A Hydrodynamic Model for Blood Penetration in Central Venous Catheters

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Abstract— **Biofilms grow wherever there exist a surface covered by substances acting as nutrients and inmuno-protective microenvironment for microbial life. Catheters provide enticing surfaces for microbial colonization and microbes often quickly take up residence. Protein deposition use to offer a proper microenvironment previous to colonization. In the present paper we propose a hydrodynamic mechanism responsible for upstream blood penetration based on the flow limited diffusion of molecules against the perfusion fluid. Diffusion of blood material constrains to a very small corridor, close to the catheter inner wall. The experimental observations in this paper are explained in the frame of this hydrodynamic model as well as previous results reported in the literature.**

Key words— **Central venous catheter, bacterial adhesion, microbial colonization, biofilm, hydrodynamics.**

I. Introduction

Central venous catheters are widely used in intensive therapeutic strategies. They are excellent tools for controlled administration of fluids, medications, blood products, and parenteral nutrition. Also, the use of central venous catheters has improved insertion of transvenous pacing electrodes and hemodynamic monitoring, with reduction of risks [1].

It is well known that central venous catheterization use to cause different undesired complications. One of the most critical and frequent is the catheter-related bloodstream infection, associated with indwelling central venous catheters [2]. Vascular catheters are irreplaceable elements for the care of critically ill patients [3], though catheter-related bloodstream infection has become a leading cause of healthcare-associated blood stream infections and is responsible for significant increase of the morbidity and mortality [4-7]. More than 250000 vascular catheter-related bacteraemias and fungaemias occur every year in the USA with attributable mortality ranging from 12% to 25% in critical patients [8, 9].

Catheter colonization is associated to bacterial adhesion mediated by physico-chemical interactions. Van der Waals, electrostatic and hydrophobic attraction forces cause serum protein deposition and structuring on a thin layer, where microorganisms are able to trigger a second adhesion process between its membrane receptors and the layer fibrin or fibrinogen. Once the adhesion process in progress, microorganism forms successive slime-layers, which acts against antibiotic treatment [10].

Previous to microorganism colonization, it is necessary upstream migration of biological material to form a multilayer on the internal catheter wall. Blood has to penetrate against the perfusion fluid drag that naturally opposes this penetration.

To illustrate this idea, Figure 1 shows some Scanning Electron Microscopy (SEM) pictures that make obvious the presence of early protein multilayer structures growing on the internal catheter surface, for both catheter tip and middle part. The catheter was donated by Torrecadenas Hospital, from a collection of discarded catheters whose removal, fifteen days after implantation following catheter care protocol which recommends systematical change of placement in this period.

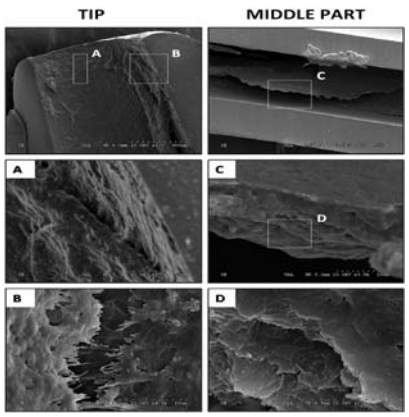

Fig. 1 SEM pictures of a two-lumen catheter. Tip-48 hours after implantation. Internal lumen (x120). A) non-infectious multilayer protein structure. Deployment area (x1000). B) first nanolayer edge with fibrillar stratified architecture (x4500). Middle Part-10 days after implantation-5 cm far from the tip. Marginal lumen (longitudinal cut), showing a folded foil. The upper edge is separated from the polymer surface as a consequence of the cutting technique (x100 expanded). C) free laminar stratified edge (x3500). D) magnified free edge (x10000)

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The physical mechanism associated to this material transport is up to now unknown. In the present paper, we propose a hydrodynamic mechanism responsible for upstream blood penetration based on the flow limited diffusion of molecules against the perfusion fluid. The predictions using this model describe fairly well the experimental results.

II. Hydrodynamic Model for Catheter Blood Penetration

Two fluids have to be considered: a perfusion flow injected into the venous system (composed basically by dissolved medical drugs into water) and the blood, trying to rise against the perfusion stream, forced by pressure. The perfusion fluid dominates the hydrodynamics at the catheter tip since blood pressure into veins cannot counteract the perfusion pressure.

It is well known that a fluid flowing through a region bounded by walls exhibits a parabolic velocity profile. The fluid velocity just on the walls is ideally zero, while it reaches its maximum value at the center. The parabolic velocity distribution is only valid under laminar flow, for which dissipative forces dominate over kinematic ones, his regime keeps for Reynolds number < 2000. Otherwise, the velocity distribution becomes disordered and turbulence becomes apparent. A small lumen section, low injection flow, and the value for the viscosity of the perfusion fluid (roughly water) warrant a laminar flow over all working conditions. The Reynolds number for the catheter under clinical conditions in this study is about few tenths. Laminar Poiseuille flow is then warranted and phenomena as fluid entrainment, produced by a boundary layer separation and/or turbulent diffusion are not expected to occur.

We propose flow limited diffusion of blood into the perfusion fluid as responsible for upstream blood penetration. The key point is the parabolic shape of the velocity profile. The velocity of the perfusion flow is very low close to the wall and the blood can diffuse counter-stream slipping on the wall. Far from the wall, the relatively high velocity frustrates upstream blood diffusion, avoiding counterstream blood penetration.

The flow limited diffusion depends on the intrinsic diffusion of blood along the perfusion fluid and on the motion of that fluid, influenced by viscosity, pressure gradients, and geometry. Since the problem involves a competition between diffusion and advection, the system behavior will depend on the Péclet number:

$$Pe = \frac{R^3 \nabla P}{D\eta} = \frac{\tau_D}{\tau}$$

being D the diffusion coefficient for blood into the perfusion fluid, ∇P is pressure's gradient along the longitudinal axis (variation of fluid pressure along the catheter length), η the perfusion fluid viscosity, and R the tube radius. This adimensional number is easily interpreted as a competition between the time scale corresponding to the molecular diffusion $\tau_D=R^2/D$, and the characteristic time for the flowing fluid $\tau=\eta/R\nabla P$. The Péclet number for the catheters in this paper is of the order of 10^6, showing that diffusion is many times slower than advection.

Assuming that molecular diffusion and convective mass transport are the only two relevant processes in the fluid, a partial differential equation including Fick diffusion and mass transport in a cylinder of radius R can be written. The mass fraction of biological material ρ is then given by the solution of:

$$\left(\frac{\partial \rho}{\partial t} + \mathrm{v}\frac{\partial \rho}{\partial z}\right) = \frac{1}{r}\frac{\partial}{\partial r}\left(rD\frac{\partial \rho}{\partial r}\right) + \frac{\partial}{\partial z}\left(D\frac{\partial \rho}{\partial z}\right) \qquad (1)$$

where z is the longitudinal coordinate along the catheter (z=0 corresponds to the catheter's tip). Axial symmetry has been assumed.

There, v is the velocity of the fluid in the catheter, given by

$$\mathrm{v} = \frac{1}{4\eta}|\nabla P|\left(R^2 - r^2\right)$$

what corresponds to a Poiseuille flow.

As a consequence of this parabolic velocity profile and the very low fluid velocity just on the walls, there exists a very thin corridor next to the catheter's wall, where biological material can diffuse against the main stream. This can explain why the biodeposit grows forming very thin layers of several microns on the internal wall. The detailed treatment of this phenomenon is reported in a more technical document to be published elsewhere [11], in which the same problem is boarded using the tools of dimensional analysis instead of solving equation (1) with the corresponding boundary conditions as we do here. A more phenomenological but less quantitative description is given in [12].

III. Results

Measurements:

Premature protein multilayer structure is observed for both kinds of catheters not only at the tip but also at five centimeters far from the tip. This dynamical structure is already present 48 hours after catheters implantation.

Physical modeling:

The calculated *Pe* for real conditions is of the order of 10^6, which means that diffusion is about a million times slower than advection and diffusive effects are much weak-

er than drag effects. For this calculation the considered parameters were characteristic values in clinical practice: a flux of about 350 milliliters per hour, millimetric catheter's diameter, liquids of ordinary viscosity $\eta \sim 10^{-3}\ \frac{Kg}{m.s}$, and diffusion coefficient in the range of those typical for diffusion of materials into solvents like water ($D \sim 10^{-9}\ \frac{m^2}{s}$).

Taking R as unit of length and τ_D as unit of time in equation (1), an adimensionalized form is obtained, with the Péclet number as control parameter. Assuming that along the z direction the mass fraction decreases exponentially, the resultant equation for the dependence of mass fraction with adimensional radius can be analytically solved in terms of Legendre's polynomials, which show that diffusion is significant only in a very thin corridor close to catheter's lumen.

With this model it was computed the density ρ depending on the radius *r* and length *z,* that are expressed in units of catheter's radius. The result is shown in Figure 2. The magnitude ρ is in units of the blood density at the catheter's tip.

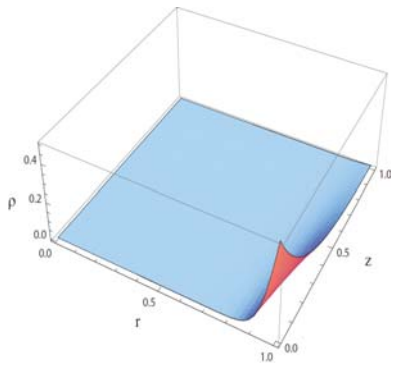

Fig. 2 Tridimensional profile of density illustrating Counterstream Blood Penetration. The value of Pe=1000 was used to make the graph. The values of the density, ρ, of diffused substance are expressed in units of blood density at catheter´s tip. Density decays exponentially along catheter's length *Z*. Both *Z* and radius *r* are expressed in units of catheter's radius. The values of *r* = 1 and *r* = 0 correspond to catheter's wall and centre, respectively. Near the wall, there is a sharp increase of ρ, expressing the formation of a diffusion layer, a region where the density of diffused substance differs substantially from its environment

IV. Discussion

Catheter infection develops in three steps: i) transport of bacteria from the skin to the catheter tip via a marginal way of fibrin, ii) attachment of microorganism and slime production through cell-cell aggregation. An optimal microenvironment for colonization and multilayer formation develops, iii) micro-colonies growth into the biofilm [13, 14]. Finally, bloodstream infection becomes apparent. A great deal of the antibiotic bacterial resistances is caused by the biofilm properties against the host immune system [15].

SEM pictures confirm the existence of non infectious protein multilayer structure already for the second day of the central venous catheters implantation. The real microorganism adhesion mechanism must then be the interaction between the microorganism adhesins and the protein multilayer network, since the initial naked polymer surface is rapidly covered by organic material after catheter implantation. This could be the reason why treatments and catheter funtionalizations previous to implantation are not sufficiently effective [16].

An important question at this point concerns the mechanism of upstream blood penetration. The hydrodynamic model proposed in this work provides a consistent answer to this question. The diffusion of blood for real clinical conditions against the perfusion fluid is extremely slow compared to advection.

When drag increases, the upstream blood diffusion is hindered by the flow. Since the velocity is zero at the walls, diffusion occurs only very close to the wall. The larger the value of *Pe*, the closer to the wall diffusion occurs. The time necessary for counterstream blood penetration to attain a given distance inside the catheter becomes predictable [11]. Using this model the distance of about 5 cm, at which protein multilayer structure was experimentally detected two days after implantation, is attainable into this period of time.

Protein multilayer structure manifest after counterstream blood penetration and could be controlled through the geometrical and physical parameters in equation (1). Increasing injection flow leads to a reduction of the diffusion layer thickness. The same effect occurs through an increase of the diffusion time. This last decreases for high diffusion coefficient and large perfusion fluid´s viscosity. The catheter diameter, pressure applied to move the perfusion fluid and its viscosity are the three parameters of control (the diffusion coefficient depends on the hydrodynamic of the diffusing elements in blood, which is determined by nature).

The application of ultrasonic waves delays microbial biofilm formation as reported by Hazan et al [17]. The hydrodynamic model we propose in this paper offers an explanation for this interesting experimental finding. Transversal oscillations induced by ultrasonic waves produce an alteration of the thin layer close to the wall, pushing out the diffusing counterstream material to the central region of the catheter where the main flow drags it back to the circulatory system. This opens a new field for future modelations based on our viewpoint.

V. Conclusions

A Protein Multilayer Structure is detected onto the catheters inner wall already 48 hours after its implantation. It implies that the microorganism adhesion mechanism bases on the interaction between the microorganism adhesins and the protein multilayer network, being irrelevant the polymer nature of the catheter.

The upstream blood penetration is well described by a hydrodynamic mechanism based on the flow limited diffusion of blood molecules against the perfusion fluid. It constraints the protein multilayer to a very small corridor very close to the catheter inner wall. Out of this region, the main flow sweeps away everything in its path.

The hydrodynamic model in this paper predicts early presence of Protein Multilayer Structure as experimentally detected.

Acknowledgments

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