The geometry of unstented and stented pig common carotid artery bypass grafts

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Abstract. The long-term success of arterial bypass grafting with autologous saphenous veins is limited by neointimal hyperplasia (NIH), which seemingly develops preferentially at sites where hydrodynamic wall shear is low. Placement of a loose-fitting, porous stent around end-to-end, or end-to-side, autologous saphenous vein grafts on the porcine common carotid artery has been found significantly to reduce NIH, but the mechanism is unclear. In a preliminary study, we implanted autologous saphenous vein grafts bilaterally on the common carotid arteries of pigs, placing a stent around one graft and leaving the contralateral graft unstented. At sacrifice 1 month post implantation, the grafts were pressure fixed in situ and resin casts were made. Unstented graft geometry was highly irregular, with non-uniform dilatation, substantial axial lengthening, curvature, kinking, and possible long-pitch helical distortion. In contrast, stented grafts showed no major dilatation, lengthening or curvature, but there was commonly fine corrugation, occasional slight kinking or narrowing of segments, and possible long-pitch helical distortion. Axial growth of grafts against effectively tethered anastomoses could account for these changes. CFD studies are planned, using 3D MR reconstructions, on the effects of graft geometry on the flow. Abnormality of the flow could favour the development of vascular pathology, including NIH.

Keywords: Graft geometry, graft casts, graft elongation, graft buckling

1. Background and methods

Almost 50% of deaths in industrialised societies are attributable to atherosclerosis, the principal complications of which include myocardial infarction, stroke and peripheral vascular disease. Coronary artery bypass surgery (CABG) and infra-inguinal bypass graft surgery (IBBS) have revolutionised the treatment of coronary artery disease and peripheral vascular disease, respectively, but the methodology is of great importance and has been the basis of extensive research.

Despite refinements in prosthetic materials, autologous saphenous vein remains the principal conduit for CABG [1,17] and IBBS [14]. However, the long-term clinical success of arterial bypass grafting with autologous saphenous veins is limited by neointimal hyperplasia (NIH) and, eventually, by superimposed atherosclerosis. Anti-platelet agents and minimization of vessel injury at the time of graft implantation [12,16] reduce the incidence of early thrombotic occlusion. Nevertheless, there is failure of over 50% of coronary artery bypass grafts within 10 years [4] and of 25–40% of infra-inguinal grafts within
5 years [21] because of NIH. The biological/pathological changes accompanying NIH are the subject of intensive study [14]. They include proliferation and migration of vascular smooth muscle cells across the internal elastic lamina in response to endogenously generated growth factors, the deposition of extracellular matrix proteins and encroachment on the lumen and, ultimately, the formation of atherosclerotic plaque and graft stenosis.

The placement of a porous, non-restricting polyester Dacron™ stent around saphenous vein–carotid artery interposition, or end-to-side, grafts in a porcine model significantly reduces NIH and total wall thickness [3,9,13,19]. Mechanisms considered to underlie this improvement include reduction of graft wall tangential (or hoop) stress by the stent [21]. However, the presence of a well-organized adventitial neovasculature in association with loose-fitting porous stents suggests that improvement of graft wall mass transport is a determinant of the reduction of NIH [9].

Recent investigations may shed further light on this question. The local flow field markedly influences vascular biology [6,11] and, apparently, the development of vascular pathology [5,10,17]. Consistent with these observations, NIH is reported to develop preferentially at sites at arterial bypass grafts where hydrodynamic wall shear is low [2,20]. We have in a preliminary study constructed autologous saphenous vein grafts on both common carotid arteries in 12 healthy pigs (11 animals – end-to-end grafts, 1 animal – end-to-side grafts). In the ‘end-to-end’ animals, a porous non-restricting polyester Dacron™ stent was placed around the graft on one carotid artery, while the contralateral carotid artery graft was unstented. In the ‘end-to-side’ animal, both grafts were unstented. At sacrifice, one month after surgery, the grafts were formalin fixed in situ at physiological transmural pressure, in order to preserve in vivo geometry and, after their excision, resin casts were made (Biresin G49, Sika Chemie, GmBh) again at physiological transmural pressure. The grafts were incised longitudinally to free the casts, the tissues being kept for histological examination.

The geometry of the unstented graft casts, in particular, was highly irregular, involving non-uniform dilatation, curvature, kinking, and possible long pitch helical distortion (Fig. 1). The methods used to measure the 3D graft cast geometry were crude. Maximum and minimum graft cast diameters were measured at several stations and related to host artery cast diameter. The length of graft casts was determined by running a fine solder wire axially along them and measuring its length when straightened. The
grafts were taut at implantation, but neither graft length nor inter-anastomosis separation was measured then. As a means of assessing whether grafts lengthened following implantation, graft cast length was related to inter-anastomosis separation, determined from the casts. The justification for this approach was the assumption that tethering of the host artery proximally and distally would inhibit change of inter-anastomosis separation.

2. Results

The unstented graft casts were irregularly highly curved, and showed in addition irregular dilatation and narrowing, kinking, and possible long pitch helical distortion. Away from sites of kinking, the grafts were approximately circular in cross-section, with diameters ranging from 0.6–1.0 cm to 0.3 cm. Near sites of kinking, maximum diameters were 0.6–1.0 cm and minimum diameters were 0.3–0.4 cm. The host artery casts had diameters of 0.3–0.4 cm. Mean graft cast length was 4.33 cm, variance = 1.57, \( n = 13 \) and mean inter-anastomosis separation was 3.0 cm, variance 0.54. The ratio mean graft cast length/mean inter-anastomosis separation took a value of 1.45, variance = 0.09. The data for the two end-to-side grafts are included in the above analysis. Their length ratios took values of 1.68 and 1.55, generally in line with those for the end-to-end grafts.

The stented graft casts tended to be finely corrugated, but generally showed no major curvature or kinking (Fig. 2). In several instances there was a suggestion of long pitch helical distortion. The diameters of the casts ranged from 0.4–0.5 cm. The host artery casts had diameters of 0.3–0.4 cm. In 3 graft casts, there were narrowed segments of length 0.5–1.0 cm, with diameters of about 0.2 cm (Fig. 3). Mean graft cast length was 2.91 cm, variance = 0.34, \( n = 11 \), and mean inter-anastomosis separation was 2.62 cm, variance = 0.26. The ratio mean graft cast length/mean inter-anastomosis separation took a value of 1.11, variance = 0.01.

The diameters of the unstented graft casts away from sites of kinking (range 0.6–1.0 cm) considerably exceeded those of the stented graft casts away from narrowed segments (range 0.4–0.5 cm). The value of the ratio mean graft cast length/mean inter-anastomosis separation was 1.45 for the unstented grafts.
A 2-tailed t-test (two samples with unequal variance) showed the means to be significantly different ($p < 0.002$).

### 3. Discussion

The geometry, particularly of the unstented graft casts, was highly complicated, and relatively crude methods were used for its measurement. The complexity of the geometry also made evident the need for additional measurements at the time of graft implantation. It seems possible nevertheless to derive significant conclusions from the work, given the validity of certain assumptions.

Graft diameter was not measured at implantation. However, if veins of similar diameter were used for the unstented and stented grafts, it is permissible to conclude that the unstented grafts dilated substantially during the post-operative period, and that external stenting inhibited such dilatation. Graft length was also not measured at implantation. However, if as is likely tethering of the host artery inhibited change of inter-anastomosis separation, it is permissible to conclude that the unstented grafts, in particular, lengthened substantially during the post-operative period. The range of increase of length relative to inter-anastomosis separation was for the unstented grafts 11–220% (mean 45%) and for the stented grafts 3–25% (mean 11%), implying that external stenting inhibited graft lengthening.

It is known that unstented vein arterial bypass grafts tend to dilate, but there does not appear to be wide recognition that they may also lengthen substantially. In an effort to clarify mechanisms, we acutely elevated the transmural pressure of segments of human saphenous vein, excess to requirement for arterial bypass grafting, to 100 cm H$_2$O. There was dilatation and an approximately 10% increase of length. Some segments also showed slight kinking if their ends were clamped a fixed distance apart. Moreover, helical distortion was evident if the segments ran axially in a tube of diameter somewhat exceeding their own.

These results make it unlikely that passive mechanical extension accounted for the marked lengthening of the unstented grafts and suggest that there had been instead axial growth and re-modelling. External stenting inhibited dilatation, gross curvature, lengthening and buckling of the grafts. Nevertheless, the graft casts showed fine corrugation and probable long-pitch helical distortion, consistent with
axial growth constrained by effectively tethered anastomoses. The triggering of these various changes requires elucidation. Our conjecture is that it involves exposure of the vein grafts to arterial blood pressure and unaccustomed hydrodynamic wall shear, in the absence of adequate adventitial tethering.

There is accumulating evidence consistent with wall mass transport playing an important role in the development of NIH. As noted above, the process affects preferentially low wall shear regions [2,20] and accompanying the marked reduction of NIH by loose-fitting porous external stents there was development of an abundant adventitial microvasculature [9].

We propose to use 3D MR surface reconstructions of unstented and stented grafts (Fig. 4) to investigate computationally the effect of luminal geometry on the flow. Pending such studies we speculate, on the basis of the observed geometric distortion, that there was abnormality of the luminal flow field. If that assumption is correct, loose-fitting porous external stents may additionally inhibit the development of NIH by improving luminal flow, whether via effects of wall shear rate on blood:wall mass transport [7,8] or via effects of wall shear stress [6,11].

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References


