# ARE LOCAL FLOW PHENOMENA RELATED TO THE DEVELOPMENT OF SMALL PITS BETWEEN THE STRUTS OF SIROLIMUS-ELUTING STENTS?

**Frank J.H. Gijsen, Jolanda J. Wentzel, Johan C.J. Schuurbiers, Patrick W. Serruys and Cornelis J. Slager**

Hemodynamics Laboratory, Thoraxcenter, Erasmus MC
Rotterdam, The Netherlands

## INTRODUCTION

Recent results of the RAVEL trial show that application of stents coated with a sirolimus-eluting polymer virtually abolishes neointimal growth and virtually eliminates restenosis in human [1]. In a previous study, we have shown that a global inverse relationship between the small amount of neointima thickness (NIT) and blood flow induced wall shear stress (SS) was present in the sirolimus-eluting stent [2]. This global relationship was found after axial averaging of the data.

We also observed the presence of shallow pits between the stent struts. In this study we investigate how these pits influence local flow phenomena.

## METHODS

We combined biplane angiography with intravascular ultrasound (IVUS) to obtain the 3D geometry of 6 human coronary arteries. IVUS images were acquired during an ECG-gated motorized pullback, contours of the lumen of the artery were drawn in the IVUS images and subsequently stacked on the 3D reconstruction of the path of the catheter [3].

We solved the Navier-Stokes equations to obtain the SS distribution in the stent at the moment of implantation on a finite element mesh that represents the total reconstructed 3D lumen for the global analysis. Furthermore, we computed velocity and SS

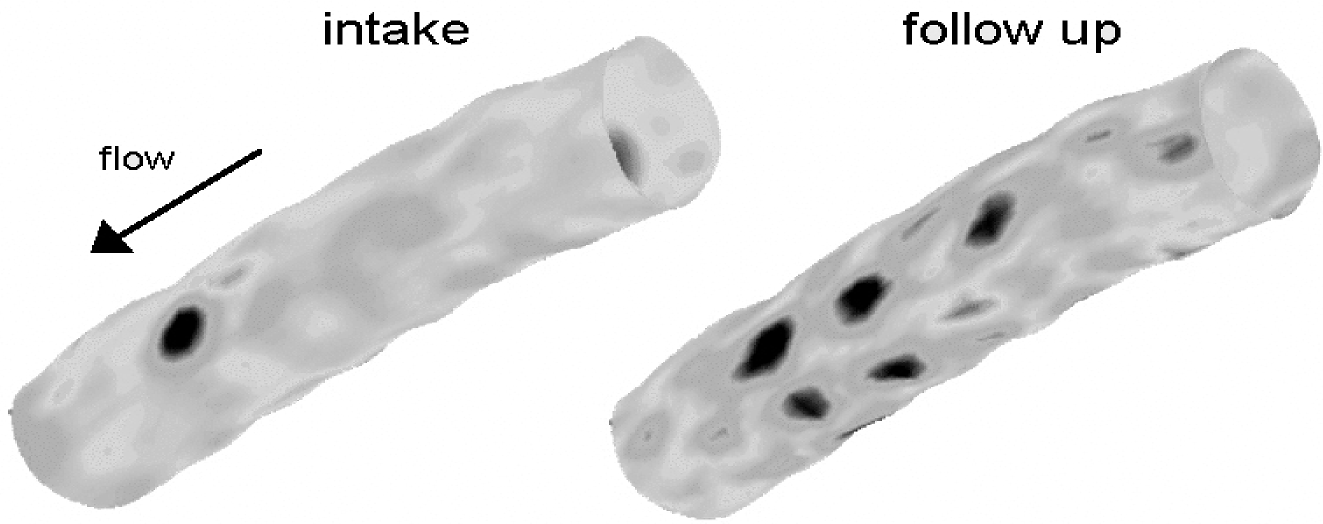


**figure 1: An example of the NIT distribution (gray-scale coded on the stent surface) in a sirolimus-eluting stent just after the procedure at intake (left) and at 6 months follow up. Note the development of negative NIT in black, indicating the presence of shallow pits.**

distribution in 2D intersections of the stented segment at follow up to investigate local flow phenomena. The boundary conditions for the analyses consisted of patient-specific data. Flow at the inlet of the artery was derived from the average peak velocity, which was measured with a Doppler flow wire. We applied a Newtonian model for blood using the viscosity measured with a capillary viscometer. The Navier-Stokes equations were solved with a validated finite element code.

NIT was defined as the distance between the extrapolated luminal stent surface and the (neo)intimal tissue border. Negative NIT implies that the tissue border position is behind the extrapolated luminal stent surface, while positive NIT implies encroachment of the neointima into the lumen.

## RESULTS

Average NIT was -0.03 ± 0.03 mm (vs. 0, t-test, $p < 0.05$). The NIT distribution in the stent showed a regular pattern. Generally, we observed negative NIT between the stent struts and positive NIT on top of the struts. The shallow pits (figure 1) between the stent struts were observed in all patients. For the individual patients, a borderline significant ($p = 0.09$, $n = 1$) or significant ($n = 4$) inverse relationship between NIT and SS was found after averaging the data in the axial direction. One patient with a minimal SS range showed no relationship. Normalizing SS using the mean for each patient ($n = 6$) and pooling all data, an inverse relationship was found:

$$NIT = -0.24 * SS + 0.21 \text{ mm } (r^2 = 0.24,\ p < 0.001)$$

These global averaged results indicate that deeper pits are preferentially located at the outside curve of an arterial segments. The 2D computations in the arterial geometry at follow up reveal that flow recirculation zones develop between the stent struts at the outside curve (figure 2). These recirculation zones are small and are not present in all the pits. However, low SS values in the pits are indicative of low velocities near the wall this might have an important impact on the elution process and retention time of sirolimus in these pits. At the inside curve, SS is much more homogeneous, and flow recirculation zones are not present.

Further research is required to investigate the impact of the presence of regions with prolonged retention time of sirolimus on the development of these shallow pits. The arterial tissue concentration of sirolimus determines its biological effect and is governed by blood flow and transport of sirolimus through the arterial wall [4]. Some of the clinical data seem to suggest that sirolimus reduces neointimal growth outside the stented region. Notably, the reduction of neointimal growth in the upstream segment 5 mm proximal to the sirolimus-eluting stent [1] suggests that the effective radius of diffusion of sirolimus through the vessel wall may be much larger than the size of the observed pits. However, other clinical data are inconclusive about the effect of sirolimus outside the stented region.

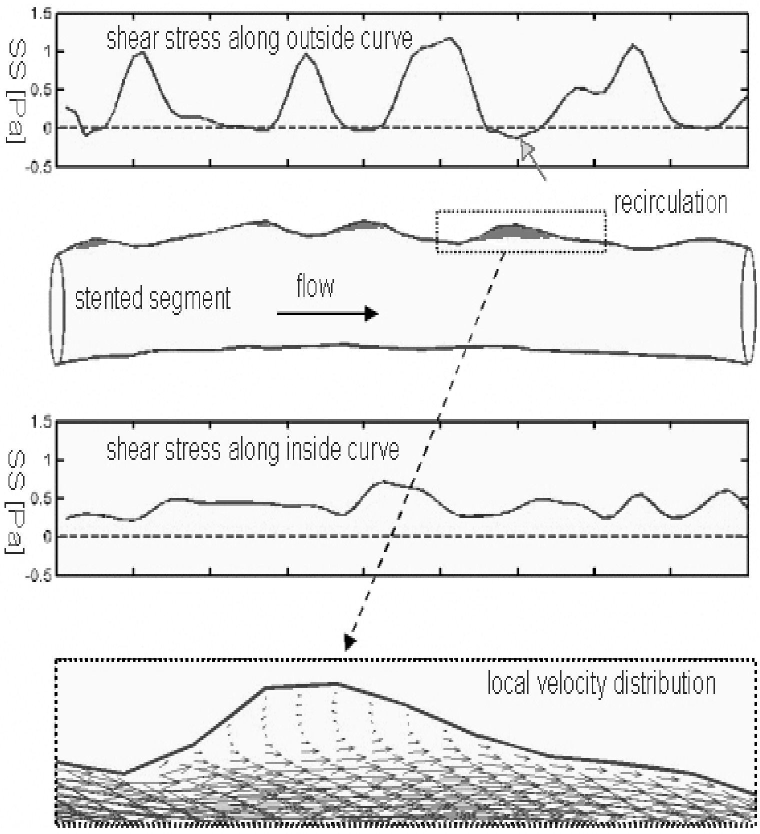


**figure 2: 2D computation in the stented segment reveal the presence of flow recirculation and areas with low shear stress along the outside curve.**

## CONCLUSION

Sirolimus-eluting stents effectively reduce neointima growth. The NIT distribution shows a regular pattern with shallow pits between the stent struts. In the deeper pits, present along the outside curve, flow recirculation might develop, leading to a prolonged retention time of sirolimus in these pits. The biological impact of these observations require further research.

## REFERENCES


1 Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med*. 2002;346:1773-80.

2 Gijsen FJH, Oortman RM, Wentzel JJ, et al. Blood flow pattern predicts neo-intima thickness distribution in sirolimus coated stents. Circulation 2002, 106, 19II, Abstract.

3 Slager CJ, Wentzel JJ, Oomen JAF, et al. True reconstruction of vessel geometry from combined X-ray angiographic and intracoronary ultrasound data. *Semin Intervent Cardiol*. 1997;2:43-47.

4 Hwang CW, Wu D, Edelman ER. Physiological transport forces govern drug distribution for stent-based delivery. Circulation 2001;10:600-605.