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Evaluation of embolic deflection device using optical particle tracking

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Abstract

Trans-aortic valve replacement is a new endovascular procedure which has started to be used routinely in cardiac interventional suites. During such procedures a stent-like device containing new aortic valves is placed over the damaged ones, possibly causing calcifications to be dislodged and released in arteries leading to stroke. To prevent such events, new devices are being developed to provide distal protection to the brain supplying arteries. Currently there is a need to evaluate such device efficacy in a repeatable manner. We are proposing and investigating such a method based on particle optical tracking. We simulated such protective devices using two porous screens (150 and 200 μm pore size) which were placed in an arterial bifurcation phantom connected to a clinically relevant flow loop. A mask was acquired and gold embolic particles (100–300 μm) were injected at a steady rate using a motorized injector. Optical images with 2 ms exposure were acquired at 30 fps. Images were subtracted, thresholded and filtered using a 5 $\times$ 5 median filter. ROI's were drawn over the main and bifurcating arteries and a particle counting algorithm was used to estimate particle flow rates in each artery for each run. The unprotected and the two protected cases were evaluated. Before filter placement, the particle flow rate was 60 and 40 %, respectively, of the main artery. After the filter placement, the particle flow rate in the protected branch was 4% and 8% of the particle flow rate in the main artery. We present a method to assess the efficacy of such devices using an optical particle tracking and counting technique.

Keywords

embolic deflection device; optical particle tracking; Trans-aortic valve replacement

Description of purpose

Trans-aortic valve replacement (TAVR)^{1–6} is a new endovascular procedure, where damaged or calcified aortic valves are replaced with artificial or animal-origin valves using a balloon deployed stent-like device. The procedure is minimally invasive and is done under x-ray guidance. In recent cases secondary cerebral stroke events were observed after the procedure.^{3, 4, 6} During placement, micro-calcifications and thrombus may be dislodged from the calcified valves and travel to the brain vasculature causing ischemic stroke events.

To prevent such events, new embolic deflection^{3, 4} or distal protection devices⁶ are proposed (Figure 1). They are retrievable porous devices which are placed in the aortic arch covering the arteries leading to the brain. The devices need to be porous to allow blood flow, but stop the potential stroke causing particle to reach the brain. Some of the devices are self-aligning however there are questions about the device fitting perfectly on any aortic arch geometry and hence stopping 100% of the calcified particles.

The efficacy of such devices is studied in vitro using phantoms; however, the task is not trivial since it involves tracking or counting micro particles in relatively large flow volumes and rates. One approach is to monitor the particles after each experiment by effectively counting them.⁷ This is an extremely precise method, very effective for devices such as distal protectors where particles are captured during the experiment. For embolic deflectors such methods could be cumbersome and time consuming. We are proposing a dynamic way to evaluate such devices using an optical particle tracking method.

Materials and Methods

Problem Description

The analysis presented in this article is a typical particle tracking/counting problem. We imaged gold embolic particles to simulate micro-calcification and thrombus, while the particles flow in a transparent bifurcation arterial phantom, under physiological blood flow conditions. More precisely, the conditions were similar to those encountered in the aorta, where the typical average velocity is about 40 cm/sec, however, the instantaneous velocity oscillates between 0 cm/sec and 120 cm/sec. These flow conditions combined with the limitations of our imaging system, 30 frames per second and about 2 cm field of view (FOV), set a few constraints on our experimental setup and counting algorithm.

The imaging camera used in this experiment was a 1M30 CCD (DALSA, Waterloo ON), which has an effective pixel size of 26 μm . The first limitation of the system was the FOV. If a particle moves with maximum peak velocity, a simple calculation reveals that a particle travels about 4 cm between two adjacent frames. Hence, it is nearly impossible to track all the particles during the one cardiac cycle. To overcome this issue we injected the particles at a steady rate (0.1 ml/sec) during the entire measurement, using a programmable injector.

To increase particle detectability we acquired an average image mask before particle injection and each subsequent frame was log-subtracted from the mask according to the formula:

$$\mathbf{I}_s^K = \langle \mathbf{I}_{mask} \rangle \frac{\mathbf{I}_{mask}}{\mathbf{I}_{acquired}^K} \quad (1)$$

where $\mathbf{I}_s^K$ is the k-th subtracted image, $\mathbf{I}_{mask}$ is the mask image, $\mathbf{I}_{acquired}^K$ is the k-th acquired image, and $\langle \mathbf{I}_{mask} \rangle$ stands for the average pixel value in the mask image. Bold letters stand for image matrices, and the operations are done at each element (pixel).

Particle motion blurring was another issue which we limited by synchronizing an LED array with the camera at very short exposures. Short exposures however cause a decrease in the particle detectability due to the particle signal-to-noise ratio (SNR) decrease. So, we searched for a balance between reducing the blurring while keeping an acceptable SNR. We used various exposure times and measured SNR for various stationary particles in subtracted optical images. SNR was calculated as:

$$SNR = \frac{S_p - S_{bckg}}{\sigma_{bckg}} \quad (2)$$

where S_p is the particle average pixel intensity, S_{bckg} is the background average pixel intensity and σ_{bckg} is the variance of the noise in the background. All quantities were measured in the subtracted images.

Camera exposures of 2 ms and higher gave an SNR of 4 and higher. Also if we assume that the particles move with the peak velocity, they will travel about 240 microns (~9 pixels) in a frame, which was of the same order as the size of the larger particles used in this study.

We assembled a system and a software method for testing two embolic deflection prototypes built from stainless steel. The particle detection algorithm is a standard IMAQ LabVIEW subroutine (National Instruments, Austin TX). Prior to detection, the subtracted images were thresholded and filtered using a 5×5 median filter. The particle detection method was validated using simulated particle signals and later used for experimental verification of the embolic deflection prototypes.

Detection Algorithm Validation

We simulated particle images with known positions and sizes. The particle diameters were between 100 and 300 μm which corresponds to approximately 4 and 11 pixels on our imaging system. Flat images were created using a Poisson noise distribution:

$$F(N) = e^{-\bar{N}} \frac{\bar{N}^n}{n!} \quad (3)$$

where $\bar{N}$ is the average signal which is the same as the average background measured in the subtracted images acquired experimentally, for an exposure of 2 ms (Figure 2, top row)

Particle signal was generated using the following distribution:

$$N(i, j) = \begin{cases} F(S) & \sqrt{(i - i_0)^2 + (j - j_0)^2} \leq \frac{D_{i_0, j_0}}{2} \\ 0 & \text{else} \end{cases} \quad (4)$$

where S was the signal of the particles, i and $j = \overline{0:1023}$ are the pixel locations and i_0 and j_0 are the location of the particles of diameter D . In total we generated 64 particles (8 rows × 8 columns) uniformly distributed. In each row the particle diameters were the same and increased monotonically in each column from 4 to 11 pixels.

Particle signal S was chosen to match the SNR observed in particle images acquired with an exposure of 2 ms. In addition we simulated motion blurred images by changing the location of the particle in one direction. This was an acceptable approach since the flow through the arterial phantom is mostly unidirectional. We generated nine images by incrementing j_0 by one pixel in equation (4). The images were averaged and added to the background.

In each image we took a Region of Interest (ROI) and constructed a histogram (Figure 2, bottom row). For low particle SNR, their signal is embedded in the tail of the histogram. To isolate the signal we implemented an automatic threshold technique based on the background intensity mean value $\overline{N}$ and the standard deviation $\sqrt{\overline{N}}$ the Poisson noise. The threshold limit was assigned using the following formula:

$$N^T(i, j) = \begin{cases} 1 & N(i, j) \leq \overline{N} + \alpha \sqrt{\overline{N}} \\ 0 & \text{else} \end{cases} \quad (5)$$

where α is adjustable parameter between 0 and 1 and $N^T(i, j)$ is the thresholded image. The optimal parameter value was selected based on the simulations.

The thresholded images were passed through a 5×5 median filter and finally inserted into the particle finding algorithm. The results were compared with the initial simulated data for various particle signals. To verify the algorithm robustness, during the simulations the background noise was kept constant and the particle signal was changed to be lower or equal to the experimentally measured value.

The algorithm returns the particle number, their positions and other various parameters such as bounding rectangle diagonal (BRD). Using the binary image, BRD is calculated by fitting the smallest enclosing rectangle to a connected cluster of pixels, and calculating the diagonal. We used such a feature to discriminate between possible false positives corresponding to the higher background noise values. A simple Pythagorean calculation applied to the particle diameter range yields a BRD range of ~ 6 to 16 pixels.

Experimental Setup

The experimental setup is shown in Figure 3. The fluid was pumped using a pulsatile blood pump (1400 Series, Harvard Apparatus, Holliston MA), which was operated at 40 pulses per minute, 35/65 systole/diastole cycle ratio and 15cm^3 volume per cycle. The pressure wave was measured using a research grade blood pressure transducer (MA1 72-4496 Series, Harvard Apparatus, Holliston MA). The transducer was connected to a 5 Fr straight Envoy catheter (Boston Scientific, Natick, MA) and advanced to the vicinity of the bifurcation phantom. The catheter tip did not protrude into the main flow. The main vessel of elastomer bifurcation was 5.12 mm in diameter. Gold embolic particles (EmboGold, BioSphereMedical, France) with diameters between 100 and 300 microns were injected using an automatic injector at a constant rate during data acquisition.

The optical setup is shown in Figure 4, the light source was an array of eight large LEDs. The individual LEDs have a border where no light is produced, and to compensate we used a 1 to 2 large area magnifying fiber optic taper which was offset about 2 cm to blur the inner

edges of the LED array. A pulse generator was used to synchronize the DALSA CCD camera and the LED array. The pulse width was 2 ms.

We acquired ~300 frames at 30 frames/second. Prior to particle injection a mask was acquired, all subsequent images were subtracted from the mask. Each subtracted image was thresholded to isolate the particle signal, and filtered with a 5×5 spatial median filter. Three ROIs were selected over the main vessel and the daughter branches (Figure 4 (d)), and particles were counted automatically in each ROI in each frame using an available National Instruments vision subroutine. The subroutine uses a connectivity condition to count only those signals which are 4 pixels or larger. Also selected ROI's had to avoid overlapping the phantom edge because, due to the pulsation, there is a mismatch between mask and the image sequence which could lead to errors. Each count was normalized to the number of pixels in the ROI and added to the previous frame:

$$n(j) = \frac{\sum_{k=0}^j N(k)}{A_{ROI}} \quad (6)$$

where $n(j)$ is the average summed number of the particles per ROI area (A_{ROI}) and $N(k)$ is the particles counted in a k^{th} frame in a given ROI. Finally, for plot representation we divided each $n(j)$ for each ROI to the $n(300)$ for the main vessel.

Two experimental mesh flow diverters were inserted into the phantom to block one of the branches. The pore sizes were 200 and 150 μm . We evaluated the effectiveness of the flow diverter by comparing the average particle flow rate passing through the three ROI's indicated in Figure 4. Finally, the particle flow rate in each of the branches was normalized to the flow rate in the main artery and reported as a percent for comparison purposes.

The pulse wave was controlled using a flow dampener and a pressure controlled reservoir which were connected to the flow loop as shown in figure 2. Two rubber pressure balls were used to adjust the air cap pressure inside the dampener and reservoir. We adjusted the pressures in the dampener and the reservoir until we obtained a pulsed wave with a minimum of 70 mmHg and maximum of 120 mmHg.

Results

Analysis of the signal to noise ratio for known particle positions are shown in Figure 5. The smallest SNR encountered was 3. The standard deviation for the background was approximately 3% of the average background signal.

Using signal and noise measurements as shown in Figure 5, we generated particle images as described in the methods section equations 3 and 4. The resulting images are shown in Figure 6. The simulated images were processed as described above and inserted into the particle detection algorithm. For $\text{SNR} > 2$ the algorithm worked 100% in recovering the number of particles and positions. For the threshold condition in equation 5 we used $\alpha = 1$. However, for values of $\text{SNR} < 2$ the algorithm gives significant errors. For $\alpha = 1$ in equation 5, particles with diameter > 8 pixels appear fragmented and direct particle counting yields one order of magnitude larger particle count than the one generated in the simulated image.

By imposing a counting condition of BRD = 5 pixels, most of the false positives are removed within the range of the generated particles.

To test the algorithm at SNR = 1 we changed the threshold in equation 5 using $0.8 < \alpha < 0.9$. For SNR = 1 and using BRD = 5 we were able to improve the results (Figure 6, middle row). For even lower SNR's the algorithm practically fails to return any reliable results.

Blurring due to motion further degrades the ability to count particles. Assuming the worst case scenario, when particles move with peak velocity of 120 cm/sec (9 pixels/2ms), the algorithm detected 97% of the particles simulated with SNR = 2. More precisely, the algorithm found all the particles with diameters > 5 pixels and missed only a few of the smallest particles (Figure 7).

The experimental data showed that the algorithm can be used reliably to count particles in the flow experiment. Results are shown in Figure 8. Such snapshots were derived for every frame; particles were counted in three ROI's in each frame and they were normalized to the ROI area.

The results of the particle counting are shown in Figures 9 and 10. Since we injected particles at a steady rate, the counting summation followed a linear trend; however small ripples are observed in the plots behavior and they coincide with the pump pulsation. The background histogram, to find the mean value and the standard deviation for thresholding, was selected outside the phantom; in equation 5 we used $\alpha = 1$ for the entire study. We repeated the data acquisition 3 times for each situation, and the deviations observed were less than 5% between the runs.

For the no diverter case the particle flow rate in the daughter branches was ~60 and 40 %, respectively, of the main artery. After the embolic deflection device placement the particle flow rate in the protected branch was 8% and 4% of the particle flow rate in the main artery for the two diverters respectively.

To verify what kind of particles passed by the filters, we used selective counting, setting the BRD equal to the diagonal of the largest particle allowed to pass the devices. For both devices the algorithm still detected a negligible number of particles passing into the protected artery. Most probably they were an artifact due to motion blurring, or an incomplete seal of the arterial inlet.

Discussions

In summary, we presented an in-vitro method to evaluate the efficacy of embolic flow diverter devices designed to provide protection to the superior circulation from the calcifications and thrombi dislodged during trans-aortic valve replacement procedures. The particles were simulated using gold embolic spheres. An optical system and a particle counting software were tested using simulated images and physiological relevant flow conditions.

The image simulations (Figure 6 and Figure 7) demonstrated that the algorithm could count and measure reliably particles with low signal to noise ratio. The low SNR was mostly due to increased noise in the low exposure time per frame required to image particles in a high velocity flow. This issue could be overcome if fluorescent particles and a laser were used for data acquisition. However, such particles are designed specifically for particle image velocimetry, they are usually designed to follow the flow lines in order to give accurate fluid dynamics description. On the other hand, the embolic materials we used are more likely to behave as real thrombi or calcifications.

The flow conditions used in our experiment were in the higher extreme of those where an embolic deflection device would be used. In general, patients undergoing such procedure are sedated and received beta-blockers to decrease the heart rate. In such conditions, it is nearly impossible to reach peak velocities ~ 120 cm/sec as reported in normal people. Even in these conditions, the particle counting algorithm identified reliably the particles embedded in the flow.

Some artifacts were observed at the edges of the phantom. Since we used an elastic phantom there was a mismatch between the location of the vessel wall in the mask and in certain images in the acquired sequence. To eliminate errors we selected the ROI's close but not including the wall area.

The experimental flow diverters were built from stainless steel with two pore sizes in the range of the particle diameters. We choose them as such in order to allow certain particle passage. This was the case as shown in figures 9 and 10. As expected, the denser diverter stopped more particles; however, the conditioned counting indicated that particles with BRD larger than expected passed the deflector. This is due to some motion blurring during the acquisition.

Overall, the purpose of this study, which was establishment of a reliable method to evaluate embolic deflection devices, was achieved. This sets the stage for evaluation of real devices in an aortic arch phantom. While tracking all the particles in all the branches at the same time might not be possible due to the small field of view of the camera, the proposed method of using a continuous injection of particles could be used to track each location individually.

Conclusions

We present a method to evaluate embolic flow diverters proposed to be used during trans-aortic valve replacement. The next step is to apply the presented method to clinically relevant situations by using an aortic arch phantom and experimental embolic flow diverter devices.

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Figure 1.
Placement of the distal protection/embolic deflection device

Figure 2. Top row simulated flat image and particles using Poisson distributed noise. Bottom row: histogram of the background simulated image, arrow indicates the threshold selection. Bottom row 3rd figure: final image after automatic threshold.

Figure 3.
Experimental flow loop

Figure 4.

Optical Setup; a) overview, bifurcation phantom is placed on a transparent plate under the camera on top of the blue spacers, (b) light source and (c) the LED array used for light pulse generation d) selection of ROI for particle counting

Figure 5. Stationary particle images on uniform background acquired using the optical system described in the methods section. Line profile locations are shown by the dotted black lines and values are represented in the right plots. The line profiles are normalized to the average background value. The SNR values are calculated using equation 2.

Figure 6. Results of the simulations for stationary images for various SNR's without/with bounding rectangular diagonal constraint where n indicates the number of particles found.

Figure 7. Results of the simulations for blurred images for various SNR's without/with bounding rectangular diagonal constraint. Blurred motion is downward.

Figure 8. Snapshots of particles passing through the phantoms. Arrows indicate particle in the DSA and the corresponding particles in the binary image

Figure 9.

Particle counting $n(j)$ for no flow diverter and for the two flow diverters. Each plot is normalized to $n^{max}(300)$, which is the total particle count recorded in ROI-1 selected in the parent vessel (Figure 8, first column)

Figure 10.

Particle counting $n(j)$ in the protected branch for two flow diverters. Each plot is normalized to $n^{max}(300)$, which is the total particle count recorded without any BRD conditions.