Anastomotic intimal hyperplasia: Mechanical injury or flow induced

Hisham S. Bassiouny, MD, Scott White, MS, Seymour Glagov, MD, Eric Choi, MS, Don P. Giddens, PhD, and Christopher K. Zarins, MD, Chicago, Ill and Atlanta, Ga.

All anastomotic intimal thickening may not be the same, and the underlying mechanism(s) regulating the different types may vary. We investigated the localization of experimental anastomotic intimal thickening in relation to known biomechanical and hemodynamic factors. Bilateral iliopelvic and vein grafts were implanted in 13 mongrel dogs. The distal end-to-side anastomotic geometry was standardized, and the flow parameters were measured. After 8 weeks, seven of 10 animals (group I) with patent grafts were killed and the anastomoses fixed by perfusion. Histologic sections from each anastomosis were studied with light microscopy, and regions of intimal thickening were identified and quantitated with use of oculomicrometry. To characterize the anastomotic flow patterns, transparent silicone models were constructed from castings of the distal anastomosis of three animals (group II), and flow was visualized with use of helium-neon laser-illuminated particles under conditions simulating the in vivo pulsatile flow parameters. Histologic sections revealed two separate and distinct regions of anastomotic intimal thickening. The first, suture line intimal thickening, was greater in polytetrafluoroethylene anastomoses (0.35 ± 0.23 μm) than in vein anastomoses (0.15 ± 0.03 μm, p < 0.05). The second distinct type of intimal thickening developed on the arterial floor and was the same in polytetrafluoroethylene (0.11 ± 0.11 μm) and vein anastomoses (0.12 ± 0.03 μm). Model flow visualization studies revealed a flow stagnation point along the arterial floor resulting in a region of low and oscillating shear where the second type of intimal thickening developed. High shear and short particle residence time were observed along the hood of the graft, an area devoid of intimal thickening. Regions of relatively low shear and long particle residence time formed along the lateral walls and heel of the anastomoses and were not specifically related to intimal thickening at the suture line. We conclude that at least two different types of anastomotic intimal thickening exist. Suture line intimal thickening represents vascular healing; greater prominence with prosthetic grafts may be related to compliance mismatch. Arterial floor intimal thickening is unrelated to graft type and develops in regions of flow oscillation and relatively low shear. In either situation the response is associated with altered flow conditions. Prevention of graft failure caused by occlusive intimal hyperplasia requires precise understanding of the hemodynamically modulated mechanisms that control each different type. (J VASC SURG 1992;15:708-17.)

Intimal thickening is a feature of the normal healing response of arteries at graft anastomoses. Progression of intimal thickening to a hyperplastic occlusive lesion at distal end-to-side anastomoses remains a major cause of prosthetic bypass graft failure. To date, accurate characterization of anastomotic intimal thickening is lacking. Whether the lesion occurs at the suture line, host artery, or both and how it relates to graft type and anastomotic flow patterns remain unclear.

Although mitogenic factors, platelet activation, and injury have been implicated in the pathogenesis of intimal hyperplasia, pharmacologic agents to minimize or inhibit these processes at vascular anastomoses have been unsuccessful. Hemodynamic factors, specifically low and oscillatory wall shear, have been shown to correlate with regions of intimal thickening at arterial branch points.

From the Departments of Surgery and Pathology, the University of Chicago, and the Department of Aerospace Engineering, Georgia Institute of Technology.

Supported by the National Institutes of Health grant 5 RO1-HL 41267.


Reprint requests: H. S. Bassiouny, MD, Department of Surgery, the University of Chicago, 5841 South Maryland Ave., Chicago, IL 60637.

24/6/33849
and in experimental stenoses. The de novo anastomotic geometry and implanted graft engender major alterations in flow velocities, near wall flow patterns, wall shear, and compliance mismatch. These hemodynamic and biomechanical forces may therefore play a significant role in the development of anastomotic intimal thickening.

In this study we determined and compared the precise location and severity of anastomotic intimal thickening in canine end-to-side polytetrafluoroethylene (PTFE) and vein anastomoses. These findings were qualitatively correlated with flow patterns characterized in a model constructed with the identical geometric features of the anastomoses and with use of pulsatile flow conditions similar to those measured in vivo.

MATERIAL AND METHODS

In vivo studies

Animal model. Adult male mongrel dogs (n = 13) weighing 20 to 25 kg were used for the study. After general anesthesia was induced with intravenous sodium pentobarbital (30 mg/kg), an endotracheal tube was placed in the animals, and anesthesia was maintained with use of halothane 1% to 3%. The iliofemoral arterial segments were exposed retroperitoneally through bilateral inguinal incisions extending to the upper thigh. Femoral artery diameter was measured with calipers before veins were manipulated. The greater saphenous vein was harvested from the hind limb. Bilateral iliofemoral bypasses were implanted with use of reversed saphenous vein on one side and 6 mm thin-walled PTFE on the other. The proximal anastomosis was constructed end to end to the common iliac artery, and the distal anastomosis was constructed end to side with 6-0 Prolene (Ethicon Inc., Somerville, N. J.) suture. All anastomoses were performed by one investigator (H. S. B.). The external iliac artery was ligated 1 cm above the inguinal ligament to simulate an arterial occlusion and to produce an inflow-outflow pressure gradient. Distal anastomotic geometry was standardized with a hood length-to-vessel diameter ratio of 4:1 and a maximum hood width of 6 mm at the center of the anastomosis. To standardize outflow conditions all distal anastomoses were constructed 1 cm beyond the deep femoral artery in a segment of superficial femoral artery devoid of side branches. Housing and handling of animals were in compliance with “Principles of Laboratory Animal Care” and “Guide for the Care and Use of Laboratory Animals” (NIH publication no. 80-23, revised 1985).

Fig. 1. Anastomotic measurements used in flow model construction. Major geometric features of anastomosis were replicated including slope of hood and anastomotic sinus.

Hemodynamic measurements. Blood flow was measured in the common iliac artery proximal to the bypass grafts and in the proximal and distal outflow limbs of the distal end-to-side anastomosis with use of two electromagnetic flow probes (Carolina Medical Electronics, Inc., King, N.C.). Systemic blood pressure was monitored with an indwelling 21-gauge brachial arterial cannula connected to a Statham pressure transducer and a strip chart recorder (Gould Inc., Test and Msm. Rec. Syst. Div., Cleveland, Ohio). The in vivo hemodynamic data were recorded simultaneously on a four-channel FM tape recorder and thereafter digitized and stored on a Masscomp (Concurrent, Westford, Mass.) computer for subsequent analysis.

Long-term animal studies. After operation, all animals received 125 mg of aspirin every day to reduce platelet aggregation and promote graft patency. The 10 animals (group 1) were fed an atherogenic diet consisting of 2% cholesterol to enhance intimal proliferation. After 8 weeks, the animals were killed with an intravenous overdose of pentobarbital, and the distal infrarenal aorta was cannulated. The distal aorta, iliac arteries, bypass grafts, and distal anastomoses were fixed by pressure perfusion with 3% glutaraldehyde at 100 mm Hg. The distal anastomosis including the graft hood, suture line, and proximal and distal outflow tracts were harvested en bloc and sectioned in the sagittal
Fig. 2. Illustration of sagittal section of end-to-side anastomosis depicts sites of localization of intimal thickening at suture line and artery floor.

Fig. 3. Suture line intimal thickening in anastomotic sinus (transverse section). Pannus of proliferating smooth muscle cells (IH) extends from artery (A) to graft surface (GH), thus covering triangular deformity at anastomotic junction. (Hematoxylin-eosin stain; original magnification × 40.)

and transverse planes (20 to 24 samples/specimen). The samples were embedded in paraffin, and adjacent 5 mm sections were stained with hematoxylin and eosin, and the Gomori-trichrome-aldehyde fuchsin procedure for connective tissue differentiation. Regions of anastomotic intimal thickening were identified by use of light microscopy, and their location in relation to anastomotic junction (sinus, toe, heel) and host artery (floor, proximal, distal outflow tracts) was mapped. Intimal thickness was measured with a Zeiss (Carl Zeiss Inc., Thornwood, N.Y.) oculomicrometer. The mean of six different measurements at each anastomotic junction was used to represent suture line intimal thickness.

**Model flow studies**

**Model construction.** To characterize the flow patterns in regions of anastomotic intimal thickening, three animals (group II) were killed 1 hour immediately after completion of the anastomoses, and the iliofemoral bypass grafts were fixed by pressure perfusion as described previously to preserve the in vivo vessel diameters and geometry. Vinyl polysiloxane (3M Company, St. Paul, Minn.) was injected into the grafts and allowed to cure for 5 minutes to produce casts of the distal anastomoses. Dimensions of the silicone casts were measured at specific sites by calipers (Fig. 1). A scaling factor of 7.5 was selected to permit the use of standard clear acrylic tubing at the inlet and exits of the model. A clay mold of the end-to-side anastomotic region was created replicating the major geometric features of the anastomosis including the slope of the hood and the relative size and configuration of the anastomotic sinus. The mold with the clear acrylic tube extensions representing inflow and outflow tracts was posi-
Table I. Maximum intimal thickness (in micrometers)

<table>
<thead>
<tr>
<th></th>
<th>PTFE</th>
<th>Vein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture line</td>
<td>0.35 ± 0.23*</td>
<td>0.15 ± 0.01</td>
</tr>
<tr>
<td>Artery floor</td>
<td>0.12 ± 0.03</td>
<td>0.11 ± 0.11</td>
</tr>
</tbody>
</table>

*Differences significant at p < 0.05.

mentioned in an acrylic box into which Sylgard elastomer (Dow Corning Corp., Midland, Mich.) was poured and allowed to cure for 3 days. The core was subsequently removed, and a transparent Sylgard model of the end-to-side anastomotic region remained. The hood length–to–host artery diameter ratio of 4:1 and hood width were the same in the model and in vivo anastomoses.

Flow visualization studies. The in vivo pulsatile flow conditions were simulated in the model with use of an electric centrifugal Tc1 (Dayton Electric Mfg., Chicago, Ill.) pump with a servo-valve controlled by a Dell PC computer (Dell Computer Corp., Austin, Texas). The system is capable of producing the desired flow velocity waveforms. Details of its construction and operation have been previously described.14 Two 12.7 mm electromagnetic flowmeters (Carolina Medical) were used to measure inflow and proximal outflow volumetric flow rates.

An upstream acrylic reservoir was used to infuse neutrally buoyant 200 μm Amberlite (Sigma Chemical Co., St. Louis, Mo.) particles (Rohm and Haas Co., Philadelphia, Pa.) into the flow system. The fluid used was a water and glycerine mixture in a volume ratio of 42:58, which was maintained at a temperature of 27.0°C ± 0.1°C by use of a downstream heater-mixer. This solution provides an index of refraction of 1.41 that matches that of the Sylgard material, thus eliminating optical distortions. The kinematic viscosity of the fluid was 0.078 cm²/sec as measured by a Wells-Brookfield cone-in-plate viscometer. Measurements of both viscosity and index of refraction were repeated frequently during the experiments to check for water evaporation, and appropriate volumes of water were added as necessary to maintain the corrected parameters. The pulsatile flow experiments were conducted with use of waveforms modeled after the typical shape measured in animal studies.

Particle trajectory in the pulsatile flow field was visualized by use of two methods. A 15 mW helium-neon laser beam was diffracted by a glass rod interfacing a thin (1.6 mm) laser light sheet in the horizontal plane of the model. Light reflected off the particles as they passed through the laser sheet, and particle path lines were photographed on black and white film at six selected times in the pulsatile cycle with an exposure time of 0.5 second. To determine three-dimensional particle movement, a videocamera recorded flow phenomena in the vertical plane under incandescent lighting.

Statistical analysis. Maximum intimal thickness at the suture line and beyond in the artery was expressed as mean ± SD. Differences between intimal thickness in vein and PTFE anastomoses were analyzed by use of a two-tailed Student's t test. Differences were considered to be significant if p < 0.05.

RESULTS
In vivo hemodynamic measurements

Mean systemic blood pressure was 93 ± 9.5 mm Hg (range, 75 to 110). Mean blood flow in the PTFE grafts was 192 ± 84 ml/min and in the vein grafts was 160 ± 68 ml/min. At the distal anastomosis, mean flow through the proximal outflow limb of PTFE bypass was 54 ± 26 ml/min and of vein bypass 59 ± 32 ml/min. Mean flow through the distal
outflow limb of PTFE grafts was $149 \pm 74$ ml/min and $121 \pm 82$ ml/min. No significant differences were observed between inflow or outflow volumetric flow rates in PTFE and vein grafts. The in vivo distal-to-proximal outflow division ratio was 75:25. The average diameter of the host artery was 4.2 mm and that of the vein grafts was 4.0 mm. Peak Reynolds numbers for these conditions were 650 based on graft diameters and assuming a kinematic viscosity of blood, $\nu$, to be 0.035 cm$^2$/sec. The average Reynolds number for the entire cycle was 260, and the frequency, $f$, of the waveforms was 2 Hz, yielding a Womersley parameter of 3.8.

$$\alpha = \frac{R}{\sqrt{\frac{2 \pi f}{\nu}}}$$

**Long-term animal studies**

After 8 weeks seven animals had patent grafts (77% patency rate). One animal died within the immediate postoperative period, and graft thromboses developed in the other two at 2 and 4 weeks, and they were excluded from the analysis.

**Topography of intimal thickening.** Histologic sections from anastomoses ($n = 154$ sections) revealed two separate and distinct regions of anastomotic intimal thickening: one at the suture line and the other on the floor of the artery. Suture line intimal thickening was observed in all PTFE and vein anastomoses and developed at the graft–vessel wall junction: in the sinus, at the toe, and at the heel of the anastomoses (Fig. 2). Arterial floor intimal thickening was noted in 12 of 14 (84.3%) anastomoses. No arterial floor intimal thickening occurred in two anastomoses: one PTFE and one vein anastomosis. The arterial lesion was located in the midplane opposite the distal portion of the graft hood and was relatively closer to the distal than the proximal outflow tract. No regions of intimal thickening were identified in the proximal or distal outflow arterial segments.

**Histopathologic findings.** Intimal thickening consisted of proliferating cells, predominantly smooth muscle and myofibroblasts, within a loose connective tissue matrix above the intimal elastic lamina. The overlying endothelium was intact, with no evidence of immediate surface thrombosis or organization of previous thrombi. Along the lateral walls of the anastomoses, at the suture line, a hyperplastic tissue pannus consisting of a structured layer of subintimal cells migrated from the artery onto graft surface. This covered the triangulation deformity at the anastomotic junction in the sinus region resulting in a more circular lumen configuration (Fig. 3). In the heel and toe regions intimal thickening projected slightly into the lumen (Fig. 4). The morphologic features of suture line and floor intimal thickening (Fig. 5) were similar.

**Lesion thickness in PTFE and vein anastomoses.** Maximal intimal thickness along the suture line was greater in PTFE anastomoses ($0.35 \pm 0.23$ μm; range, 0.10 to 0.90) than in vein anastomoses ($0.15 \pm 0.010$ μm; range, 0.05 to 0.34). The differences were significant at $p < 0.05$. No significant difference occurred, however, between arterial floor maximal intimal thickness in PTFE anasto-
Fig. 6. Model flow visualization studies. Neutrally buoyant particles are illuminated in the pulsatile flow field by use of helium-neon laser sheet of light. Early in the acceleration phase of laminar flow (LF) is observed along the hood of graft. A starting vortex (V) develops at the heel near the proximal outflow tract. At stagnation point (SP) flow attaches on the arterial floor and divides to enter the proximal and distal outflow tracts.

Fig. 7. In mid systole, the vortex structure rolls into the sinus region. The stagnation point (SP) has moved distally during the acceleration phase of systole.

morses (0.12 ± 0.03 μm; range, 0.09 to 0.16) and vein anastomoses (0.11 ± 0.11 μm; range, 0.04 to 0.24) (Table 1).

Model flow visualization studies

A distal-to-proximal outflow division ratio of 80:20 was used in the flow model to simulate the in vivo flow conditions. End-to-side graft anastomosis to the arteriotomy produced lumen cross-sectional enlargement and an adverse pressure gradient. As a result of this geometric transition, distinct secondary flow patterns developed in the anastomosis and varied during the different phases of the pulse cycle. Regions of relatively high and low particle velocities were indicative of high and low shear.

During the acceleration phase in early systole, flow entering the anastomosis was laminar, with skewing of particles toward the hood of the anastomoses (Fig. 6). On the arterial floor a flow stagnation point, which oscillated in the proximal/distal direction, was identified. Streamlines entering the anastomosis, which traversed lateral to the midplane, exhibited a circumferential velocity component toward the sinus region, with particles becoming entwined into the separation region along the side walls. Particles traversing near the midplane assumed a laminar trajectory to the proximal or distal outflow tracts. The location of the stagnation point oscillated in direction and shear throughout the pulse cycle, moving distally during the acceleration phase of systole and in a reverse direction proximally during the deceleration phase (Figs. 7 and 8).

In the region of the suture line and lateral walls (anastomotic sinus), secondary flow patterns were observed. Early in each cycle, flow separated from the heel of the anastomosis where vortex formation started and rolled into the sinus region (Fig. 6). This vortex became larger as velocity increased at peak systole and broke up during early diastole (Fig. 9). Particle motion during this vortex disruption appeared to have random characteristics in the video recordings of the flow visualization studies, giving the impression that turbulence occurred. Flow separation also occurred along the lateral sinus walls.
where particle residence time was prolonged, with delayed clearing and accumulation of the particles.

**Qualitative correlation (in vivo and model)**

Intimal thickness was absent along the graft hood where flow was laminar and high shear, short particle residence times were observed. Arterial floor intimal thickening developed in a region corresponding to the stagnation zone where low and oscillatory shear prevailed. Flow patterns consistent with separation, relatively low shear, and long particle residence time also formed along the heel and lateral wall of sinus where suture line intimal thickness was also present.

**DISCUSSION**

In this study intimal thickening developed at two distinct and separate sites: at the suture line and along the floor of the artery opposite the anastomotic hood. Suture line intimal thickening may represent vascular healing and remodeling in response to mechanical injury or compliance mismatch. The prominence of this lesion with prosthetic grafts in this study may be a consequence of the greater cyclic deformations associated with the marked differences in the mechanical properties between PTFE and native artery as compared with vein wall and native artery.\(^{15}\)

Considerable attention has been focused on compliance mismatch as a significant determinant of graft patency and intimal hyperplasia.\(^{16,17}\) It is suggested that differences in the mechanical properties of graft and artery may promote anastomotic intimal thickening. Regions of hypercompliance have also been demonstrated in end-to-end isocompliant arterial anastomoses suggesting that the mere existence of a suture line can produce this biomechanical perturbation.\(^{18}\) Although hypercompliance may result in increased smooth muscle cyclical stretch and collagen synthesis,\(^{19}\) in vivo experimental evidence supporting this tenet is lacking. Conversely, reduction of arterial wall motion has been shown to reduce arterial wall metabolism, biosynthesis of matrix components, and atherosclerotic lesion formation.\(^{20}\) Further studies correlating perianastomotic strain and compliance measurements with intimal thickening are needed to clarify the role of compliance mismatch.

Although surgical trauma and endothelial injury have been shown to induce smooth muscle cell proliferation and subsequent intimal thickening, the
role of acute vascular injury has been questioned by a number of investigators,21 and conflicting reports exist on the efficacy of antiplatelet agents in promoting graft patency and limiting intimal hyperplasia.22,23 Clowes et al.7 have demonstrated that the smooth muscle proliferative response to acute injury is short lived and eventually regresses. In this study, platelet function was inhibited with use of acetylsalicylic acid. No evidence of mural thrombus was apparent at the suture line or beyond on the arterial floor where smooth muscle cell proliferation was evident.

In our study, model flow visualization studies revealed complex secondary flow patterns in the vicinity of the suture line. The adverse pressure gradient created by the relatively large anastomotic sinus resulted in flow separation along the lateral walls at the anastomotic heel where helical formations developed and rolled into the sinus region during the acceleration phase of systole. These secondary flow patterns may interact with other biomechanical and humoral factors to modulate suture line intimal thickening. The process may be self-limiting and abate once the local intimal thickening has remodeled the surface irregularities that result in the secondary flow patterns.

Arterial intimal thickening at the floor of the anastomosis was identified in all but one PTFE and one vein anastomosis. This change developed where flow entering the anastomosis reattached along the arterial floor and oscillated during the pulsatile cycle. The stagnation zone appeared similar to the three-dimensional separation region observed along the outer wall in the sinus of the human internal carotid artery. In other studies by White,14 this stagnation point moved distally if proximal outflow increased from 0% to 50% or the hood length doubled. In addition, significant changes in the secondary flow patterns along the lateral sinus and heel of the anastomosis were observed. Hence the anastomotic flow field is greatly influenced by the anastomotic geometry and outflow divisions. Ojha et al.24 and Crashaw et al.25 studied steady and pulsatile flow fields in an end-to-side arterial anastomosis model and noted that low axial wall shear stress was present at the stagnation point on the artery floor, the toe of the anastomosis, and the proximal region of the host artery. The hemodynamic patterns elucidated in our study are similar to their findings.

It is well recognized that arteries adapt to chronic changes in flow or pressure by alterations in dimension, configuration, or wall composition.26-28 These adaptations appear to be self-limiting and cease when ideal hemodynamic conditions are established at the endothelial surface. Increased flow velocity results in artery enlargement until lumen radius results in restriction of normal baseline wall shear levels.27,29,30 Conversely, a reduction in flow velocity may result in lumen narrowing to achieve the same goal.31 In both human and experimental vessels, intimal thickening is a common response to lowered or oscillatory shear. Moreover, the degree of intimal thickening is inversely related to wall shear stress levels.13 Inflow, outflow resistance, and geometric configurations such as end-to-side anastomoses create adverse local hemodynamic conditions that may incite an intimal proliferative response.

The topography and morphologic features of anastomotic intimal thickening observed in the present study suggest an adaptive or remodeling response to the imposed biomechanical and flow conditions. If baseline conditions are achieved, intimal proliferation would be expected to cease. However, with persistence of abnormal configurations and low flow velocities, the stimulus of intimal proliferation may continue, and progressive intimal hyperplasia would occur, leading eventually to lumen stenosis and graft occlusion.

In conclusion, we have identified two different types of anastomotic intimal thickening and the conditions underlying their initiation. Suture line intimal thickening may be related to compliance mismatch and focal geometric deformations that result in complex secondary flow patterns. Arterial floor intimal thickening remote from the suture line develops in regions of flow reattachment and low and oscillating shear. Further study is needed to determine which of these lesions is responsible for anastomotic stenosis and the mechanisms regulating these responses.

REFERENCES

4. Barrett TB, Benditt EP. Sis (platelet-derived growth factor B chain) gene transcript levels are elevated in human atherosclerotic lesions compared to normal artery. Proc Natl Acad Sci USA 1987;84:1099-103.


DISCUSSION

Dr. William Abbott (Boston, Mass.). This study sheds light on a long-standing interest of ours and that of many others: anastomotic intimal hyperplasia.

Distal end-to-side anastomoses were constructed of venous and PTFE grafts in dogs and studied morphometrically and hemodynamically. The key findings were (1) intimal hyperplasia was observed at two sites, at the suture line and the floor of the artery below the hood of the graft, (2) the suture line hyperplasia was greater in PTFE reconstructions than that in vein, and the arterial floor hyperplasia was the same in the two grafting situations. I generally agree with these interesting and provocative results. However, I would like your comments on some points.

In the manuscript you state that these results mean that two differing types of hyperplasia exist. I disagree slightly with that concept because the data merely represent the fact that intimal hyperplasia is an extremely complex issue and that no single inciting event occurs. Indeed many occur, and your work just amplifies that point.

I agree that shear forces are a factor. I think most of us accept that fact, but is it really low shear? Much evidence
exists that suggests the culprit is high shear. What do you really think it is? And, furthermore, what can really be done about these abnormal shear forces?

You have implicated compliance mismatch as a likely cause of suture line hyperplasia. I agree with you on that point, and that is supported by extensive work from our own group and others, but I counsel you that many would disagree regarding the importance of compliance mismatch. I also point out that other important variables are involved, such as differences in flow surfaces and differences between polymeric versus biologic biomaterial substrates. But, if you do think it is a compliance problem, I would then like to hear further what you think the problem is.

Finally, this work suffers from problems that are similar to those of our previous publications and those of others, and one problem is that although hyperplasia is easily measurable, it does not seem to be present in significant or pathologic amounts. Apparently no good animal model exists for this, and the dog may be one of the worst. Unfortunately, this point blunts much of the significance of a lot of the good studies in this area. But, in your work was any hyperplasia found that we might all agree was of clinically relevant proportions?

Dr. Bassiouny, intimal hyperplasia is a devastating clinical problem and may be the most significant unresolved problem in the field of vascular surgery. It is very complicated and has defied simple solutions. We need much more good work in the field, and I appreciate hearing yours.

Dr. Hisham Bassiouny. In this study we observed two different types of intimal thickening. Both types were histopathologically similar. The first type, suture line intimal thickening, developed at the anastomotic junction where transition in compliance, strain, and wall motion occurs between the vein or prosthetic graft and the native artery. The finding of greater intimal thickening with the PTFE grafts compared with the vein grafts suggests that compliance mismatch may be related to the initiation of this type of intimal thickening. Perturbation of the arterial wall biomechanics and increased cyclic stretch may trigger increased smooth muscle cell mitogenic activity and collagen production. Secondary flow patterns also occur in the suture line region along the lateral wall of the anastomotic sinus and may also contribute as a cause of suture line intimal thickening.

In this experiment, qualitative correlation between the histopathologic findings and the flow patterns characterized in the model flow studies indicate that low and oscillatory wall shear is associated with intimal thickening. This is similar to the outer wall of the carotid bifurcation where intimal thickening develops in regions where wall shear oscillates. The second type of intimal thickening, arterial floor intimal thickening, developed opposite the hood of the graft in a region where flow reattached and formed a stagnation point that oscillated in both the proximal and distal direction along the midaxial plane of the arterial floor during the pulse cycle. Intimal thickening was not found in regions of high shear. Thus different mechanisms may be associated with each type of anastomotic intimal thickening. Proper characterization of the anastomotic flow field will help identify the optimum geometry and outflow conditions that favor or inhibit anastomotic intimal thickening.

The findings of this study suggest that the arterial wall response to biomechanical and hemodynamic changes engendered by an end-to-side anastomosis could well be an adaptive phenomenon until baseline conditions are restored. To date, development of a model of progressive intimal thickening and occlusive intimal hyperplasia remains a challenge to many investigators. It is conceivable that anastomotic intimal thickening, particularly on the arterial floor, may progress to an occlusive lesion if the artery wall senses a perpetual low and oscillatory shear situation. This can occur either by increasing the peripheral vascular resistance or by reducing inflow.