

DIFFERENCES IN CONDUIT AND BUFFERING FUNCTION AMONG ARTERIES, VENOUS GRAFTS AND SYNTHETIC PROSTHESIS: IMPLICANCES IN THE DEVELOPMENT OF INTIMAL HYPERPLASIA

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Abstract— Usually vascular surgeons consider the use of vein grafts as the materials of first choice for bypass or reconstruction of small arteries, while synthetic prosthesis (i.e. polytetrafluoroethylene, ePTFE) plays a secondary role in this matter. However, the causes for the superior performance of vein grafts respect ePTFE remain unclear. Our aim was to compare the conduit (CF) and buffering function (BF) of arteries, with those of vein grafts and ePTFE. *In vitro* pressure (Konigsberg) and diameter (Sonomicrometry) were measured in ovine arteries and veins, and ePTFE prosthesis, under isobaric and physiological pressures levels. From stress-strain relationship the Kelvin-Voigt time constant was calculated to quantify the BF. The CF was evaluated as $1/Z_C$, where Z_C is the characteristic impedance. Vein graft CF and BF were more similar to native arteries than those of ePTFE prosthesis. Consequently, the higher performance of vein grafts could be related with their superior matching with arteries.

Keywords— vascular prostheses, conduit function, buffering function, intimal hyperplasia.

I. INTRODUCTION

The arteries conduit function (CF) allows the distribution of blood to different tissues, while their buffer function (BF) is responsible for the smoothing of pressure and flow pulsatility determined by the intermittent ventricular ejection (Nichols and O'Rourke, 1998; Bia *et al.*, 2003; 2004; 2005a). Both functions are related and depend on the geometrical and mechanical properties of the arteries, which in turn are determined by passive (elastin and collagen fibers) and active components (smooth muscle cells) of the arterial wall. In this sense, its dynamic behavior depends on the viscoelastic individual contribution of each wall constituent and the structural arrangement among them (Bia *et al.*, 2003; 2004; Nichols and O'Rourke, 1998).

In several circumstances in which an arterial segment is altered, an arterial bypass or reconstruction is performed, in order to restore the functional capability. Looking for improving the arterial substitute patency rate, there have been described several conditions that the ideal graft should fulfill. Related to this, taking in to

account that the mechanical and/or impedance mismatch between the native artery and the alternative conduit may induce graft failure, it is accepted that an ideal arterial substitute must share identical viscoelastic and geometrical properties with the native artery (Tai *et al.*, 1999). Therefore, in theoretical terms, an autologous artery would be the ideal arterial substitute. However, except in certain limited situations, it is difficult to obtain an autologous artery of adequate length and size without the sacrifice of an organ or essential part of the body.

Several synthetic prosthesis have been employed, and nowadays, among the most widely used are expanded polytetrafluoroethylene (ePTFE) prosthesis. However, occlusion rates of ePTFE when used in small or medium size arterial reconstruction are high. For instance, patency rates for 175 ePTFE femoropopliteal bypasses were 62% at 35 months (Veith *et al.*, 1980). Better results have been obtained with venous grafts. So, the use of autologous veins (mainly the human great saphenous vein) is the first choice in bypass or reconstruction of medium and small arteries, while non-biological prosthetic materials (i.e. ePTFE) assume a secondary role in this position (Dardik and Howard, 1999).

The causes of the superior performance of veins respect to the ePTFE, in the medium and small size arteries' reconstruction, remain to be elucidated (Cabrera Fischer *et al.*, 2005; Norberto *et al.*, 1995; Kissin *et al.*, 2000). The main cause of ePTFE graft failure within a short period of time is the development of intimal hyperplasia (IH) in the distal anastomosed artery (Vijayan *et al.*, 2002; Echave *et al.*, 1979), causing outflow stenosis of prosthetic bypass and tissue ischemia. The mechanical mismatch between the ePTFE and the native artery is considered a major cause of intimal hyperplasia and graft failure (Dardik and Howard, 1999).

The pathogenesis of this lesion is described as proliferation of smooth muscle cells of the arterial media and their migration into the intima, in response to injury at the junction of the graft and the native artery. Over the past years, IH in the bypassed or reconstructed arteries has been extensively studied; however the mechanism through which it develops has not been exactly resolved (Dardik and Howard, 1999). It has been de-

scribed that early failure, secondary to IH, is merely a consequence of a thrombotic process; posterior obstruction involves an intimal hyperplastic development (Tsui and Dashwood, 2002). In the latter process, smooth muscle cells belonging to the tunica media, migrate through the elastic laminae to the tunica intima releasing a protein matrix. This produces an intimal thickening and is the beginning of the obstruction (Tsui and Dashwood, 2002). This IH, as sequelae of a thrombus organization, determines changes that resemble closely a non-thrombotic genesis (Trubel *et al.*, 1995). In addition, the IH has been related with the trauma during vein harvesting; consequently, the role of handling would be very important in avoiding graft occlusion (Seifalian *et al.*, 2002).

Moreover, two other main factors that affect the development of IH are compliance and wall shear stress mismatch between the native artery and the graft (Trubel *et al.*, 1995; Cabrera Fischer *et al.*, 2005). Since it is very difficult to isolate compliance mismatch from other intervening factors, the direct relationship between compliance mismatch and IH has been confounding. To start with, shear stress and flow rate are linearly correlated, such that a higher flow rate will induce a higher shear stress and vice versa (Tanaka *et al.*, 1996). In turn, shear stress is believed to alter the movement of smooth muscle cells (migration to the intima layer) (Loth *et al.*, 2002). In particular, localized low wall shear stress has been associated with the development of IH, making its first appearance along the suture line and migrating onto the native vessel and graft (Loth *et al.*, 2002; How *et al.*, 2000; Giddens *et al.*, 1993). Therefore, it can be said that there is mounting evidence that flow hemodynamic disturbances induce IH (Loth *et al.*, 2002). One reason for this pathologic behavior might be the deterioration of the endothelium as a consequence of disturbed flow that produces vortices (Vijayan *et al.*, 2002).

Finally, with independence of the mechanism that determine the genesis, IH during high pressure conditions has been stated as an adaptive and natural mechanism to maintain circumferential wall stress, and recently to maintain wall strain, within a normal and uniform level (Dardik and Howard, 1999; Dobrin, 1995). This behavior is called vessel remodeling. Our group has showed that the arterial wall remodeling (i.e. hypertrophy of medial smooth muscle cells) in hypertensive patients occurs with wall viscosity and inertia increase (Armentano *et al.*, 1998; Gamero *et al.*, 1999). This allows not only the stress reduction, but also keeping the wall buffering or filtering function close to the normotensive patients' levels (Armentano *et al.*, 2004). For this mechanism, the arterial system appears to preserve the BF, in order to prevent deleterious high frequency components to damage wall constituents. In the same way, the veins grafts wall remodeling (i.e. intimal and/or medial hyperplasia) (Dobrin, 1995; Jacot *et al.*, 2004; Cabrera Fischer *et al.*, 2005), after interposition in the arterial system could be analyzed as a protective

mechanism that reduces the wall stress (Dobrin, 1995), as well as, increases the BF capability maintaining the vein wall buffering performance as arterial segments, in spite of high levels of pressure. In addition, in hypertensive patients, an increase in the arterial internal diameter ("arterial dilatation") has been reported (Armentano *et al.*, 1998). Possibly, the arterial dilatation could be interpreted as an adaptive mechanism to maintain elevated the arterial conduit function, despite of the peripheral resistance increase.

Several groups have investigated and developed techniques to improve ePTFE arterial by-pass results (Kreienberg *et al.*, 2002). Some of these studies showed that the interposition of a vein conduit or segment, known as "vein cuff", between the ePTFE and the distal artery increased the by-pass patency rates (Piorko *et al.*, 2001; Miller *et al.*, 1984). About this, we have demonstrated previously significant quantitative inhibition of IH formation at outflow anastomoses by vein cuff interposition between ePTFE prosthesis and femoral arteries in an ovine model (Cabrera Fischer *et al.*, 2005). It is suggested that vein cuff could reduce the IH, by reducing the mechanical mismatch between the ePTFE prosthesis and the native artery. However, this important topic remains unclear. Additionally, despite of the fact that there are studies that suggest that the venous grafts' major patency rates in small and medium size arteries reconstruction could be related to their biomechanical properties (Dardik and Howard, 1999), until now, there are not studies evaluating and comparing the functional performance of native arteries, vein grafts and synthetic prosthesis, under identical arterial hemodynamic conditions.

Therefore, it remains to be explained if there are differences in arterial and grafts wall behavior during arterial hemodynamic condition; differences that should be taken into account during graft selection.

In this context, our aim was to evaluate and compare the CF and BF of native arteries, with those of veins grafts and ePTFE prosthesis. In addition, we discuss several biomechanical aspects that could be related with the genesis of IH. Our hypothesis was that the vein grafts or cuffs reduce the vascular CF and BF mismatch between the arterial substitute and the native artery, diminishing the mechanical injury to the distal arterial wall.

II. METHODS

A. Surgical procedure

All experiments were performed in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1996).

Nine adult healthy male Merino sheep ranging in weight from 25 to 35 kg were used in this study. All animals were vaccinated and treated for skin and intestinal parasites. During 20 days before surgery they were appropriately fed, watered, and assessed for adequate clinical status. Each sheep was anaesthetized with intra-

venous administration of pentobarbital (35 mg/kg). The animals were mechanically ventilated.

The distal descending aorta (DDA), and the right common carotid artery (CA), external jugular vein (JV) and femoral vein (FV) were dissected simultaneously in each animal. Segments of 6 cm of DDA, CA, JV and FV, were accurately measured with a caliper and marked with two suture stitches. Afterwards, they were excised and immersed in Tyrode solution, and were destined to *in vitro* mechanical study. At the end of the surgery, the animals were sacrificed with an overdose of sodium thiopentane followed by potassium chloride.

B. *In vitro* study: mechanical test

To perform the mechanical tests, each vascular segment was non-traumatically mounted (at *in vivo* length) on specifically designed cannulas of the flow circuit loop, and immersed and perfused with a thermally regulated (37°C) and oxygenated Tyrode's solution, with pH= 7.4 (Cabrera Fischer *et al.*, 2002; 2005). A full description of this device (named *in vitro* system or circulation mock, Fig. 1) has been published previously (Bia *et al.*, 2005b).

Each vessel was instrumented with a pressure microtransducer (1200 Hz frequency response, Konigsberg Instruments, Inc., Pasadena, CA, USA) inserted in the vessels through a stab wound. Each pressure transducer had been previously calibrated using a mercury manometer. To measure vein or arterial external diameter a pair of ultrasonic crystals (5MHz, 2 mm diameter) was sutured to the adventitia of the vessels. The transit time of the ultrasonic signal (1580 m/s) was converted into distance by means of a Sonomicrometer (1000 Hz frequency response, Triton Technology Inc. San Diego, CA, USA). Optimal positioning of the dimensional gauges was assessed by an oscilloscope (model 465B, Tektronix).

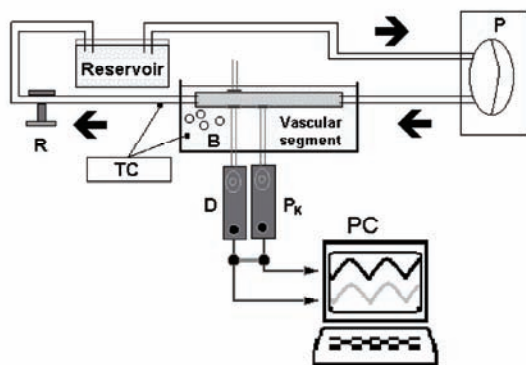


Figure 1. Circulating loop showing a pneumatic pump (P) and a perfusion line with an organ chamber, a resistance modulator and a reservoir. Tyrode's solution is oxygenated through bubbles (B) and thermally controlled (TC). Pressure (P_k) and Diameter (D) are obtained using a solid transducer and ultrasonic crystals. Both signals are stored in a personal computer (PC) (For more details see reference, Bia *et al.*, 2005b).

Furthermore, seven ePTFE grafts of 6 mm diameter, thin wall (Gore-Tex Vascular graft, W.L.Gore & Associates, Inc., Flagstaff, Arizona, USA) and 6 cm long, were mounted on the *in vitro* system described above. In order to characterize its mechanical behavior, the ePTFE grafts were instrumented with a pressure microtransducer and a pair of ultrasonic crystals; using the same procedure that was used for DDA, CA, JV and FV. To ensure minimal transmural solution loss and the subsequent decrease of intraluminal pressure, grafts were subjected to a preclotting procedure (Tai *et al.*, 2000). To this end, the graft was perfused several times with 10 ml of fresh sheep blood until no fluid loss was observed. Afterwards, all grafts were washed in normal Tyrode solution.

Once placed in the organ chamber, the vascular and ePTFE segments were allowed to equilibrate for a period of 10 minutes.

C. Experimental protocol and data acquisition

After the equilibration time, a similar protocol was followed for all segments, in order to characterize their mechanical properties.

The pneumatic device of the circulation mock, was regulated by an air supply machine that allowed fine adjustments of heart rate, pressure values and waveforms. Recordings were done submitting the segments to a stretching rate of ~110 cycles/min, an intravascular pulse pressure of ~50 mmHg and mean pressure of ~90 mmHg. In all cases the pump, and tubing resistance were regulated so as to generate adequate pressure waveforms (Bia *et al.*, 2005b).

Vascular and ePTFE segments pressure and external diameter signals were displayed in real time, digitized every 5 ms and digitally stored for later analysis. Approximately 20-30 consecutive beats were sampled and analyzed under steady-state condition.

D. Data analysis

Buffer function

For each segment, to calculate the arterial elastic and viscous modulus the arterial stress-strain loops were constructed (Bia *et al.*, 2005b; Armentano *et al.*, 1995; Barra *et al.*, 1993). The incremental elastic modulus (E_{INC}) and the viscous modulus (η) were calculated using a Kelvin-Voigt viscoelastic model (spring-dashpot) accordingly with previous works (Bia *et al.*, 2003; 2004; 2005a).

The buffer function (BF) was obtained by analyzing the temporal response of the arterial strain to an abrupt increase of stress, performed via a Kelvin-Voigt model of the arterial wall (Bia *et al.*, 2004; 2005a). Accordingly, the σ - ϵ relationship was established using E_{INC} and η

$$\sigma(t) = \sigma_0, t > 0 \Rightarrow \epsilon(t) = \frac{\sigma_0}{E_{INC}} \left(1 - e^{-t/\eta/E_{INC}} \right), t > 0$$

where the η/E_{INC} ratio would characterize the exponential temporal response of strain due to a stress change. This ratio, the time constant of the Kelvin-Voigt model or “time retardation” (Westerhof and Noordergraaf, 1970), characterizes the intrinsic capacity of the material to cushion the stress or pressure exerted over its surface. As the material involved in this case is the arterial, venous or ePTFE wall, the conduit wall BF from Kelvin-Voigt model was calculated as (Bia *et al.*, 2003; 2004; 2005a):

$$BF = \frac{\eta}{E}$$

An elevated value of BF is related with a slow response, suggesting an augmented buffering effect with an increased attenuation of stress or pressure oscillations (Bia *et al.*, 2004; 2005a; 2005b).

Conduit function

The conduit function (CF) was evaluated by means of the local hemodynamic impedance, as was previously reported (Bia *et al.*, 2005a). It was quantified in terms of the characteristic or local impedance (Z_C), following Water Hammer equation (Nichols and O'Rourke, 1998):

$$Z_C = PWV \cdot \rho_B / CSA_M$$

where ρ_B is the blood density ($\rho_B=1.06$ g/mL), CSA_M is the mean cross-sectional area (assuming a cylinder geometry for the artery, $CSA=\pi \cdot R_i^2$), where R_i is the internal radius, and PWV is the pulse wave velocity. The PWV was calculated theoretically by the Moens-Korteweg equation (Nichols and O'Rourke, 1998):

$$PWV = \sqrt{(E_{INC} \cdot h_m) / (2 \cdot \rho_T \cdot R_{im})}$$

where h_m is the mean wall thickness, R_{im} is the mean internal radius, and ρ_T is the wall tissue density. An increased Z_C will determine an increase in the resistance against blood flow (Cholley *et al.*, 2001) and consequently a diminished capacity to conduct blood, without a decrease of pressure. Therefore, in this study the conduit function, CF, was analyzed as (Bia *et al.*, 2005a):

$$CF = 1/Z_C$$

E. Statistical analysis

Hemodynamic and biomechanical parameters were compared using one-way analysis of variance and the Bonferroni t test. Values reported are expressed as mean value \pm standard deviation. A $p<0.05$ threshold was adopted as statistically significant. All statistical analysis were performed using a specific program (Systat 10, Chicago, Illinois, USA).

III. RESULTS.

In Table 1 we reproduced the hemodynamic values measured in ovine arteries and veins, and ePTFE conduits.

Values obtained of pumping rate, and systolic, diastolic, pulse and mean pressure showed non-significant differences among arteries, veins and ePTFE ($p>0.05$), ensuring an isobaric and isofrequency

Table 1: hemodynamics measurements.

	Carotid Artery	Distal Aorta	Jugular Vein	Femoral Vein	ePTFE
SP	126 \pm 4	125 \pm 5	125 \pm 6	127 \pm 4	126 \pm 3
DP	74 \pm 3	75 \pm 4	74 \pm 5	72 \pm 4	73 \pm 5
PP	53 \pm 4	52 \pm 5	51 \pm 5	54 \pm 4	54 \pm 3
MP	91 \pm 2	93 \pm 3	94 \pm 3	91 \pm 5	92 \pm 3
MD	6.2 \pm 0.4	15.9 \pm 1.2 ^a	13.9 \pm 3.3 ^a	6.4 \pm 0.6 ^{b,c}	6.2 \pm 0.1 ^{b,c}
PR	110 \pm 4	111 \pm 3	110 \pm 4	111 \pm 2	110 \pm 4

All vessels are submitted to specific hemodynamic parameters similar to those observed in arteries. SP, DP, PP and MP: systolic, diastolic, pulse and mean pressure (in mmHg), respectively. MD: mean diameter (in mm), respectively. PR: pumping rate (bpm). Values are mean \pm SD. P values determined by ANOVA + Bonferroni test: ^a, ^b, ^c, and ^d, $p<0.05$ with respect to carotid artery, distal aorta, jugular vein and femoral vein, respectively.

comparison (Table 1). Note that the external diameter was similar among carotid arteries, femoral veins and ePTFE segments. Additionally, the external diameter, was similar between the distal aorta and the jugular vein.

In Table 2 we reproduced the functional parameters, CF and BF, calculated from measurements in ovine and ePTFE segments. As can be seen, the CF did not show statistical differences between the carotid artery and the femoral vein. Additionally, the CF of the jugular was higher respect the CF of the carotid artery ($p<0.05$) and lesser respect to the CF of the distal aorta ($p<0.05$). In contrast the CF of the ePTFE segments was lesser respect the CF of arteries and veins ($p<0.01$).

The BF of jugular and femoral veins showed statistically significant differences with respect to arteries ($p<0.05$) and ePTFE conduits ($p<0.05$). The BF of the ePTFE segments was lesser respect the BF of both, arteries and veins ($p<0.01$).

IV. DISCUSSION.

The aim of this work was to characterize, and compare the CF and BF of native arteries, with those of vein grafts and ePTFE prosthesis. In addition, we analysed several biomechanical factors that could play important roles in the genesis of IH.

The following discussion focuses on three central aspects of this work.

- Methodological strategy.
- Vascular Grafts Functionality.
- Final Remarks.

Table 2: Functional Parameters

	CF	BF
Carotid Artery	1.79 \pm 0.26	5.22 \pm 0.70
Distal Aorta	16.50 \pm 3.39 ^a	4.71 \pm 0.77
Jugular Vein	5.18 \pm 1.36 ^{a,b}	2.77 \pm 0.38 ^{a,b}
Femoral Vein	1.87 \pm 0.46 ^{b,c}	3.00 \pm 0.46 ^{a,b}
ePTFE	0.35 \pm 0.01 ^{a,b,c,d}	0.01 \pm 0.01 ^{a,b,c,d}

BF: wall buffering function (10^{-2} s). CF: conduit function (10^{-4} cm²/dyn.s). Values are mean \pm SD. p values were determined by ANOVA + Bonferroni test: ^a, ^b, ^c, and ^d, $p<0.05$ with respect to carotid artery, distal aorta, jugular vein and femoral vein, respectively.

A. Methodological strategy

We studied ovine vascular segments taking into account that the ovine cardiovascular system has shown to be an excellent (and widely used) model to study the hemodynamic performance of vascular grafts, due to its similarity to the human cardiovascular system (Kohler and Kirkman, 1999; Cabrera Fischer *et al.*, 2005). In previous works we have employed this model to evaluate the performance of biological and synthetic grafts (Cabrera Fischer *et al.*, 2005; Bia *et al.*, 2005a; 2005b).

We opted for vascular segments, instead of the most used strips or rings (Silver *et al.*, 2003; Mavrilas and Tsapikouni, 2002), because the former are better to reproduce the *in vivo* hemodynamic conditions, and to preserve the shape and integrity of vascular/graft wall (Dobrin, 1995).

The technique employed to register pressure and diameter with the *in vitro* circulation mock (Figure 1), has been previously used and validated by our group (Armentano *et al.*, 1995; Cabrera Fischer *et al.*, 2002; Bia *et al.*, 2005b). This methodology, allows accurate and reproducible measurements due to the high frequency and linearity of response of both, dimension gauges and pressure transducers. The 200 Hz sampling rate used in the digitalization of the data was larger than the highest frequency components in the pressure and diameter spectra, enabling signal reconstruction without distortion.

The stress-strain relationship analysis allows the characterization of the vascular wall mechanical behavior (Armentano *et al.*, 1995; Bia *et al.*, 2005; 2005b). This analysis illustrates that the vascular wall has a non-linear, and frequency-dependent mechanical behavior (Armentano *et al.*, 1995; Bia *et al.*, 2005c). Although static analyses (i.e. incremental stress-strain test) allow the evaluation of frequency-dependent mechanical properties (i.e. wall viscosity) (Mavrilas and Tsapikouni, 2002; Silver *et al.*, 2003), an adequate characterization of the functional meaning and contribution of this properties requires dynamic analysis, in which the vascular wall is submitted to conditions similar to real hemodynamic situations. Consequently, in order to adequately characterize the arterial and vein wall mechanical functional behavior, in this work we performed a dynamic analysis of the vessels' wall. To this aim, physiological pressure and diameter waveforms, and arterial pressure and stretch frequency levels were simulated in the mock system (Table 1).

Once used in arterial reconstruction, vein grafts or ePTFE prosthesis, and native artery diameter or strain, may not necessarily be the same. In fact, when a vein is interposed in the arterial system, the blood pressure induced strain in the vessel, makes the vein graft to operate in its high strain region of the pressure-diameter or stress-strain curve (Cabrera Fischer *et al.*, 2005). On the contrary, it has been estimated that the blood pressure induced strain in the ovine femoral artery is between 10-15%, suggesting that the arteries physiologically operate in the low strain region and/or in beginning part of the

high strain region of the stress-strain curve (Bia *et al.*, 2003; 2005c). Therefore, an isometric analysis or comparison, whereas biomechanically interesting (Mavrilas and Tsapikouni, 2002; Silver *et al.*, 2003), may not reproduce what does really happen when vein grafts are used in arterial reconstruction. In opposition, when a vein graft is interposed in the arterial system, both native artery and vein and ePTFE graft are subjected to the same vascular pressure and frequency of stimulation, corresponding to that of the arterial system. Therefore, in order to perform an appropriate mechanical characterization and comparison we did an isobaric and isofrequency dynamic study of arteries, veins and ePTFE segments submitted to hemodynamic conditions similar to that of systemic arteries (Armentano *et al.*, 1995; Bia *et al.*, 2005c). To perform this kind of study an *in vitro* evaluation was compulsory. To our knowledge, similar studies have not been previously reported.

B. Vascular Grafts Functionality

The CF of the arteries, veins and ePTFE segments was evaluated by means of the characteristic impedance (Z_c). Z_c correlates directly with the elastic properties and inversely with the cross-sectional area of the conduit or vascular bed. An increased Z_c will determine an increase in local impedance against blood flow resulting in a decreased capacity to conduct blood (Cholley *et al.*, 2001). Therefore, by inverse reasoning, the CF was computed as $1/Z_c$.

The CF of the arteries allows the blood transference from the heart to the peripheral vessels. To maintain an adequate level of mean pressure and to minimize ventricular work and wave reflections, low arterial impedance must be presented to the pulsatile blood flow ejected by the heart (Pepine and Nichols, 1982; Morita *et al.*, 2002). The implantation of a rigid graft into the arterial tree –comparable to the introduction of an impedance into an oscillating electrical circuit– diminishes the perfusion efficiency and, in low-flow situations, may lead to further flow stagnation and graft thrombosis (Tai *et al.*, 2000), with concomitant increase in ventricular afterload when the rigid graft is implanted in a large artery location (Morita *et al.*, 2002).

Our results showed that the CF calculated isobarically did not evidenced significant differences between the carotid artery (a small artery) and the femoral vein. Furthermore, the jugular vein showed a higher conduit function respect to the carotid artery. In contrast, the ePTFE conduit showed a lesser CF, that it is to say a higher impedance, respect to all the arteries and veins segments. Consequently, the vein grafts reproduce and/or increase the *in vivo* conduit performance of the small native arteries. Therefore, at least in theoretical terms, the implantation of a vein grafts into the carotid region would not increase the impedance in the vascular circuit, allowing to maintain the arterial perfusion efficiently, and maintaining the ventricular afterload similar to normal values. In contrast the ePTFE, diminishes the perfusion efficiency, generating non physiological impedance levels.

C. Buffering function

Recently, our group proposed the characterization of wall BF by means of the arterial wall time constant, obtained as the ratio η/E_{INC} when a Kelvin-Voigt model represents the arterial wall (Bia *et al.*, 2005a). A large η/E_{INC} value, associated with a slow response, suggests an enhanced wall buffering function by means of a more pronounced attenuation of the pressure or stress oscillations.

The η/E_{INC} has the elastic modulus as denominator and has a dissipative term as numerator. The elasticity is responsible for the storage capacity of the arterial wall. The energy dissipation is related to the viscous properties of the arterial wall (Bia *et al.*, 2005a) and helps to attenuate traveling pressure pulses along the arteries, and prevents reflected pressure waves from resonating in the arterial system (Shadwick, 1999). In turn, wall elasticity and viscosity influence the propagation and interaction of pressure and flow waves throughout the arterial tree and, consequently, the energetic demands placed on the heart (Shadwick, 1999; Morita *et al.*, 2002). Thus, vascular viscosity and elasticity are not only important determinants of the arterial functions, but also of the whole cardiovascular system performance (Morita *et al.*, 2002).

In addition, the arterial wall BF, that is to say the capability of the arterial wall to store, transmit, and dissipate energy, is key to prevent early mechanical failure or disruption of the arterial wall components. As a law, high frequency vibrations produce structure injuries, and the aim of filtering is to reduce accelerated oscillations. The wall energy dissipation avoids the transference of the high frequency components of the pressure wave to vascular diameter, exerting a protective effect on the arterial wall.

In agreement to previous works, we found no differences in the BF between both arterial segments (Bia *et al.*, 2005a). Interestingly, the BF of veins was lesser respect to arteries. This seems that the veins submitted to arterial hemodynamic conditions do not have the "arterial" buffer or filtering capacity, allowing the high frequencies of pressure wave to be present in the diameter signals. This effect of high frequencies, provokes a detriment in the mechanical protection of the vein wall segment (Pontrelli and Rossoni, 2003). This could be related to the recognized frequent progression of the atherosclerotic disease in the vein grafts, and/or with the vein grafts intimal hyperplasia and/or remodeling (Dobrin, 1995; Berceli *et al.*, 1990).

However, the ePTFE segments showed a lesser BF respect arteries and veins. Consequently, if an ePTFE segment were interposed in the arterial system, its lower buffering capacity would provoke a high pressure and/or flow pulsatility in the distal artery. About this, when the incident pulse pressure wave enters the stiff synthetic graft, its amplitude could increase abruptly. Therefore, when the pressure waves arrive to the distal arterial segment, their high pulsatility could provoke a non-physiological wall stress level. The high stress level

in the distal anastomosis has been related to the recognized high incidence of the intimal hyperplasia in the distal graft-artery anastomosis (Dobrin, 1995).

D. Final Remarks

At date, it is accepted that, when an arterial segment is replaced, the ideal arterial graft used for arterial bypass and/or reconstruction, must share identical geometric and viscoelastic properties with the host artery (Seifalian *et al.*, 2002). However, the commercially available prosthetic vascular grafts (i.e. ePTFE), are far from that ideal, as our and other authors results showed (Seifalian *et al.*, 2002). The synthetic prostheses are extremely rigid compared to elastic and muscular native arteries (Cabrera Fischer *et al.*, 2005; Tai *et al.*, 2000).

In this work we evaluated the vascular functions – conduit and buffering functions) of arteries, vein grafts and ePTFE prosthesis in order to determinate if functional differences among them could be related with the IH development. Our data showed that the vein graft conduit and buffering performance were more alike to arteries than synthetic prosthesis.

Consequently, the graft functionality could be related with the higher patency rates of vein grafts respect ePTFE prosthesis in small and medium size arteries reconstruction.

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