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Compliance properties of a composite electrospun fibre – hydrogel blood vessel scaffold

Y. Liu [a], H. Zahedmanesh [b], C. Lally [c], P.A. Cahill [a,d], G.B. McGuinness [a,*]

[a] Centre for Medical Engineering Research, School of Mechanical and Manufacturing Engineering, Dublin City University, Ireland
[b] Imec, Leuven, Belgium
[c] Trinity Centre for Bioengineering, Trinity Biomedical Sciences Institute, Trinity College Dublin, Ireland
[d] Vascular Biology and Therapeutics Laboratory, School of Biotechnology, Faculty of Science and Health, Dublin City University, Dublin 9, Ireland

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ABSTRACT

Compliance properties are considered critical to the long term functionality of vascular grafts and tissue engineered blood vessels in vivo. This study considers the compliance characteristics of vessels constructed from an inner layer of electrospun PVA-SbQ fibres incorporated in a PVA/Gelatin cryogel. The effect of the reinforcement on mechanical compliance in pulsatile flow is characterised over a wide range of mean pressure values (40–140 mmHg). Both the reinforced and non-reinforced vessels exhibit pressure-dependent compliance, a property shared with natural blood vessels. While the non-reinforced cryogel is excessively compliant, the incorporation of electrospun fibre reinforcement results in a compliance profile similar to that found in the literature for a human superficial femoral artery.

1. Introduction

Mechanical properties play a significant role in the function of many tissues and also in the performance of implanted grafts and tissue engineering scaffolds. In particular, there is convincing evidence that the dynamic mechanical compliance properties of vascular bypass grafts influence their long term prospects of becoming re-occluded with plaque or thrombus (Fig. 1) [1]. Compliance relates vessel dilation to changes or fluctuations in internal pressure, and it is known to affect the hemodynamics of pulsatile blood flow and hence the mechanical regime experienced by cells in the endothelium and vessel wall [2].

For natural arteries, compliance is found to depend in a non-linear fashion on the mean pressure of the pulsatile blood flow (e.g. femoral artery, Fig. 2(a) [3]). This non-linear response modulates the elastic response of the artery in response to altered or heightened pressure regimes with progressively reducing compliance. This characteristic is not, however, reflected in many synthetic grafts which exhibit relatively constant compliance over a wide range of physiological or pathological mean blood pressures (e.g. PTFE graft, Fig. 2(a, b)) [1,3].

Compliance mismatch between an implanted arterial bypass graft and contiguous natural vessel can alter blood flow, potentially increasing the risk of thrombosis and intimal hyperplasia. Salacinski et al. have summarized the compliance of grafts and their patency rates [1]. Their study showed a clear relationship between compliance and patency rates (Fig. 1), which suggests that better patency rates can be obtained when graft compliance characteristics are carefully tailored to match that of the host artery.

Synthetic grafts made from Dacron and variants of PTFE exhibited low compliance that remains constant across mean blood pressures between 30 and 100 mmHg [3]. A more compliant vascular graft fabricated from poly(carbonate)polyurethane (CPU) showed a steady compliance value of the order of 8.1% per mmHg $\times 10^{-2}$ over the same mean pressure range [3]. Significant compliance mismatch would therefore arise at mean pressures both above and below 50 – 60 mmHg, including at physiological blood pressures.

Hydrogels typically exhibit non-linear stress versus strain responses of a similar character to those of soft tissues. However, they also suffer from inherent strength and stiffness limitations which impede their suitability for some applications. Electrospinning, on the other hand, can produce fibres that are similar in morphology to the collagen fibres present in the ECM of various tissues, and can also offer some control over fibre structure and

* Corresponding author.
E-mail address: garrett.mcguinness@dcu.ie (G.B. McGuinness).

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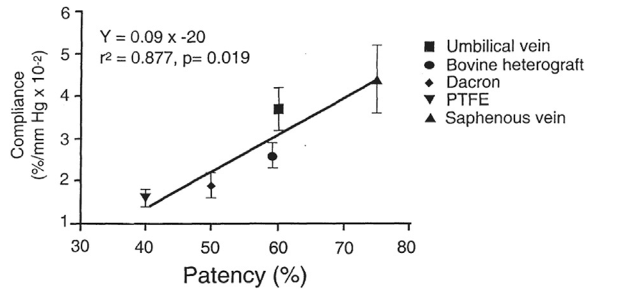

Fig. 1. Correspondence between compliance of selected grafts and their long term patency [1].

alignment. However, most electrospinning processes result in flat or tubular constructs, composed of densely arranged fibres with limited thickness, that have good strength but do not exhibit the non-linear "J-shaped" stress versus strain response of vascular tissue. There is, therefore, currently much interest in the reinforcement of suitable hydrogels to impart mechanical properties comparable with those of fibrous tissues [4–6].

A number of such studies target the development of vascular grafts or tissue engineered blood vessel scaffolds. In uniaxial testing, non-linear J-shaped responses have been obtained from ring segments fabricated from electrospun elastomer mesh (PEUUR) infiltrated with a hydrogel matrix of fibrin, with fibre-gel bonding aided by PEGDA grafted to the gel [7]. Static compliance values comparable with natural vessels have been reported for a hydrogel (PEG based) – electrospun fibre (polyurethane) vascular graft subjected to a ramped (but not pulsatile) internal pressure (0–150 mmHg) [8]. Another recent study utilised a physically cross-linked polyvinyl alcohol (PVA) cryogel as a middle layer between two electrospun layers of polycaprolactone (PCL), reporting uniaxial tensile, suture retention and burst pressure tests to confirm satisfactory mechanical properties [9]. While these studies underscore the promise of the fibre-gel approach, the feasibility of matching the non-linear compliance response of typical natural vessels over a range of pressures is as yet unexplored.

The present study addresses this question by investigating the effect on compliance characteristics of incorporating PVA-SbQ electrospun fibres in a PVA/gelatin cryogel vessel compared with the unreinforced case. PVA/gelatin cryogel samples have been extensively mechanically and biologically characterised in terms of suitability for vascular tissue engineering applications [10,11]. PVA-SbQ (Polyvinyl alcohol with styrylpyridinium pendent groups) is a photosensitive polymer which becomes water insoluble when photocrosslinked, and is widely used in photolithographic processes [12]. Parameters for electrospinning of PVA-SbQ have previously been determined [13,14].

2. Material and methods

2.1. Electrospinning

PVA-SbQ was sourced from Polysciences Inc. (USA) with a concentration of 13.3%, 45,000 molecular weight and 4.1 mol% SbQ content. PVA-SbQ fibres were electrospun onto a flat plate using a Gamma High Voltage Research power supply and process parameters of voltage 10 kV, distance 10 cm and feed rate 0.3 mL/h for 20 min.

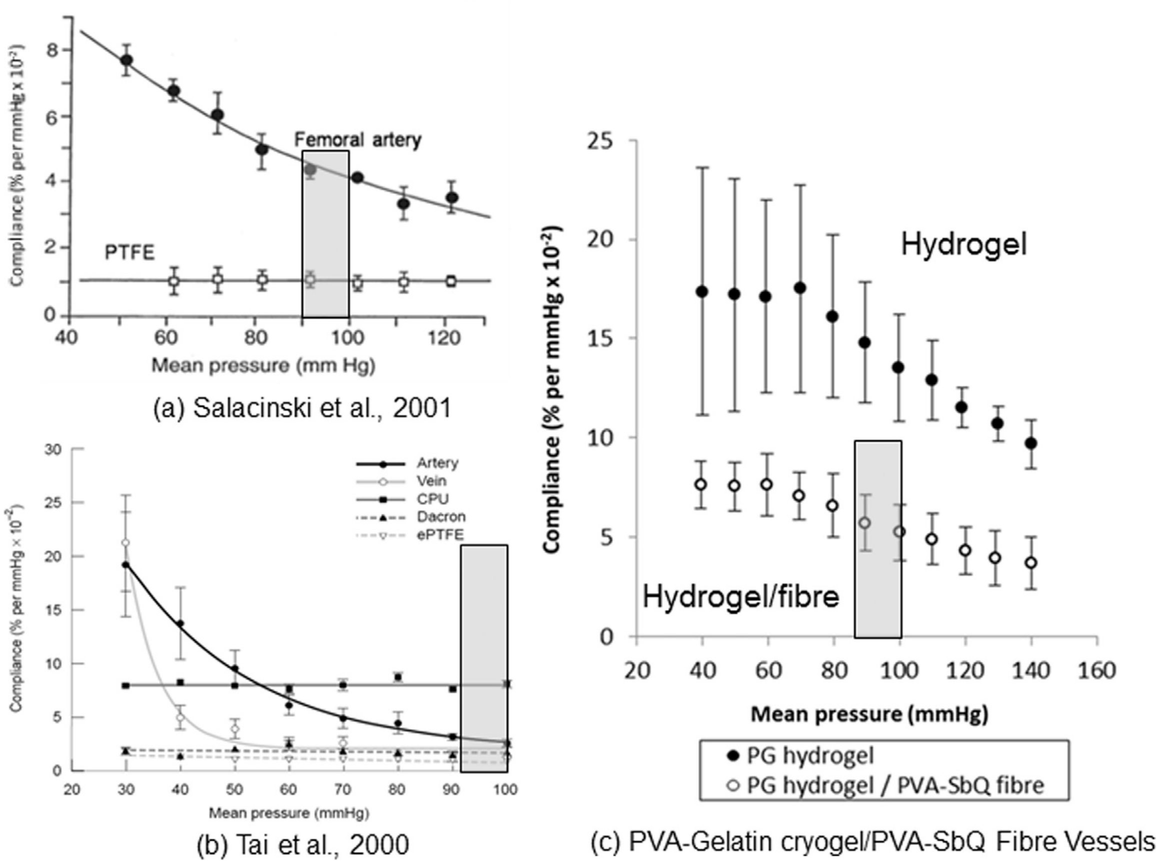

Fig. 2. (a) Non-linear compliance characteristic of human femoral artery as compared to PTFE graft (modified from [1]), (b) Compliance versus mean pressure curves for vessels and CPU, Dacron and ePTFE grafts (modified from [3]), (c) Compliance profiles with respect to mean pressure for PVA/Gelatin cryogels (1 freeze thaw cycle) and PVA/Gelatin cryogels reinforced with electrospun PVA-SbQ fibres.