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Effect of injection technique on temporal parametric imaging derived from digital subtraction angiography in patient specific phantoms

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Abstract

Parametric imaging maps (PIM's) derived from digital subtraction angiography (DSA) for the cerebral arterial flow assessment in clinical settings have been proposed, but experiments have yet to determine the reliability of such studies. For this study, we have observed the effects of different injection techniques on PIM's. A flow circuit set to physiologic conditions was created using an internal carotid artery phantom. PIM's were derived for two catheter positions, two different contrast bolus injection volumes (5ml and 10 ml), and four injection rates (5, 10, 15 and 20 ml/s). Using a gamma variate fitting approach, we derived PIM's for mean-transit-time (MTT), time-to-peak (TTP) and bolus-arrivaltime (BAT). For the same injection rates, a larger bolus resulted in an increased MTT and TTP, while a faster injection rate resulted in a shorter MTT, TTP, and BAT. In addition, the position of the catheter tip within the vasculature directly affected the PIM. The experiment showed that the PIM is strongly correlated with the injection conditions, and, therefore, they have to be interpreted with caution. PIM images must be taken from the same patient to be able to be meaningfully compared. These comparisons can include pre- and post-treatment images taken immediately before and after an interventional procedure or simultaneous arterial flow comparisons through the left and right cerebral hemispheres. Due to the strong correlation between PIM and injection conditions, this study indicates that this assessment method should be used only to compare flow changes before and after treatment within the same patient using the same injection conditions.

Keywords

Parametric Imaging Maps; DSA; Mean Transit Time; Time to Peak; MTT

1. Introduction

The work presented here is an analysis of the correlation between parametric imaging maps derived from 2D angiographic runs in a neurovascular phantom, and the contrast injection techniques used for the PIM's. Parametric imaging, also referred to as colored coded Digital Subtraction Angiography (DSA), is done by analyzing the contrast behavior at each pixel in an angiographic image sequence. The method is based on DSA[1, 2] which is the golden investigational tool for neurovascular imaging due to its broad availability and high imaging resolution.

In general, DSA is used to evaluate the structural aspects rather than the physiological aspects of neurovascular disease. Conventional CT, perfusion CT and MRI, and ultrasound studies [3–5] have all been proposed as methods by which to study physiological aspects of cerebral flow, especially in stroke patients with cerebral ischemia and sub-arachnoid hemorrhage. However, many patients are treated and assessed in angiography suites using x-ray image guidance and diagnostic information provided by a C-arm unit. A DSA based cerebral perfusion or physiological measurement that can be done in the angiogram suite would be highly beneficial for evaluation of the procedure.

Since the early development of neuro-DSA, there were many attempts to incorporate the temporal information of the contrast propagation.[6] The neurological applications are preferred due to reduced patient motion, use of biplane systems which offers a second view plane, and selective injection. Selective injection refers to the practice of placing the injection catheter directly into an artery such that only the arteries in a particular area of the brain are perfused. This particular situation results in a reduced number of overlapping vessels when the contrast is injected. The temporal information obtained during such neuro-DSA runs could be used to create a blood flow parametric description over the entire imaged vasculature. Such parameters could also be used to calculate physiological aspects of the flow [7, 8] or evaluate treatment effects.[7, 9–16]

The main way to analyze flow is by monitoring the contrast media flowing in the arteries through a method referred to as videodensitometry. This method uses time density or contrast curves to calculate parameters such as Mean Transit Time (MTT), Time to Peak (TTP), and Bolus Arrival Time (BAT). Such parameters, which are common to other imaging modalities such as CT perfusion, have been investigated in detail to understand how they relate with various pathologies or medical conditions.[4, 7, 17]

Despite various attempts, this image processing method has not become a clinical reality. The delays were due to various considerations such as computational speed, flow dependence on injection technique, or limited knowledge of the correlation of flow parameters with the patient's physiology or condition. The computational aspect has been meanwhile addressed using faster hardware and advanced programming techniques. The other two challenges still require study and testing before they are completely understood.

In this paper, we investigated the PIM dependence on the catheter position relative to the main flow and the injection technique, including contrast bolus volume and injection rate. In addition, we investigated how the presence of a stenosis changes the maps. We found that

the PIM's change significantly with the injection; however, they do this in a predictable way. The PIM's acquired in the same conditions had variations smaller than 5%, while the presence of a stenosis significantly changed the parameters in the region distal to the lesion by 25% to 50%. This result indicates that this method could be employed as a tool to quantify changes following an endovascular intervention as long as a reference is established.

2. Methods and Materials

This study has two parts: data acquisition and data analysis. In the first part, we will present details of the flow setup, the hardware and software used for data acquisition and flow control as well as the x-ray imaging acquisition. In the second part, we will describe the program we developed to create the PIM's based on x-ray image sequences followed by the analysis of PIM's correlation with the injection conditions.

2.1 Experimental Setup

We designed a flow circuit, as shown in Figure 1, using a patient-specific internal common carotid artery phantom. A pulsatile blood pump (Model 553305 Harvard Apparatus, Holliston, MA) was operated at a rate of 70 pulses per minute, an output phase ratio of 30/70 systole/diastole, and a stroke volume of 20 cc. A damper was connected in series with the circuit between the pump and the phantom to dampen the pulse wave from the pump. A contrast injector catheter and a pressure transducer probe were placed between the damper and the phantom. The iodine contrast (Visipaque, 320 mgI/ml) was injected automatically using a MEDRAD Mark V ProVis injector via a 7Fr catheter (Cordis, Miami FL). The pressure transducer (Harvard Apparatus, Holliston, MA) probe was inserted through a catheter port so that the tip of the probe did not disrupt the flow. The ultrasound probe of a transit time flowmeter module (Hugo Sachs Elektronik, Harvard Apparatus, Transonic Systems Inc.) was placed on the main branch of the phantom to record the velocity of the fluid entering the phantom. To attain a good connection between the flowmeter probe and phantom, non-spermicidal sterile lubricating jelly (Priority Care 1) was used.

The average velocity of our circuit was 1.91 l/min, and the diameter of the vessel phantom at the location of the flowmeter probe was 0.8 cm. With these conditions, the carotid fluid velocity of our experiment was equivalent to 63.3 cm/s, which is within the range of normal arterial velocity through the carotid, 60–100 cm/s. The post-phantom flow was returned to the main reservoir using a y-connector with one of the returns emptying into a smaller bottle within the larger container to collect the contrast during an injection. During an injection, the return that entered directly into the water reservoir was clamped. The contrast was collected in the smaller bottle so as not to contaminate the reserve water flowing through our circuit. Once the contrast bottle was nearly filled, it was removed, drained, and the equivalent amount of clean water was added back to the reservoir. A hand pump was connected to the water reservoir as a second pressure regulator within our circuit. Before running a trial, the pump was used to increase the initial pressure of the system. The initial pressure value (~70 mm Hg) was set such that the system pressure was near the normal physiologic blood pressure of 120 mm Hg systolic and 80 mm Hg diastolic while the pump

was working. The flowmeter and pressure transducer were connected to a digital phosphor oscilloscope 5054 (Model DPO 5054 Tektronix, Beaverton, OR), which recorded the data as waveforms.

For the experiment, two contrast bolus injection volumes were studied: 5 ml and 10 ml. For each volume, injection rates of 5 ml/s, 10 ml/s, 15 ml/s, and 20 ml/s were studied. These injection parameters were repeated with the catheter placed in two different locations, outside of the main flow (catheter tip placed at the orifice of a Y-connector not entering the main flow, Point A in Figure 1a) and directly in the flow of the circuit (catheter tip advanced in the main flow loop close to the carotid origin, Point B in Figure 1a). The contrast injections were studied using biplane-DSA. The DSA runs were acquired at 30 frames per second, and the x-ray parameters remained unchanged throughout the experiment. Each run was performed three times

We performed a second round of experiments where the vessel corresponding to the Middle Cerebral Artery was constricted using a suture to simulate a 75% stenosis, Figure 2 (right). This data was acquired only for the case of the injection catheter tip outside the main flow (Point A, Figure 1a). Our decision to not include the case of the catheter tip in the main flow (Point B, Figure 1a) was based on our initial results done in an unmodified phantom, which indicated that advancing the catheter in the vessel causes disturbances of the flow which are hard to quantify.

2.2 Data Analysis

We analyzed the data using the sequence of steps in the diagram in Figure 3. To speed up the processing, the size of the acquired images was reduced from 1024×1024 to 256×256 using 4×4 binning. Next, we recorded the intensity of each pixel during the entire sequence. To speed up the data processing and avoid unnecessary analysis of pixels outside the vessels, we set a calculation threshold. The threshold was based on the RMS calculation of pixel variation during a sequence. The RMS limit was set to 10% above the background RMS, which was established by tracking operator-selected background pixels (without vessels). For those pixels with the RMS below the threshold, the values of temporal parameters in the PIM were set to zero. For those pixels with the RMS above the threshold, we fitted the intensities with a gamma variate function [18, 19]:

$$D(t)=K(t-t_0)^\alpha e^{-\frac{(t-t_0)}{\beta}}$$

where K is a constant scale factor, t_0 is the time of appearance of the contrast medium, and α and β are parameters of the distribution. Using the definition of MTT⁵ and the properties of the gamma variate functions, it can be shown that:

$$MTT=t_0+\beta(\alpha+1)$$

The TTP can be calculated by finding the maximum of the gamma variate function:

$$TTP = \beta\alpha$$

For each run, a PIM was derived for each parameter (MTT, TTP and BAT). For the runs acquired with the same injection conditions, catheter position, or pathology (stenosis or no-stenosis), we averaged the PIM for each parameter. To report our results more accurately, we selected eight locations in the vasculature (Figure 2, left) to record the parameters and compared them amongst the various runs. We also calculated the standard variance for runs acquired in the same conditions to verify experimental reproducibility.

3. Results

The waveform recorded using the pressure and flow sensors showed changes in flow for all recorded data (Figure 4). For the case where the catheter was advanced closer to the phantom (point B in Figure 1), the observed disturbances were more pronounced: 40 mmHg (40% of the mean pressure) increase and 10 cm/s (13% of the mean) increase. For the case where the catheter was more proximal (Point A, Figure 1), the disturbances were about 40–50% less than the case of Point B.

PIM results are shown in Figures 5, 6, 7, and 8. Below the parametric images, we show the distribution of values recorded at each point indicated in Figure 2. The legend between the PIM and the plots indicates the acquisition conditions for each curve. All parameters changed with the injection. For the 5 ml bolus with catheter obstructing the flow, the bolus was diluted and the contrast signal at each pixel was reduced. To be able to find all the points in the flow, we reduced the selection value for the RMS (Figure 3) from 10% above the ground RMS to only 5%. By doing so, we included some areas outside the phantom, especially around the plastic container enclosing the phantom where the noise variations were more pronounced.

PIM's acquired in the same conditions showed an average standard variation of less than 5%. All parameters changed with the injection technique. MTT, BAT and TTP decreased as the injection rate for a given bolus increased. For a given velocity, the parameters increased with a larger bolus. At point #0 which corresponds to the inlet, the recorded MTT for advanced catheter, 5ml bolus, 5ml/s was 5 seconds compared with 2 seconds when having no catheter in the flow and using the same injection conditions. As we track the bolus through the arterial network, the shift tends to keep the same proportions. The same ratios are also maintained for various injection rates.

Bolus arrival time (BAT) in Figure 6 shows the same patterns as MTT. However, in the case of BAT, the advanced catheter position had a longer arrival time, which is counterintuitive since the catheter was advanced closer to the phantom inlet. We believe that the main cause of this result is the disturbances caused by a 7Fr (2.1 mm) catheter placed in an 8 mm vessel. Despite this impediment, the behavior of the BAT through the arterial network followed reliable trends: the farther away was the point with regard to inlet (Point #0 Figure 2, left), the longer it took for the bolus to arrive, and the higher the injection rate the shorter the

BAT. The plot analysis shows that it took less than 0.2 seconds (6 frames) for the bolus to reach the most distal part of the phantom.

The Time to Peak (TTP), Figure 7, was the parameter that changed the least with the changing of the injection parameters and catheter position. In addition, the TTP did not change throughout the arterial network as much as the parameters changed, and any trends were not predictable

The stenosis case is shown in Figure 8 and Figure 9. All the PIM's show changes in the affected areas when compared to the previous results. The analysis in Figure 9, performed only for point #2, shows a reliable change between the stenosis and regular case, which is maintained for all injection rates and bolus sizes.

4. Discussions

Our results show that the temporal parameters in the parametric imaging map or color DSA depend significantly on the injection rate, the bolus size, and location of the catheter. Even though this dependence is well behaved, this variation raises questions about using such maps for diagnosis purposes. Advancement of the catheter tip in the flow demonstrated significant changes in the flow parameters, as indicated by the sensors used in the experiment, but also caused unexplained behavior of the bolus, such as large dilution and delayed arrival time. One of the explanations for such behavior could be the given by the turbulence caused by the act of injecting directly into the artery, and it is well known that turbulence can cause nonlinear phenomena, which could be the source of such behavior.

Our measurements were performed in a controlled experiment using a phantom mimicking a portion of the anterior brain circulation and demonstrated a PIM behavior similar to previously reported data.[6] The farther the point with regard to the inlet, the more diluted the bolus became, as shown in the MTT maps. In addition, the difference observed in the inlet between MTT's and BAT's were maintained through the entire PIM.

The stenosed case shows that there are significant changes in the PIM's between the normal vessel and the diseased one, especially in the post-stenosed circulation area. This indicates that this method could be used interactively during endovascular procedures to assess the effect of the treatment. We believe that such an approach is far more reliable than a qualitative evaluation such as Thrombolysis in Myocardial Infarction (TIMI) scores. In addition to stenosis, AVM treatments could be another procedure which could benefit from this type of analysis. As embolizing material is deposited in the vasculature, one could use such technique to assess the time delay required for the bolus to reach the venous phase.

The results shown in this paper indicate that one PIM cannot be treated as a standalone diagnosis tool. The dependence of the parameters on the injection techniques, catheter position, and bolus size makes it nearly impossible to relate one parameter with a certain health condition. The PIM's should only be used in relative situations when a region containing a pathology is compared with a healthy region. For example, one could use the right hemisphere of the brain which contains a pathology compared to the left hemisphere which does not. Another situation could be to assess treatments such as angioplasty and

embolizations to quantify changes at various phases of the procedure. By establishing a relation between such changes and the patient outcomes, we believe that the PIM's could become a tool routinely used in the angiographic suite.

5. Conclusions

The injection parameters affect the parametric DSA images, thus obstructing establishment of standardized values for MTT, TTP, and BAT, which can be applied to all patients at any given time. In a clinical setting, additional physiologic factors will affect the images including the patient's blood viscosity, cardiac output, and vasculature structure. Since these factors are unpredictable and directly impact the PIM, only PIM images taken from the same patient can be compared. These images can be created by taking DSA images of the cerebral arterial blood flow in both brain hemispheres and comparing the flow with the assumption that one hemisphere is normal. Alternatively, physicians can compare DSA images taken directly pre- and post-treatment, as long as the bolus volume, injection rate, catheter position, and any other controllable conditions are kept constant when each image is taken. Within these constraints, the PIM will offer immediate and reliable information to the attending physician about the status of the patient's condition. Given that the patient is already in the angiographic suite in preparation for treatment of an aneurysm or acute stroke, being able to perform such descriptive studies within the treatment room could be invaluable.

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Figure 1. Experimental setup. (a) Flow circuit. Points A and B indicate the two positions where the injection catheter tip was placed. (b) Phantom artery. (c) Pulsatile blood pump, flowmeter, pressure transducer, and oscilloscope.

Figure 2. DSA snapshots of the unmodified phantom (left), and stenosed phantom (right). The points indicated in the left picture identify the locations at which we recorded the values in PIM's for comparison amongst runs. (ICA-internal carotid, ACA- Anterior Communicating Artery, MCA-Middle Cerebral Artery, M1 and M2 segments of MCA, A2 segment of ACA)

Figure 3.
Algorithm Description

Figure 4. Velocity and pressure graphs of a 10 ml contrast injection bolus at 5 ml/s and 20 ml/s performed with and without the advancement of the catheter within the flow. The time of injection is indicated by the arrow. Flow velocity is not significantly disturbed; however the pressure shows a significant increase over a short period of time.

Figure 5. Mean Transit Time: Top PIM acquired for various injection rates (5, 10, 15 and 20 ml/s) and two boluses (5 and 10 ml). All runs were done for two cases with no catheter in the flow and with the catheter partially obstructing the flow. The bottom plots show the parameters as a function of injection rate, recorded at the points indicated in Figure 2, left. The legend above the plots indicates the contrast bolus size and catheter position for a particular curve.

Figure 6.

Bolus Arrival Time: Top PIM acquired for various injection rates (5, 10, 15 and 20 ml/s) and two boluses (5 and 10 ml). All runs were done for two cases with no catheter in the flow and with the catheter partially obstructing the flow. The bottom plots show the parameters as a function of injection rate, recorded at the points indicated in Figure 2, left. The legend above the plots indicates the contrast bolus size and catheter position for a particular curve.

Figure 7. Time to Peak: Top PIM acquired for various injection rates (5, 10, 15 and 20 ml/s) and two boluses (5 and 10 ml). All runs were done for two cases with no catheter in the flow and with the catheter partially obstructing the flow. The bottom plots show the parameters as a function of injection rate, recorded at the points indicated in Figure 2, left. The legend above the plots indicates the contrast bolus size and catheter position for a particular curve.

Phantom with Stenosis

Figure 8. Parameters recorded for the stenosed cases. PIM's acquired for various injection rates (5, 10, 15 and 20 ml/s) and two boluses (5 and 10 ml). The catheter tip was placed at point A (Figure 1) to minimize the disturbance of the main flow.

Figure 9.
Comparison of parameters for the non-stenosed phantom and the stenosed case measured at Point #2 indicated in Figure 2, left.