# QUANTITATIVE ASSESSMENT OF THE LOWER LIMB DIGITAL SUBTRACTION ANGIOGRAPHY POST SUCCESSFUL REVASCULARIZATION USING OPTICAL FLOW METHOD (syngo iFlow)

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My family whom have injected me the morale to regain the hope after despair, to restart the journey after every detour, to revive the strength after the defeat and to resurrect the dream after rejections. Above all, this is also as a symbol of submission to the Great Almighty, the author of knowledge and wisdom for the countless love to His servant.

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### LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMNS

DSA	Digital substraction angiography
TTP	Time to peak
TDC	Time density curve
СТ	Computed tomography
MRI	Magnetic resonance imaging
SIR	Society of interventional radiology
PTA	Percutaneous transarterial angioplasty
PCC	Parametric color coding
FT	Blood flow time

#### ABSTRAK

Latar belakang: Digital subtraction angiografi (DSA) merupakan prosedur yang diterima pakai secara am dalam memberikan diagnosis tepat dan merancang rawatan endovaskular bagi masalah penyakit pembuluh darah yang komplex. Tujuan kajian ini adalah untuk menentukan masa aliran darah dalam arteri kaki sebelum dan selepas revaskularasi yang berjaya dalam bentuk time density curve pada aplikasi syngo iFlow pada imej angiografi.

**Metodologi:** Seramai 45 pesakit telah dikaji dari imej substraksi angiografi sebelum dan selepas revaskularasi salur darah kaki yang berjaya. Masa yang diperlukan untuk mencapai kepekatan maksima kontras di dalam salur darah ini di tentukan melalui aplikasi syngo iFlow. Purata dan sisihan piawai yang diperolehi bagi setiap pengukuran, dan tahap kepentingan telah ditentukan (P < 0,05).

**Keputusan:** Seramai 45 pesakit yang berjaya dirawat mealui kaedah revaskularasi dikaji (25 lelaki, 19 perempuan). Kesempitan salur darah dikategori kepada kurang dari 50% sempit 2 pesakit; 50-75% sempit 37 pesakit; 76-99% sempit 6 pesakit. Terdapat signifikan perbezaan masa aliran darah antara kawasan pangkal and hujung salur darah sempit untuk pesakit yang belum dirawat (p-<0.001) . Purata perbezaan ini adalah 0.84s dengan purata setiap kawasan salur darah pangkal dan hujung sempit adalah 3.94s(0.43) dan 4.78s(0.80) masing-masing. Terdapat juga kepentingan perbezaan masa aliran darah antara kawasan pangkal dan hujung salur darah sempit untuk pesakit yang sudah dirawat (p-<0.001) . Purata perbezaan ini adalah 0.34s dengan purata setiap kawasan salur darah pangkal dan hujung sempit adalah 3.90s(0.39) dan 4.16s(0.52) masing-masing. Sebelum rawatan, purata TTP antara kawasan salur darah sempit bagi kawasan pangkal dan hujung adalah 3.94s dan 4.78s. Kemudian selepas rawatan berubah kepada 3.90s dan 4.16s. Peratusan kemajuan masa

yang terbanyak adalah 62% (n=10), kedua terbanyak adalah 83% (n=6) dan 78% (n=6). Dengan menggunakan analisis t-test terdapat kepentingan kemajuan masa yang diperoleh pada salur darah sebelum dan selepas dirawat (p < 0.01).

**Konklusi:** Terdapat kepentingan kemajuan perubahan masa dalam parameter bagi pesakit sebelum dan selepas rawatan revaskularasi yang berjaya. Ini membuktikan aplikasi syngo iFlow bole dijadikan aras penanda awal dalam menentukan keberjayaan proses revaskulari salur darah kaki.

**Kata kunci:** *time density curve; time to peak; digital subtraction angiography (DSA); revascularization; parametric color coding* 

**Background:** Digital subtraction angiography (DSA) remains the gold standard in diagnosing complicated peripheral vascular disease and is the only imaging modality capable of visualizing endovascular treatments in all contexts. The purpose of the study is determine the means different of arterial flow time (FT) of DSA on the lower limb circulation pre and post successful revascularization using time density curve (TDC) on syngo iFlow application.

**Methodology:** A total of 45 patients, retrospectively review the pre and post successful revascularization blood flow time using syngo iFlow application. The blood flow time (TTP) of the successful arterial flow is determined by using the application. Mean and SDs were obtained for each measurement, and level of significance for pre and post treatment was studied (P < 0.05).

**Result:** In total of 45 subject was studied (26 male, 19 female, means age 59.3). Stenoses were graded as follows based on the angiographic finding: less than 50% stenosis 2 patients; 50-75% stenosis 37patients; 76-99%, 6 patients. There was a significant difference in means between proximal and distal stenosis for pre treatment (p-value<0.001). The mean difference of pre treatment was -0.84 with mean(SD) for pre and post stenotic segment were 3.94s(0.43) and 4.78s(0.80) respectively. There was also significant mean difference between proximal and distal stenosis for post treatment ( p-value<0.001). The mean difference of post treatment was -0.34 with mean(SD) for pre and post stenotic segment were 3.94s(0.43) and 4.78s(0.80) respectively. There was also significant mean difference between proximal and distal stenosis for post treatment ( p-value<0.001). The mean difference of post treatment was -0.34 with mean(SD) for pre and post stenotic segment were 3.90s(0.39) and 4.16s(0.52) respectively. Before treatment, means TTP time (time to peak time) between contrast time curve proximal and distal to the treated vessels segment was 3.94s and 4.78s respectively, after treatment was 3.90s and 4.156s respectively. Gain percentage of the improvement time was highest at 62% (n=10), second most 83% (n=6) and 78%

(n=6). Using pair t- test analysis, decrease in TTP time was stastistically significant pre and post treatment (p < 0.01).

**Conclusion:** With the significant changes in blood flow parameter pre and post treatment as well as improvement of the gain percentage blood flow time, syngo iFlow application can be the first marker to determine the successful rate of the revascularization technique objectively.

**Keyword:** *time density curve; time to peak; digital subtraction angiography (DSA); revascularization; parametric color coding* 

## **CHAPTER 1: INTRODUCTION AND**

## LITERATURE REVIEW

#### 1. INTRODUCTION & LITERATURE REVIEW

Peripheral vascular disease (PVD) is common diseases which can be categorize to be affected noncardiac and nonintracranial arteries. The most common cause of the peripheral vascular disease is an artherosclerosis disease and less common cause such as inflammatory disorders of arterial wall (vasculitis), and noninflammatory arteriopathies includes fibromuscular dysplasia (1). PVD will cause problem to the patient when there is obstruction or narrowing of the vessels to the supplied organ. There are many treatment approach recommended for these disease. There are includes medical treatment such as single- agent antiplalete agent and statins in conjunction with efforts to reduce risk factors such as smoking cessation and getting away from sedentary lifestyle (2). However these treatments are mainly concern in slowing the progression of artherosclerotic disease systemically and when those treatments are fail, then endovascular approach will be introduce as the next step of management (2). However, the timing and need for revascularization should be evaluated and the hemodynamic condition of the vascular lesion should be assessed.

Understanding the hemodynamic conditions of vascular lesions in the lower limb is important to obtain the correct diagnoses of peripheral vascular disease and strategizing treatment (3). Non-invasive imaging modalities, such as CT and MR perfusion, provide information on the hemodynamic status within the vessels. Contrasted CT angiography is now a standard and well-validated method for obtaining the information on level of stenosis/ obstruction as well as the severity of the disease. Digital subtraction angiography (DSA) remains the gold standard in diagnosing complicated peripheral vascular disease and it is the only imaging modality capable of visualizing endovascular treatments in all contexts (3). Currently, the morphology of vasculature is well-demonstrated in modern flat-panel angiography suites using high spatial and temporal resolution. Recently, several vendors provide software for dynamic flow velocity evaluation with the visualization of a complete run in full color (Siemens SyngoiFlow, GE AngioViz, Philips 2D Perfusion) (4). Previous studies were represented the new approaches for blood flow velocity measurement using X-ray angiographic images. Pereira, Ouared (5) proposed a method for the estimation of arterial hemodynamic flow from X-ray video densitometry data and validated using an in vivo setup. Bogunović and Lončarić (6) developed two new algorithms for the measurement of blood flow from dynamic X-ray angiographic images. Shpilfoygel, Close (7) reviewed over 100 manuscripts related to blood flow quantification from digital subtraction angiography and illustrated the advantage of using optical flow-type methods in combination with DSA.

Some of the advantages of this method (optical flow method) which has been described in previous study are used for blood flow rate and velocity measurements (8). The calculation of the movement of the contrast material is assumed to be a good representation of the blood flow in the field of view. With the introduction of the optical flow method, physiological information can be obtained using post-processing techniques without additional contrast use and/or radiation exposure (8). For optical flow method there is parametric color coding of DSA run colors assigned to different contrast time arrival to the specific region and this image can be generated with one click from the application and allows us for fast visual assessment of blood flow and

perfusion in the angiography suite (9). Further time- density curve will be generated from the color coding imaging for region of interests (ROIs) which placed within the vascular structure, allowing us to quantify the blood flow and give us the objective assessment of the revascularization (10).

Yet one of the main remaining problem in assessment post revascularization is that it cannot be quantified and it solely dependent on the experience of the examiner by eye balling measurement. There is other method for visualizing and quantifying the blood flow however it cannot be measures or performed immediately during an angiographic intervention session. Examples of those method includes computational fluid dynamic models, time of flight magnetic resonance angiography or time-resolved MRA which some of these method have shown their high diagnostic value. Unfortunately it needs to be done in different setting and different modality.

In this study, we investigated the use of DSA images as in the form of optical flow to quantitatively compare blood flow in the time density curve between pretreatment and post-treatment stenotic vessel. The quantitative results using this approach can be assessed and can be utilized in the future for clinical evaluations.

#### **REFERENCES:**

1. Kullo IJ, Rooke TW. Peripheral Artery Disease. New England Journal of Medicine. 2016;374(9):861-71.

2. O'Donnell ME, Reid JA, Lau LL, Hannon RJ, Lee B. Optimal Management of Peripheral Arterial Disease for the Non-Specialist. The Ulster Medical Journal. 2011;80(1):33-41.

3. Hennion DR, Siano KA. Diagnosis and treatment of peripheral arterial disease. American family physician. 2013;88(5):306-10.

4. Zenteno M, Moscote-Salazar Luis R, Lee A. Roles and rules of Syngo iFLOW in neuroendovascular procedures. Romanian Neurosurgery2013. p. 305.

5. Pereira VM, Ouared R, Brina O, Bonnefous O, Satwiaski J, Aerts H, et al. Quantification of internal carotid artery flow with digital subtraction angiography: validation of an optical flow approach with Doppler ultrasound. AJNR American journal of neuroradiology. 2014;35(1):156-63.

6. Bogunović H, Lončarić S. Blood Flow and Velocity Estimation Based on Vessel Transit Time by Combining 2D and 3D X-Ray Angiography. In: Larsen R, Nielsen M, Sporring J, editors. Medical Image Computing and Computer-Assisted Intervention – MICCAI 2006: 9th International Conference, Copenhagen, Denmark, October 1-6, 2006 Proceedings, Part II. Berlin, Heidelberg: Springer Berlin Heidelberg; 2006. p. 117-24.

7. Shpilfoygel SD, Close RA, Valentino DJ, Duckwiler GR. X-ray videodensitometric methods for blood flow and velocity measurement: a critical review of literature. Medical physics. 2000;27(9):2008-23.

8. Su H, Lou W, Gu J. Clinical values of hemodynamics assessment by parametric color coding of digital subtraction angiography before and after endovascular therapy for critical limb ischaemia. Zhonghua yi xue za zhi. 2015;95(37):3036-40.

9. Ho Y-J, Chang M-B, Lin Y-H, Yao C-H, Huang T-C. Quantitative Portal Vein Velocity of Liver Cancer Patients with Transcatheter Arterial Chemoembolization on Angiography. The Scientific World Journal. 2012;2012:830531.

10. Bonnefous O, Pereira VM, Ouared R, Brina O, Aerts H, Hermans R, et al. Quantification of arterial flow using digital subtraction angiography. Medical physics. 2012;39(10):6264-75.

**CHAPTER 2 : STUDY PROTOCOL** 

#### 2. STUDY PROTOCOL

#### **2.1 TITLE**

Quantitative assessment of lower limb digital subtraction angiography post successful revascularisation using optical flow method (Syngo iFlow).

#### **2.2 OBJECTIVES**

#### 2.2.1 General objective

To determine blood flow timing on time density curve of DSA using Syngo I-flow application on the lower limb circulation pre and post successful revascularization.

#### 2.2.2 Specific objectives:

1. To determine the blood flow time (FT) to reach the maximum contrast opacification based on time density curve of lower limb vessels (artery) pre and post revascularization by using syngo iFlow application.

To compare the mean difference of blood flow time (FT) between proximal and distal stenotic vessels in the pre treatment using paired t-test. And also to compare mean difference of blood flow time (FT) between proximal and distal stenotic vessels in the post successful revascularization using paired t-test.
To determine the gain percentage of blood flow time (gain flow time) between pre and post revascularization by using equation:

**FTpre** = difference blood flow time (FT) to reach the maximum contrast opacification based on time density curve of lower limb vessels (artery) pre treatment (flow time at distal stenosis (pretreatment vessel) – flow time at proximal stenosis (pretreatment vessel)) **FTpost** = difference blood flow time (FT) to reach the maximum contrast opacification based on time density curve of lower limb vessels (artery) post treatment (flow time at distal stenosis (post treatment vessel) – flow time at proximal stenosis (post treatment vessel))

Gain = FT post - FT pre x 100%

#### FT pre

4. To compare mean difference of blood flow time (FT) in proximal stenosis vessels between pre and post successful revascularization using independent t-test. And also to compare mean difference of blood flow time (FT) in distal stenosis vessel between pre and post successful revascularization using independent t-test.

#### 2.3 METHODOLOGY:

#### 2.3.1 Study Design

This is a cross sectional study which will be conducted in Hospital Universiti Sains Malaysia (HUSM).

#### 2.3.2 Study location and duration

Study was conducted in Hospital Universiti Sains Malaysia (HUSM) from January 2013- December 2016

2.3.3 Study population and Sample

#### 2.3.3.1 Reference Population:

Subject age 18 years old and above in Kelantan

#### 2.3.3.2 Source Population:

Subjected for revascularization with successful revascularization in Hospital Universiti

Sains Malaysia, Kubang Kerian, Kelantan

2.3.4 Sampling technique

Non probability purposive sampling

2.3.5 Sampling frame

#### 2.3.5.1 Inclusion Criteria

1. 18 years old and above.

2. Males and females with peripheral vascular disease subjected for revascularization with successful revascularization. (Revascularization included the angioplasty, stenting as well as the drug coated angioplasty)

#### 2.3.5.2 Exclusion criteria

- 1. Patients with chronic renal insufficiency
- 2. Patient with congestive heart disease
- 3. Suboptimal imaging quality due to motion artifacts.
- 4. Missing images from PACS.

#### 2.3.6 Sample Size Calculation

1. For objective 1, the sample size was calculated using Sample Size Calculator version 1.7, updated August 2015 from website: www.medic.usm.my/biostat that are analysed by single proportion. Based on the successful prevalence of angioplasty review and prevalence of 10% of peripheral vascular disease of worldwide population by Michael et al 2015 corresponding 95% confidence interval, estimated proportion 10%, an interval of width 5% and drop out 10% sample size needed is 42.

2. For objective 2, the sample size was calculated using Sample Size Calculator version 1.7, updated August 2015 from website: www.medic.usm.my/biostat that are analysed by two means comparison (paired). Based on previous literature review in 2012 by Huang et al, using power of study 0.8, significant level 0.05, standard deviation of 2.357, means paired difference of 0.982 with drop out 0.1, sample size needed is 38 with corrected sample of 45.

3. For objective 3, there was no previous literature was found with identical measurement. Therefore, sample size will be based on highest sample size.

4. For objective 4, the sample size was also calculated using Sample Size Calculator version 1.7, updated August 2015 from website: www.medic.usm.my/biostat that are analysed by two means comparison. Based on previous literature review in 2012 by Huang et al, using power of study 0.8, significant level 0.05, standard deviation of 1.948, means difference of 0.974 with drop out 0.1 sample size needed is 32 with corrected sample of 36.

Total actual sample needed 45.

#### 2.3.7 Research Tools

- 1. Artis Zee Biplane (AXIOM-Artis Zee® Siemens Health Care, Germany)
- Picture Archive Communication System (PACS) in HUSM.(PACS Universal Viewer Version 5.0 SP6)
- Diagnostic workstation with 2 Mega Pixel monitor- (Barco MPG 2121 monitor- resolution 2048 x 1536)
- 4. Scan protocol Scanning parameters used: 120 kV, 410 mAs, and scan: AP, lateral

#### **Motion artefact**

Abnormal radiographic images which usually appear as shading or streaking in the reconstructed image due to voluntary motion or involuntary motion of the subject during body scanning.

#### Revascularization

Restoration of the blood circulation of an organ or area by interventional radiologist using angioplasty, stenting as well as the drug coated angioplasty.

#### Successful revascularization

Defined as restoration of inline flow through the affected vessel with <30% stenosis at the end of the procedure.

#### Patients with chronic renal insufficiency

Progressive loss of glomerular function caused by a long-standing renal parenchymal disease with the glomerular filtration rate (GFR) is less than 60 ml/min/1.73  $m^2$  (calculation according to National Kidney foundation)

#### Patient with congestive heart disease

Inability of the heart to pump sufficiently to maintain blood flow to meet the body's needs with reduction of the ejection fraction is less than 40%.

#### **Digital Subtraction angiography**

Is a fluoroscopy technique used in interventional radiology to clearly visualize blood vessels in a bony or dense soft tissue environment.

#### Syngo iFlow

Application on DSA that provides the visualization of complete DSA run in color coded single image that can calculate and display flow curves for single pixels which clinician can evaluate the inflow and outflow of contrast in dedicated pixels or region of interest (ROIs) such as time to maximal opacification or area under curve.

#### Angioplasty

Minimally invasive endovascular procedure to widen the narrowed or obstructed arteries or vein.

#### 2.3.9 Data Collection

- 1. Data of age, gender, and race will be collected from Radiology Information System (RIS) and Picture Archive Communication System (PACS) in HUSM.
- 2. All subjects will be labelled with serial number in order to maintain privacy and confidentiality of subject.
- 3. Data collected will be kept in subjects' data sheet.

#### 2.3.10 Image acquisition

 Subjects will be collected from the PACS. Subject will be screened against the inclusion/exclusion criteria. The clinical and angiographic information were retrospectively collected.

- 2. Images will be selected in anterior-posterior (AP) or lateral (LAT) position obtained at 6 frames/s. To prevent bias each sample will be determine the leading artery by an interventional radiologist and diagnostic radiologist.
- 3. The beginning of the arterial phase was defined as the first time frame when the contrast appeared in the artery, and the end of the arterial phase was defined as the first time frame when the contrast disappeared.
- Both pre and post treatment AP or lateral views of DSA were acquired. The selected regions of interest (ROIs) were chosen to represent intravascular regional blood flow of lower limb artery.
- 2.3.11 Image analysis
- All subjects underwent successful revascularization in the Advance Minimally Invasive Endovascular Neurointerventional Unit (AMIEN) in angiography room by using imaging system installed by Global Siemens Healthcare Company called Artis Zee Biplane (AXIOM- Artis Zee® Siemens Healthcare, Germany). Successful revascularization is defined as restoration of inline flow through the affected vessel with <30% stenosis at the end of the procedure.</li>
- 2. A method for blood flow velocity estimation using optical images based on the optical flow method (OFM) that links all the motion subjects between the phases on optical images will be used. The gradient-based OFM basically calculates the flow information according to the changes in image intensity on successive images in pixels per second.
- 3. In this study, the OFM algorithm was applied to estimate the blood flow time at the arterial phase for both the AP or lateral DSA images for pre and post treatment evaluations.

- 4. In all of the patients, the mean arterial blood flow time was defined as the average blood flow time needed to reach the maximum contrast enhancement at selected ROIs in the arteries.
- 5. Selected ROIs specific at proximal part of the respective artery and used as reference point (ROI *ref*), two further ROIs were placed within respective artery directly proximal (ROI 1) and distal (ROI 2) to the stenotic vessel segment. All ROIs had identical surface area of 6.9mm2.
- 6. For ROI *ref*, point of interest was allocated at the normal main vessel which proximal to the stenotic vessel, for ROI *l*(proximal to stenotic vessel) point of interest was allocated at least 1cm just before the stenotic vessel, meanwhile for ROI 2(distal to stenotic vessel) point of interest was also allocated at least 1cm just after the stenosis.
- For each ROI, data points of acquired time density curve (TDC) were exported for further analysis. Time to reached maximum contrast intensity in the ROI *1* and ROI *2* of treated vessel segment was computed in the pre and post treatment data, which refer to time to peak (TTP) in the following.
- 8. The perioperative changes were evaluated to assess the efficacy of revascularization. Parametric color coding of blood flow velocity was applied to facilitate visual comparison. The percentage gains of the treatments in blood flow velocity time among the patients were obtained using the following equation:

## Gain = F<u>T *post* – FT *pre*</u> x 100% FT pre

where FTpre and FTpost are the pre and post treatment blood flow velocities.

**FTpre** = difference blood flow time (FT) to reach the maximum contrast opacification based on time density curve of lower limb vessels (artery)

pre treatment (flow time at distal stenosis (ROI2) – flow time at proximal stenosis (ROI1))

**FTpost** = difference blood flow time (FT) to reach the maximum contrast opacification based on time density curve of lower limb vessels (artery) post treatment (flow time at distal stenosis (ROI2) – flow time at proximal stenosis (ROI1))

Larger values of gain indicate better restoration of blood flow velocity time.

- Statistical analysis will be perform using PASW Statistics software version 17.0.2 for Windows (SPSS) for comparison of average blood flow time within ROIs before and after treatment.
- 2.3.12 Statistical analysis
  - The blood flow time of proximal and distal stenotic of pre and post revascularization of lower limb will obtain in means and difference of blood velocity time was compared using paired t test.
  - 2. The gain percentage (gain time) of blood flow time between pre and post revascularization will be calculated by using

 The mean difference of blood velocity between pre and post successful revascularization of proximal and distal stenotic vessel will be compared using independent t-test.

## **CHAPTER 3: MANUSCRIPT**

#### **3.1 TITLE PAGE**

## QUANTITATIVE ASSESSMENT OF THE LOWER LIMB DIGITAL SUBTRACTION ANGIOGRPAHY POST SUCCESSFUL REVASCULARIZATION USING OPTICAL FLOW METHOD (Syngo iFlow)

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I have the genuine respect and being thankful to my mentor and philosopher Associate Professor Dr. Mohd Shafie for granting me the opportunity to do this project. With his support and guidance, I was able to complete it within the stipulated time. His dedication, keen interest and overwhelming attitude to assist his student have definitely eased off the uphill task. Apart from that, his timely advice, meticulous scrutiny, scholarly advice and scientific approach have helped me to a great extent to accomplish this project.

Alhamdulillah, I would like to dedicate this research to my wife, my sons and my family whom have injected me the morale to regain the hope after despair, to restart the journey after every detour, to revive the strength after the defeat and to resurrect the dream after rejections. Above all, this is also as a symbol of submission to the Great Almighty, the author of knowledge and wisdom for the countless love to His servant.

#### 3.2.1 TITLE

QUANTITATIVE ASSESSMENT OF THE LOWER LIMB DIGITAL SUBTRACTION ANGIOGRAPHY POST SUCCESSFUL REVASCULARIZATION USING OPTICAL FLOW METHOD (Syngo iFlow)

#### 3.2.2 ABSTRACT

**Background:** Digital subtraction angiography (DSA) remains the gold standard in diagnosing complicated peripheral vascular disease and capable of visualizing endovascular treatments plan. The purpose of the study is determine the means different of arterial flow time of DSA on the lower limb circulation pre and post successful revascularization using time density curve (TDC) on Syngo I-flow application.

**Methods:** A total of 45 patients, retrospectively review the pre and post successful revascularization blood flow time using Syngo i-flow application. Mean and SDs were obtained for each measurement, and level of significance for pre and post treatment was studied (P < 0.05).

**Result:** In total of 45 subject was studied (26 male, 19 female, means age 59.3). Stenosis were graded as follows based on the angiographic finding: less than 50% stenosis 2 patients; 50-75% stenosis 37patients; 76-99%, 6 patients. There was a significant mean difference between pre and post stenosis for pre treatment (p-value<0.001). The mean difference of pre treatment was -0.84 with mean(SD) for pre and post stenotic segment were 3.94(0.43) and 4.78(0.80) respectively. There was also significant mean difference between pre and post stenosis for post treatment ( p-value<0.001). The mean difference between pre and post stenosis for post treatment ( p-value<0.001). The mean difference between pre and post stenosis for post treatment ( p-value<0.001). The mean difference between pre and post stenosis for post treatment ( p-value<0.001). The mean difference of post treatment was -0.34 with mean(SD) for pre

and post stenotic segment were 3.90(0.39) and 4.16(0.52) respectively. Before treatment, means TTP time (time to peak time) between contrast time curve proximal and distal to the treated vessels segment was 3.94s and 4.78s respectively, after treatment was 3.90s and 4.156s respectively. Gain percentage of the improvement time was highest at 62% (n=10). Using t- test analysis, improvement in TTP time was statistically significant between pre and post treatment (p < 0.01).

**Conclusion:** With the significant changes in blood flow parameter as well as improvement of the gain percentage blood flow time, syngo iFlow application can determine the successful rate of the revascularization technique objectively.

**Keyword:** *time density curve; time to peak; digital subtraction angiography (DSA); revascularization; parametric color coding* 

#### 3.2.3 INTRODUCTION

In obtaining correct diagnosis and strategizing treatment for peripheral vascular disease, it is important to understand the hemodynamic conditions of the vascular lesion. CT and MR perfusion can provide the information on hemodynamic status within the vessels as a non-invasive imaging modalities. Contrasted CT angiography is now a standard and well-validated method for obtaining the information on level of stenosis/ obstruction as well as the severity of the disease.

According to Hennion and Siano (3) digital subtraction angiography (DSA) remains the gold standard in diagnosing complicated peripheral vascular disease and is the only imaging modality capable of visualizing endovascular treatments. Morphology of the vasculature can be visualized and demonstrate in modern flat-panel angiosuites using high spatial and temporal resolution. In current setting there are software that have been provided by several vendors to evaluate the dynamic flow of the blood vessel with visualization of complete run in color coding setting for example ; Siemens SyngoiFlow, GE AngioViz and Philips 2D Perfusion. In previous studies, they were represented as the new approaches for blood flow velocity measurement using X-ray angiographic images.

Study by Pereira, Ouared (5) has proposed a method for the estimation of arterial hemodynamic flow from X-ray video densitometry data and validated using an in vitro setup. Other study by Bogunović and Lončarić (6) has developed two new algorithms for the measurement of blood flow from dynamic X-ray angiographic images. Critical review of literature has been done by Shpilfoygel, Close (7) and over 100 manuscripts related to blood flow quantification from digital subtraction angiography and illustrated the advantage of using optical flow-type methods in combination with DSA. This has been proved that color coding angiography has big impact in evaluating physiological information that can be obtained using postprocessing technique without additional contrast use and/or radiation exposure.

In this study, we investigated the use of DSA images in the form of optical flow to quantitatively compare blood flow in the time density curve between the pretreatment and the post-treatment stenotic patients. The quantitative results using this approach can be assessed and can be utilised in the future for clinical evaluations.

#### 3.2.4 MATERIAL/ SUBJECT METHOD

This study was a cross sectional study which was approved by our ethical review board, 45 patients with successful revascularization in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan from 2013-2017 was included. Subject age are 18 years old and older.

#### **3.2.4.1** Angiography and Optical flow imaging

All angiography examinations were performed by using Artis Zee Biplane (AXIOM-Artis Zee® Siemens Health Care, Germany). Scan protocol are scanning parameters used: 120 kV, 410 mAs, and scan: AP or lateral. Images will be selected in anteriorposterior (AP) or lateral (LAT) position obtained at 6frames/s. All this imaging were archived from Picture Archive Communication System (PACS) in HUSM (PACS Universal Viewer Version 5.0 SP6). Conventional imaging AP or lateral also obtain pre and post revascularization. Both pre and post treatment AP or lateral views of DSA were acquired and color coded images are generated automatically by using syngo