DEPENDENCE OF PORCINE ARTERIAL ENDOTHELIAL PERMEABILITY ON WALL SHEAR STRESS AND ITS RELATED INDICES

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INTRODUCTION

The onset of atherosclerosis may be related to changes in vascular endothelial permeability to macromolecules, which may in turn be induced by wall shear stress or its related indices. We report here an initial experiment that correlates, site-by-site, the albumin uptake in a porcine aortic trifurcation with several measures of wall shear obtained by computational fluid dynamic (CFD) simulation in the same artery segment. The results suggest that the permeability of the vessel decreases monotonically with increasing time-averaged shear stress, while its relationship to other shear related indices is weak or absent.

METHODS

All experimental procedures were performed in accordance with an established protocol approved by the Ohio State University Institutional Animal Care and Use Committee. A 72-kg domestic female swine was anesthetized with sodium pentobarbital and both femoral arteries were surgically exposed. Perivascular flow probes (Transonic Systems, Ithaca NY) were placed around each femoral artery to monitor the blood flow rate. Evans Blue Dye (EBD) was administered intravenously at a 2:1 molar concentration ratio with blood serum albumin and allowed to circulate in the bloodstream for 90 minutes prior to sacrifice. Immediately following sacrifice, the arterial tree was flushed with saline to clear the animal of blood and EBD. Silicone casting material was injected at 100 mm Hg into the abdominal aorta just proximal to the renal artery ostia. The cast replicated the infrarenal aorta and iliac-femoral arteries (Fig. 1). Once the casting material had cured, the rigid cast and surrounding tissue were carefully excised from the animal and placed in neutral buffered formalin overnight. The arterial tissue was removed from the cast with a dorsal cut. The tissue was pinned out for quantitation of the distribution of EBD uptake using en face photographic densitometry [1]

The cast was laser scanned to generate a three-dimensional cloud of 150,000 points representing the luminal surface. Using a custom mesh generator, a three-dimensional 8-node brick element mesh representation of the terminal aorta and the common internal, external and circumflex iliac arteries was created (Fig. 2). The mesh contained 175,968 volume elements and 18,016 surface elements. Mesh sensitivity tests were performed by iterative refinement of the mesh until further refinement did not change the computational results.

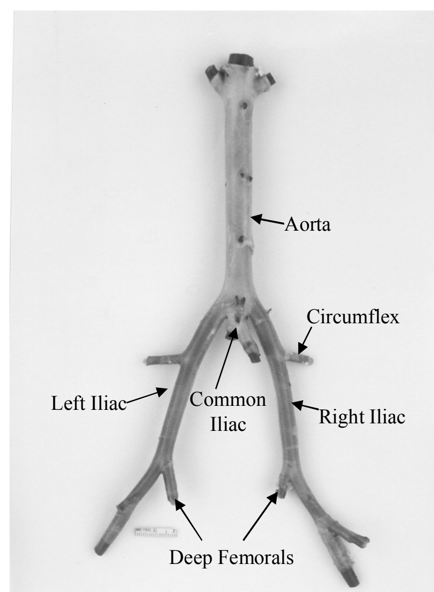

Figure 1 Dorsal view of the luminal cast of the porcine aortic trifurcation prior to removal of the tissue.

The measured femoral artery flow rates were used to estimate the flows through the iliac and circumflex arteries and aorta, using flow relationships established previously [2]. The porosities of porous plugs placed at the vessel termini were adjusted to obtain the desired flow partition. Pulsatile flow calculations were performed using the finite-element code FIDAP (Fluent, Inc., Lebanon, NH). A uniform inlet velocity profile and no-slip conditions at the rigid walls were applied.

The aorta segment was sufficiently long that a fully developed velocity profile existed immediately proximal to the trifurcation. The fluid was assumed to be Newtonian, with a kinematic viscosity of 3.3 cs. The inlet flow waveform was typical for the iliac region, had a period of 0.75 seconds and was discretized into 60 time steps. The mean and peak Reynolds numbers and the Womersley number based on the diameter at the inlet were 985, 3034, and 9.0, respectively. Four cycles were computed and the fourth cycle was used for wall shear calculation.

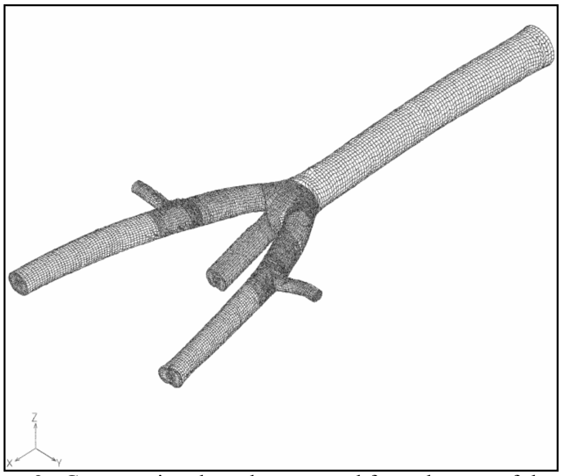

Figure 2 Computational mesh generated from the cast of the porcine aortic trifurcation

The three-dimensional distribution of the computed wall shear stress indices in the right and left external iliac arteries, from the trifurcation to the deep femoral ostia, was mapped to a two-dimensional image by a numerical transform that simulates the cutting and pinning out of the tissue. The transformed shear image and the en face photographs of the corresponding tissue were deformed to a common template using an affine transformation based on selected geometric features of the vessel [1]. The distributions of selected shear stress indices were then compared on a pixel-by-pixel basis (20,000 pixels total) with the optical density (OD) distribution of the templated image of the EBD-stained tissue. The optical density measures albumin uptake during the dye exposure and is proportional to local permeability [3]

RESULTS

The transformed and templated images displaying the time-averaged shear stress in the left and right external iliac arteries are shown with the corresponding templated tissue OD images in Fig. 3. The highest shear stress, depicted by the darkest spot in the image, occurred near the flow divider in both arteries. The shear stress in this region ranged between 50 and 95 dyn/cm^2. However, patches of much lower shear (10-15 dyn/cm^2) are immediately adjacent to this region. The nearly white region opposite the flow divider experienced shear stresses less than 5 dyn/cm^2. The distal portion of the arteries, which accounted for the majority of pixels in the image, had a more uniform distribution of shear, which ranged between 15 and 20 dyn/cm^2.

To enable a more quantitative presentation of the data, for each artery the pixels were sorted according to shear stress into 19 bins with increments of 5 dyn/cm^2 from 0 to 95 dyn/cm^2. Next, the average optical density and shear stress for the pixels within each shear bin were calculated. A normalized permeability was then obtained for each bin by dividing the average optical density in that bin by the average OD of the entire segment; this was done separately for both the left and right iliac regions. The resulting normalized permeability is plotted against time-averaged shear stress in Fig. 4.

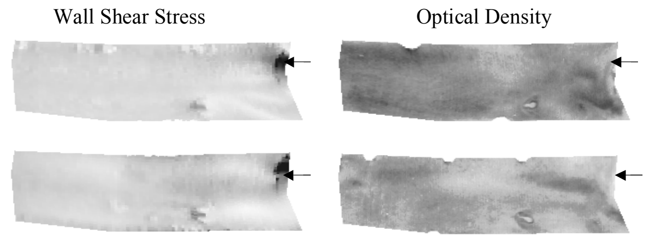

Figure 3 Templated time-averaged wall shear stress and optical density. Top: left iliac artery. Bottom: right iliac artery

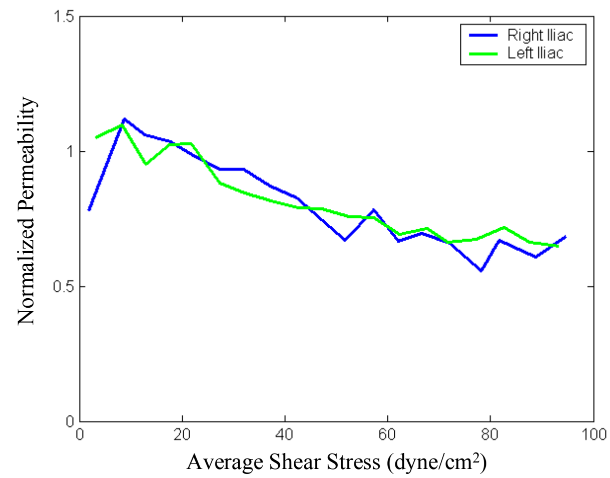

Figure 4 Normalized permeability vs. time-averaged wall shear stress

The same analyses were performed for other shear-related indices including maximum and minimum wall shear stress, the variance and pulse of shear stress, oscillatory shear index, and the maximum temporal shear stress gradient during the cardiac cycle. For this single case, no relationship was observed between the normalized permeability and any of these shear-related indices.

SUMMARY AND CONCLUSIONS

The distribution of normal permeability at the porcine aortic trifurcation was measured densitometrically. The corresponding distribution of wall shear stress was obtained computationally using an arterial cast to define the computational region. Pixel-by-pixel comparisons of the permeability and shear distributions in the external iliac arteries revealed (1) a monotonic decrease in permeability with increasing time-averaged wall shear stress, (2) weak or absent dependence of permeability on other shear-related indices, and (3) consistency between the left and right arteries.

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