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THE INSTITUTE OF MEDICAL & DENTAL
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THE UNIVERSITY OF LIVERPOOL

Dedicated Session C
King's Suite

VASCULAR PROSTHESES

Chair	G Soldani Centro Studi Processi Ionici del CNR, Universita de Pisa, Italy
13.45	Chairman's Introduction **Small diameter vascular prostheses: present status and future developments**
14.00	R Eloy Cardiovascular Surgery and Biomaterials, INSERM, Bron, France
14.35	R Barbucci, F Tempesti, M Benvenuti, A Magniani and A Albanese CRISMA, University of Siena, Italy **Preparation, physico-chemical and biological characterisation of heparinisable materials**
15.10	Tea Break
15.30	J Jozefonvicz and M Jozefowicz Laboratoire de Recherches sur les Macromolecules, Universite Paris-Nord, France **A new concept for the tailoring of biocompatible materials**
16.05	PB van Wachem, JM Schakenraad and B van der Lei University of Groningen, The Netherlands **Aspects of improved vascular graft healing; an overview of the 'Groningen' experience**
16.40	C Baquey, L Bordenave, MY Jablonski-Bernasconi, T Darnis and M Rabaud INSERM, Universite de Bordeaux, France **New approaches to enhance vascular prostheses performances**
17.15	End of Session

Small-diameter vascular prostheses: present status and future developments.

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Clinical experience with vascular grafts has demonstrated that a satisfactory vascular prostheses which could serve as a replacement in the venous system or as a small-diameter artery has been and, even after 30 years of research and development, continues to be a most difficult problem in vascular surgery. Specific autologous veins and arteries are now considered the small diameter grafts of choice for peripheral and cardiovascular applications. In all cases, however, these vessels are limited to a finite supply in any one individual and/or are of unsuitable quality. Vascular prostheses made of porous fabrics such as expanded polytetrafluoroethylene (Teflon®) and woven or knitted polyethylene-terephthalate (Dacron®), although successful in the replacement of large-diameter arteries, have not proven useful for long-term applications as venous or small-diameter arterial substitutes. Therefore, the development of new biomaterials and/or new concepts in the design and manufacture of small-diameter vascular prostheses are still warranted.

The challenge is to realize a tubular structure 1 to 4 mm internal diameter (i.d.) which can remain patent in a low blood flow configuration, does not induce anastomotic hyperplasia, and promotes a minimal connective tissue growth on the luminal surface to support the formation of a thin, stable, mature neointima. Many characteristics of the prosthesis, such as chemical composition, method of fabrication, compliance, porosity, and bioresorbability have been investigated for their possible roles in promoting appropriate neointima formation. Among these characteristics, wall porosity plays an essential role in affecting patency and long-term wound healing properties of small-diameter vascular prostheses. Porosity is important both on the blood-contacting side and on the soft-tissue external side of the graft, where tissue ingrowth is a critical factor in the long-term compliance of the vessel. If the surface chemistry is constant controlled porosity is important in determining blood response, tissue response, and compliance. However, also the kind of material used in the fabrication process affects the thromboresistance of the graft. One approach is to use relatively thromboresistant materials. These materials may be thromboresistant either because they do not cause significant coagulation or thrombosis, or because pharmacological agents (such as heparin) are incorporated in these materials which will inhibit adverse blood response. The relative thromboresistance of polyurethanes as a class of materials makes them suitable for this strategy.

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Our laboratory has initiated an extensive program to study porous polyurethane vascular prostheses made by a processes which relies on a thermodynamically unstable polymer solution which can readily form a gel upon exposure to a relatively small excess of a nonsolvent, producing a material which displays a fine interconnected pore structure. This process involves the formation of gel-like tubular membranes by a phase-inversion effect derived from simultaneous but separate spraying of a polyurethane - polydimethylsiloxane solution and water (as nonsolvent) over a sliding and rotating mandrel. The major advantage of this technique is its flexibility. By varying the amount of nonsolvent in the polymer solution and adjusting the mechanical parameters of the spinning process, one can vary the porosity of the tube wall over a wide range, and as a result obtain wall compliance values ranging from venous to arterial to rather rigid tube properties.

To understand the role of inner surface geometry in affecting the patency of small-diameter vascular grafts we are producing asymmetric structure depositing a nonporous or minimally porous skin on the inside or outside of the tube. An experiment was performed using two kinds of 1.5 mm ID tubular membranes, with and without a dense skin. Both types featured a porous, communicating cell wall structure and an outer porous surface. Membrane segments were implanted in the infrarenal abdominal aorta of rats by the same surgeon. The results showed all the skinned grafts occluded in 3 days, while at 12 weeks the degree of patency of the porous grafts was related to their water permeability (w.p.), the highest degree of patency was obtained with w.p. in the range of 20-40 $ml/min/cm^2$.

As future developments we are working to use the technique described here to incorporate bioactive polypeptides, anticoagulants, and other growth stimulating or inhibiting factors into the gel-like structure of the graft. For example, this can be achieved by dissolving them in the nonsolvent (in this case, water), afterwards a composite devices can be fabricated using separate solutions of synthetic and biological polymers which are simultaneously blended and layered by a spraying-interfacial coprecipitation process. Using this approach we are studying the feasibility of a second generation of synthetic small-diameter vascular prostheses, that is porous, distensible, tubular membranes which incorporate albumin and basic Fibroblast Growth Factor (bFGF) to achieve a slow, local release which could influence the healing process. In preliminary experiments we have demonstrated that albumin and bFGF can be released at an approximately constant rate for at least 2 weeks and that the bFGF initially incorporated in the membrane remained biologically active as shown by *in vitro* proliferation of human endothelial cells.

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