Evaluation of flow velocities after carotid artery stenting through split spectrum Doppler optical coherence tomography and computational fluid dynamics modeling

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Abstract: Hemodynamics plays a critical role in the development of atherosclerosis, specifically in regions of curved vasculature such as bifurcations exhibiting irregular blood flow profiles. Carotid atherosclerotic disease can be intervened by stent implantation, but this may result in greater alterations to local blood flow and consequently further complications. This study demonstrates the use of a variant of Doppler optical coherence tomography (DOCT) known as split spectrum DOCT (ssDOCT) to evaluate hemodynamic patterns both before and after stent implantation in the bifurcation junction in the internal carotid artery (ICA). Computational fluid dynamics (CFD) models were constructed to simulate blood velocity profiles and compared to the findings achieved through ssDOCT images. Both methods demonstrated noticeable alterations in hemodynamic patterns following stent implantation, with features such as slow velocity regions at the neck of the bifurcation and recirculation zones at the stent struts. Strong correlation between CFD models and ssDOCT images demonstrate the potential of ssDOCT imaging in the optimization of stent implantation in the clinical setting.

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References and links
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Stroke is a significant global medical issue and is recognized as the third most frequent cause of death in Canada, as well as a leading cause of long-term disability [1]. Carotid atherosclerotic...
disease is characterized by a decrease in arterial lumen size and is well known to contribute to ischemic stroke. The disease is often treated using carotid endarterectomy in patients who are symptomatic with a large amount of stenosis [2]. However, carotid artery stenting has recently proved to be an effective and less invasive treatment for high-risk patients [3]. There are several complications associated with the procedure such as restenosis, which results in a narrowing of the arterial lumen by either neointimal hyperplasia or arterial remodeling [4]. To date, there is still an incomplete understanding of the mechanism behind restenosis, though it is known that stent implantation causes changes in vasculature geometry and influences hemodynamics. Bifurcations and curved vessels have been reported to have a higher risk of plaque formation, suggesting that the irregular flow patterns found in these regions contribute to shear stress and the development of atherosclerosis [5]. Implantation of stents also interferes with flow patterns as stent struts protrude into the arterial lumen, causing vortices and stagnation zones, which influence wall shear stress patterns and exposure time of platelets [6]. These local variations in shear stress can affect endothelial cells and result in inflammation and greater plaque formation or remodeling [7]. As a result, thrombus formation may occur which can increase the risk of a stroke [8].

Currently, there is no standard imaging modality that can evaluate the irregular flow patterns in diseased blood vessels. Recent developments in optical coherence tomography (OCT) and its Doppler variant (DOCT) demonstrated clinical potential for real time intravascular in vivo imaging. OCT is a high resolution (1 to 10 μm) optical imaging modality that can provide near histological evaluation. The physical principle of OCT is analogous to ultrasound, where backscattering of light (instead of sound) is measured using interferometry. Doppler shifts are simultaneously resolved by using mature ultrasound algorithms [9]. We have previously shown in vivo DOCT imaging of a misplaced stent in the carotid artery [10]. Due to the low signal-to-noise ratio around its struts, the Doppler signal was cluttered by noise. As a result, additional signal processing techniques were required in order to increase sensitivity of velocity measurements. A previously demonstrated technique known as split spectrum DOCT (ssDOCT) was utilized to reduce phase noise without incorporating external bulk optical devices.

In this study, blood profiles at the bifurcation junction within subclavian artery (SA) and common carotid artery (CCA) of a porcine model were evaluated with ssDOCT imaging both before and after stent implantation. Hemodynamic changes within the vessels due to stent intervention were visualized. To further understand these changes, computational fluid dynamics (CFD) models were employed to assist in the analysis of the ssDOCT images.

2. Materials and methods

2.1. Split spectrum Doppler optical coherence tomography system

The DOCT system used in this study was a commercial rotary catheter OCT system (C7-XR, LightLab Imaging, St. Jude Medical Inc., USA) and has been described in our previous work [11]. Briefly, the C7-XR contains a 50.4 kHz swept source laser, which has a spectral bandwidth of 110 nm centered at 1310 nm. The sweep trigger, k-clock and OCT fringe signals of the C7-XR system were coupled into a PC DAQ card (AT9350, AlazarTech, Canada) in order to acquire the DOCT signal. The detectable flow velocity before phase wrapping was measured to be from ∼ 2 mm/s to ∼ 3.4 cm/s (with a Doppler angle of 70 degrees) [11].

DOCT measurements in OCT rotary probes are susceptible to inherent rotational motion artefacts, non-uniform rational distortion, and bulk tissue motion. We have previously shown that a signal processing technique known ssDOCT decreased the noise clutter from the aforementioned sources of noise [10]. This technique involved the splitting of the interferogram into multiple windows in which each window was used to calculate the Doppler shift via Kasai autocorrelation. In this study, the interferogram was split into dual bands (B=2), each with a
Kasai kernel of 4 by 20 (axial and transverse direction) for all ssDOCT measurements. Due to the high absorption coefficient of blood, a 1.5% blood/saline mixture was injected to provide visualization of the vessel wall and scatterers for Doppler shift measurements [11]. Additional histogram filtering was employed by isolating the region of the outer LightLab C7 dragonfly OCT catheter as a reference to reduce bulk motion noise [10, 12].

Porcine models (N=3) were anesthetized with ketamine and their vitals were constantly monitored. The femoral artery was exposed and the standard catheterization protocol was followed in order to guide the LightLab C7 dragonfly OCT catheter to the carotid or subclavian artery [13]. Both fluoroscopy and volumetric OCT images were acquired to locate a side branch in the subclavian or carotid artery of the porcine model to simulate a bifurcated human carotid artery, where the internal carotid artery (ICA) originates. In this paper, this simulated location will be referred to as the ICA. The OCT catheter was positioned near the bifurcation of the vessel and ssDOCT flow images were acquired. Additional ssDOCT images were collected after a stent was deployed along the ICA, which obstructed the entrance of the side branch, as seen in Fig. 1. The animal protocol in this study was approved by the Animal Care Committee at Sunnybrook Health Sciences Centre (Toronto, Canada).

2.2. In vivo Doppler imaging model

![Image](image1)

![Image](image2)

Fig. 1. a) Fluoroscopic image of the stent placement. b) Contrast was injected into the artery in order to visualize the gross flow distribution of the vessel after stent implantation. Scale bar: 10 mm. c) Magnified view of the region marked with dashed box in a), showing details of catheter and guidewire positions. d) Magnified view with contrast injection, showing blood in-flow, mild spasm distal to the stent edge in an out-flow branch. Notice in this particular setting, the OCT imaging catheter and its guidewire are placed through the stent in one of the out-flow branches. Scale bar: 3 mm.

2.3. Computational fluid dynamics simulations

The dimensions of the ICA were measured from the structural OCT image and used to generate the virtual geometry in SolidWorks (V2014, Dassault Systèmes SolidWorks Corp., France).
A virtual stent was created to approximate the shape and size of the stent used in the in vivo experiments. This virtual stent was placed near the location of the bifurcation, as observed in the volumetric OCT image. Time-dependent flow analysis was performed using a multi-physics simulator (COMSOL V4.4, USA). Blood flow was modeled using incompressible Newtonian fluid with the fluid dynamic properties of blood and arterial wall accounted for during the simulation. Inlet velocity was modeled after a previously reported human cardiac blood velocity profile [14] with a peak velocity of 2.3 m/s. It has been shown that a peak velocity of 2.3 m/s or greater has been associated with severe stenosis of the ICA [15]. During simulation, the CFD models were assumed to have a laminar flow profile with a non-slip condition and solved using the Navier-Stokes equations.

3. Results

3.1. Computational fluid dynamics simulations

Figure 2(c) and 2(f) depicts the flow distribution of a virtual 3-dimensional bifurcation viewed in the transverse and longitudinal plane, respectively. The OCT catheter was eccentrically positioned from the arterial wall resulting in a laminar-like flow in the parent vessel (Fig. 2(c)), while the side branch consisted of a diverted flow at the entrance, which revealed higher velocity proximal to the carina and low to stagnant velocity regions distal to the carina (Fig. 2(d)). The corresponding CFD model without the influence of the OCT catheter is shown in Fig. 2(e) and 2(f). Similarly, a laminar-like flow was observed in the parent vessel while diverted flow was observed in the side branch.

These flow distributions changed after a virtual stent was placed across the neck of the side branch with and without the influence of the OCT catheter (Fig. 3). In both scenarios, velocity slipstreams at the neck formed between each of the stent strut and redirected the flow. Closer observation revealed eddy current formation around various stent struts at the entrance of the side branch (Fig. 3(a) and 3(b)). The slipstreams were apparent throughout the cardiac cycle. Stagnant flow regions were also observed approximately 1.5 mm away from the carina within the side branch. Perturbation of flow from the stent struts was present and had low velocity profiles. The overlaid streamlines in Fig. 3(a) and 3(b) demonstrated these low velocity flow patterns, which had enveloped around the strut. Contralateral to the placement of the OCT catheter, recirculation zones were observed near the stent strut. These recirculation zones were also observed in the CFD models without the placement of the OCT catheter. However, in the parent vessel, the flow distribution had a laminar profile with increased velocity compared to before stent deployment with the OCT catheter. For the case without the OCT catheter, lower laminar-like velocity profile was observed in the parent vessel.

In the transverse plane of the CFD model (Fig. 3(d) and 3(e)), similar to the OCT imaging plane, slipstreams had also created stagnant flow regions distal to the neck of the bifurcation. The overlaid streamline revealed stagnant flow regions that were lateral to the center of the side branch. In the parent vessel, the flow distribution exhibited a non-uniform flow profile along the outlier of the peak velocity.

3.2. In vivo ssDOCT imaging

Over the course of ssDOCT imaging of porcine models, bifurcations were analyzed both before and after stent implantation. Prior to the intervention, the OCT catheter was positioned proximal to the neck of the side branch entrance. Flow distribution was perceived as phase contours, which were bounded to $-\pi$ to $\pi$. High velocities could be measured by the number of phase wrapping or aliasing rings. Fig. 4 depicts high velocities at the neck of the bifurcation. Distal to the entrance to the side branch and within the parent vessel, lower velocity (less phase contours) were visualized. Increased blood concentration in the center of the side branch exhibited
Fig. 2. a) Structural OCT image in the transverse plane, demonstrating the parent vessel (*pv), side branch (*b), and the stent struts with shadows. b) Reconstructed longitudinal plane of the blood vessel from OCT pull-back imaging was employed as a reference for the 3D geometry of the CFD model. c) The velocity distribution before stent implantation with the OCT catheter from the CFD simulation of the carotid artery in the transverse plane with flow velocity contours. d) Streamlines overlaid on the CFD simulated velocity distribution with the OCT catheter in the longitudinal plane. e) The CFD simulation of the velocity distribution before stent placement without the OCT catheter. f) The corresponding streamlines that was overlaid on the CFD simulated velocity distribution without the OCT catheter in the longitudinal plane. Scale bar: 1 mm.
Fig. 3. a) The velocity distribution from the CFD simulation with the OCT catheter present after stent implantation covering the bifurcation in the longitudinal plane. Streamlines were overlaid onto the velocity distribution. An eddy was observed close to the stent strut near the entrance of the bifurcation (dashed region). b) The corresponding CFD simulation without the OCT catheter within the lumen wall. Similarly, an eddy current was also observed around the stent strut near the entrance of the bifurcation (dashed region). c) Contralateral to the position of the OCT catheter, a recirculation zone near a stent strut was observed. d) The CFD simulation was re-sliced to view the distribution in the transverse plane without the OCT catheter. e) The corresponding CFD simulation without the OCT catheter image. Scale bar: 1 mm.
unresolvable velocity measurements. Overall there was a higher velocity within the neck of the bifurcation during systolic period.

The introduction of a stent over the neck of the side branch vessel had exhibited hemodynamic flow changes to the vessel. When the OCT catheter was placed distal to the neck of the bifurcation, several stent struts were not completely anchored on the vessel wall (Fig. 5). The blood flow profile around the stent struts distal to the neck of the branch vessel wall appeared to envelop around the struts for a portion of the cardiac cycle with minimal perturbation. This limited disruption in flow profile was also seen in the cluster of stent struts located at the mid-left section of the image. However in between this cluster of stent struts, low velocity estimates were observed.

At the neck of the stented bifurcation, low signal-to-noise Doppler signals can be visualized at the corner of a protruded stent strut. In this particular frame, the phase contours extended beyond the stent strut and into the side branch. Similar to Fig. 6, certain struts had an enveloped phase contour surrounding its location. Stent struts that were densely positioned along the wall exhibited disturbances in its phase contour (Fig. 6(d)), while the protruded stent strut produced low flow velocities. After the initial frame, an eddy current formation was noted around the struts in the ssDOCT image. This dissipated slowly into a low to stagnant region.
In one particular instance during the experiment, the ssDOCT images captured a decrease in velocity within the ICA (Fig. 7). From the structural 3D OCT image, two struts had bridged the neck of the bifurcation. Throughout the collected ssDOCT sequence, a decrease in velocity was seen as a reduction in phase aliasing with time. Low signal-to-noise Doppler signals were also observed beyond the stent and bifurcation. Following the decrease in flow, a backflow of blood from the side branch to the parent vessel had occurred. Due to this injection of blood in the main artery, a sudden increase in the concentration of blood in saline occurred, resulting in the inability to resolve the stent struts and thus, the bifurcation diminished.

4. Discussion
4.1. In vivo ssDOCT imaging

The differentiation between ssDOCT images of the bifurcation before and after stenting was distinct. Prior to stent implantation, higher velocity was observed at the neck entrance of the side branch, while the stented entrance resulted in the formation of eddies and low velocity flow regions. Previous studies have associated formation of thrombus to low wall shear stress (or endothelial shear stress) and stagnant / low velocity area [16]. Furthermore, increasing evidence has suggested the presence of low wall shear stress contributes to in-stent restenosis [16]. During ssDOCT imaging, low velocity zones were observed in between the poorly deployed stent.
struts and the arterial vessel wall. This could interrupt the overall homeostasis of vessel wall, as the pressure and forces differs from the non-stented region. These hemodynamic changes could be detected by the endothelium, which would trigger vascular remodeling (leading to intimal hyperplasia), atherosclerosis or early embolization [16–18]. These low to stagnant velocity zones were also present at the intersection of the neck with a protruded stent strut. The intact vascular endothelium of the arterial wall is generally assumed to be nonthrombogenic. As a result, adhesion of platelets along the wall would not accumulate due to defects or injury. In stagnant regions, the accumulation of fibrin activates platelets leading to thrombogenesis [17, 19].

Proper placement of the stent had exhibited laminar-like flow during the cardiac cycle. There were clear differences between the flow patterns in the parent vessel and the stented side branch. The presence of laminar flow in a parent vessel of the ICA has been reported in stented bifurcation studies through both phantom and CFD [20]. Similar flow measurements in bifurcation using Doppler ultrasound and digital particle imaging were reported. However, Doppler ultrasound lacked the resolution to provide detailed qualitative flow visualization and digital particle imaging and would not be suitable for in vivo imaging [20, 21]. These studies also did not suggest backflow of blood from the side branch to the parent vessel after stent placement.

4.2. Comparison between CFD and ssDOCT

Simulations of the ICA and side branch showed separation in flow. Consistent streams that flowed through the neck of the side branch were visualized as low signal-to-noise Doppler
signals. From the transverse plane of the CFD simulations, the flow streams did not exhibit a uniform pattern as there was a marginal increase in velocity at the lateral region of the side branch. This was also observed in the ssDOCT image as one of the sides of the velocity profile was larger.

In terms of stented bifurcation, local flow disturbances were observed along the stent struts in the CFD simulation. When the struts were properly placed in the ICA, the parent vessel revealed a laminar-like contour, which was predicted by the CFD model. In some of the ssDOCT frames, the phase contours appeared to envelop over the stent strut. Isolated eddies from the stent were only noticed at the entrance of the side branch. These isolated eddies were also observed in the longitudinal view in the CFD model. However, it was also noted that there were increased phase contours that transition to phase aliasing in the parent vessel. This signified high velocities in the parent vessel and was more evident prior to stent intervention, as seen in the CFD simulation. The increase in velocity after stent placement within the parent vessel is due to a number of factors and assumptions made in the simulations (see limitation of the study). One potential factor that could have contributed to the increase velocity within the parent vessel is the presence of the OCT catheter. However, in-depth analysis of the hemodynamic effects of the OCT catheter within the lumen wall will be left for future investigations. Lastly, the rare phenomenon of backflow from the side branch was not predicted in the CFD model. The backflow within a vessel may only occur under specific pressure and velocity conditions. Unfortunately, due to the complexity of the in vivo experiment, we were unable to recreate this phenomenon.

4.3. Limitations of the study

One of the technical hurdles of CFD modeling is its idealization and simplification of the in vivo environment. In this study, the ICA and its side branches were modeled as ideal rigid cylinders and without stenosis. In normal vasculature, rhythmic expansion and contraction of the vessel wall from the pressure changes with the cardiac cycle lead to the deformation of its shape. This would introduce a time-dependent mechanical effect on the CFD model, which was not included in this study. Furthermore, from the 3D pullback of the OCT rotary catheter, the lumen of the ICA was different than the ideal cylinder. This would contribute to the deviation between the CFD and the measured ssDOCT. Furthermore, we had assumed that the CFD inlet had a peak velocity of 2.3 m/s, as well as a human cardiac velocity profile. This would also contribute to the deviation of the velocity measurements.

The stent structure was modeled using a generic strut pattern. Diameter, length and the thickness of the stent struts were based on the stent used in the in vivo pig experiment. Additionally, the position of the stent relative to the bifurcation was approximated using the 3-Dimensional OCT image. However, extensive studies have shown that the shape of the stent strut, its spacing and its position affects the flow slipstreams [22]. As a result, the difference between the in vivo stent placement and virtual stent placement would explain the deviation.

During in vivo imaging, the OCT catheter was introduced in the lumen. This external device would affect the normal flow distribution in post-operative intervention. Furthermore, the flow distributions studied were in a healthy carotid artery. During clinical interventional treatment, the vessel wall and its surrounding environment could consist of hypertension, calcification, atherosclerotic plaque, or other factors resulting from vascular diseases.

It should also be noted that during ssDOCT imaging, a diluted concentration of blood was introduced in order to provide both visualization of the lumen wall and scattering for Doppler phase estimates. However, the injection of this Doppler “contrast agent” would reduce the local viscosity and influence the hemodynamics. This was not accounted for in the CFD models and further investigation of time-dependent changes in viscosity is left for future studies.
In spite of these approximations and imaging catheter insertions, similarities between the ssDOCT images and simulations were observed. These results could provide feedback to the surgeon on the quality of the stent placement in order to reduce post-operative complications. This same feedback could provide further developmental insights in the design of carotid stents.

5. Conclusion

Results from this study demonstrate the feasibility of ssDOCT imaging for studying hemodynamic changes both before and after stent deployment in the bifurcation junction within the carotid artery. Both ssDOCT images and CFD models displayed significant differences in blood flow profiles following stent implantation. Specifically, slow velocities were observed at the neck of the bifurcation, which may lead to the development of thrombosis. Moreover, flow disturbances were also visualized at the stent struts. Overall, ssDOCT images correlated well with cross-sectional flow profiles from the CFD models, and can potentially provide critical feedback for stent intervention in a clinical setting.

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