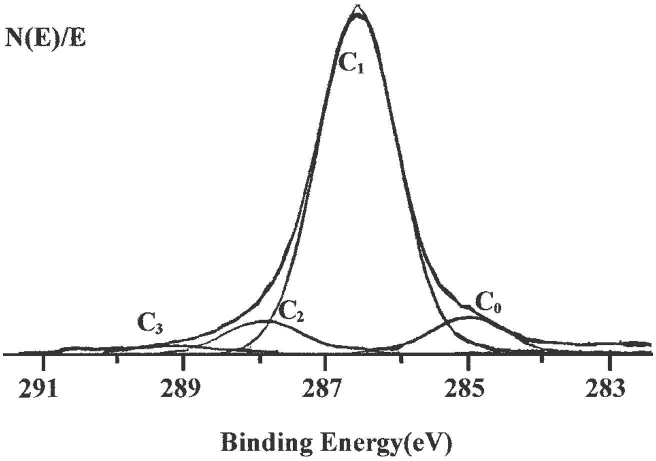

Figure 1. C1s XPS signal of the film deposited at 2Wand 400 mTorr (adopted from [1]).

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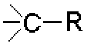
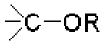
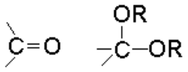
[1] Although alcohol groups C–OH could also contribute to the C1 component, their contribution was negligible since no O–H stretching absorption was revealed by FT-IR

Table II. Curve-Fitting Components of XPS C1s Peak (R = H or Organic Radical).

Chemical groups	Position, eV
(C_0) 	285.0 (reference)
(C_1) 	286.5 ± 0.2
(C_2) 	288.0 ± 0.2
(C_3) 	289.5 ± 0.2

Another employed monomer was diethylene glycol vinyl ether (EO2V), which was used for the deposition of PEO-like films by CW and pulsed discharges [3]. The authors deconvoluted the XPS C(1s) spectrum into four separate binding energy peaks corresponding to C-C bonds (284.6 eV), C-O-C and C-O-H (285.4 eV), C=O (286.9 eV), and a higher energy peak corresponding to C atoms triply bonded to O atoms (figure 2). The plasma polymer films obtained from EO2V exhibited essentially no change in XPS spectra when subjected to 15 days soaking in PBS solution at 37°C. However, the non-fouling properties of the plasma-generated films were clearly dependent on the plasma duty cycles employed during polymerization: improved non-fouling properties correlated with increasing ethylene oxide (EO) content observed for longer off period used. Simultaneously with the increasing EO content, there was an increase in the hydrophilicity of the surfaces.

As shown in Figure 2, there is a dramatic variation in the relative intensities of the peaks at 284.6 and 285.4 eV with decreasing plasma duty cycle during film formation. Whereas the C–C peak dominates for the 1/20 ms duty cycle film, it is less in the lower duty cycle films. Overall, the relative importance of the higher binding energy peaks corresponding to C=O and –C(O)O functionalities are significantly diminished with decreasing plasma duty cycle during film formation. Finally, it is apparent that essentially no change in film composition is achieved when the plasma duty cycle during film deposition is changed from 1/100 to 1/200 ms.

As it was discussed above, proteins adsorbed on implanted biomedical devices mediate platelet and leukocyte adhesion [4, 5]. Radio frequency plasma deposited tetraethylene glycol vinyl ether (tetraglyme) ($CH_3O(CH_2CH_2O)_4CH_3$), which forms a PEO-like coating, has been shown to resist protein adsorption and monocyte adhesion *in-vitro*. These studies demonstrated that plasma power has a large effect on the surface chemistry of plasma-deposited tetraglyme thin films and that these chemical changes greatly influence the resistance of the surface towards protein adsorption and cell adhesion.

In the works [6, 7, 8, 9], the authors used glow discharge fed by a mixture of diethylene glycol dimethyl ether (DEGDME) vapours and argon at different (5-100 W) RF power values. Best fitting procedures of the C1s XPS spectra are shown in Figure 3. The major peak for samples prepared at 5 and 10 W is centred at 286.5 eV (C_1 component), which is indicative of their high PEO character. On the contrary, for films prepared at 15 W the most important component is the one centred at 285.0 eV (C_0 component) suggesting higher hydrocarbon nature of PEO coatings deposited at higher RF power.

Also the studies [10, 11] showed good non-fouling properties of PEO-like plasma polymers employing either tri(ethylene glycol) monoallyl ether [10], or oligoglyme, dioxin and crow ethers [11] deposited by RF plasma polymerization of these monomers under both continuous wave (CW) and pulsed plasma operation.

A study [12] described a combination of plasma and photolithographic processes for production of micro-structured surfaces. In a first step, a layer which is non-adhesive towards cells and proteins was obtained by pulsed plasma polymerization of diethylene glycol dimethyl ether monomer (P-PEO-like). The second step combined pattern generation with the help of photolithography and fabrication of bio-adhesive areas by activation of the first layer by a second plasma treatment with a mixture of Ar and H_2. After the patterning the samples were immersed into bovine serum albumin solution and analysed by the ToF-SIMS mapping.

As can be seen in Figure 4, the map of the $C_3H_7O^+$ ion, which is a representative of the P-PEO-like domain, shows a negative contrast (very low intensity on the pattern), whereas the map of the S^- ion, which is a marker of the presence of proteins, exhibits a positive contrast with a very low

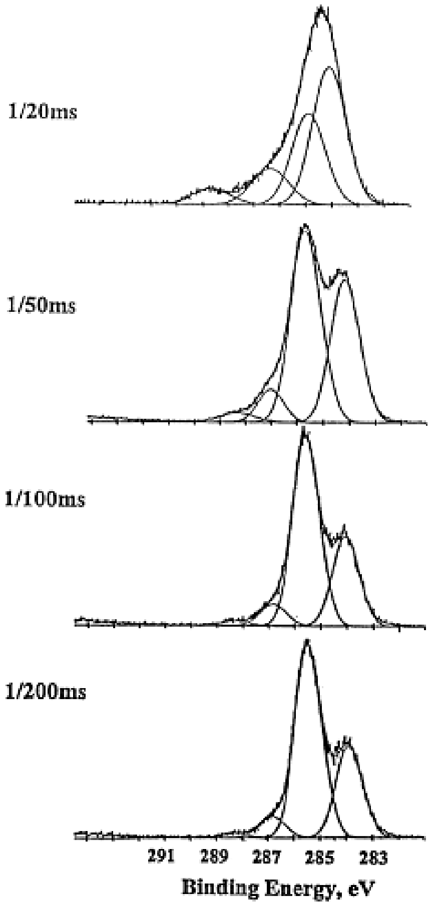


Figure 2. C(1s) high resolution XPS spectra of EO2V polymer films synthesized using 1 ms plasma on times and plasma off times of 20, 50, 100 and 200 ms, all runs carried out at 200 W peak power (adopted from [3]).

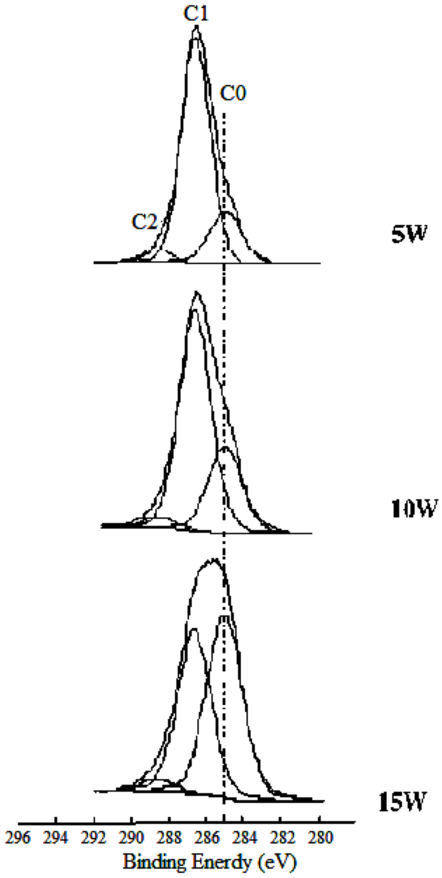


Figure 3. C1s spectra of PEO-like films (60 nm thick) deposited at different power values and 1 h deposition time (adopted from [8]).

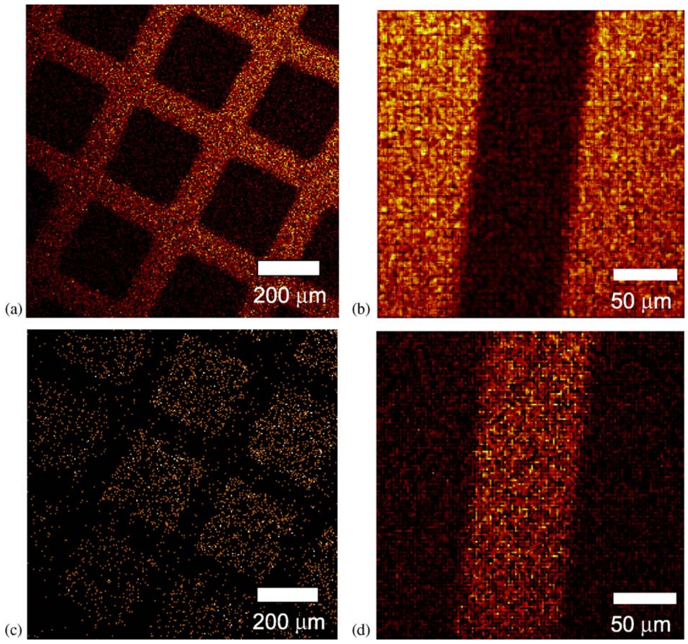


Figure 4. ToF-SIMS images of different structures of P-PEO-like layer after the patterning process and protein adsorption (a), (b) $C_3H_7O^+$ ion and (c), (d) S^- ion (180 s, 15 Pa, 10% of H_2 in Ar, 1000 W, pulsed plasma polymerization), adopted from [12].

background intensity. Thus, the proteins are only localized on the active patterns (bright field), while the dark background remains uncovered. These images demonstrate clearly the well-defined chemical contrast on the surface and consequently the success of the patterning by a combination of the plasma processes and photolithography.

As it was shown above, several research groups have successively prepared the non-fouling PEO-like plasma polymer from low molecular weight precursors. However, another method using directly PEO was suggested recently [13]. This method is based on vacuum thermal degradation of conventional PEO with activation of its vapours by a glow discharge. It has been shown that thermal degradation of PEO proceeds via fragmentation of the macromolecular chains and elimination of the oligomeric PEO fragment into a gas phase. Such oligomeric species built up the film on the substrate. The aim of this study is to further investigate chemical composition and non-fouling behaviour of PEO-like plasma polymer deposited by this method. Figure 5 shows the schematic diagram of experimental arrangement.

Experimental

Solid polyethylene oxide (PEO) was used as starting material for deposition process. PEO granules were loaded into a copper crucible, which rested on two molybdenum stripes heated by electric current. The crucible was placed 4 cm above a magnetron with a graphite target. The magnetron was used to ignite a glow discharge when required, while graphite was chosen as a material with low-sputter yield to minimize the contribution of sputtered carbon to deposited films. A radio frequency (Dressler Ceasar 13.56MHz) generator was used to deliver power to the magnetron. A quartz crystal microbalance (QCM) was placed in the plane with the substrates 10 cm above the crucible to control the deposition rate. The entire arrangement resided in a vacuum chamber brought by rotary and diffusion pumps to a base pressure of 1×10^{-3} Pa. The experiments were performed with argon used as a gas to initiate the plasma. The pressure of 1 Pa and 5 cm^3 (STP) min^{-1} flow rate were used.

Fourier Transform Infrared Reflection Absorption Spectroscopy (FTIR-RAS, Bruker Equinox 55) and X-ray Photoelectron spectroscopy (XPS, Phobios 100, Specs) were used to characterize chemical composition of deposits. QCM (Maxtek, inc.) was used to analyze the protein adsorption on the plasma polymers in a liquid phase. All the chemicals were purchased from Sigma-Aldrich, Inc. Fibrinogen from bovine plasma, bovine serum albumin (BSA) and bovine immunoglobulin (IgG) were used for the adsorption tests as the most abundant proteins in blood. Their freshly prepared solutions in Phosphate Buffered Saline (Dulbecco’s PBS) were used. A concentrated protein solution in PBS (1 mg/ml, 5 ml) was added afterwards to the beaker to receive a final protein concentration about 50 µg/ml and kinetics of the protein adsorption was then measured. The measurements were performed at room temperature in a static regime without stirring applied.

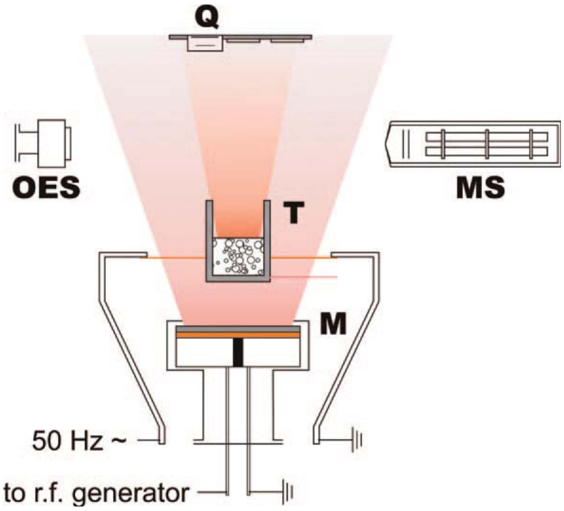


Figure 5. Experimental arrangement: Q, quartz crystal microbalance; OES, optical emission spectroscopy; MS, mass spectrometry; C, crucible; T, thermocouple; M, magnetron (adopted from [13]).

Results and discussion

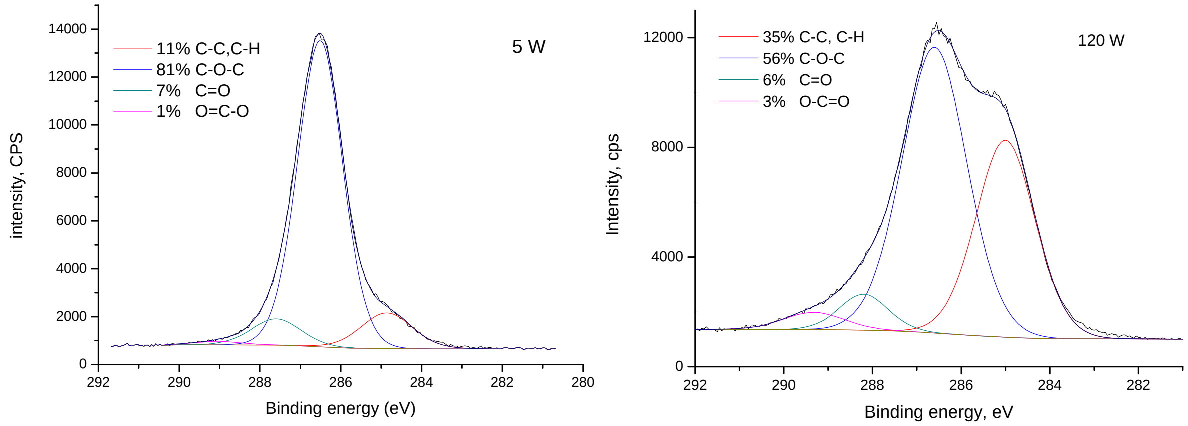
Figure 6 shows the C1s XPS of PEO-like plasma polymer deposited by plasma assisted vacuum thermal degradation of PEO at different power of discharge. According to data given in literature, this peak was fitted with four components and the ether groups were located at 286.5 eV. As can be seen, the shape of the C1s peak changes drastically with increasing delivered RF power: the relative fraction of the C-O-C species decreases from 81 to 56% as the power increases from 5W to 120W. This decrease is accompanied by the rise of the aliphatic hydrocarbon content that increases from 11 to 35%.

Such changes in chemical composition, which indicate the loss of PEO character of the deposited films with increasing RF power, are further manifested in the loss of non-fouling properties of coatings as measured by QCM in terms of enhanced protein adsorption. This is demonstrated in Figure 7, where is depicted adsorption kinetics of selected blood proteins on samples prepared at different power of discharge.

In the case of 5 W power used, the frequency of QCM acoustic resonator does not change with time when immersed to the solution of blood proteins (albumin, immunoglobulin, fibrinogen, Figure 7a). In other words, this proves that the proteins do not adsorb on the surface of the plasma polymer deposited at lower power and hence with higher representation of ether groups. On the contrary, the film deposited at 120W loses its non-fouling properties as it can be seen from figure 7b: strong adhesion of blood proteins to such surface can be observed in this case with the QCM frequency shift proportional to the molecular mass of the proteins.

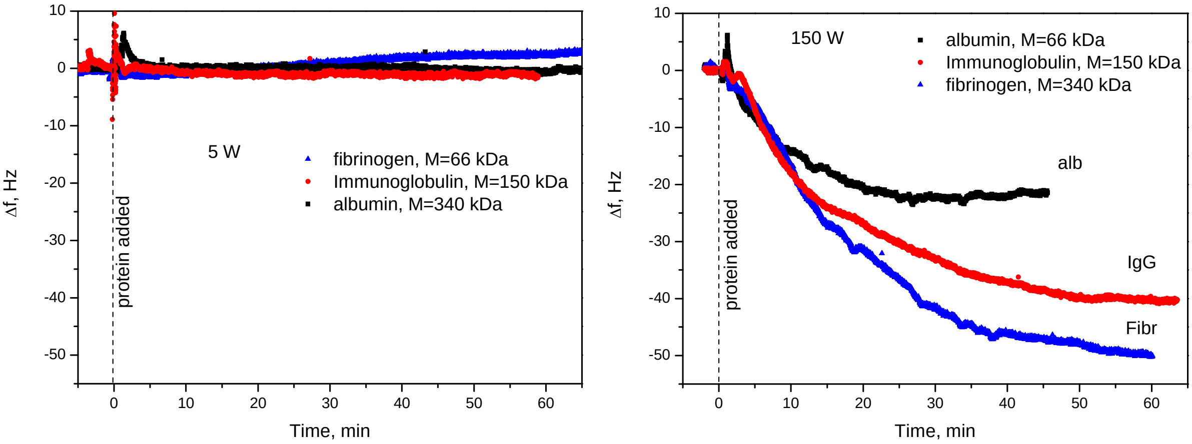
Conclusions

In this study, plasma polymerization as a method for the deposition of plasma polymer on the base of polyethylene oxide by glow discharge at low pressure was presented. Experimental part introduced



(a) (b)

Figure 6. The C1s spectra of PEO-like films deposited a) at 5W and b) at 120W.



(a) (b)

Figure 7. Adsorption of blood proteins on PEO-like plasma polymers: a) at 5W and b) at 150W.

the first results obtained by using plasma assisted vacuum thermal degradation of PEO as an alternative strategy for production of non-fouling surfaces. It was determined that PEO-like films prepared at high power of discharge lost non-fouling properties; however the plasma polymer films prepared at low power showed good protein-resistant properties. The further research will be focused on deposition of PEO-like films by dielectric barrier discharge (DBD) at atmospheric pressure at the Institute of Plasma Physics and their comparison with the results of the low pressure deposition.

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