AD Early Detection: Carotid Artery Reactivity Comparison between Healthy Young and Aged People

Mohd A. Jamlos, Eko Supriyanto

Abstract**—**Early detection of Alzheimer Disease (AD) is very important in order to have high chance to be cured from this disease. It could be done through assessing the carotid artery condition since the impairment of this artery leads to the central process of Alzheimer. Ability of the artery to dilate shows it is in a good shape. This kind of dilation is called carotid artery reactivity (CAR) where the more the artery able to dilate, the better the condition of the artery. The artery dilation could be measured using its blood flow velocity as the parameter. High blood flow velocity is the sign of wide dilation of the carotid artery. Healthy people and Alzheimer patient is believed to have different carotid artery reactivity value. At the same time, different age of healthy people also have different value. Hence, this study emphasize on finding the normal reactivity value belong to the group of young and aged healthy people. This normal value could be used to differentiate between healthy people and Alzheimer patient. All 40 subjects whose are less than 30 years old for young subjects and people aged more than 50 years old for aged people have been scanned with ultrasound machine using Doppler technique before and after having exercise to achieve 85% of their Maximal Heart Rate (MHR). Readings of carotid artery blood flow velocity before exercise (rest) and after exercise (stimulated) are taken to be compared to obtain its percentage increment value (reactivity). Based on the result, the young normal carotid artery reactivity value is 143.6% for male and 103.3% for female meanwhile for aged normal carotid artery reactivity value is 105% for male and 74% for female.

Keywords**—**Alzheimer disease (AD), Doppler imaging, carotid artery reactivity (CAR), healthy aged people

I. Introduction

Alzheimer disease is known as progressive neurodegenerative disorder primarily resulted in neuronal function disruption and cognitive and behavioral dysfunction due to the accumulation of neuritic plaques and neuropathological tangles [2]. Hippocampus and entorhinal cortex are two significant structures located in medial temporal lobe suggested to be affected in the earliest phase of the disease while temporal, frontal and parietal cortices are involved during the rest of the disease progresses. Age is always related as the main risk factor for almost all neurodegenerative diseases especially AD. Eventhough aged people is always have higher chance to get AD, it does not mean healthy young people are totally safe from AD. Healthy young people also have the potential to get AD if they do not take any precaution measurements needed and always check their health status from time to time [7].

Due to the expectation of increasing in life span particularly in developed countries' citizens, more people will have higher risk and potential to get AD [4]. Within the period of 25 years, efforts done to have more understanding on basic principle of AD are based on two independent lines of research. The first line is the study on molecular level of the protein deposits in order to obtain the identification of their major components while the second line is the study on rare and inherited disease. [23]. AD has a widely variety of presentation and clinical course made it among one of the heterogeneous disorder disease. Because of that, it is quite difficult to measure the severity of AD as the cognitive decline rate is different among AD patient [3]. Among the biggest risk factors to get AD are age, insulin resistance or diabetes and genetic [24]. However, all these factors do not ensure in increasing the rate of AD progress as a lot of patients experienced either slow or fast rate without any present of those risk factors [3].

Early detection among potential individuals to get AD is very essential in order to reduce the risk of AD where it has affected 24.3 million people worldwide in 2010 with increment around 4.6 million yearly [3]. In Malaysia only, it is estimated that there are currently about 50,000 people with this disease. However, most of them are not diagnosed due to relatives think that the symptoms displayed are a normal part of growing old and lack of awareness about the dangerousness of AD [6].

Treatment in the early stage is very efficient in treating AD especially before any clinical symptoms shown [4]. For the sake of detecting AD at early stage, structural and functional brain has to be evaluated first. Fundamentally, single photon emission tomography (SPECT) and positron emission tomography (PET) are used for brain functional imaging while computed tomography (CT) and magnetic resonance imaging (MRI) are used for brain structural imaging. SPECT and PET will show reduced neuronal function in human brain such as altered cerebral glucose and

Manuscript received October 3, 2011
Mohd Aminudin Jamlos is with the Diagnostics Research Group, Biotechnology Research Alliance, Universiti Teknologi Malaysia (UTM) Skudai, 81310, Johor Bahru, Johor Malaysia (e-mail: mohdaminudin86@gmail.com).
Eko Supriyanto is with the Diagnostics Research Group, Biotechnology Research Alliance, Universiti Teknologi Malaysia (UTM) Skudai, 81310 Johor Bahru, Johor Malaysia (e-mail: eko@biomedical.utm.my).

altered cerebral blood flow while CT and MRI will show tissue atrophy due to loss of synapses and neurons because of AD process [5]. However, the developed methods are high risk due to radiation utilization for PET, SPECT and CT scanning meanwhile high cost and long scanning duration for MRI scanning. Hence, ultrasound machine is utilized in order to replace those conventional methods since this modality is quickly, safely, accurately and cost effectively in detecting AD at early stage [18,19].

It has been proven before that AD could be accurately detected by analyzing carotid artery structure. This is due to vascular abnormalities have the great potential to lead to vascular dysfunction which able to stimulate synaptoxic B-amyloid (AB) accumulation in the brain considered as the central process for AD formation [6]. This kind of protein is known as amyloid-like filaments that formed plaques and tangles of AD. Amyloid-like filaments are made up of Amyloid-b (AB) and tau where they are normally soluble proteins at the beginning [24]. The problem rises when overproduction of beta-amyloid occurred and the brain fails to dispose it at the same time. It will cause excess jams signaling at the synapses, blocking information flow and the worst is leading to brain cell death [13].

Thus, a lot of new techniques have been explored to study vascular function in term of cerebral blood flow (CBF) including diffusion weighted imaging (DWI), diffusion tensor imaging (DTI), arterial spin labeling (ASL) and blood oxygenated level dependent (BOLD) [7]. However, doppler imaging technique using ultrasound machine is the most suitable one compared to other method since this modality has been used safely, accurately, cost effectively and quickly in measuring carotid artery blood flow velocity [1]. Hence, it is very important to assess carotid artery structure and its condition using ultrasound machine. This could be done through analyzing of carotid artery reactivity (CAR) in term of its blood flow velocity as previous studies found that AD could be accurately detected by analyzing of cerebral vessel reactivity (CVR) [6]. CAR indicates the capacity of blood vessels to dilate when being stimulated by several particular stimuli where the bigger the dilation, the better the condition of carotid artery (CA) [8]. Well-functioned carotid artery has the ability to dilate for reserve capacity reacted towards any dilatory stimulus is a very essential method in regulating and maintaining constant cerebral blood flow in healthy human. It has been suggested that in order to have a continuous physiologic blood supply for brain, CAR must be in normal range of reading for healthy human [12].

Determining the CAR value could be done with measuring the carotid artery blood flow [9,11] which automatically increase the carotid blood flow (CBF) [10]. In order to confirm that carotid artery reactivity can be used to detect AD in early stage, characterization of carotid artery blood flow in healthy people need to be obtained first so that it can be compared and analyzed with Alzheimer patient later. All the subjects have undergone adequate exercise to stimulate carotid artery reactivity under hypertension condition. In this study, a significant value has been acquired for normal carotid artery reactivity among young and aged healthy people since everyone has the potential to get AD. With this value, someone can use it as a reference value to categorize either he or she has Alzheimer disease or not. Currently, most of the studies related to diagnosing AD are always use cerebral vessel as the main indicator and drug or CO2 as the stimulator [17]. However, cerebral vessel study needs expert personnel to handle the expensive transcranial Doppler ultrasound to obtain good and accurate result. According to Kolb B. et al, carotid artery blood flow could replace the cerebral blood flow [14]. Hence, carotid blood flow will be the main indicator in this study which allows utilization of conventional Doppler ultrasound and easy to handle in obtaining accurate and good result.

II. MATERIALS AND METHODS

This study is divided into two different parts which are carotid artery wall reactivity measurement for young healthy people as well as for aged healthy people. Carotid artery wall reactivity for young people is done first followed by measurement for aged healthy people. Reactivity measurement is done to observe dilation capability of carotid artery under hypertension condition (exercise condition). Human subjects' carotid artery consist of 20 each of male and female being scanned using doppler ultrasound scan technique during normal (rest) and stimulated (exercise) condition.

A. *Data acquisition*

In this study, 20 subjects of male and female each are selected to be participated for data collection. They are invited to have free scanning on the carotid artery using Doppler ultrasound imaging technique. 40 healthy subjects which are below than 30 years old for young meanwhile 50 years old and above are considered as aged subject. All of them are non smoker, free from any vascular disease and have normal blood pressure. Before start data collection, their details such as name, identification card number, age, weight, height, blood pressure and oxygen concentration are taken. Personal interview between the subject and the researcher also done to ensure the subjects are really fit and suitable to participate in this study. Table 1 and 2 shows the average value for young and old subject details respectively. Carotid artery wall reactivity are being measured in this part. The measurement results are considered as the normal carotid artery wall reactivity value.

Table 1
Details of young subjects

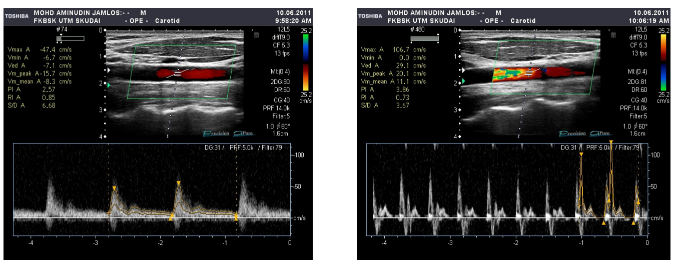
Characteristics	Average Value
Mean age	22.5 ± 3.3
Mean weight	70 kg ± 8.5
Mean height	165.7cm ± 5.4
Mean blood pressure	125/83 mm Hg ± 8.4/6.2
Mean oxygen concentration	99% ± 1.5

Table 2
Details of aged subjects

Characteristics	Average Value
Mean age	59.5 ± 5
Mean weight	73kg ± 10
Mean height	163cm ± 7.8
Mean blood pressure	130/90 mm Hg ± 10.2/5.7
Mean oxygen concentration	95% ± 3.5

B. Measurement

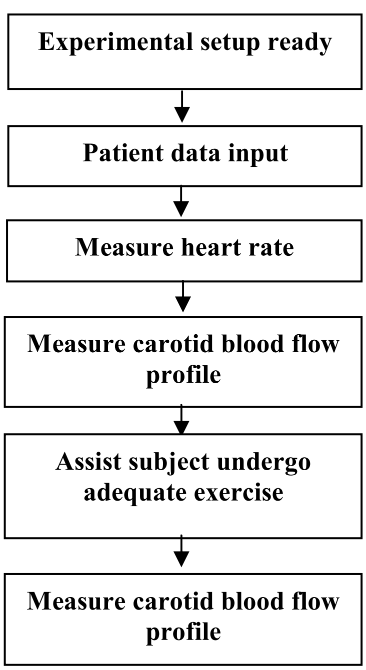
For the measurement, there are some steps to be done to get the data acquired. Figure 1 shows the data acquired which is image of Doppler ultrasound carotid artery during rest and exercise.



(Rest) (Exercise)

Figure 1: Doppler ultrasound carotid artery images during rest and exercise

Meanwhile figure 2 show the flow chart of carotid artery characterization process in human.



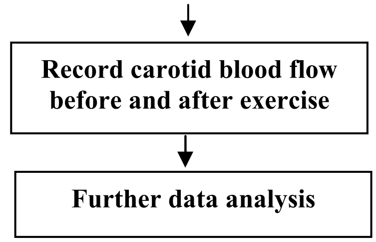


Fig. 2: Flow chart of carotid artery characterization

This measurement is done with two different parts which are under rest condition (normal) and under exercise condition (stimulated). After being explained by the researcher, the subject started the process of the experiment. The heart rate and carotid artery blood flow velocity under rest condition are taken simultaneously. Heart rate reading is taken using patient monitor while ultrasound machine with doppler imaging technique have been utilized to record the carotid artery blood flow. Figure 3 shows how the velocity of carotid artery blood flow determined. It could be obtained through two different methods which are manually measure the amplitude of the graph or automatically calculated by the ultrasound machine.

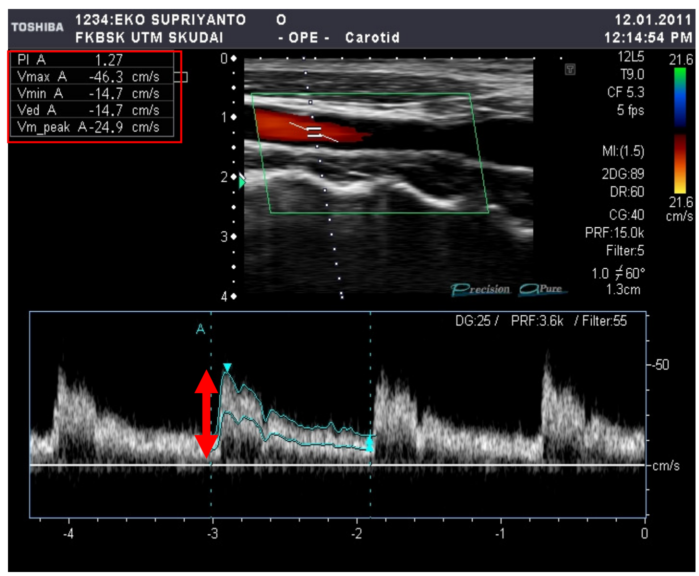


Figure 3: Carotid artery blood flow velocity

Heart rate and carotid artery blood flow velocity are recorded in beat per minute and centimeter per second respectively. When all the required data are taken, subject asked to have adequate exercise on the treadmill. The period of the exercise and the speed of the treadmill are not fix as long as the heart rate of the subject achieve 85% of maximal heart rate. Adequate exercise has been used as the stimulator to create carotid artery reactivity. The reactivity state could be achieved when the subject heart rate reach 85% of its maximal heart rate after having adequate exercise [16]. Maximal heart rate (MHR) is calculated in beat per minute (bpm) and determined with specific formula [15]. The formulas are shown as followed:

Male MHR : 220 – age (1)
Female MHR : 200 – age (2)

Subjects asked to warm up their body first to avoid any injury during the exercise period. The subject heart rate is being observed during all the time of exercise and once the subject achieves the target heart rate, he or she will be scanned immediately using ultrasound machine to record his or her carotid artery wall structure. This is because to avoid decline of the subject heart rate in order to remain the target heart rate during the recording process of carotid artery structure. Subjects are asked to have rest first and being ensured they are in good condition before leaving examination room.

C. Doppler Scan Protocol

Doppler ultrasound scan is used in this study to evaluate carotid artery reactivity. It provides carotid artery blood flow velocity reading. Doppler scan is done due to it is able to detect the changes of carotid artery blood flow velocity due to responds for human body physiology. The highest reading of blood velocity during rest and exercise are selected to find the changes of the velocity. The differences between these two data are compared and analyzed in order to find its reactivity value.

Structure of carotid artery is being scanned using Toshiba Diagnostic Ultrasound System machine (Aplio MX SSA-780A). The probe used is PLT-1204 MV linear transducer. The 12-MHz transducer is placed at the middle right of the subject neck to obtain the desired images. The transducer has to be in contact with subject neck and remain static during the recording and reconstructing process. The data desired is taken or record only when the image of 2D carotid artery is shown at the monitor of ultrasound machine clearly and constantly. Otherwise, the data obtained can not be considered as accurate data. The highest signal is determined at depth ranging from 1 to 2 cm and gain of 80 dynamic range (DR) [20-22].

D. Data Analysis

The condition of the carotid artery is being assessed in this study. The assessment is based on its reactivity. The reactivity of carotid artery could be determined through the blood flow velocity passed it. The faster the blood flow, the more the carotid artery reacted. The more the carotid artery reacted, the better the condition of the carotid artery. Figure 4 and 5 shows the image of normal (rest) and stimulated (exercise) carotid artery image respectively. The normal image has slower velocity blood flow while the stimulated image has higher velocity of blood flow.

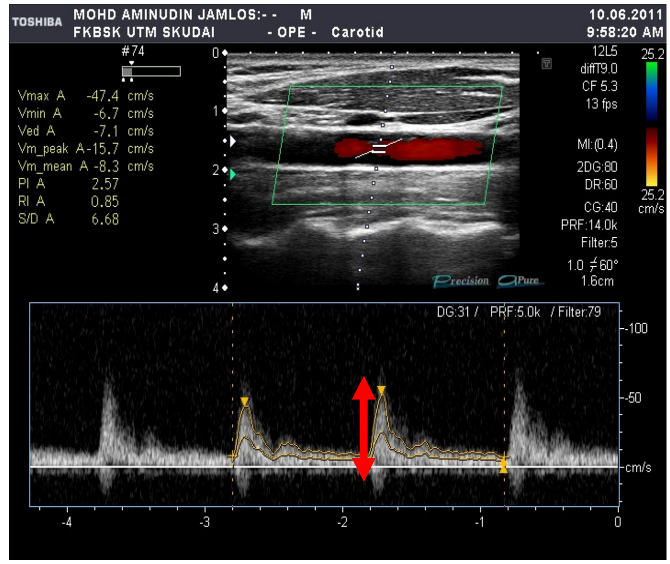


Figure 4: Normal (rest) Doppler carotid artery image

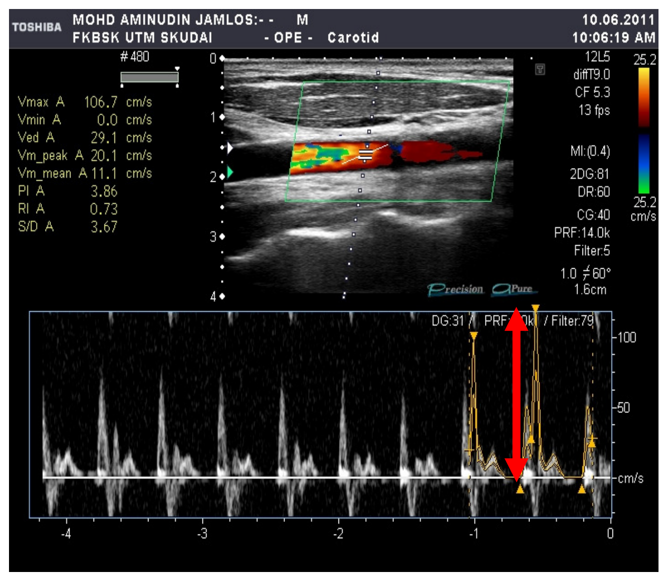


Figure 5: Stimulated (exercise) Doppler carotid artery image

In this study, unharmed exercise method has been selected as the stimulator for the carotid artery to react or dilate as big as possible. Hence, the maximum carotid artery blood flow velocity before and after having exercise will be compared and analyzed to find the increment percentage and at the same time find the normal carotid reactivity among young and aged healthy people. This normal value could be used to compare with the value belong to Alzheimer patient so that it could be used as the main indication to categorize healthy people and Alzheimer patient. The normal carotid reactivity value could be obtained through below formula:

$$\Delta V = \frac{V_{CAS} - V_{CAN}}{V_{CAN}} \times 100 \quad (1)$$

Where ΔV= percentage of increment, V_{CAS} = Stimulated carotid artery velocity, V_{CAN}= Normal carotid artery velocity

$$\Delta V = V_{CAS} - V_{CAN} \quad (2)$$

Where ΔV= Increment value, V_{CAS} = Stimulated carotid artery velocity, V_{CAN} = Normal carotid artery veloity

III. Result and Analysis

All results from this study are shown in this section. It includes the readings of carotid artery blood flow velocity and subject heart rate which are taken during rest and exercise state for young and aged healthy people.

A. Carotid Artery Reactivity Measurement

The results of carotid artery reactivity measurement are shown in this part. The reactivity values show the ability of the carotid artery wall to dilate under hypertension technique. It includes the readings of carotid artery blood flow velocity and subject heart rate which are taken during rest and exercise state.

Table 3: Carotid artery blood flow velocity changes of young male subject

n^{th} subject	Rest (normal)(cm/s)	Exercise (stimulated)(cm/s)
1	51.5	99.9
2	60.5	130
3	47.4	106.7
4	70.9	169.7
5	60.8	151.3
6	49.9	124.2
7	54.5	139.7
8	51.8	138.8
9	45.5	123
10	44.8	121.5
Average value	53.76	130.48

Table 3 shows the result for 10 young male subjects. The results show the reading carotid artery blood flow velocity (cm/s) during rest (normal) and exercise (stimulated) condition. From the result, the lowest velocity for rest condition is 44.8 meanwhile the highest one is 70.9. The average velocity for rest condition is 53.76 cm/s. On the other hand, the lowest velocity for stimulated condition is 99.9 meanwhile the highest one is 169.7. The average velocity for stimulated condition is 130.48 cm/s.

Table 4: Carotid artery blood flow velocity changes of young female subject

n^{th} subject	Rest (normal)(cm/s)	Exercise (stimulated)(cm/s)
1	110.5	163.2
2	67.2	104.1
3	60.2	102.3
4	59	117.2
5	51.5	111.2
6	53.7	120.8
7	50.6	115.7
8	50	124.6
9	47	127.3
10	42.5	117.2
Average value	59.2	120.4

Table 4 shows the result for 10 young female subjects. The results show the reading carotid artery blood flow velocity (cm/s) during rest (normal) and exercise (stimulated) condition. From the result, the lowest velocity for rest condition is 42.5 meanwhile the highest one is 110.5. The average velocity for rest condition is 59.2 cm/s. On the other hand, the lowest velocity for stimulated condition is 102.3 meanwhile the highest one is 163.2. The average velocity for stimulated condition is 120.4 cm/s.

Table 5: Carotid artery blood flow velocity changes of aged male subject

n^{th} subject	Rest (normal)(cm/s)	Exercise (stimulated)(cm/s)
1	55.3	99.1
2	54.9	100.5
3	47	90.1
4	49.8	93.7
5	60.4	125.8
6	46.7	100.2
7	42.1	90.8
8	50.5	111.2
9	44.5	98.7
10	44.9	105.5
Average value	49.6	101.6

Table 5 shows the result for 10 aged male subjects. The results show the reading carotid artery blood flow velocity (cm/s) during rest (normal) and exercise (stimulated) condition. From the result, the lowest velocity for rest condition is 42.1 meanwhile the highest one is 60.4. The average velocity for rest condition is 49.6 cm/s. On the other hand, the lowest velocity for stimulated condition is 90.1 meanwhile the highest one is 125.8. The average velocity for stimulated condition is 101.6 cm/s.

Table 6: Carotid Artery blood flow velocity changes of aged female subject

n^th^ subject	Rest (normal)(cm/s)	Exercise (stimulated)(cm/s)
1	61.5	87.9
2	64.4	93
3	58	88.3
4	63.5	107.1
5	51.2	94.5
6	45.1	85
7	47	88.8
8	47.5	90.3
9	48	91.9
10	51.8	101.2
Average value	53.8	92.8

Table 6 shows the result for 10 aged female subjects. The results show the reading carotid artery blood flow velocity (cm/s) during rest (normal) and exercise (stimulated) condition. From the result, the lowest velocity for rest condition is 45.1 meanwhile the highest one is 64.4. The average velocity for rest condition is 53.8 cm/s. On the other hand, the lowest velocity for stimulated condition is 85 meanwhile the highest one is 107.1. The average velocity for stimulated condition is 92.8 cm/s.

D. Analysis carotid artery blood flow and heart rate increment

The percentage increment values which are the target data consist of normal carotid artery reactivity percentage are shown in these following tables.

Table 7: Carotid Artery blood flow velocity increment in young male

n^{th} subject	Increment value(cm/s)	Increment percentage (%)
1	48.4	94
2	69.5	114.8
3	59.3	125.1
4	98.8	139.3
5	90.5	148.8
6	74.3	148.9
7	85.2	156.3
8	87	167.9
9	77.5	170.3
10	76.7	171.2
Average value	76.7	143.6

Table 7 shows the lowest increment value among young male subjects is 48.4 cm/s while the highest one is 76.7 cm/s. The average increment value is 76.7 cm/s. On the other hand, the lowest carotid artery blood flow velocity increment percentage is 94% while the highest one is 171%. The average for this increment percentage is 143.6%.

Table 8: Carotid Artery blood flow velocity increment in young female

n^{th} subject	Increment value (cm/s)	Increment percentage (%)
1	52.7	47.6
2	36.9	54.9
3	42.1	69.9
4	58.2	98.6
5	59.7	115.9
6	67.1	124.9
7	65.1	128.6
8	74.6	149.2
9	80.3	170.8
10	74.7	175.8
Average value	61.2	103.3

Table 8 shows the lowest increment value among young female subjects is 52.7 cm/s while the highest one is 74.7 cm/s. The average increment value is 61.2 cm/s. Apart from that, the lowest carotid artery blood flow increment percentage is 47.6% while the highest one is 175%. The average for this increment percentage is 103.3%.

Table 9: Carotid Artery blood flow velocity increment in aged male

n^{th} subject	Increment value(cm/s)	Increment percentage (%)
1	43.8	79.2
2	45.6	83.1
3	43.1	83.7
4	43.9	88.2
5	65.4	108.3
6	53.5	114.6
7	48.7	115.7
8	60.7	120.2
9	54.2	121.8
10	60.6	135
Average value	52	105

Table 9 shows the lowest increment value among aged male subjects is 43.1 cm/s while the highest one is 65.4 cm/s. The average increment value is 52 cm/s. Apart from that, the lowest carotid artery blood flow increment percentage is 79.2% while the highest one is 135%. The average for this increment percentage is 105%.

Table 10: Carotid Artery blood flow velocity increment in aged female

n^{th} subject	Increment value (cm/s)	Increment percentage (%)
1	26.4	42.9
2	28.6	44
3	30.3	45.6
4	43.6	68.6
5	43.3	84.6
6	39.9	88.5
7	41.8	88.9
8	42.8	90.1
9	43.9	91.5
10	49.4	95.4
Average value	39	74

Table 10 shows the lowest increment value among aged female subjects is 26.4 cm/s while the highest one is 49.4 cm/s. The average increment value is 39 cm/s. Apart from that, the lowest carotid artery blood flow increment percentage is 42.9% while the highest one is 95.4%. The average for this increment percentage is 74%.

Table 11
Heart rat increment in young male subject

n^{th} subject	Increment value (bt/m)	Increment percentage (%)
1	59	79
2	77	88
3	71	102
4	82	127
5	87	128
6	83	139
7	90	139
8	99	140
9	82	149
10	111	179
Average value	82	127

Table 11 shows the lowest heart rate increment value among young male subjects is 59 while the highest one is 111. The average increment value is 82 bt/m. On the other hand, the lowest heart rate increment percentage is 79% while the highest one is 179%. The average for this increment percentage is 127%.

Table 12
Heart rate increment of young female subject

n^{th} subject	Increment value (cm/s)	Increment percentage (%)
1	58	70
2	61	71
3	60	75
4	63	77
5	69	78
6	66	79
7	70	88
8	65	105
9	85	119
10	84	121
Average value	69	88

Table 12 shows the lowest heart rate increment value among young female subjects is 58 while the highest one is 85. The average increment value is 69 bt/m. On the other hand, the lowest heart rate increment percentage is 70% while the highest one is 121%. The average for this increment percentage is 88%.

Table 13: Heart rate increment in aged male subject

n^{th} subject	Increment value (cm/s)	Increment percentage (%)
1	77	88
2	65	89
3	73	90
4	69	91
5	80	97
6	63	98
7	66	99
8	62	101
9	71	104
10	81	111
Average value	70	97

Table 13 shows the lowest heart rate increment value among aged male subjects is 62 while the highest one is 81. The average increment value is 70bt/m. On the other hand, the lowest heart rate increment percentage is 88% while the highest one is 111%. The average for this increment percentage is 97%.

Table 14: Heart rate increment of aged female subject

n^{th} subject	Increment value (cm/s)	Increment percentage (%)
1	51	60
2	70	65
3	63	66
4	55	69
5	61	69
6	50	70
7	54	70
8	58	87
9	67	91
10	55	95
Average value	58	74

Table 14 shows the lowest heart rate increment value among aged female subjects is 51 while the highest one is 70. The average increment value is 70bt/m. On the other hand, the lowest heart rate increment percentage is 60% while the highest one is 95%. The average for this increment percentage is 74%.

E. Correlation between heart rate and carotid artery blood flow velocity

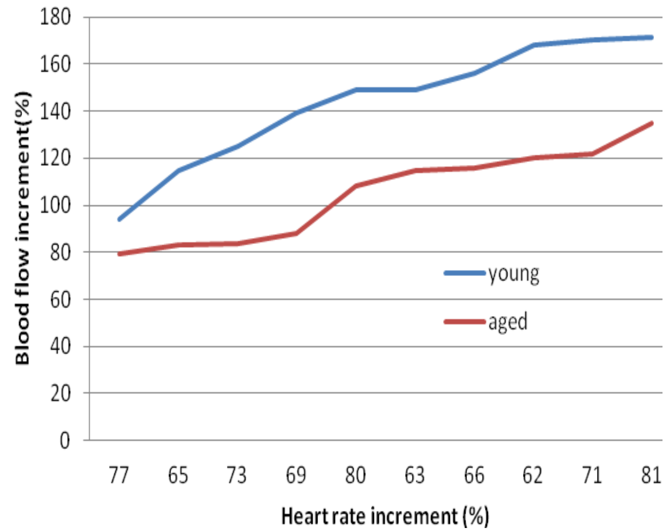


Fig. 3: Correlation between heart rate and CA blood flow in male subjects

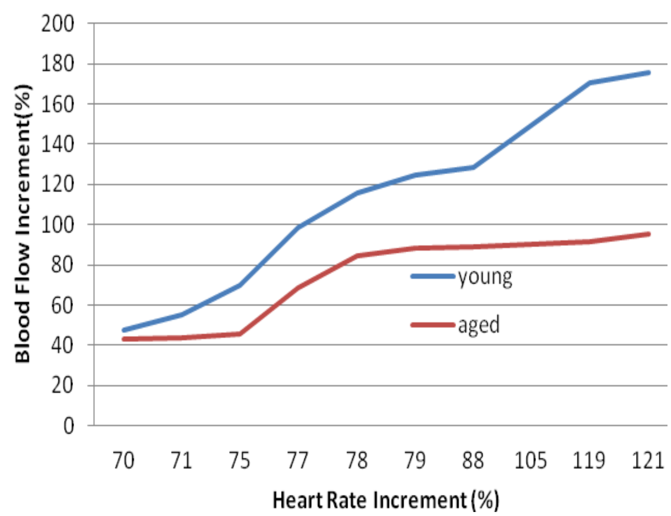


Fig. 4: Correlation between heart rate and CA blood flow in female subjects

Figure 3 and 4 represent the correlation between heart rate and carotid artery blood flow velocity for male and female respectively. Both figures show that the carotid artery blood flow velocity is directly proportional to heart rate. It also shows that young healthy people whether male or female have higher value of blood flow increment percentage when the heart rate is increase. The faster the blood flow, the higher the heart rate will be. Hence, the higher the heart rate, the more the carotid artery dilates. This is due to compensate the

faster and higher amount of blood flow from heart towards brain to fulfill high metabolic demands of neural activity
.

F. Comparison between young and aged on carotid artery characterization

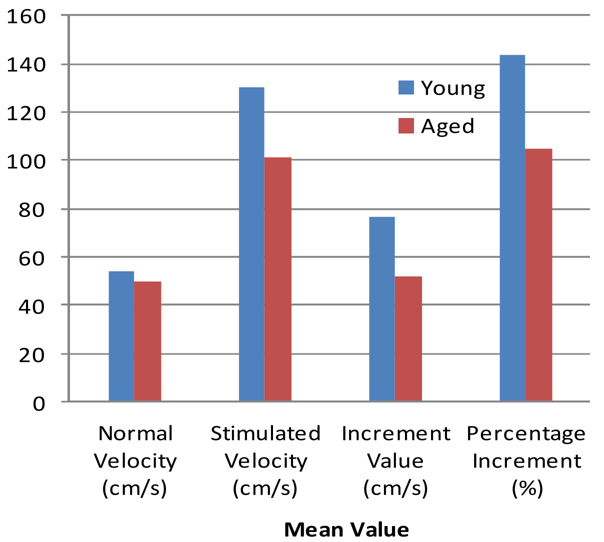


Fig. 5: Overall comparison between young and aged male

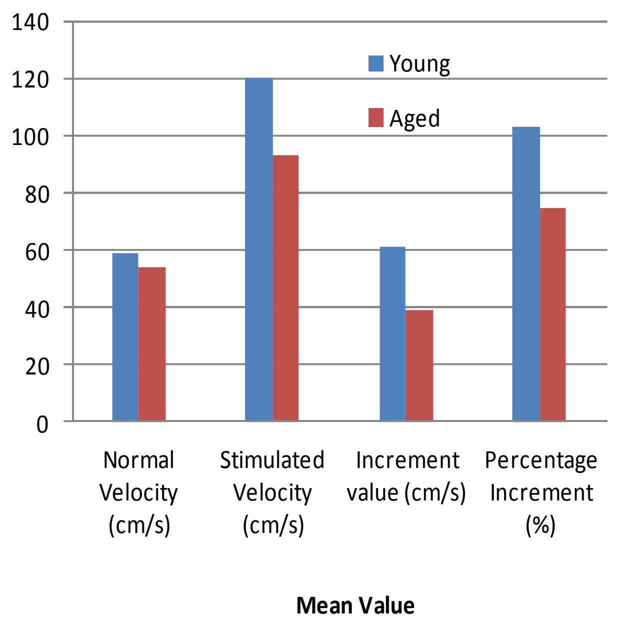


Fig. 6: Overall comparison between young and aged female carotid artery characterization.

Figure 5 and 6 show the overall comparison between young and aged male and female carotid artery characterization respectively. It shows that young healthy people will have higher value than aged healthy people regardless the gender in all parameters which are normal carotid artery blood flow velocity, stimulated carotid artery blood flow velocity, carotid artery blood flow increment value and carotid artery blood flow percentage increment. This might be due to young people still have actively dividing cell to generate new cell in order to maintain the good structure of carotid artery. On the other hand, aged people experience degeneration of the cell due to the natural aging process will lead to impairment of carotid artery structure that cause lower carotid artery reactivity value.

IV. CONCLUSION

As conclusion, this study is successfully in assessing the reactivity of human carotid artery. It is able to measure the carotid artery blood flow velocity changes due to the reaction from the carotid artery or the dilation effect of the carotid artery. This is because the carotid artery responded towards the hypertension condition realized by adequate exercise. This study found that the normal carotid reactivity value among young healthy people is 143.6% for male and 103.3% for female meanwhile the normal carotid reactivity value among aged healthy people is 105% for male and 74 % for female. This normal carotid artery reactivity value can be used as an indicator to evaluate the risk to get AD. Apart from that, this study also found that carotid artery blood velocity is directly proportional to heart rate. Hence, carotid artery reactivity measurement method can be projected as a new approach to contribute in early detection of Alzheimer disease.

V. ACKNOWLEDGEMENT

This work is fully support by Ministry of Science, Technology and Innovation (MOSTI) Malaysia under grant of Science Fund Vot No. Q: J130000.7136.00H25. The authors would like to thank to Research Management Centre (RMC), Biotechnology Research Alliance (RA), and Faculty of Health Science and Biomedical Engineering, Universiti Teknologi Malaysia (UTM) for their support.

REFERENCES

[1] E. Supriyanto, M. A. Jamlos, N. Humaimi, and L. K. Kheung, " Segmentation of Carotid Artery Wall towards Early Detection of Alzheimer Disease" in Proceedings of the 15th WSEAS International Conference on Circuits, Corfu Island, Greece, July 14-16, 2011, pp. 201-206.

[2] Prince S. E., Woo S., Doraiswamy P. M., Petrella J. R., "Functional MRI in the early diagnosis of Alzheimer's disease: is it time to refocus?", Expert Rev. *Neurotherapeutics* (2008) 8 (2), 169-175

[3] Lopez O. L. et al, "Predicting cognitive decline in Alzheimer's disease: An integrated analysis", Alzheimer's & Dementia 6 (2010) 431–439

[4] Mueller S. G. et al, “Alzheimer’s Disease Neuroimaging Initiative” (2008), University of California, San Francisco, California, USA
[5] Wierenga C. E., Bondi M. W., “Use of Functional Magnetic Resonance Imaging in the Early Identification of Alzheimer’s Disease”, *Neuropsychol Rev* (2007) 17: 127-143
[6] Wong S. H. et al, “Antioxidant Intake and Mild Cognitive Impairment Among Elderly People in Klang Valley: A Pilot Study”, Sains Malaysiana 39(4)(2010): 689–696
[7] Morris J. C., Storandt M., Miller P., McKeel D. W., Price J. L., Rubin E. H., Berg L., “Mild Cognitive Impairment Represents Early-Stage Alzheimer Disease”, *Arch Neurol*. (2001) 58:397-405
[8] Mueller S. G., Weiner M. W., Thal L. J., Petersen R. C., Jack C. R., Jagust W., Trojanowski J. Q., Toga A. W., Beckett L., “Ways toward an early diagnosis in Alzheimer’s disease: The Alzheimer’s Disease Neuroimaging Initiative (ADNI)”, *Alzheimer’s & Dementia 1* (2005) 55–66
[9] Yeshuvath U. S., Uh J., Cheng Y., Cook K. M., Weiner M., Arrastia R. D., Osch M. V., Lu H., “Forebrain-dominant deficit in cerebrovascular reactivity in Alzheimer’s disease”, *Neurobiology of Aging* (2010) 02.005
[10] Tarawneh R., Holtzman D. M., “Biomarkers in translational research of Alzheimer’s Disease”, Neuropharmacology 59 (2010) 310-322
[11] Scwertfeger N., Neu P., Schlattmann P., Lemke H., Heuser I., Bajbouj M., “Cerebrovascular reactivity over time course in healthy subjects”, Journal of the Neurological Sciences 249 (2006) 135-139
[12] Wierenga C. E. and Bondi M. W., “Use of Functional Magnetic Resonance Imaging in the Early Identification of Alzheimer’s Disease”, Neuropsychol Rev (2007) 17: 127-143
[13] Yeshuvath U. S., Amezcua K. L., Varghese R., Xiao G., “On the assessment of cerebrovascular reactivity using hypercapnia BOLD MRI”, NMR Biomed. (2009) 22 (7): 779-786
[14] Kolb B., Diane L., Rotella, Stauss H. M., “Frequency response characteristic of cerebral blood flow autoregulation in rats”, Am J Physiol Heart Circ Physiol (2007) 292: H432-H438.
[15] Tanaka H., Monahan K. D., Seals D. R., “Age-Predicted Maximal Heart Rate Revisited”, Journal of the American College of Cardiology (2001) Vol. 37, No. 1.
[16] Nishime E. O., Cole C. R., Blackstone E. H., Pashkow F. J., Lauer M. S., “Heart Rate Recovery and Treadmill Exercise Score as Predictors of Mortality in Patients Referred for Exercise ECG”, JAMA. (2000)284:1392-1398.
[17] Mitsuhashi N., Onuma T., Kubo S., Takayanagi N., Honda M., Kawamori R., “Coronary Artery Disease and Carotid Artery Intima-Media Thickness in Japanese Type 2 Diabetic Patients”, *Diabetes care,* volume 25, number 8, august 2002.
[18] Goedert M. and Spillantini M. G., “A Century of Alzheimer’s Disease”, *Science* 314 (2006) 777.
[19] Carrillo M. C., Blackwell A., Hampel H., Lindborg J., Sperling R., Schenk D., Jeffrey J. Sevigny J. J., Ferris S., Bennett D. A., Craft S., Hsu T., Klunk W., “Early risk assessment for Alzheimer’s disease”, Alzheimer’s & Dementia 5 (2009) 182–196
[20] Hum Yan Chai, Lai Khin Wee, Eko Supriyanto, Ultrasound Images Edge Detection using Anisotropic Diffusion in Canny Edge Detector Framework, WSEAS TRANSACTION, 2011
[21] Mahani Hafizah, Tan Kok, E Supriyanto, Development of 3D Image Reconstruction Based On Untracked 2D Fetal Phantom Ultrasound Images using VTK. WSEAS Transactions on Signal Processing.
[22] Yagel S. And Valsky D. V., “From anatomy to function: the developing image of ultrasound evaluation”, *Ultrasound Obstet Gynecol* 2008; 31: 615–617
[23] Goedert M. and Spillantini M. G., “A Century of Alzheimer’s Disease”, *Science* 314 (2006) 777.
[24] Carrillo M. C., Blackwell A., Hampel H., Lindborg J., Sperling R., Schenk D., Jeffrey J. Sevigny J. J., Ferris S., Bennett D. A., Craft S., Hsu T., Klunk W., “Early risk assessment for Alzheimer’s disease”, Alzheimer’s & Dementia 5 (2009) 182–19

Prof. Eko Supriyanto is a biomedical engineer. He is head of Diagnostics Research Group, Universiti Teknologi Malaysia. He obtained his PhD in medical electronics from University of Federal Armed Forces, Hamburg, Germany. His research interest is engineering application in medicine. He has more than 130 international publications in the area of medical electronics, medical image processing and medical computing. He has 22 national and international innovation awards and more than 10 patents of biomedical products.