REPEATABILITY OF MEASURES OF ARTERIAL FUNCTION

DETERMINING THE REPEATABILITY OF LOW FLOW MEDIATED CONSTRICTION AND TOTAL VESSEL REACTIVITY IN THE BRACHIAL ARTERY OF HUMANS

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TITLE: Determining the Repeatability of Low Flow Mediated Constriction and Total Vessel Reactivity in the Brachial Artery of Humans

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LAY ABSTRACT

Endothelial function is the ability of arteries to expand and contract. Endothelial dysfunction has been linked to an increased risk for cardiovascular disease (CVD). The most widely used test to assess endothelial function is the flow mediated dilation test (FMD). Two novel measures of endothelial function, low flow mediated constriction (L-FMC) and total vessel reactivity (TVR) have been introduced as supplements to FMD, however little is known about the repeatability of these measurements. Additionally, it is unknown whether L-FMC and TVR are influenced by age, sex, CVD or CVD risk factors. We investigated the day-to-day repeatability of FMD, L-FMC and TVR, and their relationships with age and the influence of sex and CVD and elevated CVD risk. We found that FMD and TVR, but not L-FMC, were repeatable and associated with age. We also found that sex or CVD did not alter the relationship between age and our measures.

ABSTRACT

Endothelial function is the ability of an artery to vasodilate and can be assessed using a flow mediated dilation (FMD) test. While FMD is a useful tool for assessing endothelial function, it has been argued that it does not capture overall vascular function. Two novel measures, low flow mediated constriction (L-FMC) and total vessel reactivity (TVR) have been introduced to compensate for the potential limitations of FMD. Unfortunately, little is known about the repeatability of brachial artery L-FMC and TVR. Additionally, it is unclear how L-FMC and TVR might be influenced by age, sex and the presence of cardiovascular disease (CVD) or CVD risk. Therefore, the main purpose of this investigation was to assess the day-to-day repeatability of FMD, L-FMC and TVR in the brachial artery. The secondary purpose was to assess if FMD, L-FMC and TVR were associated with age and if this relationship was influenced by sex or the presence of CVD or CVD risk factors. 375 participants (age:37±22) were included in the study, 98 participants (age:34±19) underwent two FMD tests and were included in the repeatability analysis. For all participants brachial artery endothelial function was assessed using a FMD test. The day-to-day repeatability of FMD was substantial (ICC=0.68), L-FMC was slight (ICC=0.01) and TVR was moderate (ICC=0.50). Age was associated with FMD and TVR (ρ=-0.24, ρ=-0.19, $p<0.005$), however there was no relationship between age and L-FMC. The relationships between age and FMD and TVR persisted in individuals with CVD and CVD risk factors, and sex did not moderate the relationship between age and any of our vascular outcomes. These results indicate that brachial artery FMD and

TVR are relatively repeatable, however L-FMC is not repeatable. As well, it appears that age is associated with a decrease in FMD and TVR, but not related to L-FMC.

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LIST OF ACRONYMS

BH_4	tetrahydrobiopterin
CAD	coronary artery disease
CP	cerebral palsy
CV	coefficient of variation
CVD	cardiovascular disease
EDHF	endothelial derived hyperpolarizing factor
EE	ethinyl estradiol
eNOS	endothelial nitric oxide synthase
ER_{α}	estrogen receptor alpha
ER_{β}	estrogen receptor beta
ET-1	endothelin-1
ET_A	endothelin receptor A
ET_B	endothelin receptor B
FMD	flow mediated dilation
GMP	guanosine monophosphate
ICC	intraclass correlation coefficient
L-FMC	low flow mediated constriction
MBV	mean blood velocity
NO	nitric oxide
NTG	nitroglycerin challenge test
OCP	oral contraceptive pill

SCI	spinal cord injury
SFA	superficial femoral artery
TVR	total vessel reactivity

LIST OF EQUATIONS

Chapter 1:

(1) $TVR\ \% = \dfrac{maximal\ diameter - occlusion\ diameter}{occlusion\ diameter}\ X\ 100$

(2) $TVR\ \% = \ |FMD\% + L - FMC\%|$

Chapter 2:

(1) $FMD\ (mm) = \ maximum\ diameter - baseline\ diameter$

(2) $FMD\ (\%) = \dfrac{maximum\ diameter - baseline\ diameter}{baseline\ diameter}\ X\ 100$

(3) $L - FMC\ (mm) = \ occlusion\ diameter - baseline\ diameter$

(4) $L - FMC\ \% = \dfrac{occlusion\ diameter - baseline\ diameter}{baseline\ diameter}\ X\ 100$

(5) $TVR\ \% = \dfrac{maximum\ diameter - occlusion\ diameter}{occlusion\ diameter}\ X\ 100$

(6) $Absolute\ NTG\ (mm) = peak\ NTG - baseline\ NTG$

(7) $Relative\ NTG\ (\%) = \dfrac{peak\ NTG - baseline\ NTG}{baseline\ NTG}\ X\ 100$

(8) $Blood\ flow\ \left(\dfrac{mL}{min}\right) = (\pi r^2\ x\ MBV)\ x\ 60\ \ where\ r = arterial\ diameter/2$

(9) $Shear\ rate\ (s^{-1}) = \dfrac{MBV\ x\ 8}{arterial\ diameter}$

DECLARATION OF ACADEMIC ACHEIVEMENT

VIR and MJM conceived the study. VIR led the study development, completed the data collection and data analysis of the prospective cohort, as well as analyzed some of the occlusion images from the retrospective data. VIR was responsible for data interpretation. MJM provided the retrospective dataset from studies previously conducted under her supervision, assisted with study development, data interpretation and provided funding for the project. Christopher Gupta assisted with study development and data collection. Kajeetha Sarvananthan and Jennifer Williams assisted with data collection.

CHAPTER 1: LITERATURE REVIEW

INTRODUCTION 1.1

Cardiovascular disease (CVD) is the second leading cause of death in Canada, claiming over 53 000 lives in 2017 (101). Evidence of early signs of atherosclerosis are present in children and progress with age (82). Results from the Framingham study, a longitudinal study assessing CVD, indicate that there are a variety of risk factors that predispose an individual to develop cardiovascular disease (45). These risk factors include inactivity, obesity, hypertension, cigarette smoking, diabetes and hypercholesterolemia (41, 44, 45). While these risk factors play a large role in the development of CVD, they are unable to predict 100% of CVD risk (18, 32). As a result, researchers have begun to focus on novel risk factors for CVD, such as endothelial function, which is a measure of the function of the arterial wall (32). Endothelial dysfunction refers to altered arterial wall function and is thought to be the first step in the development of atherosclerosis (21, 71).

1.1.1 Arterial Anatomy

Arteries consist of three main tissue layers; the tunica externa, the tunica media and the tunica intima (67, 94). The tunica externa is a layer of connective tissue, mainly comprised of collagen that surrounds the artery and helps maintain the relative position of the artery (67). The tunica media is the thickest arterial layer and consists primarily of smooth muscle that encircles the artery in a circular pattern (67, 94). The tunica media regulates arterial diameter through vasoconstriction and vasodilation (67). The tunica intima is comprised of specialized cells called endothelial cells that directly contact blood flowing through the lumen of the artery (67). It was once thought that endothelial cells

were a passive barrier between blood and the other arterial tissue layers, however research has now determined that these cells play an important physiological role in modulating arterial diameter (67).

1.1.2 Endothelial Function

The endothelium is a monolayer of cells which regulate vasomotion through the production of various vasoactive substances, as well as vessel wall inflammation, smooth muscle cell proliferation and cellular adhesion (21). The ability of the endothelial cells to influence arterial diameter is fundamental to ensuring tissue oxygen and metabolic demands are met (21).

1.1.2.1 Endothelial Dependent Vasodilation

Endothelial dependent vasodilation refers to the ability of endothelial cells to promote vasodilation (86). This function can be activated through a variety of pathways, one of which is triggered when blood flowing through the artery imposes a shear stress on the endothelial cells (17, 84, 86). The shear stress promotes the opening of calcium-activated potassium channels, which hyperpolarizes the endothelial cell, leading to calcium influx (17). Calcium influx activates endothelial nitric oxide synthase (eNOS) which converts L-arginine to nitric oxide (NO) (17, 84). From here, nitric oxide diffuses to the vascular smooth muscle where it stimulates soluble guanylate cyclase, an enzyme that converts guanosine triphosphate to cyclic guanosine monophosphate (GMP) (60). The increase in cyclic GMP causes relaxation of the smooth muscle cell layer, which ultimately results in vasodilation (60). Lower levels of endothelial function (also known as endothelial dysfunction) have been shown to be predictive of future cardiovascular

events in both symptomatic and asymptomatic individuals (32, 86). Endothelial function has been suggested to be a marker of both traditional and novel CVD risk factors and endothelial dysfunction is thought to be the first step in the progression of atherosclerosis (21, 32).

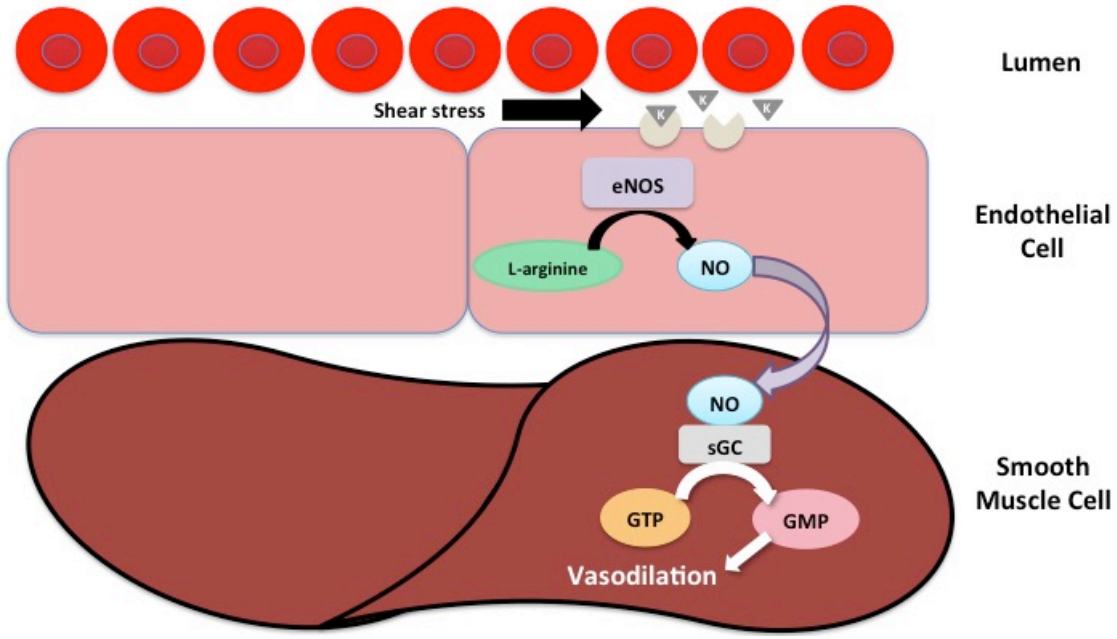

Figure 1. The mechanism of endothelial dependent vasodilation. Potassium (K), endothelial nitric oxide synthase (eNOS), nitric oxide (NO), soluble guanylate cyclase (sGC), guanosine triphosphate (GTP), guanosine monophosphate (GMP).

1.1.2.2 Endothelial Dependent Vasoconstriction

Endothelial cells also have the ability to induce vasoconstriction (21). The main vasoconstrictor substance that is produced by the endothelial cells is endothelin-1 (ET-1) (93). ET-1 was first described in 1988, and since then two other isoforms, endothelin-2 and endothelin-3 have been discovered, however only ET-1 is produced by the endothelium in humans (72, 93, 99). The release of ET-1 is mediated by a variety of factors, including shear stress (46). Specifically, low levels of shear stress have been

shown to increase the release of ET-1, intermediate levels of shear stress have been shown to result in initial increases then decreases in ET-1 release, and high levels of shear suppress the release of ET-1 (49). When ET-1 is produced it binds to endothelin receptors ET_A and ET_B (4). ET_A and ET_B receptors are located on the vascular smooth muscle and ET_B receptors are located on the endothelium (10). Binding of ET-1 to the endothelin receptors on the vascular smooth muscle produces vasoconstriction, however binding of ET-1 to the endothelium has been shown to increase NO and prostacyclin production (10). ET-1 imposes its vasoconstrictor effects on vascular smooth muscle through a complicated signaling process that involves many pathways (46). In the classical signaling pathway, ET-1 binds to ET_A on the vascular smooth muscle, which activates phospholipase C (46, 93). Phospholipase C produces inositol triphosphate and diacylglycerol from phosphatidylinositol (46). Inositol triphosphate then binds to receptors on the endoplasmic reticulum, causing in an increase in intracellular calcium, which results in vasoconstriction (46). It has been suggested that elevated plasma levels of ET-1 are involved in certain pathological states, such as hypertension (93).

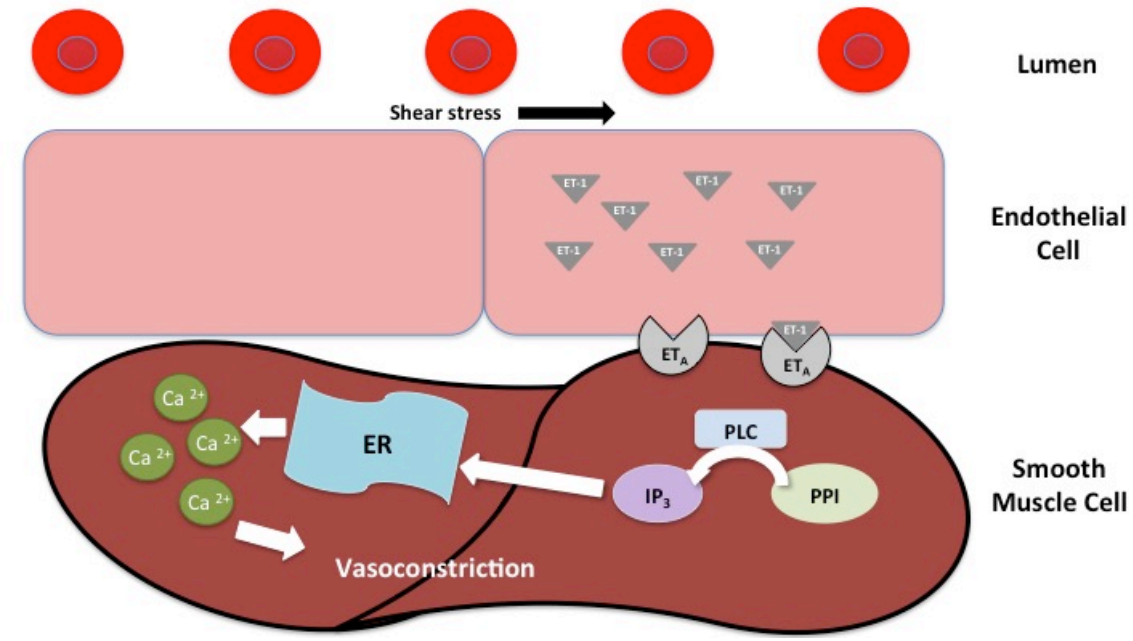

Figure 2. The mechanism of endothelial dependent vasoconstriction. Endothelin-1 (ET-1), endothelin receptor A (ET_A), phospholipase C (PLC), inositol triphosphate (IP_3), phosphatidylinositol (PPI), endoplasmic reticulum (ER), calcium (Ca^{2+}).

1.1.2.3 Measures of Endothelial Function

As endothelial function has been implicated as a marker of cardiovascular health, there have been a variety of techniques introduced to assess both the vasodilatory and vasoconstrictor capacity of endothelial cells.

Infusion Methods

The most direct method of assessing endothelial function is through angiography accompanied by the infusion of vasoactive substances, and this technique has been primarily applied to investigations of coronary arteries (92). Specifically, a guide wire along with a catheter is placed into the coronary artery of interest (53). Acetylcholine is then infused through the catheter in increasing concentrations; acetylcholine has been shown to promote vasodilation in arteries with healthy endothelial cells and

vasoconstriction in arteries with endothelial dysfunction and atherosclerosis, due to direct interaction between acetylcholine and the tunica media (53, 64, 100). Images are collected at baseline and each increment and a dose response curve is then created (53, 92). Arteries with a dose dependent increase in vasodilation are deemed healthy (92). While this method is considered the gold standard for evaluating coronary endothelial function, it is invasive, expensive and the procedure comes with potential risks for the patient (92). As a result, researchers began using a similar infusion method in the brachial artery, which is associated with fewer risks. Instead of a dose response curve however, the forearm blood flow during the acetylcholine infusion is measured using venous occlusion plethysmography and blood flow during each infusion is compared to rest to determine the level of endothelial dependent dilation that occurs (73, 92). While this infusion method is reliable and repeatable, it is still invasive and poses potential risks to participants (92).

Flow Mediated Dilation (FMD)

Flow mediated dilation (FMD), first introduced by Celermajer and colleagues in 1992, is a non-invasive measure that is used to assess the ability of endothelial cells to promote vasodilation in response to an increase in shear stress (11). FMD is performed using Duplex ultrasound to capture both the arterial diameter and blood flow of the target artery, often the brachial artery, however other arterial segments such as the radial artery, superficial femoral artery and popliteal artery can be imaged (87). Images of the artery are acquired at rest, and then a pneumatic is cuff placed around the participant's limb that is inflated to a suprasystolic level (11). The cuff can be placed either distal to the

ultrasound probe or proximal to the ultrasound probe (86). The cuff remains inflated for 5 minutes and then is released, which results in a dramatic increase in blood flow, referred to as reactive hyperemia (11, 86). An additional image of the target artery is obtained to allow determination of the maximal diameter resulting from the reactive hyperemia stimulus (11). Percent dilation is calculated relative to baseline, to assess the relative change in diameter (11). Importantly, it has been shown that endothelial function in the brachial artery measured by FMD is correlated to endothelial function of the coronary arteries as measured by acetylcholine infusion (7). Additional studies determined that FMD was largely mediated by the release of NO (86). FMD is currently the most commonly used technique to assess endothelial function and it has been suggested that a 1% increase FMD results in a 13% decrease risk of future cardiovascular events (32, 36).

Low Flow Mediated Constriction (L-FMC)

While infusion techniques and FMD have provided valuable information about endothelial function, some have argued these measures do not capture overall vascular function (29). Gori and colleagues argued that FMD only measures the "recruitability" of endothelial cells, but fails to capture basal arterial tone (29). As a result, a relatively newer measure, low flow mediated constriction (L-FMC) has been introduced to account for the limitations of FMD (28). L-FMC is a measure of the change in arterial diameter that occurs during a period of low blood flow and can be determined from data obtained during the occlusion phase of a traditional FMD test (28, 31). Unlike FMD, L-FMC is not thought to be mediated by NO, and instead is mediated through an increase of ET-1 and an inhibition of vasodilators, specifically endothelial derived hyperpolarizing factor

(EDHF) and prostaglandins (28, 80). While there has been an increased interest in L-FMC in the last decade, it was first described by Levenson and colleagues in 1987, who observed a marked decrease in mean blood flow and mean blood velocity as well as an increase in vascular resistance after 60 seconds of wrist cuff occlusion (42, 51). In 1989, Anderson and colleagues extended these findings when they performed 10 minutes of forearm occlusion while using Doppler ultrasound to image the brachial artery (6, 42). The group observed a marked decrease in blood flow during 10 minutes of forearm occlusion that was associated with a decrease in brachial artery diameter (6). In 2008, Gori and colleagues revisited the technique and since then there has been a substantial increase in L-FMC research (28). Gori *et al.* observed the presence vasoconstriction during low flow in the radial artery in a number of studies (28, 29, 31) and additional studies have also reported similar findings (20, 96). However, responses during low flow in the brachial artery appear to be variable with multiple studies reporting individual responses that range from vasodilation to vasoconstriction or no change in diameter during the low flow period (5, 34, 38, 48).

Total Vessel Reactivity (TVR)

Some studies assessing both FMD and L-FMC have reported a relationship between the two variables. Harbin *et al.*, Harrison *et al.,* and Aizawa *et al.* found a significant positive correlation between brachial artery L-FMC and FMD, while Kranen *et al.* found no such relationship (5, 34, 38, 48). Spiro and colleagues found that there was a relationship between brachial artery L-FMC and FMD in healthy individuals, but not individuals with atherosclerosis (81). Aizawa *et al.* found that the low flow response

independently predicted FMD (5). Similarly, studies assessing radial artery L-FMC and FMD have reported conflicting findings with some reporting the two measures are related (30, 96) and others not (28, 29). Total vessel reactivity (TVR, also referred to as modified FMD, vasoactive range etc.) is a composite score of FMD and L-FMC and is thought to provide a more comprehensive assessment of overall vascular function as it takes into consideration both the vasodilatory and vasoconstrictor functions of the endothelium (38, 42). However, there has been limited investigation into this novel measure, and there is no general consensus on how best to evaluate overall vascular range, as a variety of equations have been used previously (5, 9, 20, 38, 48, 69, 70). Two commonly used equations to calculate TVR are:

$$(1)\ TVR\ \% = \frac{maximal\ diameter - occlusion\ diameter}{occlusion\ diameter}\ X\ 100$$

$$(2)\ TVR\ \% = \ |FMD\% + L - FMC\%|$$

1.1.3 Endothelial Independent Vasodilation

While the previously mentioned techniques focus on assessing endothelial dependent dilation and constriction, there are also tests used to evaluate vascular smooth muscle function, independent from the endothelium. A nitroglycerin challenge test (NTG) is often used to assess endothelial independent dilation (17). This challenge test can be performed along with either the infusion technique or FMD technique for assessing endothelial dependent dilation (11, 92). For the less invasive FMD test, sublingual nitroglycerin is administered to the participant (11). Nitroglycerin is a nitric oxide donor, and has been shown to promote vasodilation by directly operating on the vascular smooth

muscle (11, 17). The percent change in diameter resulting from the administration of nitroglycerine is then calculated to determine endothelial independent vasodilation (11).

1.2 REPEATABILITY OF MEASURES OF ENDOTHELIAL FUNCTION

1.2.1 Overview

In recent years there has been a general scientific focus on ensuring study results are reproducible or repeatable. In preclinical research it is estimated that 75-90% of study findings are not reproducible (8). Groups in both physiology and psychology have attempted to address these reproducibility issues. In 2014, the National Institute of Health put forward a plan to improve reproducibility that included improved training for researchers, ensuring a more systematic approached is used for assessing grant applications and introducing a data bank where researchers could access unpublished data (15). Similarly, peer reviewed scientific journals such as *Nature* have removed restrictions on the length of methods sections to improve reporting of procedural details (15). In psychology, the Open Science Collaboration created the Reproducibility Project, which sought to understand the level of reproducibility in psychological science (66).

While improving reproducibility across studies is important, researchers can also work to ensure the methods they use are repeatable. In this case, the aim is to determine how precise or variable the measurement is from a research test (26). This type of repeatability is referred to as test-retest reliability, and is determined by performing a test multiple times on the same individual, under the same conditions (26). There are a variety of statistical methods used to assess test-retest reliability, two of which are intraclass correlation coefficients (ICC) and Cohen's Kappa. ICCs provide a measure of both the

correlation and agreement between two or more measurements (47). In general, ICCs are a ratio of the variance over the sum of the variance plus error (47, 77). ICC calculations produce a coefficient between 0-1, with 1 meaning perfect repeatability and 0 meaning poor repeatability (47). There are various forms of ICCs however, it is recommended that a two-way mixed effects model with absolute agreement be used for test-retest studies (47). Cohen's Kappa (κ) is similar to ICC in that it measures the degree of agreement or consistency between two different measurements (54). Cohen's κ can be performed on data that consists of at least two mutually exclusive categories (54). The calculation of Cohen's κ quantifies the agreement or consistency present in the measurement that is beyond the level of agreement that is expected by pure chance (54). Values of κ range from -1 to 1, a $\kappa = -1$ indicates a level of a agreement poorer than what is expected by chance, $\kappa = 0$ signifies that the level of agreement is no greater than what is expected by chance and a $\kappa = 1$ signifies perfect agreement (54).

1.2.2 Flow Mediated Dilation

There has been extensive research assessing the repeatability of FMD since its inception. In 1995, Sorensen *et al*. assessed the repeatability of brachial artery FMD in 40 adults (20 males, 20 females) aged 22-51 (79). The group measured FMD at 4 time points to assess between-day, between-week and between-month repeatability (79). The overall coefficient of variation (CV), a measure of variability, was 1.8%, indicating FMD was repeatable (79). Importantly, it appeared variation was not higher for the between-week and between-month analysis when compared to between-day variation, and variation between the sexes was similar (79). In contrast, Hardie and colleagues found that FMD

was poorly repeatable in a sample of 19 (6M, 13F) healthy adults (35). The group assessed FMD at two time points, separated by an average of 90 days, and found the mean between day difference in FMD was 0.57% with a standard deviation of 6.83% (35). Additionally, there appeared to be more variability in women when compared to men (35). However, neither of these studies controlled for the time of day the test was performed or the caffeine and food intake of the participants prior to testing (35, 79). Liang *et al.* assessed FMD in 30 (10M, 20F) healthy adults at two time points separated by an average of 2.5 weeks (52). Participants in this study were instructed to refrain from ingesting caffeine 8 hours prior to testing and ask to maintain their typical lifestyle for diet, physical activity and alcohol ingestion (52). The group reported a CV of 10.8% and concluded that FMD had satisfactory repeatability (52). Malik *et al.* assessed FMD in a group of 20 healthy men twice within a 10 day period (55). Their results indicated poor repeatability of FMD with a CV of 41% and an ICC=0.10 (55). Onkelinx and colleagues assessed the within-day and between-day repeatability of FMD in a cohort of 18 men with coronary artery disease (CAD) (65). They reported that FMD had excellent within-day (ICC=0.94) and between-day (ICC=0.99) repeatability (65). Charakida *et al.* assessed short (48 hours apart), medium (3 months apart) and long term (9 months apart) FMD repeatability in a group of 67 patients with coronary heart disease participating in a multi-site trial (14). They found that short and medium term repeatability of FMD was similar (ICC=0.80, ICC=0.74), but long term repeatability was poorer (ICC=0.58) (14).

As there appears to be lack of consensus on the repeatability of FMD within and between studies, three guideline papers have been released in 2002, 2011 and 2019

outlining recommendations for researchers to improve FMD repeatability and standardized protocols (17, 86, 87). One major recommendation centered around the pneumatic cuff placement during FMD, as some groups place the cuff distal to the ultrasound probe and others place the cuff proximal (86). It was determined that FMD assessed with the cuff placement distal to the probe was largely mediated by NO, whereas FMD with the cuff placed proximal is mediated by NO and other factors (86, 87). Therefore, it was recommended that the cuff be placed distal to the probe to ensure the FMD measured is largely endothelial NO dependent (86, 87). Some recommendations have centered on participant preparation, as more is understood about factors that influence FMD. It is recommended that participants are fasted, avoid exercise, caffeine, medication and supplements prior to testing, as these are all known to influence FMD (17, 86, 87). As well, testing should be performed in a quiet temperature controlled room at approximately the same time of day if measures are repeated (17, 86). For premenopausal women it has also been recommended that testing occur at the same time point during the menstrual cycle, optimally between day 1-7 of the menstrual cycle when estrogen levels are low (86). Guidelines for image acquisition and analysis, protocols and sonographer training have also been introduced (17, 86, 87). Importantly, Greyling and colleagues performed a systematic review of studies assessing FMD repeatability and found that greater adherence to the 2011 guidelines was associated with less variation and improved repeatability of FMD (33).

1.2.3 Low Flow Mediated Constriction

Relatively few studies have investigated the repeatability of L-FMC, and there appear to be important differences between arteries in this measure. Gori and colleagues assessed the repeatability of L-FMC in the radial artery of 25 young healthy participants (28). They found that radial artery L-FMC had substantial repeatability, reporting an ICC of 0.80 (28). Similarly, Weissgerber and colleagues investigated the repeatability of radial artery L-FMC in a cohort of 23 pregnant and 27 non-pregnant women (96). They found that L-FMC had moderate and substantial repeatability within the two groups (ICC=0.56 non pregnant women, ICC=0.86 pregnant women) (96). In contrast, studies assessing the repeatability of brachial artery L-FMC have reported conflicting findings, with some reporting low levels of repeatability and others reporting high levels of repeatability. Harbin and colleagues assessed the repeatability of brachial artery L-FMC in a cohort of 26 young adults and reported that L-FMC diameters had weak intra- and interday repeatability (34). Similarly, Kranen *et al.* assessed the day-to-day repeatability of brachial artery L-FMC in 27 adolescents using both ICCs and Cohen's κ (48). The group found there was poor agreement for L-FMC between days (κ =0.04) as well as poor repeatability between days (ICC=0.17) (48). In contrast, Bell and colleagues assessed the day-to-day repeatability of brachial artery L-FMC in a sample of 5 healthy young men and found almost perfect repeatability (ICC=0.87). Spiro *et al.* found that in a cohort of 10 healthy young adults, L-FMC was repeatable across a two hour time period (81). Unfortunately, there are currently no guidelines for L-FMC measurement and differences

in methods used exist between groups. Therefore, more work needs to be done to comprehensively understand the repeatability of L-FMC.

1.2.4 Total Vessel Reactivity

Only two studies have assessed the repeatability of TVR. Inaba and colleagues assessed TVR (calculated as the absolute value of FMD+L-FMC) in a cohort of 25 healthy men and found the measure had excellent repeatability (ICC = 0.93) (43). In contrast, Kranen *et al.* found that TVR (calculated as the difference between peak diameter and occlusion diameter relative to baseline diameter) had only moderate repeatability (ICC=0.52) in a group of 27 adolescents (48). Due to the relative lack of information regarding the repeatability of TVR, more research is required.

1.3 FACTORS INFLUENCING VASCULAR FUNCTION

1.3.1 Biological Sex

It is well known that differences in the cardiovascular system exist between males and females, and in the past few decades some research has focused on identifying and understanding these biological differences. Differences in baseline diameter between boys and girls have been documented in children as young as 6 years old, where as differences in FMD between the sexes have been shown to appear around age 17 (40). One main difference between the sexes is that unlike males, natural cycling females experience fluctuations in sex hormones (mainly estrogen and progesterone) across their menstrual cycle (1, 16). The menstrual cycle is comprised of three phases: the menstrual phase, the follicular phase and the luteal phase (25, 94). During the menstrual phase of the cycle both estrogen and progesterone levels are low (25). In the follicular phase estrogen

increases, with peak levels occurring just prior to ovulation (1, 25). Finally, during the luteal phase estrogen levels fall and progesterone levels increase (1, 94). Importantly, estrogen has been shown to influence endothelial function through two main pathways; the genomic and non genomic pathways (13). Endothelial cells express estrogen receptors, mainly estrogen receptor alpha (ERα) and estrogen receptor beta (ERβ). In the genomic pathway, estrogen diffuses through the endothelial cell plasma membrane and binds to either ERα or ERβ, which causes the receptors to dimerize into homo- or hetero-dimers (13). These dimers then enter the nucleus and initiate gene transcription, which leads to an increase of eNOS expression (13). In the non-genomic pathway, estrogen binds to cell surface ERα which results in the phosphorylation of eNOS, increasing the capacity of eNOS to produce NO (13). There is also limited evidence that fluctuations in estrogen may lead to fluctuations in ET-1 expression (68). Polderman and colleagues found that ET-1 was highest during the menstrual phase of the cycle and lowest during the follicular phase, when estrogen is elevated (68). Therefore, it has been suggested that fluctuations in estrogen that occur throughout the menstrual cycle may lead to fluctuations in vascular function.

In 1995, Hashimoto and colleagues were the first to investigate if fluctuations in endothelial function occurred across the menstrual cycle in healthy young naturally cycling females (39). The group assessed FMD in 17 males and 17 females, testing females in the menstrual phase, follicular phase and luteal phase (39). Their results indicated that females had similar levels of FMD when compared to males during the menstrual phase, but that in females FMD increased during both the follicular and luteal

phases of the cycle (39). Since this landmark paper, many groups have assessed endothelial function across the menstrual cycle and have reported conflicting findings. Some group have found similar results (3, 37) whereas others have found no change in FMD across the menstrual cycle (19, 76, 98). However, there has been limited investigation of how L-FMC or TVR may fluctuate across the hormonal cycle. Rakobowchuk *et al.* found that neither L-FMC nor TVR fluctuated across the menstrual cycle (70). Additionally, there has been limited research evaluating potential sex differences in L-FMC or TVR. A study performed in in adults with varying levels of coronary artery disease found that radial artery L-FMC was lower in males when compared to females (31). In contrast, Norioka *et al*. found that male sex was an independent predictor of the presence of brachial artery L-FMC in a group of smokers (63). Therefore more research is warranted to understand if sex differences exist in L-FMC and TVR.

In addition to fluctuations of endogenous sex hormones, millions of females take oral contraceptive pills (OCP) that create a different pattern of hormonal fluctuation (78). There are two main OCP dosing patterns: monophasic dosing and tricyclic dosing; in monophasic dosing active pills with a stable concentration of ethinyl estradiol (EE) and progestin (synthetic form of progesterone) are taken for 21 days, with a 7 day placebo phase (78). In contrast, tricyclic dosing has a constant EE dose with an incremental increase in progestin every 7 days across the 21-day active pill phase, followed by a 7-day placebo phase (78). Researchers have assessed whether fluctuations of sex hormones that occur across an OCP cycle also influence vascular function. Similar to the lack of

consensus in findings in natural cycling females, some groups have found increases in FMD in the active phase compared to the placebo phase (59, 89), while others have found no differences (76, 89, 90) or decreases in FMD (90). To our knowledge, no study to date has assessed L-FMC or TVR in females using OCPs.

1.3.2 Aging

It is well known that the risk for CVD increases with age (74). While endothelial dysfunction is often seen in association with CVD, evidence suggests that endothelial dysfunction occurs as a result of aging in the absence of CVD or CVD risk factors (74). It is thought that this dysfunction is mainly due to decreases in bioavailability of NO and increases in oxidative stress and inflammation (75). NO bioavailability is impacted by the availability of tetrahydrobiopterin (BH_4), an important cofactor necessary for the production of NO (75, 95) and BH_4 availability is lower in older adults (74, 95). As we age, there is also an increase in superoxide production without an concomitant increase in antioxidant production, leading to more oxidative stress overall (74). Donato and colleagues assessed brachial artery FMD and the level of oxidation present in the endothelial cells of both younger and older men (23). They found that brachial artery FMD was 50% lower in older men when compared younger men, and that decreases in FMD were associated with higher levels oxidative stress (23). Additionally, inflammatory markers such as interleukin-6 and C-reactive protein appear to be higher in older adults (22). Donato *et al.* assessed markers of inflammation and endothelial dependent vasodilation in older and younger adults and found higher levels of some inflammatory factors (interleukin-6, tumor necrosis factor-α and monocyte chemoattractant protein-1)

and a transcription factor that increases inflammation (nuclear factor κ B) in older adults compared to younger adults (22). They also found lower levels of endothelial dependent dilation in the older adults when compared to the younger adults (22). It has also been suggested that an increase production of ET-1 might be responsible for lower levels of endothelial dependent vasodilation in older adults. Donato *et al.* found that the expression of ET-1 in vascular endothelial cells was greater in older men when compared to young men, and that ET-1 expression was inversely related to FMD (24). Wenner *et al.* found that ET_B receptor blockade increased vasodilation in response to local heating in postmenopausal women, whereas ET_B receptor blockade decreased vasodilation in young women (97). The group concluded these result indicate that ET_B receptor function is altered in women with aging (97).

Importantly, the impacts of aging on endothelial function appear to differ between men and women. Celermajer *et al.* was the first to report the presence of sex based differences in the age associated decline of endothelial function in 1994 (12). The group assessed FMD in 238 healthy individuals aged 15-72 and found that FMD begins to decline in men at approximately age 40, whereas women experience a decline in FMD around age 50 (12). Additionally, the rate of decline in FMD was greater in women when compared to men (12). The group concluded that the loss of estrogen that occurs during menopause was likely the reason for the different pattern of decline seen in women (12). In 2012, Moreau *et al.* evaluated FMD across the phases of the menopause transition in 132 healthy women (61). They observed a stepwise decrease in FMD from premenopause to postmenopause and found that lower FMD was associated with lower levels of

estrogen (61). Gavin and colleagues assessed if changes in estrogen status from pre- to postmenopause altered endothelial ERα expression, and whether not this influenced FMD (27). They noted that ERα was lower in postmenopausal women when compared to premenopausal women in the late follicular phase, but the same as premenopausal women in the menstrual phase (27). Additionally, FMD was approximately 30% lower in postmenopausal women and was positively related to ERα expression in the overall group and in postmenopausal women (27). In contrast, it is unclear if aging influences L-FMC and TVR. One study found that brachial artery occlusion diameters were different between children and adults when compared to older adults (85).

1.3.3 Cardiovascular Disease

Both CVD and the presence of CVD risk factors have been shown to influence vascular function. Kuvin *et al.* found that individuals with coronary artery disease (CAD) had a significantly lower FMD when compared to those without CAD (50). Additionally, the group found that individuals with more CVD risk factors had a lower FMD than those with fewer risk factors (50). Celemajer *et* al. found children with familial hypercholesterolemia had lower levels of FMD compared to healthy children (11). Adachi *et al.* assessed FMD in 75 individuals with and without stroke and found that individuals with stroke caused by either large artery atherosclerosis or cardioembolism, but not small vessel occlusion had a significantly lower FMD when compared to those without stroke (2). The impact of CVD and CVD risk factors on L-FMC and TVR is less clear. L-FMC and TVR in the radial artery appears to be lower in individuals with CAD compared to those without CAD (28, 29). Importantly, Gori *et al.* found that L-FMC

progressively declines with worsening CAD severity (31). Dawson *et al.* found that radial artery L-FMC and TVR were reduced in individuals after radial artery catheterization (20). Gori *et* al. found that the addition of FMD and L-FMC to a model including CAD risk factors improved the model's ability to predict the presence of CAD (31). In the brachial artery, Spiro and colleagues found that L-FMC was greater in patients with unstable CAD compared to those with stable CAD (81). Aizawa and colleagues found that the presence of CVD risk factors did not influence L-FMC (5). Harrison *et al.* investigated FMD, L-FMC and TVR in a cohort of 46 adults with varying CVD risk factors and found that while there were no differences in FMD and L-FMC in the group with multiple risk factors when compared to healthy individuals, TVR was significantly lower in those with multiple risk factors (38).

1.3.4 Elevated Cardiovascular Disease Risk – Spinal Cord Injury and Cerebral Palsy

There are various populations that are thought to be at elevated risk for cardiovascular disease, two of which are individuals with spinal cord injury (SCI) and cerebral palsy (CP). Individuals with SCI appear to have a greater prevalence of CVD, as well as higher mortality from CVD when compared to ambulatory individuals (62). CVD risk factors, such as metabolic syndrome, dyslipidemia, obesity and physical inactivity, are also more common in individuals with SCI (62). These risk factors, along with autonomic dysfunction that often accompanies SCI, contribute to the development of CVD in this population (62). Our lab, along with others have assessed FMD in this population to determine how endothelial function may be altered by SCI (83, 88, 91).

Thijssen *et al.* assessed FMD in the superficial femoral artery (SFA) of 14 men, including 6 men with SCI (88). The group found greater SFA FMD in SCI individuals when compared to controls, however this difference was no longer apparent after correction for shear rate area under the curve (88). Our group assessed both brachial artery and SFA FMD in 8 individuals with SCI and 8 ambulatory individuals (91). We found that there were no differences in FMD in either of the arterial segments, however when FMD was scaled to baseline diameter, SCI individuals appeared to have lower SFA FMD than ambulatory individuals (91). It is unclear if L-FMC or TVR might be altered in SCI individuals.

Cerebral palsy (CP) is a disorder that results in motor impairments that impact an individual's physical activity levels (58). It has been show that physical activity levels of individuals with CP decline with age and worsening disease status (57, 58). Low levels of physical activity in this population have been associated with increased risk for cardiovascular disease (57). Researchers from our lab have worked to understand if endothelial function of adolescents and adults with CP is altered (56, 58). Martin *et al.* assessed brachial artery FMD in adolescents with and without CP and found children with CP participated in less vigorous physical activity, however there were no differences in FMD between adolescents with CP and those without (56). Similarly, McPhee and colleagues assessed FMD in ambulatory and non-ambulatory individuals with CP and found that there were no differences in FMD, even though individuals who were non-ambulatory participated in fewer minutes of moderate-vigorous physical activity (58). To our knowledge, no study has evaluated L-FMC or TVR in this population.

1.4 STUDY OBJECTIVES AND HYPOTHESES

The main purpose of this study was to assess FMD, L-FMC and TVR in a diverse population of individuals to determine:

(1) The repeatability of brachial artery FMD, L-FMC and TVR. We hypothesized that the repeatability of FMD, L-FMC and TVR would be moderate.

(2) How brachial artery FMD, L-FMC and TVR are influenced by age and how this relationship is moderated by sex, elevated cardiovascular disease risk and the presence of overt CVD. We predicted that FMD, L-FMC and TVR would decrease with aging, and that differences between the sexes would be evident. We hypothesized that the presence of CVD and elevated CVD risk would lead to a reduction in FMD, L-FMC and TVR.

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CHAPTER 2: MANUSCRIPT

Determining the Repeatability of Low Flow Mediated Constriction and Total Vessel Reactivity in the Brachial Artery of Humans

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2.1 ABSTRACT

Endothelial function is the ability of an artery to vasodilate that is often assessed in the peripheral vasculature using a flow mediated dilation (FMD) test. While FMD has been shown to be a valuable tool, it may not ideally capture overall vascular function. Two novel measures, low flow mediated constriction (L-FMC) and total vessel reactivity (TVR) have been introduced to provide a complementary vascular assessment to FMD, however little is known about the repeatability of L-FMC and TVR, particularly in the brachial artery. Additionally, it is unclear how L-FMC and TVR might be influenced by aging or the presence of cardiovascular disease (CVD) or elevated CVD risk and if these measures differ between the sexes. Therefore the main purpose of this investigation was to assess the day-to-day repeatability of FMD, L-FMC and TVR in the brachial artery of humans. The secondary purpose was to assess how FMD, L-FMC and TVR change with aging and if this relationship was influenced by sex or the presence of CVD or elevated CVD risk. 375 participants (age: 37 ± 22) were included in the overall study, which included both retrospective and prospective data. 98 participants (age: 34 ± 19) underwent two FMD tests; as such they were included in the repeatability analysis. For all participants brachial artery endothelial function was assessed using a FMD test. A 30 second image was taken at 4 minutes of cuff occlusion to capture the low flow response. The between day repeatability of FMD was substantial (ICC = 0.68), TVR was moderate (ICC = 0.50) and L-FMC was slight (ICC = 0.01). FMD and TVR (ρ= -0.24, ρ= -0.19, $p<0.005$) were associated with age, however there was no relationship between age and L-FMC. These relationships persisted in individuals with CVD and elevated CVD risk,

and sex did not moderate the relationship between age and any of our vascular outcomes. These results indicate that brachial artery FMD and TVR are relatively repeatable, however L-FMC is not repeatable. As well, it appears that while age is associated with a decrease in FMD and TVR, there is no such relationship between age and L-FMC.

2.2 INTRODUCTION

Arterial endothelial function refers to the ability of endothelial cells to produce vasodilation (4, 43). Endothelial function is commonly assessed in the peripheral vasculature using the non-invasive flow mediated dilation (FMD) dilation test (44). Importantly, FMD has been shown to be predictive of future cardiovascular events in both symptomatic and asymptomatic individuals (43). While FMD has been shown to be a valuable tool for assessing endothelial function, some have argued that it does not capture overall endothelial function, particularly the full expression of vascular range including vasoconstriction and vasodilation (17, 25). As a result, two novel measures of endothelial function, low flow mediated constriction (L-FMC) and total vessel reactivity (TVR) have been introduced to address some of the apparent limitations of FMD (16). L-FMC is a measure of arterial diameter during a low blood flow state that is meant to provide information on resting vascular tone and vasoconstriction capacity (16, 17, 19). The information required to determine L-FMC can be acquired during the occlusion phase of a traditional FMD test (16). It is thought that L-FMC is mediated by an increased production of endothelin-1 (ET-1) and a decreased production of certain vasodilators (endothelial derived hyperpolarizing factor, prostaglandins) (16). TVR is a composite score of both FMD and L-FMC and is thought to provide a more comprehensive

assessment of vascular function in comparison to either index alone (23, 25). While these two novel measures of vascular function can potentially improve our understanding of endothelial function, little is known about their repeatability, particularly when assessed in the brachial artery. Previous studies assessing the repeatability of brachial artery L-FMC have reported conflicting findings, with some reporting that L-FMC has good within and between day repeatability, while others reporting that L-FMC has poor repeatability in adolescents and young adults (3, 21, 27, 42). The very limited research available that assessed the repeatability of brachial artery TVR has found either almost perfect (26) or moderate repeatability (27) in adolescents and healthy young adults.

It is well known that aging influences endothelial function and it is thought that a combination of a decrease in nitric oxide (NO) bioavailability, an increase in inflammatory factors and reactive oxygen species are responsible for the age related decline in vascular function (38). As such, studies have reported higher levels of reactive oxygen species and inflammation along with lower FMD (11, 12). While decreases in FMD with age have been well documented, little is known about how aging influences L-FMC and TVR. A study by Gori *et al.* found that older age (>65 years) was associated with lower L-FMC (19). To our knowledge, no study has comprehensively the effects of aging of L-FMC and TVR.

Endothelial function has been shown to vary between the sexes. Hashimoto *et al.* were the first to show that natural cycling women have higher levels of FMD during the follicular and luteal phase when compared to men, however in their study FMD during the menstrual phase was similar between men and women (24). Since that early report, a

variety of studies have assessed FMD across the menstrual cycle and have either reported increases or no change in FMD across the menstrual cycle (1, 10, 22). Recent work from our lab found there were no changes in FMD across both a natural menstrual cycle or oral contraceptive pill cycle, however once scaled to baseline diameter, women had lower levels of FMD when compared to men (40). Important sex differences are also present with aging, as women appear to show a decline in FMD later in life compared to men, and the rate of decline in FMD with aging is greater in women compared to men (5). Additionally, Moreau *et al.* found FMD progressively decreased across the phases of the menopause transition (34). Until now, very little work has assessed potential sex differences in L-FMC and TVR. One study found that L-FMC did not change across the menstrual cycle (37). A study by Gori *et al.* found that male sex was associated with lower radial artery L-FMC and Norioka *et al.* found that male sex was associated with the presence of brachial artery L-FMC (19, 35).

Endothelial function has been shown to be reduced in individuals with CVD and elevated CVD risk. Kuvin *et al.* found individuals with coronary artery disease (CAD) had lower levels of FMD and that the number of cardiovascular disease (CVD) risk factors was associated with FMD (28). Little is known about the influence of CVD and CVD risk factors on L-FMC. Gori *et al* found that both radial artery L-FMC and TVR were lower in individuals with CAD and that L-FMC was negatively correlated with CAD severity (16, 17, 19). Aizawa *et al.* found the presence of CVD risk factors did not influence L-FMC (2). In agreement with this finding, Harrison *et al* found no differences in FMD and L-FMC between individuals with and without CVD risk factors, however

TVR appeared lower in those individuals with CVD risk factors when compared to those without CVD risk factors. (23).

Given the work to date, the main purposes of this study were to assess FMD, L-FMC and TVR in a diverse population of individuals to determine: (1) the repeatability of brachial artery FMD, L-FMC and TVR and (2) how brachial artery FMD, L-FMC and TVR are influenced by age, sex, elevated cardiovascular disease risk and the presence of overt CVD. We hypothesized that the repeatability of FMD, L-FMC and TVR would be moderate and that FMD, L-FMC and TVR would decrease with aging. Furthermore, we hypothesized that differences between the sexes would be evident, such that men would show a decline in both FMD and L-FMC earlier in life than women and that the presence of CVD or elevated CVD risk would lead to a reduction in FMD, L-FMC and TVR.

2.3 METHODS

2.3.1 Participants

Retrospective data along with prospective data were used for the present investigation. Our retrospective data set included 355 participants that previously underwent at least one FMD test in our laboratory. This data set consisted of individuals ranging from six to eighty-one years of age, including healthy young adults, individuals with spinal cord injury, individuals with cerebral palsy, individuals with stroke, individuals with coronary artery disease and healthy older adults. The FMD results from many of these studies have been published elsewhere (6–9, 32, 33, 39–41, 45). All of the data was collected using a similar FMD protocol as described below. This cohort also consists of data from forty participants (age <18 years old) taking part in the SKIP

(School-age Kids" health from early Investment in Physical activity) study (data not yet published).

80 participants from the retrospective cohort had undergone repeated testing; therefore, the data from these individuals were used for the day-to-day repeatability analysis. We controlled for hormonal fluctuations in both natural cycling women and women taking oral contraceptive pills. For natural cycling women we used data from two visits that occurred during the menstrual phase of the menstrual cycle. For women on oral contraceptive pills we used two visits that occurred during the active phase of a pill cycle, as repeat data was not available during the placebo phase. As some studies were intervention studies that had randomized baseline visits, we used the first two visits based on chronological order. Additionally, we only utilized baseline (or pre-intervention) data from any study that had an intervention component.

For our observational analysis, we utilized the first visit for any participants that underwent multiple testing visits. Additionally, the SKIP study is a longitudinal study assessing various measures within school-aged children across a three-year period. As such, we only utilized data from the first year of the study.

In addition to our retrospective data set, we collected prospective data from 20 individuals (14 women, 6 men) who were recruited from McMaster University using poster advertisements as well as advertisements in a local newspaper. Individuals were required to be 35-80 years of age to address the age ranges where our retrospective data was most sparse. Postmenopausal women were included if they had not experienced menses for >1 year and were not currently taking hormone replacement therapy. No

premenopausal women were recruited in the prospective cohort. Participants needed to be free of active cardiovascular or cerebrovascular disease to be included in the prospective portion of the study. The study was approved by the Hamilton Integrated Research Ethics Board (HiREB #5291).

Table 1. List of Studies

Study ID	Number of Participants
RAM	50
SFCP	39
CAMO	34
SKIP	40
SCI	34
CAD	26
TR	25
TVR	20
NESTLE	18
CAMS	12
AC	16
AM	20
ASPEN	10
SPEC	9

AB - SCI	8
ACUTEENDO	7
EDS	4
COS	3
TOTAL	**375**

RAM – Repeatability of Arterial Measures, SFCP – Stay Fit Cerebral Palsy: Cardiovascular Health, CAMO – Cardiovascular Health and Mobility in community older adults, SKIP – school-age kids health from early investment in physical activity, SCI – Cardiovascular and metabolic health in spinal cord injury, CAD – Vascular adaptations to low-volume HIIT in coronary artery disease, TR – Endothelial adaptations to SIT vs END vs Control, TVR – Total Vessel Reactivity, NESTLE – Step reduction in older adults, CAMS – Cardiovascular Health and Mobility after stroke, AC – Sex-differences in response to a single bout of SIT, AM – Arterial Measures, ASPEN – Artery Function Responses to Changes in Blood Flow, SPEC – Speckle Tracking Study, AB – SCI – Cardiovascular and metabolic health in able bodied individuals, ACUTE ENDO – acute endothelial function, EDS – exercise dilation study, COS - CHOICES: Cardiovascular/Health Outcomes in spinal cord injury.

2.3.2 Study Design

All study visits for prospective data collection took place in the Vascular Dynamics Lab at McMaster University. All participants attended one familiarization visit. At the familiarization visit participants were screened to ensure they were eligible to take part in the study. Participants provided informed consent and were given a demonstration of the FMD technique, however no data was acquired at this visit.

Prior to the testing visits, participants were instructed to refrain from vigorous physical activity for 24 hours, as well to have fasted overnight for at least 10 hours. Testing visits took place in the morning between the hours of 7:00am-12:00pm to control for diurnal variation. At the start of the first testing visit anthropometric measurements including body weight and height were collected.

For postmenopausal women and men, data was collected during two study visits

scheduled at the same time of day on two different days separate by at least 24 hours. For postmenopausal women a blood sample was collected at the start of all visits. For men, one blood sample was collected at the start of one of the two visits, of which was randomized for each participant. Immediately following the blood draw, participants were fitted with three electrocardiography electrodes (AD Instruments, Colorado Springs, CO) that were used to record heart rate throughout the duration of the protocol. Participants had ten minutes of supine rest, after which blood pressure was assessed using an automated, oscillometric blood pressure device (Dinamap ProSeries, Batesville, IN). Blood pressure was assessed once every minute, for at least three minutes. The first measure of blood pressure was discarded, and the second and third measures were averaged. However, if the second and third measures were greater than 5mmHg apart, one additional measurement was collected. The two closest measures of blood pressure were then averaged.

2.3.3 Outcome Measures

2.3.3.2 Venous Blood Draw

A 16.0mL venous blood sample was collected at the start of each visit for women and at the start of one visit for men. Blood was collected in four 4.0mL serum blood collection tubes (BD Vacutainer Plus, Red BD Hemogard Closure, Franklin Lakes, NJ) and set aside to clot for at least 45 minutes. Following coagulation, the tubes were spun at 4000rpm for ten minutes in a centrifuge set to 4°C (Sorvall Legend XTR Centrifuge, Thermo Fisher Scientific, Waltham, MA). Serum was aliquoted into three 1.5mL eppendorfs and frozen at -20°C. Frozen serum samples were brought to the Core

Laboratory at the McMaster University Medical Centre for analysis of endogenous estradiol (Architect Estradiol Chemiluminescent Microparticle Immunoassay, Abbott Laboratories, Abbott Park, IL), progesterone (Architect Progesterone Chemiluminescent Microparticle Immunoassay, Abbott Laboratories, Abbott Park, IL), and testosterone (Immulite 2000 Total Testosterone Chemiluminescent Enzyme Immunoassay, Siemens Healthcare Diagnostics, Tarrytown, NY).

2.3.3.3 Flow Mediated Dilation (FMD)

A Duplex ultrasound (Vivid Q, GE Medical Systems, Horten, Norway) along with a 12 MHz linear array probe was used to simultaneously assess brachial artery diameter and mean blood velocity. A single lead ECG was connected to the ultrasound to simultaneously collect heart rate. At the start of the test, a pneumatic cuff was placed on the participant's right forearm and a baseline image of the right brachial artery was taken for thirty seconds. The cuff was then rapidly inflated to 200 mmHg and remained inflated for five minutes. An additional Duplex image of the brachial artery was acquired at four minutes of occlusion for thirty seconds. The cuff was then rapidly deflated at five minutes, and a cineloop was taken in Duplex mode for three minutes to capture the reactive hyperemia response. Ultrasound images were then prepared for offline analysis using a software program (Sante DICOM Editor). First raw images were transferred from the ultrasound to a computer. Individual frames were then extracted at or before every R spike of the cardiac cycle. The extracted frames were then merged into a single loop for all baseline, four-minute and reactive hyperemia images. For analysis, a semi-automated edge tracking software (Arterial Measurement System II Image and Data Analysis,

Gothenburg; Sweden) was used to determine brachial artery diameter at all three time points.

Flow mediated dilation was calculated by subtracting the mean baseline diameter from the maximum diameter reached during reactive hyperemia using the following equations to determine absolute and relative FMD:

$$(1)\ \text{FMD (mm)} = \text{maximum diameter-baseline diameter}$$

$$(2)\ \text{FMD (\%)} = \frac{\text{maximum diameter-baseline diameter}}{\text{baseline diameter}}\ \text{X } 100$$

Low flow mediated constriction was calculated by subtracting the mean baseline diameter from the mean occlusion diameter using the following equations to determine absolute and relative L-FMC:

$$(3)\ \text{L-FMC (mm)} = \text{occlusion diameter-baseline diameter}$$

$$(4)\ \text{L-FMC \%} = \frac{\text{occlusion diameter-baseline diameter}}{\text{baseline diameter}}\ \text{X } 100$$

Total vessel reactivity was calculated by subtracting the occlusion diameter from the maximum diameter using the following equation:

$$(5)\ \text{TVR \%} = \frac{\text{maximum diameter-occlusion diameter}}{\text{occlusion diameter}}\ \text{X } 100$$

2.3.3.4 Nitroglycerin Challenge Test (NTG)

For 194 of 375 participants, a nitroglycerin challenge test (NTG) was used to assess smooth muscle function. After the FMD test participants were given 10 minutes of supine rest. Following the rest period, a thirty-second baseline image of the brachial artery was taken. A 0.4 mg dose of nitroglycerin (NTG) was then administered sublingually to the participant. Following NTG administration, a thirty-second image was

obtained every minute for ten minutes. Images were then prepared for offline analysis and analyzed as described above. The absolute and relative diameter change after NTG administration was calculated using the following equations:

$$(6)\ \text{Absolute NTG (mm)} = \text{peak NTG-baseline NTG}$$

$$(7)\ \text{Relative NTG (\%)} = \frac{\text{peak NTG-baseline NTG}}{\text{baseline NTG}}\ \text{X } 100$$

2.3.3.5 Mean Blood Velocity & Shear Rate

Mean blood velocity signals were collected during the baseline, occlusion and reactive hyperemia phases of the test while the ultrasound was in Duplex mode. A spectral analysis system (Neurovision 500M TCD, Multigon Instruments, Yonkers, NY, USA) was used to perform a Fast Fourier transformation function on the acquired audio signals from the ultrasound to generate intensity weighted mean blood velocity (MBV) signals. A Powerlab system (Powerlab model ML870, AD Instruments, Colorado Springs, CO, USA) was then used to sample the MBV signal and convert the analog signals to digital which were then analyzed offline using LabChart software (LabChart 8, AD Instruments, Colorado Springs, CO, USA). For reactive hyperemia MBV and arterial diameters were then averaged into 5-cycle rolling average bins and used to calculate blood flow and shear rate using the following equations:

$$(8)\ \text{Blood flow } \left(\frac{\text{mL}}{\text{min}}\right) = (\pi r^2 \text{ x MBV}) \text{ x } 60 \ \text{ where r} = \text{arterial diameter}/2$$

$$(9)\ \text{Shear rate } (s^{-1}) = \frac{\text{MBV x } 8}{\text{arterial diameter}}$$

Differences in the retrospective cohort

While our FMD acquisition and analysis has remained relatively consistent over

the years of the studies included in this analysis, there are some differences between studies in the retrospective cohort. Some studies included a familiarization visit (where participants were given a demonstration of the FMD technique, but no data was acquired), while others did not. The fasting period for studies included in the retrospective dataset ranged from 4-12 hours (8, 9, 32, 33, 39–41, 45). Similarly, the period of time the participant was instructed to refrain from exercise ranged from 12-24 hours. The rest period prior to vascular testing ranged from 10-20 minutes. A majority of studies utilized a GE Vivid Q ultrasound with a 12 MHz linear array probe (6–8, 33, 39–41, 45), while one study utilized the GE System FiVe with a 10 MHz linear array probe (32). Studies also utilized a slightly different cuff placement, ranging from 3-10cm away from the antecubital fossa, however all cuff placement was distal to the brachial artery assessment site. One study had a different protocol for acquiring the ultrasound images during the FMD test; they acquired a baseline image 3 heart cycles in duration, after cuff deflation they collected blood velocity signals for 30 seconds, after which they collected an image 3 heart cycles in duration every 15 seconds until 3 minutes after cuff deflation (32). The nitroglycerin challenge test protocol also varied between studies. One study gave participants 15 minutes of rest before NTG and acquired ultrasound images of the brachial artery at every two minutes after nitroglycerin administration (45). Another study acquired images that were 10 heart cycles in duration at baseline and every minute after nitroglycerin administration (8).

2.3.4 Statistical Analysis

Statistical Package for the Social Sciences (SPSS Inc., Version 25.0, Chicago IL)

was used for all analyses. We utilized intraclass correlation coefficients (ICCs, two way mixed, absolute agreement) to determine the repeatability of FMD, L-FMC and TVR. ICC cut off values are as follows: poor < 0, slight 0 - 0.2, fair 0.21-0.4, moderate 0.41 - 0.60, substantial 0.61 – 0.80, almost perfect 0.81-1 (29). Sample size calculations were based on previous research assessing the repeatability of L-FMC using ICC,Sample.Size in Rstudio (Version 1.1.423) to estimate a sample size if the ICC value is between 0.2-0.3. The sample size required to detect an ICC in this range with $\alpha = 0.05$ and $\beta = 0.80$ fell between 83 – 192 participants. As a secondary measure of repeatability for L-FMC, we utilized Cohen's Kappa to measure the level of agreement between the two repeat visits. Relative L-FMC at each visit was assigned a label as follows: > 0 was labeled "dilate", = 0 was labeled "no change" and < 0 was labeled "constriction". To determine if a relationship existed between age and our vascular measures we utilized Spearmen's correlation coefficients as our data were non-parametric upon visual inspection. To determine if sex moderated the relationship between age and our vascular measures, we utilized a moderated multiple regression with sex as the dichotomous moderator variable and also assessed potential between day differences in hemodynamic variables using a signed rank test. Potential differences in between day endothelial independent dilation were assessed using paired-sample t-tests.

2.4 RESULTS

FMD data was available in 375 participants for the observational study and repeat data was available in 98 participants for the repeatability analysis. From the 20 participants that were recruited, all 20 were included in the observational study analysis

and 18 were included in the repeatability investigation as one participant only completed one visit and another did not follow pretesting instructions at one visit. Participant characteristics are outlined in Table 2, while hemodynamic variables are outlined in Table 3 for the repeatability cohort and Table 4 for the observational cohort.

Table 2. Participant Characteristics

Observational Cohort	
Sex	253M, 122F
Age (years)	37 ± 22
BMI	24.4 ± 5.8
Repeatability Cohort	
Sex	53M, 45F
Age (years)	34 ± 19
BMI	25.2 ± 5

Data are presented as mean ± standard deviation. M – males, F - females.

Repeatability Study

There were differences in systolic blood pressure ($p<0.005$), diastolic blood pressure ($p=0.010$) and mean arterial pressure ($p=0.002$) between the two visits, however there were no differences in heart rate ($p=0.826$). Data on FMD variables can be found in Table 5. We found that FMD had substantial repeatability (ICC=0.68), L-FMC had poor repeatability (ICC= 0.01) and TVR had moderate repeatability (ICC=0.50) in our cohort. At Visit 1 40.8% of individuals presented with constriction during low flow and 59.2% presented with dilation. Similarly, at Visit 2, 39.8% of individuals presented with constriction during low flow, 59.2% presented with dilation and 1% showed no change. 19 participants consistently presented with constriction, 37 consistently presented with dilation and 41 participants presented with dilation at one visit and constriction at the other visit. In contrast, baseline, occlusion and peak arterial diameters all had almost

perfect repeatability (Table 5). Additionally, we found that there was poor agreement of L-FMC between the visits (κ = 0.12). We found that there were no differences in endothelial independent function between the two visits (Table 6). Blood analysis in the 20 prospective participants revealed all females were within normative values for postmenopausal women for estrogen and testosterone at both visits, however one female had slightly elevated progesterone at Visit 2. Males were within normative values for estrogen, progesterone and testosterone.

Table 3. Hemodynamics, Repeatability Cohort

	Visit 1	Visit 2	p
HR (bpm)	**62 (15)**	**62 (15)**	**.862**
SBP (mmHg)	**116 (20)**	**113 (17)**	**<0.005**
DBP (mmHg)	**69 (9)**	**67 (7)**	**0.010**
MAP (mmHg)	**87 (8)**	**85 (7)**	**0.002**

Data are presented as medians with interquartile range. HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure. Results are from a sign rank test. n=87.

Observational Study

Vascular variables for the observational analysis can be found in Table 7. In our cohort 190 individuals experienced vasoconstriction during the low flow period (50.7%) while 185 presented with vasodilation (49.3%). Individuals who experienced vasoconstriction during low flow appeared to be slightly older than those who presented with vasodilation (38 vs. 35 years) and the percentage of men and women who experienced vasodilation and vasoconstriction were similar. Analysis revealed that there was a negative correlation between age and FMD (ρ= -0.24) as well as age and TVR (ρ= -0.19) however there was no correlation between age and L-FMC. To assess whether the presence of CVD or elevated CVD risk would alter this relationship, we reran the

correlations excluding healthy individuals (n = 124). Similarly to the overall observation cohort, we found that FMD and L-FMC were correlated with age (ρ= -0.41 $p<0.005$, ρ= -0.43 $p<0.005$), however L-FMC was not correlated with age in the cohort with CVD and elevated CVD risk. Additionally we found that there was a positive correlation between FMD and L-FMC (ρ= 0.27, $p<0.005$). Our moderator analysis revealed sex did not moderate the relationship between age and any of our vascular measures.

Table 4. Hemodynamics, Observational Cohort

	Mean ± Standard Deviation
HR (bpm) (n=322)	65 ± 12
SBP (mmHg) (n=362)	116 ± 17
DBP (mmHg) (n=362)	67 ± 10
MAP (n=305)	86 ± 11

Data are presented as mean ± standard deviation. HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure.

Table 5. Vascular Variables, Repeatability Cohort

	Visit 1	Visit 2	CV(%)	ICC
Baseline Diameter	3.87±0.76	3.89±0.74	2.4	0.97
Occlusion Diameter	3.88 ±0.78	3.92 ±0.74	2.6	0.97
Peak Diameter	4.09±0.76	4.12±0.74	2.4	0.96
Absolute FMD	0.22±0.10	0.23±0.10	13.1	0.63
FMD%	5.90±3.10	6.15±3.09	14.4	0.68
Absolute L-FMC	0.01±0.07	0.03±0.10	-	0.01
L-FMC%	0.33±1.89	0.90±2.92	-	0.01
TVR%	5.56±2.80	5.25±3.19	36.3	0.50

Data are presented as mean ± standard deviation. FMD – flow mediated dilation, L-FMC – low flow mediated constriction, TVR – total vascular reactivity, CV – coefficient of variation, ICC – intraclass correlation coefficient.

Table 6. Nitroglycerin Challenge Test, Repeatability Cohort

	Visit 1	Visit 2	p
Baseline Diameter (mm)	3.71±0.71	3.71±0.70	0.80
Peak Diameter (mm)	4.50±0.75	4.48±0.75	0.37
Absolute NTG (mm)	0.79±0.19	0.77±0.20	0.35
NTG%	21.92±6.26	21.46±6.44	0.36
TTP (minutes)	7±2	7±2	0.47

Data are presented as mean ± standard deviation. NTG – nitroglycerin challenge test, TTP – time to peak. Results are from a paired sample t-test. N=78 for all variables except TTP V2 where n=77.

Table 7. Vascular Variables, Observation Cohort

	Mean ± Standard Deviation
Baseline Diameter	3.79±0.82
Occlusion Diameter	3.79±0.82
Peak Diameter	4.03±0.84
Absolute FMD	0.24±0.13
FMD%	6.55±3.91
Baseline Blood Flow (n = 215)	50.61±33.98
Peak Blood Flow (n = 215)	358.25±166.33
Peak Shear Rate (n = 223)	964.42±544.53
Shear Rate AUC (n = 205)	23234.50±17603.69
Absolute L-FMC	-0.001±0.12
L-FMC%	0.01±3.31
TVR%	6.61±4.55
Baseline NTG Diameter (n=194)	3.97±0.71
Peak NTG Diameter (n=194)	4.75±0.79
Absolute NTG (n=194)	0.78±0.23
NTG% (n=194)	20.09±6.11
NTG TTP (n=190)	7±2

Results are presented as mean ± standard deviation. FMD – flow mediated dilation, L-FMC – low flow mediated constriction, TVR – total vascular reactivity, NTG – nitroglycerin challenge test, TTP – time to peak. n=375 unless otherwise stated.

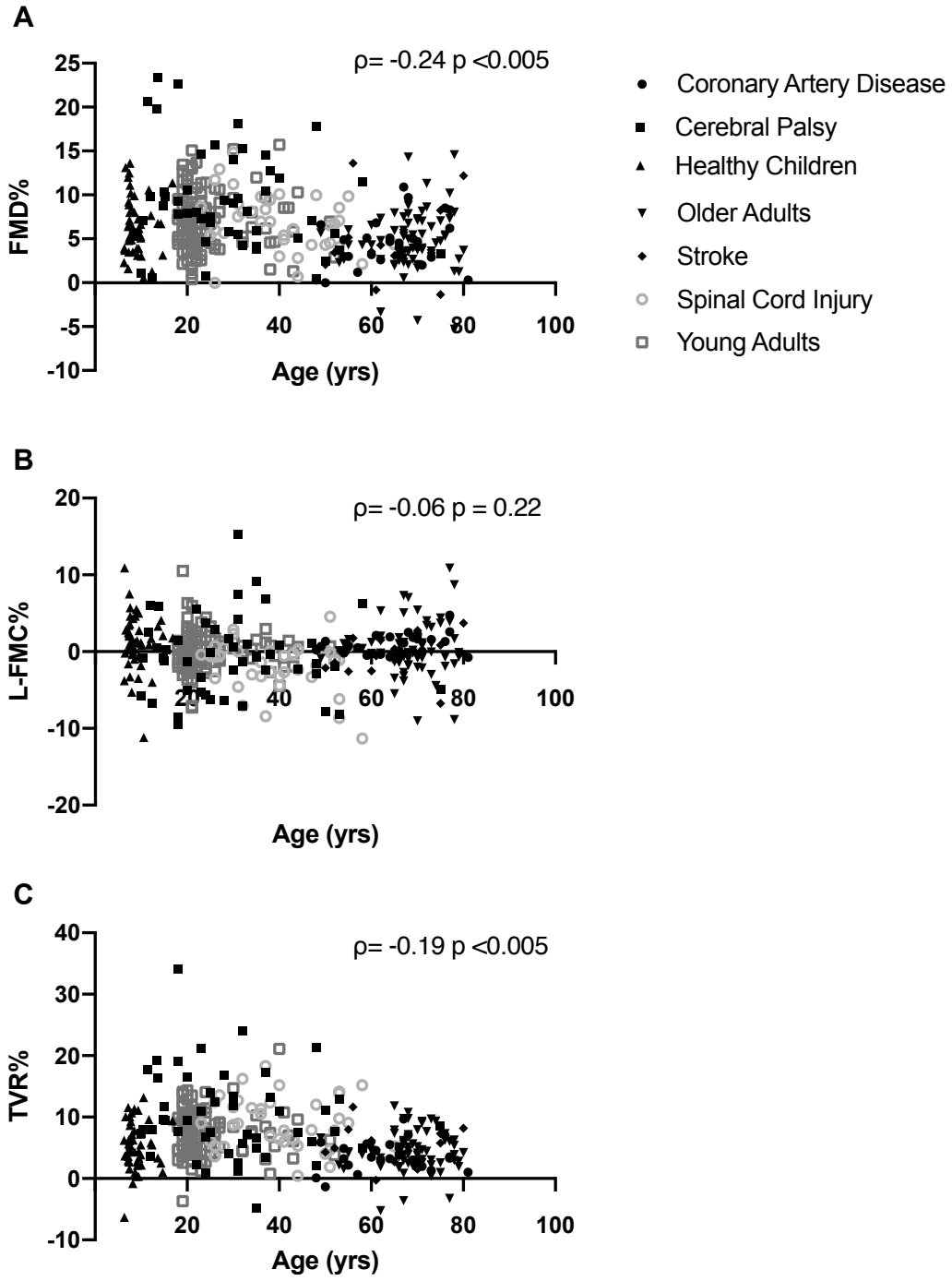

Figure 1. Associations between age and [A] flow mediated dilation (FMD), [B] low flow mediated constriction (L-FMC) and [C] total vessel reactivity (TVR). A significant association was found between age and FMD and age and TVR but not age and L-FMC.

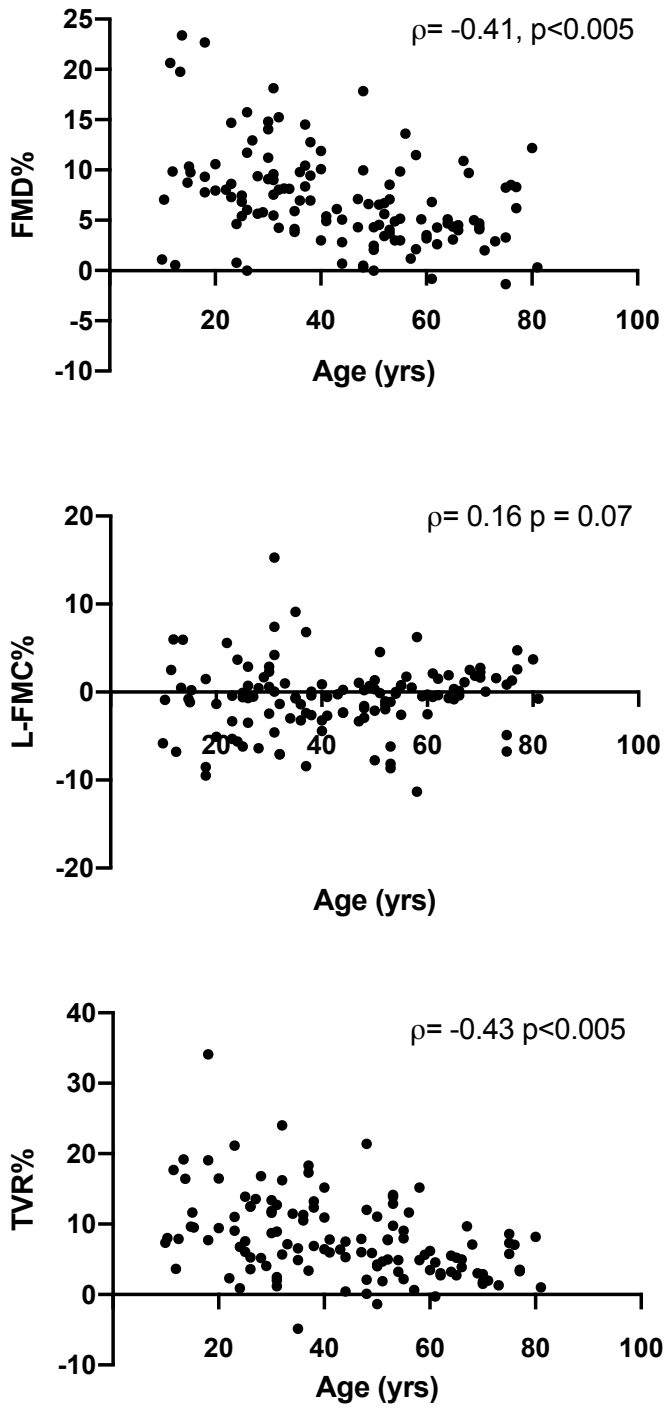

Figure 2. Associations between age and [A] flow mediated dilation (FMD) [B] low flow mediated constriction (L-FMC) and [C] total vessel reactivity (TVR) in individuals with cardiovascular disease or elevated cardiovascular disease risk. A significant association was found between age and FMD and age and TVR but not age and L-FMC.

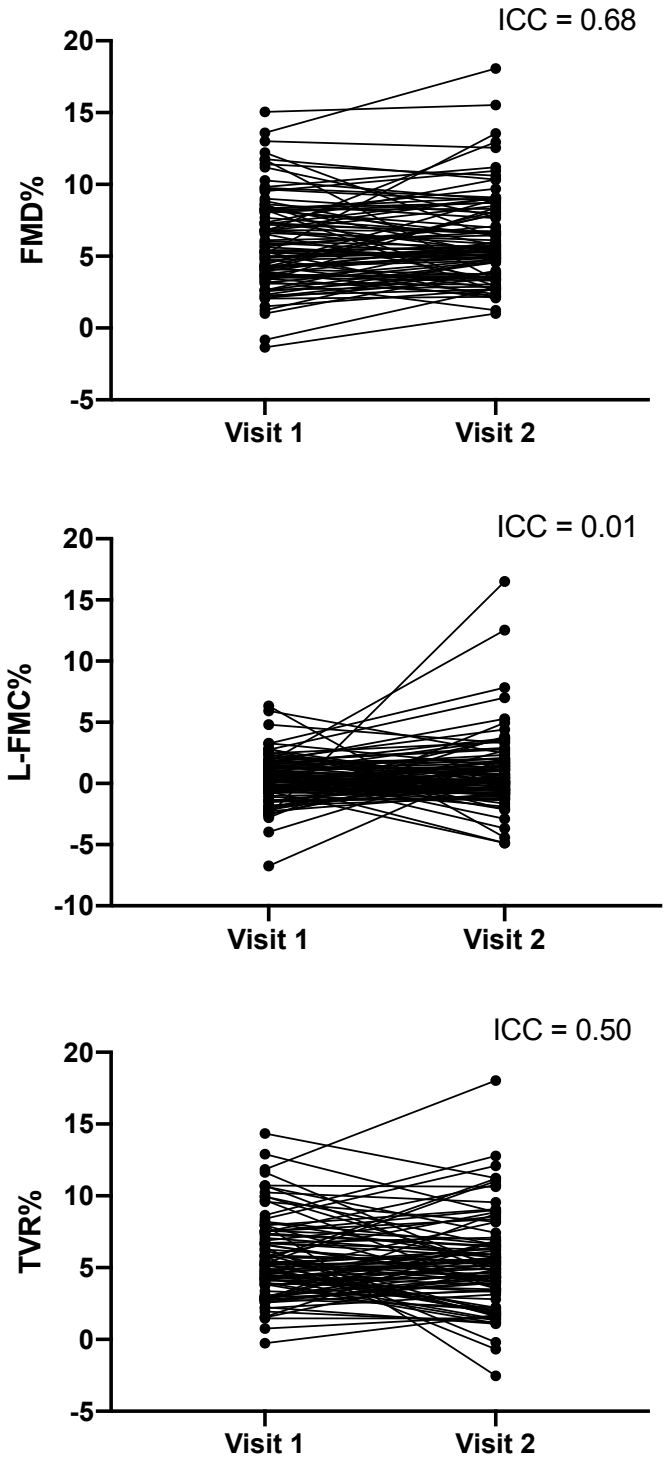

Figure 3. Lines depict individual participant responses across the two visits for [A] flow mediated dilation (FMD) [B] low flow mediated constriction (L-FMC) and [C] total vessel reactivity (TVR).

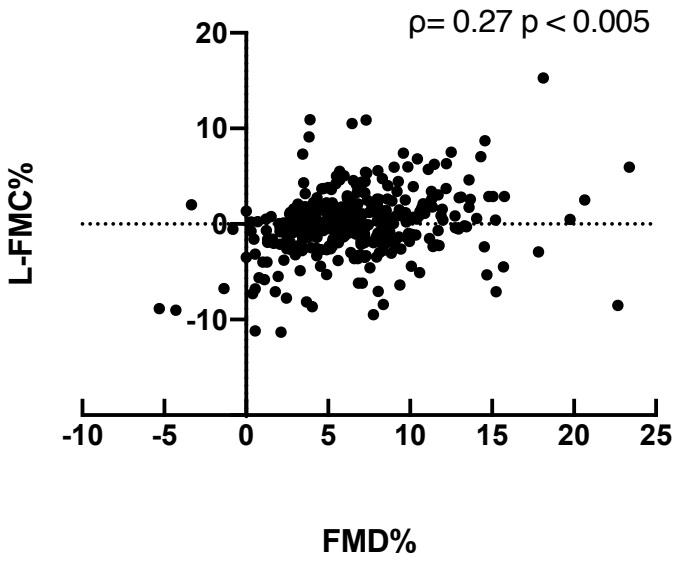

Figure 4. Correlation between low flow mediated constriction (L-FMC) and flow mediated dilation (FMD).

2.5 DISCUSSION

This is the first study to comprehensively assess the repeatability of both brachial artery L-FMC and TVR in a diverse cohort of individuals. Additionally, we are the first to directly investigate the relationship between age and L-FMC or TVR as well as the influence of sex on this relationship.

2.5.1 Repeatability Analysis

In contrast to our hypothesis, our results suggest that FMD is repeatable in the brachial artery, while L-FMC is not repeatable and TVR is only moderately repeatable. Our finding that brachial artery FMD is substantially repeatable is consistent with some, but not all, previous literature. Malik *et al.* assessed the between-day repeatability of brachial artery FMD within a ten day period in a cohort of twenty healthy men and found FMD had poor repeatability (ICC=0.10) (31). In contrast, Onkelinx *et al.* found brachial artery FMD had excellent between-day repeatability in a cohort of 18 patients with CAD (ICC=0.99) (36). Liang *et al.* assessed the repeatability of FMD in 30 adults across an average of 2.5 weeks and found a CV of 10.8% (30). In a recent systematic review, Greyling *et al.* found that greater adherence to current FMD guidelines was associated with less variation in FMD (20). As our lab follows a standard operating procedure for all FMD studies that was developed to follow the current guidelines, this may explain why we found FMD had substantial repeatability in our cohort. However, the data in our repeatability cohort came from multiple studies and was collected and analyzed by different individuals, despite a majority of repeat tests being analyzed by the same individuals within a participant. Additionally, there were some methodological

differences between studies, such as different ultrasound equipment and pre-testing instructions. This between-study variation could result in greater variation in FMD and may explain why our level of repeatability was not as high as other studies.

Our study is the largest study to date to assess the repeatability of L-FMC in the brachial artery. Consistent with previous work, we found brachial artery L-FMC is highly variable both within, and between, individuals (2, 21, 23, 27). We also found that L-FMC was not repeatable between days in the brachial artery, however the repeatability of the occlusion diameter was almost perfect. Similar to our findings, Kranen *et al.* found that in a cohort of 27 adolescents L-FMC had poor repeatability (ICC= 0.17, $\kappa = 0.04$) however the occlusion diameter had almost perfect repeatability (ICC = 0.94) (27). Additionally, Harbin and colleagues found that brachial artery L-FMC was not repeatable within, or between, days (21). In contrast, Sprio *et al.* found that L-FMC in a cohort of 10 healthy adults was repeatable within a day (42). Similarly, Bell and colleagues found brachial artery L-FMC had almost perfect between-day repeatability in a cohort of 5 healthy young men (ICC=0.87) (3). There are a variety of potential reasons why these contradictory findings exist. First, both the studies by Bell *et al.* and Sprio *et al.* used relatively small sample sizes (n=5 and n=10 respectively) when compared to our study as well as those by Kranen *et al.* and Harbin *et al.* (3, 21, 27, 42). Using a sample size calculation we determined a much larger sample than n=5 or n=10 would be required to detect the presence of poor L-FMC repeatability. Additionally, both our study and the study by Kranen *et al.* utilized retrospective data. For our study this retrospective data included studies in which the data was collected and analyzed by different individuals,

which could have increased the variability in our sample. It is also important to note that in all of the previous studies as well as our study, both the absolute and relative diameter change during low flow reported is quite small (3, 21, 27, 42). Therefore, it is possible that our equipment is not sensitive enough to accurately detect these small changes in diameter, or the error in our measurements is greater than the actual change in diameter. Either of these problems could be responsible for the variability observed in L-FMC present in the brachial artery in the current study, as well as the contradictory findings present in the literature. While guidelines exist for the assessment of FMD, no such guidelines have been developed for L-FMC. Differences in the timing of the low flow measurement and the definition of dilation/constriction exist in the literature, which could also be responsible for the observed differences seen between studies.

Our results indicate that TVR in the brachial artery is moderately repeatable (ICC = 0.50). There have been limited previous investigations into TVR, with only two groups previously assessing the repeatability of TVR in the brachial artery. Inaba *et al.* assessed TVR (calculated as the absolute value of FMD+L-FMC) in 25 healthy men and found the measure had almost perfect repeatability (ICC = 0.93) (26). In contrast, Kranen *et al.* assessed TVR (as the difference between peak and occlusion diameter relative to baseline diameter) in 27 adolescents and found brachial artery TVR had moderate repeatability (ICC = 0.52) (27). We calculated TVR as the difference between peak and occlusion diameter relative to occlusion diameter and found similar results to Kranen *et al.* In a follow up analysis, we also calculated TVR as the absolute value of FMD + L-FMC, another commonly used equation in the literature. The repeatability of this measure

(ICC=0.52) was similar to that observed for our previously calculated TVR measure. Regardless of the equation used, TVR is a composite score of FMD and L-FMC and as such, is influenced by variability present in both of these measures. As we reported poor L-FMC repeatability, the high level of variability in L-FMC likely influenced the repeatability of TVR. Importantly, we found that there were no between day differences in any of the nitroglycerin challenge test variables. These results indicate that smooth muscle function did not differ between the two visits, which is in accordance with previous work that found NTG was relatively repeatable between days (15).

2.5.2 Observational Analysis

Our study is the first to directly investigate the relationship between age and L-FMC and TVR. In agreement with our hypothesis, we found that both FMD and TVR were negatively associated with age, and in contrast we found that L-FMC was not significantly associated with age. It is thought that the age related decline in FMD is related to a decreases in NO bioavailability and increases in oxidative stress and inflammation (38). Our results are inline with previous studies that have reported a decline in FMD as age increases (5, 34). Additionally, we expected that TVR would show a similar decline with age to FMD, as TVR is a composite score of FMD and L-FMC. We postulated that L-FMC would be attenuated with age, as Gori *et al.* found that being over 65 years old was associated with lower radial artery L-FMC (19). However, our results suggest that there is no relationship between L-FMC and age. It is possible the contrasts in the results of different studies may be due to conflicting alterations in ET-1 and vascular structure that occur with aging. ET-1 has been shown to increase with age,

therefore increases in ET-1 could potentially lead to an increase, rather than a decrease in L-FMC (13, 38). However, Harrison *et al*. found that L-FMC was positively correlated with brachial artery pulse wave velocity, suggesting that increases in stiffness are related to an attenuation of L-FMC (23). Therefore, it is possible that the contradictory actions of increased ET-1 and arterial stiffening might counterbalance each other, leading to no change in L-FMC with aging. We expected that CVD and elevated CVD risk would lead to a reduction in FMD, L-FMC and TVR and thus, the relationship between age and our vascular measures would be altered. However, we found that the relationship between age and our vascular measures was maintained in our cohort of individuals with CVD and elevated CVD risk.

Surprisingly, we found that sex did not moderate the relationship between age and any of our vascular measures. Earlier work has found sex differences in FMD in both younger and older adults (5, 14, 24). It is possible that the different patient populations in our sample could have influenced our ability to detect an effect of sex. While we attempted to increase the number of middle aged and older adults through our prospective cohort, a larger portion of our sample included children and younger adults. As there are conflicting findings of sex differences in younger adults, it is possible that the greater number of these individuals in our observational cohort influenced the sex specific moderator analysis of our data. As we saw L-FMC was highly variable in our repeatability analysis, it is possible that any influence of sex on the relationship between age and L-FMC is imperceptible. As both the relationship between age and FMD and L-FMC was not moderated by sex, it was unsurprising that the relationship between TVR

and age was also not moderated by sex.

Our results indicate there is a positive relationship between FMD and L-FMC. This suggests that reactivity to low flow influences the subsequent reactive hyperemia response and highlights the importance of assessing L-FMC alongside FMD. These findings are consistent with some (2, 18, 21, 23) but not all (16, 19, 27) studies that have previously assessed FMD and L-FMC. Importantly, it appears there are differences between the brachial artery and radial artery, as a majority of studies performed in the brachial artery have found a relationship between FMD and L-FMC (2, 21, 23), whereas those performed in the radial artery have not (16, 19). These findings highlight the potential for physiological differences between the two arterial beds.

2.5.3 Limitations and Future Directions

One major limitation of the present investigation is that our retrospective data included data from multiple studies that were collected and analyzed by different individuals. It is possible that having multiple sonographers and different individuals analyzing the ultrasound images could have increased the variation seen in our measurements. Additionally, there were slight differences in certain aspects of testing between the studies, such as the ultrasound equipment used and pretesting instructions, which could have influenced our results. While we found similar results to other studies that utilized healthy individuals, the inclusion of individuals with cardiovascular disease and elevated cardiovascular disease risk could have also increased the variability seen in our sample.

Future studies should continue to assess the repeatability of L-FMC and TVR and

guidelines for both of these measures should be developed if they are to be used as supplementary measurements to FMD. More work should be done to understand the mechanisms that are responsible for the low flow response and in particular address the dichotomy of dilatory and constrictor responses both within and between individuals. Additionally, more mechanistic studies should be performed in the brachial artery, as there has been relatively little research in this area and mechanistic studies may provide insight into why large variability exists between and within individuals. Finally, studies should focus on understanding other potential physiological factors that may influence L-FMC and TVR.

2.6 CONCLUSION

Our results indicate that FMD has substantial between day repeatability, while TVR is only moderately repeatable between days and L-FMC is not repeatable between days. Additionally we found that FMD and TVR were negatively associated with age, however L-FMC showed no relationship with age. Sex did not appear to moderate the relationship between age and any of our vascular measures and relationships between age and FMD and TVR persisted in our cohort of individuals with CVD and elevated CVD risk.

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APPENDICES

APPENDIX 1: RAW DATA

Shaded areas indicate missing data.

Repeatability Cohort

Participant Characteristics

Study ID	Sex	Age	Height	Weight	BMI
CAMS01	MALE	50	1.76	102.70	33.15
CAMS02	FEMALE	75	1.52	66.30	28.70
CAMS06	MALE	62	1.69	77.90	27.27
CAMS08	MALE	60	1.745	75.40	24.76
CAMS09	MALE	52	1.63	69.70	26.23
CAMS10	MALE	65	1.79	114.10	35.61
CAMS11	FEMALE	56	1.58	94.70	37.93
CAMS12	MALE	61	1.81	87.40	26.68
CAMS13	MALE	75	1.76	99.70	32.19
CAMS14	MALE	70	1.74	111.00	36.66
CAMS15	FEMALE	55	1.58	74.80	29.96
V2 CAMS01	MALE	50	1.76	102.70	33.15
V2 CAMS02	FEMALE	75	1.52	66.30	28.70
V2 CAMS06	MALE	62	1.69	77.90	27.27
V2 CAMS08	MALE	60	1.745	75.40	24.76
V2 CAMS09	MALE	52	1.63	69.70	26.23
V2 CAMS10	MALE	65	1.79	114.10	35.61
V2 CAMS11	FEMALE	56	1.58	94.70	37.93
V2 CAMS12	MALE	61	1.81	87.40	26.68
V2 CAMS13	MALE	75	1.76	99.70	32.19
V2 CAMS14	MALE	70	1.74	111.00	36.66
V2 CAMS15	FEMALE	55	1.58	74.80	29.96
RAM01 V1	MALE	21	1.84	86.8	25.64
RAM02 V1	MALE	21	1.82	88.9	26.84
RAM03 V1	MALE	22	1.76	67	21.63
RAM04 V1	MALE	21	1.87	82.1	23.48
RAM05 V1	MALE	21	1.65	63	23.14
RAM06 V1	MALE	21	1.82	73.6	22.22
RAM07 V1	MALE	21	1.68	72	25.51

RAM08 V1	MALE	24	1.79	67	20.91
RAM09 V1	MALE	21	1.81	62.7	19.14
RAM10 V1	MALE	23	1.76	86.2	27.83
RAM11 V1	MALE	19	1.74	74.4	24.57
RAM12 V1	MALE	20	1.89	76.5	21.42
RAM15 V1	MALE	19	1.79	85.7	27.49
RAM16 V1	MALE	21	1.83	73.4	21.92
RAM17 V1	MALE	20	1.79	71.6	22.35
RAM18 V1	MALE	21	1.78	86	27.14
RAM19 V1	MALE	21	1.86	81.1	23.44
RAM20 V1	MALE	21	1.67	71.5	25.64
RAM01 V2	MALE	21	1.84	86.8	25.64
RAM02 V2	MALE	21	1.82	88.9	26.84
RAM03 V2	MALE	22	1.76	67	21.63
RAM04 V2	MALE	21	1.87	82.1	23.48
RAM05 V2	MALE	21	1.65	63	23.14
RAM06 V2	MALE	21	1.82	73.6	22.22
RAM07 V2	MALE	21	1.68	72	25.51
RAM08 V2	MALE	24	1.79	67	20.91
RAM09 V2	MALE	21	1.81	62.7	19.14
RAM10 V2	MALE	23	1.76	86.2	27.83
RAM11 V2	MALE	19	1.74	74.4	24.57
RAM12 V2	MALE	20	1.89	76.5	21.42
RAM15 V2	MALE	19	1.79	85.7	27.49
RAM16 V2	MALE	21	1.83	73.4	21.92
RAM17 V2	MALE	20	1.79	71.6	22.35
RAM18 V2	MALE	21	1.78	86	27.14
RAM19 V2	MALE	21	1.86	81.1	23.44
RAM20 V2	MALE	21	1.67	71.5	25.64
RAM21 V1	FEMALE	20	1.54	46.3	19.52
RAM22 V1	FEMALE	20	1.575	46.4	18.70
RAM23 V1	FEMALE	26	1.55	43.9	18.27
RAM24 V1	FEMALE	19	1.59	56.4	22.31
RAM25 V1	FEMALE	22	1.61	52.2	20.14
RAM26 V1	FEMALE	21	1.64	62.1	23.09
RAM31 V1	FEMALE	23	1.55	48.3	20.10
RAM32 V1	FEMALE	24	1.6	66.7	26.05

RAM34 V1	FEMALE	18	1.56	54	22.19
RAM35 V1	FEMALE	32	1.63	60	22.58
RAM36 V1	FEMALE	20	1.57	57.4	23.29
RAM38 V1	FEMALE	22	1.58	46.5	18.63
RAM21 V2	FEMALE	20	1.54	46.3	19.52
RAM22 V2	FEMALE	20	1.575	46.4	18.70
RAM23 V2	FEMALE	26	1.55	43.9	18.27
RAM24 V2	FEMALE	19	1.59	56.4	22.31
RAM25 V2	FEMALE	22	1.61	52.2	20.14
RAM26 V2	FEMALE	21	1.64	62.1	23.09
RAM31 V2	FEMALE	23	1.55	48.3	20.10
RAM32 V2	FEMALE	24	1.6	66.7	26.05
RAM34 V2	FEMALE	18	1.56	54	22.19
RAM35 V2	FEMALE	32	1.63	60	22.58
RAM36 V2	FEMALE	20	1.57	57.4	23.29
RAM38 V2	FEMALE	22	1.58	46.5	18.63
V2RAM41	FEMALE	20	1.74	66.2	21.87
V2RAM43	FEMALE	26	1.65	60.5	22.22
V2RAM44	FEMALE	24	1.58	56.8	22.75
V2RAM46	FEMALE	20	1.65	60.5	22.22
V2RAM47	FEMALE	23	1.54	54	22.77
V2RAM48	FEMALE	19	1.67	103.8	37.22
V2RAM49	FEMALE	27	1.64	58.7	21.82
V2RAM50	FEMALE	18	1.58	47.2	18.91
V2RAM51	FEMALE	21	1.67	62.4	22.37
V2RAM52	FEMALE	18	1.62	51.7	19.70
V2RAM53	FEMALE	20	1.74	65.8	21.73
V2RAM54	FEMALE	21	1.69	59.2	20.73
V2RAM55	FEMALE	23	1.68	70.5	24.98
V2RAM56	FEMALE	19	1.65	47.2	17.34
V2RAM58	FEMALE	21	1.73	73	24.39
V2RAM59	FEMALE	20	1.58	64.4	25.80
V2RAM60	FEMALE	20	1.76	58.3	18.82
V2RAM61	FEMALE	27	1.66	59.6	21.63
V3RAM41	FEMALE	20	1.74	66.2	21.87
V3RAM43	FEMALE	26	1.65	60.5	22.22
V3RAM44	FEMALE	24	1.58	56.8	22.75

V3RAM46	FEMALE	20	1.65	60.5	22.22
V3RAM47	FEMALE	23	1.54	54	22.77
V3RAM48	FEMALE	19	1.67	103.8	37.22
V3RAM49	FEMALE	27	1.64	58.7	21.82
V3RAM50	FEMALE	18	1.58	47.2	18.91
V3RAM51	FEMALE	21	1.67	62.4	22.37
V3RAM52	FEMALE	18	1.62	51.7	19.70
V3RAM53	FEMALE	20	1.74	65.8	21.73
V3RAM54	FEMALE	21	1.69	59.2	20.73
V3RAM55	FEMALE	23	1.68	70.5	24.98
V3RAM56	FEMALE	19	1.65	47.2	17.34
V3RAM58	FEMALE	21	1.73	73	24.39
V3RAM59	FEMALE	20	1.58	64.4	25.80
V3RAM60	FEMALE	20	1.76	58.3	18.82
V3RAM61	FEMALE	27	1.66	59.6	21.63
ASPEN 1 V1	MALE	22	1.84	98.00	28.95
ASPEN 2 V1	MALE	23	1.68	60.50	21.44
ASPEN 3 V1	MALE	23	1.84	103.00	30.42
ASPEN 4 V1	MALE	21	1.81	80.50	24.57
ASPEN 5 V1	MALE	18	1.75	80.20	26.19
ASPEN 6 V1	MALE	20	1.73	77.00	25.73
ASPEN 7 V1	MALE	20	1.78	73.00	23.04
ASPEN 8 V1	MALE	22	1.80	74.00	22.84
ASPEN 9 V1	MALE	21	1.78	110.00	34.72
ASPEN 10 V1	MALE	30	1.80	65.50	20.22
ASPEN 1 V2	MALE	22	1.84	98.00	28.95
ASPEN 2 V2	MALE	23	1.68	60.50	21.44
ASPEN 3 V2	MALE	23	1.84	103.00	30.42
ASPEN 4 V2	MALE	21	1.81	80.50	24.57
ASPEN 5 V2	MALE	18	1.75	80.20	26.19
ASPEN 6 V2	MALE	20	1.73	77.00	25.73
ASPEN 7 V2	MALE	20	1.78	73.00	23.04
ASPEN 8 V2	MALE	22	1.80	74.00	22.84
ASPEN 9 V2	MALE	21	1.78	110.00	34.72
ASPEN 10 V2	MALE	30	1.80	65.50	20.22
V1 ACUTEENDO 1	MALE	25	1.85	91.00	26.60
V1 ACUTEENDO 2	MALE	22	1.81	91.50	27.90

V1 ACUTEENDO 3	MALE	25	1.79	67.50	21.10
V1 ACUTEENDO 4	MALE	22	1.63	71.50	26.90
V1 ACUTEENDO 5	MALE	21	1.69	65.50	22.90
V1 ACUTEENDO 6	MALE	21	1.83	84.50	25.20
V1 ACUTEENDO 7	MALE	25	1.83	75.00	22.40
V2 ACUTEENDO 1	MALE	25	1.85	91.00	26.60
V2 ACUTEENDO 2	MALE	22	1.81	91.50	27.90
V2 ACUTEENDO 3	MALE	25	1.79	67.50	21.10
V2 ACUTEENDO 4	MALE	22	1.63	71.50	26.90
V2 ACUTEENDO 5	MALE	21	1.69	65.50	22.90
V2 ACUTEENDO 6	MALE	21	1.83	84.50	25.20
V2 ACUTEENDO 7	MALE	25	1.83	75.00	22.40
EDS01	MALE	22	1.76	72	23.24
EDS02	MALE	20	1.8	59.7	18.43
EDS03	MALE	20	1.87	89.3	25.54
EDS04	MALE	24	1.82	91.1	27.50
EDS01 V2	MALE	22	1.76	72	23.24
EDS02 V2	MALE	20	1.8	59.7	18.43
EDS03 V2	MALE	20	1.87	89.3	25.54
EDS04 V2	MALE	24	1.82	91.1	27.50
TVR2	FEMALE	53	1.68	65.50	23.21
TVR3	MALE	79	1.84	80.74	23.85
TVR4	MALE	54	1.73	103.64	34.63
TVR5	MALE	38	1.92	86.36	23.43
TVR6	FEMALE	71	1.63	74.84	28.17
TVR7	MALE	71	1.75	74.80	24.42
TVR8	FEMALE	55	1.62	93.89	35.78
TVR9	MALE	55	1.76	107.50	34.70
TVR11	FEMALE	60	1.61	60.09	23.18
TVR12	FEMALE	67	1.60	64.54	25.21
TVR13	FEMALE	80	1.64	75.28	27.99
TVR14	FEMALE	58	1.77	87.98	28.08
TVR15	FEMALE	62	1.68	73.60	26.08
TVR16	FEMALE	60	1.66	58.86	21.36
TVR17	MALE	62	1.79	84.50	26.37
TVR18	FEMALE	73	1.54	107.16	45.18
TVR19	FEMALE	65	1.61	78.60	30.32
TVR20	FEMALE	67	1.63	72.50	27.29

V2TVR02	FEMALE	53	1.68	65.50	23.21
V2TVR03	MALE	79	1.84	80.74	23.85
V2TVR04	MALE	54	1.73	103.64	34.63
V2TVR05	MALE	38	1.92	86.36	23.43
V2TVR06	FEMALE	71	1.63	74.84	28.17
V2TVR07	MALE	71	1.75	74.80	24.42
V2TVR08	FEMALE	55	1.62	93.89	35.78
V2TVR09	MALE	55	1.76	107.50	34.70
V2TVR11	FEMALE	60	1.61	60.09	23.18
V2TVR12	FEMALE	67	1.60	64.54	25.21
V2TVR13	FEMALE	80	1.64	75.28	27.99
V2TVR14	FEMALE	58	1.77	87.98	28.08
V2TVR15	FEMALE	62	1.68	73.60	26.08
V2TVR16	FEMALE	60	1.66	58.86	21.36
V2TVR17	MALE	62	1.79	84.50	26.37
V2TVR18	FEMALE	73	1.54	107.16	45.18
V2TVR19	FEMALE	65	1.61	78.60	30.32
V2TVR20	FEMALE	67	1.63	72.50	27.29

Hemodynamics

Study ID	**HR**	**SBP**	**DBP**	**MAP**
CAMS01				
CAMS02				
CAMS06				
CAMS08				
CAMS09				
CAMS10				
CAMS11				
CAMS12				
CAMS13				
CAMS14				
CAMS15				
V2 CAMS01				
V2 CAMS02				
V2 CAMS06				
V2 CAMS08				

V2 CAMS09				
V2 CAMS10				
V2 CAMS11				
V2 CAMS12				
V2 CAMS13				
V2 CAMS14				
V2 CAMS15				
RAM01 V1	58	118	68	88
RAM02 V1	59	116	63	85
RAM03 V1	55	121	69	88
RAM04 V1	73	124	77	93
RAM05 V1	65	105	62	82
RAM06 V1	63	119	60	85
RAM07 V1	77	134	70	93
RAM08 V1	64	126	67	89
RAM09 V1	67	111	65	85
RAM10 V1	72	132	71	93
RAM11 V1	47	117	68	88
RAM12 V1	83	128	68	91
RAM15 V1	55	127	67	90
RAM16 V1	71	127	64	89
RAM17 V1	72	113	66	85
RAM18 V1	55	125	65	89
RAM19 V1	73	126	66	88
RAM20 V1	72	113	65	85
RAM01 V2	57	126	69	91
RAM02 V2	72	130	67	91
RAM03 V2	54	126	63	89
RAM04 V2	79	118	76	91
RAM05 V2	58	111	64	84
RAM06 V2	59	117	60	84
RAM07 V2	56	126	67	90
RAM08 V2	53	113	65	85

RAM09 V2	64	109	65	84
RAM10 V2	79	125	65	87
RAM11 V2	47	117	68	88
RAM12 V2	49	116	62	84
RAM15 V2	52	121	65	88
RAM16 V2	78	125	65	88
RAM17 V2	68	114	62	84
RAM18 V2	50	116	63	85
RAM19 V2	75	122	61	85
RAM20 V2	48	111	62	84
RAM21 V1	68	109	76	87
RAM22 V1	54	96	62	77
RAM23 V1	60	92	64	76
RAM24 V1	53	103	65	82
RAM25 V1	61	107	69	85
RAM26 V1	53	117	78	90
RAM31 V1	59	102	66	82
RAM32 V1	79	113	73	88
RAM34 V1	64	106	66	83
RAM35 V1	45	114	70	87
RAM36 V1	58	103	68	83
RAM38 V1	66	94	64	77
RAM21 V2	71	107	82	90
RAM22 V2	52	95	64	77
RAM23 V2	61	90	63	74
RAM24 V2	57	107	68	84
RAM25 V2	56	103	68	83
RAM26 V2	49	112	75	88
RAM31 V2	57	91	63	74
RAM32 V2	73	118	73	89
RAM34 V2	64	104	65	82
RAM35 V2	49	108	67	85
RAM36 V2	60	99	70	83

RAM38 V2	65	91	59	73
V2RAM41	70	95	62	77
V2RAM43	72	94	65	78
V2RAM44	74	102	65	81
V2RAM46	68	98	68	81
V2RAM47	55	101	61	79
V2RAM48	54	108	66	84
V2RAM49	74	109	74	86
V2RAM50	61	105	71	84
V2RAM51	80	99	64	80
V2RAM52	72	106	66	83
V2RAM53	56	107	66	84
V2RAM54	72	108	80	88
V2RAM55	62	107	66	83
V2RAM56	69	96	67	79
V2RAM58	59	116	70	89
V2RAM59	64	112	79	88
V2RAM60	60	91	63	75
V2RAM61	70	103	68	83
V3RAM41	70	95	63	77
V3RAM43	67	96	64	78
V3RAM44	83	101	68	83
V3RAM46	62	97	66	80
V3RAM47	57	96	60	77
V3RAM48	56	107	66	83
V3RAM49	64	110	75	87
V3RAM50	60	103	67	83
V3RAM51	67	99	64	80
V3RAM52	58	103	63	81
V3RAM53	54	104	64	82
V3RAM54	70	101	69	83
V3RAM55	68	105	64	82
V3RAM56	72	96	67	81

V3RAM58	48	105	63	81
V3RAM59	62	112	81	89
V3RAM60	67	106	70	84
V3RAM61	70	102	70	83
ASPEN 1 V1	55	112	58	80
ASPEN 2 V1	63	115	60	81
ASPEN 3 V1	62	148	79	106
ASPEN 4 V1	74	123	60	85
ASPEN 5 V1	69	121	63	86
ASPEN 6 V1	62	122	61	85
ASPEN 7 V1	59	127	72	93
ASPEN 8 V1	60	127	60	86
ASPEN 9 V1	51	128	75	94
ASPEN 10 V1	53	103	70	82
ASPEN 1 V2	70	131	60	87
ASPEN 2 V2	66	104	58	76
ASPEN 3 V2	73	118	65	86
ASPEN 4 V2	73	129	62	87
ASPEN 5 V2	60	130	68	93
ASPEN 6 V2	60	108	60	77
ASPEN 7 V2	69	121	62	85
ASPEN 8 V2	62	119	57	83
ASPEN 9 V2	55	121	77	93
ASPEN 10 V2	55	102	68	81
V1 ACUTEENDO 1	58	124	73	90
V1 ACUTEENDO 2	56	126	73	91
V1 ACUTEENDO 3	48	133	78	96
V1 ACUTEENDO 4	50	122	70	87
V1 ACUTEENDO 5	54	131	77	95
V1 ACUTEENDO 6	75	131	69	90
V1 ACUTEENDO 7	59	106	57	73
V2 ACUTEENDO 1	59	112	66	81
V2 ACUTEENDO 2	51	127	70	89

V2 ACUTEENDO 3	52	108	64	79
V2 ACUTEENDO 4	43	115	68	84
V2 ACUTEENDO 5	53	121	70	87
V2 ACUTEENDO 6	74	133	67	89
V2 ACUTEENDO 7	64	99	55	70
EDS01	88.5	114.5	77.5	89
EDS02	72	114	68.5	87
EDS03	56	131	72	93
EDS04	67	123.7	70.3	89.3
EDS01 V2	72.5	123.5	76.5	93
EDS02 V2	54	117	72	88
EDS03 V2	77	115	65	86
EDS04 V2	68	117.7	73.3	90
TVR2	60.5	108	69.5	84.5
TVR3	59	141.5	79.5	104.5
TVR4	91.5	126	76.5	94
TVR5	49	116	71	89
TVR6	56.5	138	85.5	107.5
TVR7	65	126.5	74	95
TVR8	73	124.5	79	97
TVR9	64	115	69.5	85
TVR11	59	123	78	96.5
TVR12	60.5	117.5	75	92
TVR13	69.5	133.5	71.5	97.5
TVR14	55	112.5	75.5	76
TVR15	66	128.5	80	100.5
TVR16	51.5	92.5	58.5	71.5
TVR17	41.5	126	77	97
TVR18	60	140	69.5	98.5
TVR19	54.5	119	69.5	89
TVR20	73	139.5	76	101
V2TVR02	68	94.5	55.5	70
V2TVR03	80.5	138	85.5	106.5
V2TVR04	87.5	133	82.5	102
V2TVR05	50.5	119.5	69.5	89

V2TVR06	60.5	124	73	93.5
V2TVR07	66.5	121	73.5	91.5
V2TVR08	64.5	113	74	88.5
V2TVR09	63	113	67	84
V2TVR11	56	111	73	86.5
V2TVR12	66.5	113.5	68	85.5
V2TVR13	74.5	131	76	98.5
V2TVR14	56.5	111.5	65	83.5
V2TVR15	65.5	125	83.5	99.5
V2TVR16	63.5	96.5	67.5	78
V2TVR17	44.5	123.5	78.5	96.5
V2TVR18	58	145.5	72.5	103.5
V2TVR19	55	117.5	70	89.5
V2TVR20	75	122.7	70	91.3

Blood Analyses

Normative Values Postmenopausal Women: estradiol (<103 pmol/L), progesterone (<0.7 nmol/L), testosterone (≤1.5 nmol/L)

Normative Values Men: estradiol (<162 pmol/L), progesterone (<0.7 nmol/L), testosterone (4.5-26.6 nmol/L)

Study ID	**Estradiol (pmol/L)**		**Progesterone (nmol/L)**		**Testosterone (nmol/L)**	
	V1	**V2**	**V1**	**V2**	**V1**	**V2**
TVR01						
TVR02	<92	<92	<0.3	0.4	<0.7	1
TVR03	99	N/A	0.6	N/A	15.2	N/A
TVR04						
TVR05	N/A	<92	N/A	0.5	N/A	12.4
TVR06	<92	<92	<0.3	<0.3	<0.7	<0.7
TVR07	<92	N/A	0.6	N/A	12.8	N/A
TVR08	<92		0.4		<0.7	
TVR09						
TVR10						
TVR11	<92	<92	<0.3	0.4	<0.7	<0.7
TVR12	<92	<92	0.4	0.4	<0.7	<0.7
TVR13	<92		0.5		0.9	
TVR14		<92		<0.3		<0.7
TVR15	<92	<92	<0.3	<0.3	<0.7	<0.7

TVR16	<92	<92	0.4	0.4	<0.7	<0.7
TVR17	N/A	<92	N/A	0.3	N/A	13.7
TVR18	<92	<92	0.4	0.9	<0.7	<0.7
TVR19		<92		<0.3		<0.7
TVR20	<92	<92	<0.3	<0.3	<0.7	<0.7

Vascular Variables

Study ID	BL Diameter	Peak Diameter	Time to Peak	Abs FMD	% FMD	4 min Diameter	Abs L-FMC	%L-FMC	TVR	ABS(FMD +LFMC)	LOW FLOW RESPONSE
CAMS01	4.26	4.34		0.09	2.06	4.16	-0.09	-2.13	4.28	4.18	Constrict
CAMS02	2.80	2.76		-0.04	-1.35	2.61	-0.19	-6.75	5.79	8.11	Constrict
CAMS06	4.33	4.52		0.19	4.27	4.40	0.07	1.52	2.71	5.79	Dilate
CAMS08	4.21	4.36		0.15	3.53	4.10	-0.11	-2.51	6.19	6.02	Constrict
CAMS09	3.30	3.41		0.11	3.44	3.25	-0.05	-1.45	4.96	4.90	Constrict
CAMS10	5.66	5.83		0.18	3.09	5.68	0.02	0.34	2.74	3.44	Dilate
CAMS11	2.28	2.59		0.31	13.60	2.32	0.04	1.76	11.64	15.36	Dilate
CAMS12	3.81	3.78		-0.03	-0.82	3.79	-0.02	-0.56	-0.27	1.38	Constrict
CAMS13	3.55	3.84		0.29	8.23	3.58	0.03	0.86	7.30	9.10	Dilate
CAMS14	4.62	4.82		0.20	4.32	4.75	0.13	2.75	1.53	7.06	Dilate
CAMS15	2.67	2.81		0.14	5.16	2.60	-0.07	-2.60	7.96	7.77	Constrict
V2 CAMS01	4.33	4.42		0.09	2.18	4.36	0.03	0.73	1.43	2.91	Dilate
V2 CAMS02	2.62	2.65		0.03	1.00	2.67	0.04	1.68	-0.67	2.67	Dilate
V2 CAMS06	4.33	4.67		0.34	7.93	4.49	0.16	3.70	4.08	11.62	Dilate
V2 CAMS08	4.25	4.39		0.14	3.31	4.31	0.06	1.43	1.85	4.75	Dilate
V2 CAMS09	3.66	3.74		0.08	2.25	3.67	0.02	0.48	1.76	2.73	Dilate
V2 CAMS10	5.39	5.56		0.16	3.03	5.34	-0.05	-0.89	3.95	3.91	Constrict
V2 CAMS11	2.36	2.79		0.43	18.08	2.66	0.30	12.54	4.92	30.64	Dilate
V2 CAMS12	3.82	3.92		0.11	2.77	3.86	0.04	1.06	1.69	3.84	Dilate
V2 CAMS13	3.95	4.05		0.10	2.58	3.81	-0.14	-3.66	6.47	6.24	Constrict
V2 CAMS14	4.96	5.20		0.24	4.86	4.96	0.00	-0.01	4.88	4.87	Constrict
V2 CAMS15	2.84	3.23		0.39	13.56	3.31	0.47	16.52	-2.54	30.07	Dilate

RAM01 V1	4.27	4.61	34.28	0.34	8.03	4.31	0.04	0.90	7.07	8.86	Dilate
RAM02 V1	5.08	5.33	59.16	0.25	4.98	5.08	0.00	0.08	4.90	5.00	Dilate
RAM03 V1	4.15	4.32	48.36	0.17	4.11	4.16	0.01	0.30	3.80	4.40	Dilate
RAM04 V1	4.17	4.28	34.28	0.11	2.68	4.22	0.05	1.20	1.46	3.84	Dilate
RAM05 V1	3.62	3.95	46.37	0.33	9.02	3.83	0.22	5.95	2.90	15.07	Dilate
RAM06 V1	4.01	4.28	56.97	0.27	6.75	4.08	0.07	1.83	4.83	8.56	Dilate
RAM07 V1	4.29	4.64	25.18	0.35	8.23	4.35	0.06	1.41	6.72	9.57	Dilate
RAM08 V1	4.14	4.49	75.90	0.35	8.33	4.06	-0.09	-2.16	10.72	10.61	Constrict
RAM09 V1	4.09	4.24	35.20	0.15	3.61	4.13	0.04	0.87	2.71	4.54	Dilate
RAM10 V1	4.54	4.76	73.94	0.21	4.71	4.63	0.08	1.83	2.83	6.46	Dilate
RAM11 V1	3.83	4.02	44.99	0.19	4.88	3.81	-0.02	-0.45	5.36	5.41	Constrict
RAM12 V1	4.48	4.87	35.51	0.39	8.61	4.40	-0.08	-1.85	10.66	10.56	Constrict
RAM15 V1	4.65	4.93	29.96	0.28	5.93	4.68	0.02	0.53	5.37	6.55	Dilate
RAM16 V1	3.81	4.39	70.66	0.57	15.06	3.92	0.11	2.87	11.85	17.83	Dilate
RAM17 V1	4.25	4.53	60.57	0.28	6.61	4.33	0.08	1.90	4.62	8.49	Dilate
RAM18 V1	4.78	4.96	62.25	0.17	3.63	4.75	-0.03	-0.66	4.32	4.22	Constrict
RAM19 V1	4.35	4.64	57.97	0.3	6.80	4.36	0.01	0.19	6.59	7.09	Dilate
RAM20 V1	4.21	4.56	78.44	0.34	8.16	4.27	0.06	1.38	6.69	9.45	Dilate
RAM01 V2	4.27	4.68	50.65	0.41	9.69	4.42	0.15	3.57	5.91	13.17	Dilate
RAM02 V2	5.06	5.33	41.58	0.27	5.34	5.08	0.02	0.37	4.95	5.70	Dilate
RAM03 V2	4.02	4.26	44.39	0.23	5.77	4.07	0.05	1.19	4.52	6.91	Dilate
RAM04 V2	3.62	3.73	53.51	0.1	2.89	3.67	0.05	1.39	1.47	4.15	Dilate
RAM05 V2	3.57	3.85	29.13	0.28	7.98	3.66	0.09	2.47	5.37	10.31	Dilate
RAM06 V2	4.04	4.25	44.83	0.21	5.18	4.16	0.12	2.90	2.21	8.10	Dilate
RAM07 V2	4.22	4.50	41.69	0.27	6.49	4.25	0.03	0.70	5.75	7.09	Dilate
RAM08 V2	4.02	4.37	60.22	0.35	8.71	4.17	0.15	3.84	4.68	12.55	Dilate

RAM09 V2	3.95	4.10	42.59	0.15	3.74	3.93	-0.02	-0.52	4.29	4.32	Constrict
RAM10 V2	4.64	4.88	100.08	0.24	5.09	4.77	0.13	2.78	2.24	7.96	Dilate
RAM11 V2	3.83	4.03	40.11	0.2	5.29	3.81	-0.02	-0.62	5.95	5.84	Constrict
RAM12 V2	4.26	4.59	20.63	0.33	7.66	4.27	0.01	0.22	7.42	7.96	Dilate
RAM15 V2	4.64	4.88	41.14	0.24	5.22	4.69	0.05	1.13	4.04	6.30	Dilate
RAM16 V2	3.92	4.53	59.41	0.61	15.53	3.84	-0.08	-2.13	18.04	17.69	Constrict
RAM17 V2	4.25	4.51	44.40	0.26	6.12	4.27	0.02	0.59	5.51	6.70	Dilate
RAM18 V2	4.76	4.93	43.75	0.17	3.60	4.70	-0.06	-1.27	4.93	4.84	Constrict
RAM19 V2	4.26	4.51	47.19	0.25	5.85	4.34	0.07	1.73	4.05	7.60	Dilate
RAM20 V2	4.19	4.48	77.74	0.29	6.99	4.22	0.03	0.71	6.24	7.63	Dilate
RAM21 V1	2.47	2.76	39.77	0.29	11.76	2.42	-0.06	-2.26	14.35	14.00	Constrict
RAM22 V1	2.82	3.13	99.21	0.32	11.19	2.77	-0.04	-1.52	12.90	12.69	Constrict
RAM23 V1	2.74	2.94	25.18	0.2	7.35	2.74	0.00	-0.08	7.49	7.38	Constrict
RAM24 V1	3.55	3.63	45.39	0.08	2.16	3.54	-0.01	-0.36	2.58	2.61	Constrict
RAM25 V1	3.05	3.22	41.04	0.17	5.64	3.03	-0.02	-0.59	6.27	6.17	Constrict
RAM26 V1	2.83	3.20	34.77	0.37	13.00	2.91	0.08	2.75	9.97	15.83	Dilate
RAM31 V1	3.30	3.41	145.69	0.1	3.15	3.31	0.01	0.35	2.78	3.38	Dilate
RAM32 V1	3.07	3.28	76.00	0.21	6.78	3.05	-0.02	-0.69	7.53	7.53	Constrict
RAM34 V1	2.72	2.98	47.97	0.26	9.54	2.74	0.02	0.81	8.66	10.37	Dilate
RAM35 V1	3.47	3.66	58.98	0.18	5.25	3.50	0.03	0.76	4.45	5.95	Dilate
RAM36 V1	3.35	3.47	41.90	0.13	3.77	3.30	-0.05	-1.40	5.24	5.28	Constrict
RAM38 V1	3.18	3.31	41.86	0.13	4.07	3.17	-0.01	-0.40	4.50	4.49	Constrict
RAM21 V2	2.49	2.75	37.56	0.26	10.34	2.47	-0.02	-0.81	11.24	11.25	Constrict
RAM22 V2	2.82	3.04	45.48	0.22	7.74	2.79	-0.03	-1.04	8.86	8.84	Constrict
RAM23 V2	2.78	3.07	56.60	0.29	10.34	2.77	-0.01	-0.39	10.77	10.82	Constrict
RAM24 V2	3.53	3.67	39.62	0.14	3.86	3.51	-0.02	-0.56	4.44	4.52	Constrict

RAM25 V2	2.94	3.08	45.00	0.14	4.80	2.93	-0.01	-0.49	5.31	5.25	Constrict
RAM26 V2	2.88	3.24	52.64	0.36	12.55	3.08	0.20	7.00	5.18	19.51	Dilate
RAM31 V2	3.45	3.61	35.29	0.16	4.63	3.42	-0.04	-1.04	5.73	5.68	Constrict
RAM32 V2	3.09	3.35	83.78	0.26	8.50	3.09	0.00	0.11	8.38	8.53	Dilate
RAM34 V2	2.76	3.06	60.82	0.3	10.95	2.72	-0.04	-1.63	12.78	12.50	Constrict
RAM35 V2	3.49	3.66	38.41	0.17	4.85	3.50	0.01	0.21	4.63	5.08	Dilate
RAM36 V2	3.37	3.55	30.70	0.18	5.44	3.37	0.00	0.13	5.30	5.47	Dilate
RAM38 V2	3.11	3.37	30.83	0.25	8.13	3.17	0.06	1.84	6.18	9.88	Dilate
V2RAM41	3.10	3.32	32.65	0.23	7.32	3.18	0.08	2.51	4.69	9.90	Dilate
V2RAM43	3.12	3.33	30.97	0.21	6.83	3.16	0.04	1.29	5.47	8.12	Dilate
V2RAM44	2.86	3.16	101.83	0.29	10.29	3.00	0.14	4.82	5.22	15.18	Dilate
V2RAM46	2.94	3.29	41.20	0.35	11.72	3.00	0.05	1.85	9.69	13.42	Dilate
V2RAM47	3.31	3.54	34.07	0.23	6.87	3.29	-0.02	-0.66	7.58	7.48	Constrict
V2RAM48	3.38	3.71	28.75	0.33	9.77	3.38	0.01	0.16	9.59	10.06	Dilate
V2RAM49	3.00	3.16	38.31	0.16	5.39	3.00	0.00	0.10	5.28	5.39	Dilate
V2RAM50	2.78	3.10	36.70	0.32	11.41	2.80	0.02	0.63	10.71	12.13	Dilate
V2RAM51	3.70	3.85	25.85	0.15	4.10	3.69	-0.01	-0.16	4.27	4.38	Constrict
V2RAM52	3.36	3.69	24.66	0.33	9.82	3.42	0.06	1.73	7.95	11.61	Dilate
V2RAM53	3.85	4.06	26.78	0.21	5.39	3.83	-0.02	-0.46	5.87	5.97	Constrict
V2RAM54	2.88	3.12	41.72	0.24	8.23	2.83	-0.05	-1.82	10.23	10.07	Constrict
V2RAM55	3.51	3.80	26.58	0.29	8.32	3.59	0.08	2.37	5.82	10.69	Dilate
V2RAM56	3.25	3.50	22.80	0.25	7.68	3.26	0.01	0.28	7.38	7.99	Dilate
V2RAM58	3.31	3.60	30.55	0.29	8.84	3.27	-0.03	-1.01	9.95	9.75	Constrict
V2RAM59	3.49	3.67	32.35	0.18	5.26	3.44	-0.05	-1.37	6.72	6.69	Constrict
V2RAM60	3.37	3.58	30.66	0.21	6.12	3.31	-0.07	-1.93	8.20	8.19	Constrict
V2RAM61	3.32	3.51	28.39	0.19	5.67	3.28	-0.04	-1.12	6.88	6.88	Constrict

V3RAM41	3.16	3.37	30.65	0.21	6.56	3.17	0.00	0.13	6.42	6.56	Dilate
V3RAM43	3.02	3.23	30.56	0.20	6.73	3.09	0.07	2.35	4.28	9.05	Dilate
V3RAM44	3.00	3.27	86.22	0.27	8.94	3.10	0.10	3.31	5.45	12.27	Dilate
V3RAM46	3.17	3.28	132.94	0.11	3.36	3.17	-0.01	-0.18	3.55	3.68	Constrict
V3RAM47	3.34	3.64	25.14	0.30	9.06	3.40	0.07	1.97	6.95	11.15	Dilate
V3RAM48	3.49	3.81	29.40	0.32	9.10	3.52	0.03	0.84	8.19	9.95	Dilate
V3RAM49	3.04	3.22	57.69	0.17	5.63	2.90	-0.15	-4.86	11.03	10.56	Constrict
V3RAM50	2.90	3.21	45.18	0.31	10.61	2.90	0.00	-0.03	10.63	10.61	Constrict
V3RAM51	3.69	3.83	33.10	0.14	3.73	3.62	-0.07	-1.88	5.72	5.62	Constrict
V3RAM52	3.54	3.94	10.42	0.40	11.20	3.61	0.07	1.98	9.07	13.29	Dilate
V3RAM53	4.00	4.20	27.01	0.20	5.10	3.99	-0.01	-0.29	5.40	5.25	Constrict
V3RAM54	2.91	3.15	41.16	0.24	8.30	2.88	-0.03	-1.15	9.55	9.28	Constrict
V3RAM55	2.95	3.22	40.35	0.27	9.08	2.95	0.01	0.20	8.86	9.28	Dilate
V3RAM56	3.40	3.62	23.13	0.22	6.52	3.40	0.00	0.00	6.52	6.52	Nochange
V3RAM58	3.13	3.31	38.69	0.18	5.78	3.10	-0.02	-0.75	6.58	6.42	Constrict
V3RAM59	3.46	3.66	32.45	0.20	5.74	3.42	-0.04	-1.26	7.10	6.90	Constrict
V3RAM60	3.60	3.84	33.50	0.23	6.44	3.60	-0.01	-0.16	6.61	6.72	Constrict
V3RAM61	3.37	3.60	37.93	0.24	7.09	3.32	-0.05	-1.37	8.58	8.57	Constrict
ASPEN 1 V1	5.04	5.29		0.25	4.98	5.08	0.04	0.80	4.14	5.76	Dilate
ASPEN 2 V1	4.05	4.29		0.24	5.81	4.13	0.07	1.77	3.97	7.70	Dilate
ASPEN 3 V1	5.29	5.42		0.14	2.55	5.27	-0.02	-0.39	2.96	2.95	Constrict
ASPEN 4 V1	4.34	4.66		0.32	7.39	4.45	0.11	2.47	4.80	9.84	Dilate
ASPEN 5 V1	4.47	4.66		0.19	4.43	4.53	0.06	1.43	2.96	5.68	Dilate
ASPEN 6 V1	4.55	4.71		0.16	3.41	4.43	-0.13	-2.79	6.38	6.31	Constrict
ASPEN 7 V1	4.09	4.39		0.3	7.23	4.23	0.13	3.26	3.85	10.59	Dilate
ASPEN 8 V1	3.4	3.63		0.23	6.72	3.46	0.07	1.96	4.67	8.73	Dilate

ASPEN 9 V1	4.88	5.14		0.26	5.25	4.99	0.11	2.22	2.97	7.54	Dilate
ASPEN 10V1	4.17	4.57		0.4	9.65	4.22	0.05	1.16	8.40	10.75	Dilate
ASPEN 1 V2	4.84	5.10		0.26	5.48	4.94	0.10	2.09	3.32	7.46	Dilate
ASPEN 2 V2	4.19	4.47		0.28	6.68	4.42	0.22	5.29	1.32	11.97	Dilate
ASPEN 3 V2	5.05	5.24		0.19	3.85	5.00	-0.04	-0.84	4.73	4.61	Constrict
ASPEN 4 V2	4.39	4.62		0.23	5.34	4.54	0.15	3.39	1.88	8.63	Dilate
ASPEN 5 V2	4.47	4.87		0.4	8.96	4.56	0.09	2.07	6.74	11.02	Dilate
ASPEN 6 V2	4.37	4.58		0.21	4.76	4.59	0.22	4.97	-0.20	9.73	Dilate
ASPEN 7 V2	3.79	4.14		0.34	9.06	4.09	0.30	7.83	1.14	16.91	Dilate
ASPEN 8 V2	3.08	3.48		0.4	12.94	3.22	0.14	4.41	8.17	17.40	Dilate
ASPEN 9 V2	5.05	5.30		0.25	4.85	5.07	0.02	0.44	4.39	5.39	Dilate
ASPEN 10V2	4.35	4.74		0.39	8.86	4.23	-0.13	-2.89	12.10	11.86	Constrict
V1 ACUTEENDO 1	3.97	4.26	37.05	0.29	7.19	4.11	0.13	3.29	3.77	10.47	Dilate
V1 ACUTEENDO 2	3.91	4.07	47.87	0.17	4.27	3.88	-0.03	-0.78	5.10	5.06	Constrict
V1 ACUTEENDO 3	4.45	4.81	22.13	0.36	8.05	4.47	0.02	0.50	7.51	8.55	Dilate
V1 ACUTEENDO 4	3.27	3.38	60.60	0.11	3.25	3.20	-0.07	-2.21	5.71	5.57	Constrict
V1 ACUTEENDO 5	4.17	4.21	95.12	0.04	1.02	4.00	-0.17	-3.97	5.19	4.99	Constrict
V1 ACUTEENDO 6	4.58	4.76	63.70	0.18	3.97	4.46	-0.11	-2.48	6.61	6.45	Constrict
V1 ACUTEENDO 7	3.71	3.88	57.78	0.17	4.52	3.69	-0.02	-0.60	5.15	5.12	Constrict
V2 ACUTEENDO 1	4.06	4.34	33.35	0.27	6.70	4.12	0.06	1.41	5.22	8.11	Dilate
V2 ACUTEENDO 2	3.98	4.17	90.66	0.19	4.70	3.96	-0.02	-0.39	5.11	5.09	Constrict
V2 ACUTEENDO 3	4.43	4.81	63.84	0.39	8.74	4.42	-0.01	-0.24	9.00	8.98	Constrict

V2 ACUTEENDO 4	3.27	3.54	57.46	0.27	8.36	3.36	0.09	2.70	5.52	11.06	Dilate
V2 ACUTEENDO 5	3.78	3.93	28.84	0.15	3.98	3.85	0.07	1.91	2.03	5.89	Dilate
V2 ACUTEENDO 6	4.54	4.81	61.02	0.27	5.96	4.61	0.07	1.62	4.27	7.58	Dilate
V2 ACUTEENDO 7	3.67	3.96	57.78	0.29	7.90	3.73	0.05	1.48	6.32	9.38	Dilate
EDS01	2.94	3.20	33.49	0.25	8.62	2.96	0.02	0.62	7.95	9.24	Dilate
EDS02	3.45	3.87	58.66	0.42	12.21	3.67	0.22	6.33	5.53	18.53	Dilate
EDS03	3.95	4.16	71.32	0.21	5.41	4.00	0.05	1.27	4.09	6.67	Dilate
EDS04	4.65	5.05		0.40	8.52	4.67	0.01	0.32	8.18	8.84	Dilate
EDS01 V2	3.15	3.24	48.46	0.09	2.91	3.13	-0.02	-0.63	3.56	3.54	Constrict
EDS02 V2	3.71	3.95	58.36	0.23	6.28	3.55	-0.16	-4.42	11.19	10.70	Constrict
EDS03 V2	4.29	4.53	69.58	0.24	5.58	4.34	0.05	1.17	4.35	6.75	Dilate
EDS04 V2	4.81	5.06	48.42	0.25	5.14	4.78	-0.02	-0.51	5.68	5.66	Constrict
TVR2	4.00	4.09	58.77	0.09	2.28	4.00	0.00	0.10	2.18	2.25	Dilate
TVR3	5.71	5.78		0.07	1.23	5.67	-0.04	-0.70	1.94	1.93	Constrict
TVR4	5.69	5.84	61.46	0.15	2.64	5.75	0.06	1.05	1.57	3.68	Dilate
TVR5	5.45	5.53	40.27	0.08	1.52	5.49	0.04	0.77	0.75	2.29	Dilate
TVR6	4.73	4.92	132.43	0.19	3.95	4.77	0.04	0.80	3.12	4.75	Dilate
TVR7	4.69	4.87	80.43	0.18	3.75	4.74	0.05	1.14	2.58	4.90	Dilate
TVR8	4.39	4.65	59.35	0.26	6.03	4.46	0.07	1.59	4.37	7.52	Dilate
TVR9	4.45	4.64	55.30	0.19	4.30	4.46	0.01	0.16	4.14	4.49	Dilate
TVR11	4.78	4.98	64.34	0.21	4.32	4.77	-0.01	-0.22	4.56	4.55	Constrict

TVR12	3.62	3.81	71.54	0.19	5.30	3.60	-0.02	-0.59	5.93	5.80	Constrict
TVR13	3.74	3.88	41.30	0.14	3.69	3.72	-0.02	-0.53	4.24	4.28	Constrict
TVR14	3.36	3.51	48.34	0.15	4.32	3.37	0.01	0.41	3.90	4.76	Dilate
TVR15	4.00	4.11	74.18	0.11	2.63	4.00	-0.01	-0.17	2.80	3.00	Constrict
TVR16	3.72	3.96	57.19	0.24	6.55	3.76	0.05	1.23	5.26	7.89	Dilate
TVR17	5.46	5.72	65.52	0.26	4.81	5.53	0.08	1.39	3.37	6.27	Dilate
TVR18	3.76	3.89	63.85	0.12	3.29	3.80	0.04	1.04	2.23	4.26	Dilate
TVR19	3.16	3.23	33.97	0.07	2.09	3.14	-0.02	-0.67	2.78	2.76	Constrict
TVR20	3.99	4.09	146.58	0.09	2.33	3.97	-0.02	-0.59	2.94	2.76	Constrict
V2TVR02	3.86	3.96	115.77	0.10	2.69	3.84	-0.02	-0.44	3.14	3.12	Constrict
V2TVR03	5.46	5.73	74.15	0.27	4.93	5.66	0.20	3.70	1.19	8.63	Dilate
V2TVR04	5.42	5.67	53.77	0.25	4.60	5.30	-0.12	-2.12	6.87	6.72	Constrict
V2TVR05	5.29	5.43		0.14	2.67	5.34	0.06	1.06	1.59	3.74	Dilate
V2TVR06	5.05	5.15	78.85	0.11	2.10	5.05	0.00	0.05	2.05	2.15	Dilate
V2TVR07	4.76	4.92	68.80	0.16	3.39	4.75	0.00	-0.07	3.47	3.47	Constrict
V2TVR08	4.33	4.58	49.79	0.24	5.65	4.41	0.08	1.75	3.83	7.39	Dilate
V2TVR09	4.52	4.75	50.83	0.23	5.02	4.49	-0.03	-0.60	5.66	5.63	Constrict
V2TVR11	4.83	4.94	62.42	0.11	2.36	4.85	0.02	0.47	1.88	2.83	Dilate
V2TVR12	4.62	4.72	66.64	0.10	2.15	4.64	0.02	0.52	1.62	2.67	Dilate
V2TVR13	3.70	3.83		0.13	3.48	3.67	-0.03	-0.84	4.35	4.32	Constrict
V2TVR14	3.34	3.50	70.23	0.16	4.93	3.38	0.05	1.39	3.49	6.32	Dilate
V2TVR15	4.05	4.30		0.24	6.04	4.02	-0.03	-0.78	6.86	6.81	Constrict

V2TVR16	3.75	3.88	36.26	0.13	3.37	3.81	0.06	1.63	1.71	5.01	Dilate
V2TVR17	5.49	5.65	30.47	0.15	2.77	5.49	0.00	-0.03	2.80	2.80	Constrict
V2TVR18	3.70	3.75	69.66	0.05	1.24	3.71	0.01	0.15	1.09	1.39	Dilate
V2TVR19	3.35	3.47	53.01	0.12	3.45	3.19	-0.16	-4.87	8.75	8.33	Constrict
V2TVR20	4.10	4.29	45.21	0.19	4.58	4.15	0.05	1.17	3.37	5.74	Dilate

Nitroglycerin Challenge Test (NTG) Data

Study ID	BL NTG	PEAK NTG	Abs NTG	%NTG	TTP
CAMS01					
CAMS02	2.82	3.18	0.36	12.71	9.00
CAMS06	4.29	4.71	0.43	9.93	9.00
CAMS08	4.22	4.80	0.58	13.75	10.00
CAMS09					
CAMS10	5.65	6.11	0.46	8.17	7.00
CAMS11	2.16	2.83	0.68	31.33	7.00
CAMS12	3.93	4.33	0.40	10.28	10.00
CAMS13	3.49	4.10	0.60	17.21	10.00
CAMS14					
CAMS15	2.50	3.11	0.61	24.60	8.00
V2 CAMS01					
V2 CAMS02	2.58	2.90	0.32	12.56	7.00
V2 CAMS06	4.41	5.01	0.60	13.52	10.00
V2 CAMS08	4.19	4.90	0.70	16.81	10.00
V2 CAMS09					
V2 CAMS10	5.56	6.30	0.74	13.32	9.00
V2 CAMS11	2.13	2.72	0.59	27.92	7.00
V2 CAMS12	4.02	4.43	0.41	10.15	10.00
V2 CAMS13	3.71	4.10	0.40	10.66	9.00
V2 CAMS14	4.89	5.31	0.43	8.70	8.00
V2 CAMS15	2.40	3.27	0.87	36.05	6.00
RAM01 V1	4.20	4.80	0.60	14.34	8.00
RAM02 V1	4.69	5.48	0.79	16.91	10.00
RAM03 V1	4.29	4.92	0.63	14.65	7.00
RAM04 V1	4.01	4.91	0.90	22.43	7.00
RAM05 V1	3.67	4.47	0.80	21.78	9.00
RAM06 V1	3.93	4.72	0.79	20.24	10.00
RAM07 V1	4.17	5.17	1.00	23.88	7.00
RAM08 V1	4.00	4.99	0.99	24.74	8.00
RAM09 V1	3.80	4.65	0.85	22.44	9.00
RAM10 V1	4.22	4.96	0.74	17.61	8.00
RAM11 V1	3.78	4.45	0.67	17.59	9.00
RAM12 V1	4.41	5.50	1.09	24.69	8.00

RAM15 V1	4.96	5.63	0.67	13.59	8.00
RAM16 V1	4.06	4.78	0.72	17.74	5.00
RAM17 V1	4.21	5.16	0.95	22.53	7.00
RAM18 V1	4.58	5.39	0.81	17.58	7.00
RAM19 V1	4.42	5.37	0.95	21.57	5.00
RAM20 V1	3.92	5.13	1.21	30.83	10.00
RAM01 V2	4.23	4.87	0.64	15.25	8.00
RAM02 V2	4.89	5.61	0.72	14.84	6.00
RAM03 V2	3.86	4.52	0.66	17.04	7.00
RAM04 V2	3.91	4.71	0.80	20.35	8.00
RAM05 V2	3.77	4.49	0.72	19.23	9.00
RAM06 V2	3.86	4.60	0.74	19.31	7.00
RAM07 V2	4.16	4.94	0.78	18.63	10.00
RAM08 V2	3.98	4.79	0.81	20.41	5.00
RAM09 V2	3.88	4.70	0.82	21.16	10.00
RAM10 V2	4.35	5.25	0.90	20.75	9.00
RAM11 V2	3.63	4.42	0.79	21.62	10.00
RAM12 V2	4.14	5.18	1.04	25.16	5.00
RAM15 V2	4.65	5.37	0.72	15.51	6.00
RAM16 V2	3.84	4.74	0.90	23.39	10.00
RAM17 V2	4.17	5.20	1.03	24.84	6.00
RAM18 V2	4.67	5.37	0.70	14.99	9.00
RAM19 V2	4.06	4.91	0.85	21.04	10.00
RAM20 V2	3.90	5.35	1.45	37.11	10.00
RAM21 V1	2.57	3.34	0.77	29.88	6.00
RAM22 V1	2.79	3.38	0.59	21.36	10.00
RAM23 V1	2.63	3.38	0.75	28.63	10.00
RAM24 V1	3.53	4.53	1.00	28.33	10.00
RAM25 V1	3.06	3.48	0.42	13.87	10.00
RAM26 V1	2.74	3.44	0.70	25.46	5.00
RAM31 V1	3.10	3.92	0.82	26.47	6.00
RAM32 V1	3.04	3.54	0.50	16.62	4.00
RAM34 V1	2.89	3.62	0.73	25.21	10.00
RAM35 V1	3.55	4.35	0.80	22.39	4.00
RAM36 V1	3.31	4.17	0.86	26.15	4.00
RAM38 V1	3.09	3.78	0.69	22.42	8.00
RAM21 V2	2.52	3.13	0.61	24.05	6.00

RAM22 V2	2.83	3.45	0.62	21.86	10.00
RAM23 V2	2.80	3.37	0.57	20.42	10.00
RAM24 V2	3.53	4.26	0.73	20.62	9.00
RAM25 V2	2.86	3.28	0.42	14.53	8.00
RAM26 V2	3.00	3.87	0.87	28.80	7.00
RAM31 V2	3.25	3.89	0.64	19.82	5.00
RAM32 V2	3.17	3.66	0.49	15.63	4.00
RAM34 V2	2.73	3.50	0.77	28.05	10.00
RAM35 V2	3.49	4.30	0.81	23.15	10.00
RAM36 V2	3.14	4.17	1.03	32.87	5.00
RAM38 V2	2.96	3.73	0.77	26.18	10.00
V2RAM41	3.17	4.04	0.87	27.30	4.00
V2RAM43	3.26	3.97	0.72	22.00	5.00
V2RAM44	2.98	3.84	0.86	28.90	5.00
V2RAM46	3.00	3.85	0.86	28.50	5.00
V2RAM47	3.61	4.37	0.76	21.20	5.00
V2RAM48	3.63	4.36	0.73	20.10	3.00
V2RAM49	3.10	3.94	0.85	27.30	5.00
V2RAM50	2.74	3.75	1.01	36.70	5.00
V2RAM51	3.60	4.60	0.99	27.60	4.00
V2RAM52	3.59	4.61	1.02	28.50	5.00
V2RAM53	3.81	4.59	0.78	20.40	4.00
V2RAM54	2.92	3.65	0.73	25.00	4.00
V2RAM55	3.47	4.53	1.06	30.40	4.00
V2RAM56	3.11	4.21	1.10	35.20	4.00
V2RAM58	3.39	4.23	0.84	24.80	5.00
V2RAM59	3.51	4.24	0.72	20.60	5.00
V2RAM60	3.39	4.38	0.99	29.10	4.00
V2RAM61	3.35	4.33	0.98	29.30	4.00
V3RAM41	3.15	3.74	0.60	19.00	4.00
V3RAM43	3.31	4.11	0.80	24.10	
V3RAM44	3.10	3.97	0.88	28.30	5.00
V3RAM46	3.22	3.97	0.75	23.30	5.00
V3RAM47	3.69	4.48	0.79	21.30	5.00
V3RAM48	3.67	4.43	0.75	20.40	3.00
V3RAM49	2.76	3.66	0.90	32.60	5.00
V3RAM50	3.04	3.96	0.92	30.10	5.00

V3RAM51	3.62	4.55	0.93	25.70	6.00
V3RAM52	3.45	4.47	1.02	29.60	4.00
V3RAM53	3.84	5.08	1.24	32.30	4.00
V3RAM54	3.06	3.83	0.77	25.20	5.00
V3RAM55	3.31	4.52	1.21	36.50	5.00
V3RAM56	3.38	4.42	1.03	30.60	5.00
V3RAM58	3.17	4.04	0.86	27.20	4.00
V3RAM59	3.45	4.24	0.79	22.90	5.00
V3RAM60	3.62	4.52	0.90	24.90	4.00
V3RAM61	3.42	4.37	0.95	27.90	6.00
ASPEN 1 V1					
ASPEN 2 V1					
ASPEN 3 V1					
ASPEN 4 V1					
ASPEN 5 V1					
ASPEN 6 V1					
ASPEN 7 V1					
ASPEN 8 V1					
ASPEN 9 V1					
ASPEN 10 V1					
ASPEN 1 V2					
ASPEN 2 V2					
ASPEN 3 V2					
ASPEN 4 V2					
ASPEN 5 V2					
ASPEN 6 V2					
ASPEN 7 V2					
ASPEN 8 V2					
ASPEN 9 V2					
ASPEN 10 V2					
V1 ACUTEENDO 1	4.16	4.92	0.76	18.31	6.00
V1 ACUTEENDO 2	3.98	4.99	1.01	25.25	10.00
V1 ACUTEENDO 3	4.21	4.96	0.75	17.71	9.00
V1 ACUTEENDO 4	3.35	4.13	0.79	23.58	8.00
V1 ACUTEENDO 5	4.34	4.84	0.50	11.44	8.00
V1 ACUTEENDO 6	4.89	5.45	0.56	11.48	5.00
V1 ACUTEENDO 7	3.88	4.69	0.81	20.77	6.00

V2 ACUTEENDO 1	4.10	4.83	0.73	17.67	6.00
V2 ACUTEENDO 2	4.06	4.98	0.92	22.53	10.00
V2 ACUTEENDO 3	4.39	5.18	0.78	17.82	6.00
V2 ACUTEENDO 4	3.47	4.11	0.64	18.46	10.00
V2 ACUTEENDO 5	4.01	4.58	0.57	14.22	9.00
V2 ACUTEENDO 6	4.61	5.44	0.83	18.13	10.00
V2 ACUTEENDO 7	3.84	4.59	0.75	19.62	9.00
EDS01	3.14	3.89	0.75	23.89	8.00
EDS02	3.48	4.40	0.92	26.44	9.00
EDS03	4.01	4.74	0.73	18.20	9.00
EDS04	4.73	5.58	0.85	17.97	5.00
EDS01 V2	2.88	3.55	0.67	23.26	8.00
EDS02 V2	3.52	4.38	0.86	24.56	7.00
EDS03 V2	4.42	4.99	0.57	12.90	9.00
EDS04 V2	4.75	5.30	0.55	11.58	6.00
TVR2	3.56	4.86	1.30	36.63	7.00
TVR3					
TVR4					
TVR5	5.50	6.43	0.93	16.91	9.00
TVR6					
TVR7					
TVR8					
TVR9					
TVR11	4.59	5.80	1.22	26.50	7.00
TVR12	4.62	5.22	0.60	12.91	9.00
TVR13	3.56	4.29	0.73	20.37	5.00
TVR14	3.19	3.90	0.71	22.26	5.00
TVR15	3.80	4.46	0.66	17.45	5.00
TVR16	3.82	4.72	0.90	23.51	6.00
TVR17	5.44	6.35	0.91	16.67	6.00
TVR18					
TVR19	3.24	3.81	0.57	17.70	6.00
TVR20	3.87	4.75	0.88	22.74	8.00
V2TVR02	3.59	4.65	1.06	29.67	6.00
V2TVR03					
V2TVR04					
V2TVR05	5.46	6.30	0.84	15.47	7.00
V2TVR06					

V2TVR07					
V2TVR08					
V2TVR09					
V2TVR11	4.66	5.90	1.24	26.72	6.00
V2TVR12	4.58	5.21	0.63	13.80	5.00
V2TVR13	3.63	4.10	0.47	13.02	5.00
V2TVR14	3.30	3.82	0.52	15.63	5.00
V2TVR15	4.04	4.55	0.51	12.63	3.00
V2TVR16					
V2TVR17	5.41	6.16	0.75	13.92	6.00
V2TVR18					
V2TVR19	3.32	3.94	0.62	18.65	8.00
V2TVR20	3.94	4.84	0.90	22.88	8.00

Observational Cohort

Participant Characteristics

Study ID	**Sex**	**Age**	**Height**	**Weight**	**BMI**
SPEC02	FEMALE	19.0	1.63	63.00	23.71
SPEC03	MALE	22.0	1.86	78.70	22.75
SPEC04	MALE	21.0	1.75	66.00	21.55
SPEC05	FEMALE	18.0	1.76	62.80	20.27
SPEC06	MALE	21.0	1.75	62.00	20.24
SPEC07	MALE	19.0	1.81	73.50	22.44
SPEC08	MALE	18.0	1.94	87.00	23.12
SPEC09	MALE	22.0	1.97	94.00	24.22
SPEC10	MALE	21.0	1.79	74.00	23.10
COS01	MALE	44.0	1.88	96.70	27.36
COS02	MALE	51.0	2.00	88.90	22.23
COS03	FEMALE	26.0	1.65	47.00	17.26
SFCP01	MALE	35.0	1.57	96.70	39.23
SFCP02	FEMALE	31.0	1.52	41.70	17.93
SFCP03	FEMALE	37.0	1.64	84.00	31.42
SFCP04	FEMALE	52.0	1.53	65.70	28.25
SFCP05	MALE	31.0	1.66	71.40	25.91
SFCP06	MALE	18.0	1.80	70.50	21.76

SFCP07	FEMALE	48.0	1.59	79.70	31.53
SFCP08	FEMALE	26.0	1.47	73.00	33.78
SFCP09	FEMALE	20.0	1.39	40.00	20.70
SFCP10	FEMALE	33.0	1.41	75.90	38.18
SFCP11	MALE	32.0	1.70	53.40	18.48
SFCP12	FEMALE	24.0	1.67	64.70	23.20
SFCP13	MALE	25.0	1.50	41.20	18.43
SFCP14	FEMALE	30.0	1.61	57.40	22.14
SFCP15	FEMALE	53.0	1.45	38.00	18.07
SFCP16	FEMALE	40.0	1.45	58.50	28.02
SFCP17	MALE	25.0	1.67	68.70	24.63
SFCP18	MALE	31.0	1.65	51.10	18.77
SFCP19	MALE	47.0	1.69	47.50	16.63
SFCP21	FEMALE	23.0	1.49	49.90	22.48
SFCP22	MALE	23.0	1.75	91.60	30.08
SFCP23	MALE	18.0	1.72	69.20	23.53
SFCP24	FEMALE	38.0	1.40	41.30	21.07
SFCP26	MALE	35.0	1.70	74.00	25.61
SFCP28	FEMALE	44.0	1.60	69.20	27.20
SFCP29	MALE	20.0	1.66	53.90	19.56
SFCP30	FEMALE	29.0	1.53	57.70	24.65
SFCP31	MALE	30.0	1.79	94.20	29.40
SFCP32	MALE	28.0	1.80	122.40	37.78
SFCP33	FEMALE	75.0	1.62	131.10	49.95
SFCP34	MALE	50.0	1.74	107.10	35.58
SFCP35	MALE	35.0	1.60	50.50	19.85
SFCP36	MALE	48.0	1.60	47.00	18.47
SFCP42	MALE	58.0	1.74	90.00	29.90
SFCP43	FEMALE	24.0	1.55	42.90	17.74
SFCP45	MALE	37.0	1.62	57.10	21.89
SFCP46	FEMALE	18.0	1.43	26.90	13.25
SFCP47	FEMALE	32.0	1.53	42.90	18.33
SFCP48	MALE	22.0	1.83	76.30	22.78
AMCP1	MALE	9.9	1.38	32.90	17.40
AMCP2	MALE	15.3	1.58	46.20	18.50
AMCP3	MALE	13.7	1.39	36.40	18.90
AMCP4	MALE	14.8	1.57	58.40	23.70

AMCP5	MALE	12.4	1.49	32.60	14.80
AMCP6	MALE	15.0	1.65	49.20	18.10
AMCP7	MALE	10.3	1.37	46.30	24.60
AMCP8	MALE	13.4	1.48	35.10	16.10
AMCP9	FEMALE	11.9	1.65	40.40	14.90
AMCP11	FEMALE	11.5	1.39	32.70	17.00
AMCON1	MALE	11.7	1.48	35.10	16.10
AMCON2	MALE	12.3	1.74	63.30	20.90
AMCON3	MALE	13.6	1.72	42.80	14.40
AMCON4	MALE	14.7	1.72	59.50	20.20
AMCON5	MALE	9.4	1.34	27.40	15.30
AMCON6	MALE	12.1	1.61	71.10	27.50
AMCON7	MALE	14.3	1.70	58.70	20.30
AMCON8	MALE	9.9	1.40	38.50	19.60
AMCON10	FEMALE	16.8	1.68	58.80	20.80
AMCON11	FEMALE	10.5	1.42	34.90	17.40
TR02	MALE	20.0	1.73	69.30	23.30
TR03	MALE	34.0	1.84	76.70	22.70
TR04	MALE	19.0	1.81	64.90	19.80
TR05	MALE	24.0	1.71	66.00	22.60
TR06	MALE	35.0	1.85	126.80	37.00
TR07	MALE	20.0	1.64	76.00	28.30
TR08	MALE	38.0	1.75	70.40	23.00
TR09	MALE	21.0	1.62	80.60	30.70
TR10	MALE	19.0	1.72	64.20	21.70
TR11	MALE	22.0	1.97	128.10	33.00
TR12	MALE	21.0	1.77	81.00	26.00
TR13	MALE	19.0	1.72	53.30	18.10
TR14	MALE	25.0	1.69	68.80	24.20
TR15	MALE	44.0	1.70	108.80	37.60
TR17	MALE	39.0	1.79	107.10	33.60
TR18	MALE	37.0	1.98	89.30	22.80
TR19	MALE	21.0	1.76	69.30	22.40
TR20	MALE	24.0	1.71	73.60	25.20
TR21	MALE	22.0	1.75	63.80	21.00
TR22	MALE	26.0	1.71	75.40	25.80
TR23	MALE	34.0	1.85	102.90	30.10

TR24	MALE	26.0	1.81	84.70	25.70
TR25	MALE	24.0	1.78	85.00	26.80
TR26	MALE	41.0	1.69	55.00	19.30
TR27	MALE	27.0	1.78	119.20	37.60
CAMO01	MALE	73.0	1.82	86.00	26.08
CAMO02	MALE	73.0	1.83	82.46	24.62
CAMO03	FEMALE	75.0	1.54	52.62	22.19
CAMO04	MALE	78.0	1.78	94.44	29.74
CAMO05	FEMALE	70.0	1.65	55.40	20.35
CAMO06	FEMALE	62.0	1.61	72.10	27.82
CAMO07	MALE	74.0	1.76	68.60	22.15
CAMO08	MALE	69.0	1.90	86.80	24.04
CAMO09	MALE	78.0	1.85	80.40	23.49
CAMO10	FEMALE	68.0	1.67	74.90	26.86
CAMO11	FEMALE	72.0	1.69	67.00	23.46
CAMO12	FEMALE	68.0	1.65	52.40	19.36
CAMO13	FEMALE	76.0	1.62	77.60	29.57
CAMO14	FEMALE	72.0	1.70	60.50	20.93
CAMO15	MALE	77.0	1.68	58.10	20.59
CAMO16	FEMALE	66.0	1.63	75.80	28.53
CAMO17	FEMALE	67.0	1.65	64.86	23.83
CAMO18	FEMALE	68.0	1.58	58.40	23.39
CAMO19	MALE	78.0	1.64	71.60	26.62
CAMO20	MALE	75.0	1.83	76.90	22.96
CAMO21	FEMALE	66.0	1.66	77.10	27.98
CAMO22	FEMALE	70.0	1.64	77.20	28.70
CAMO23	FEMALE	67.0	1.71	70.70	24.18
CAMO24	MALE	66.0	1.79	57.30	17.88
CAMO25	MALE	67.0	1.75	94.60	30.89
CAMO26	FEMALE	68.0	1.61	70.30	27.12
CAMO27	MALE	77.0	1.87	79.00	22.59
CAMO28	MALE	71.0	1.70	84.40	29.12
CAMO29	FEMALE	68.0	1.66	109.00	39.56
CAMO30	MALE	73.0	1.65	82.70	30.38
CAMO31	MALE	67.0	1.81	69.80	21.31
CAMO32	MALE	70.0	1.75	102.50	33.47

CAMO33	FEMALE	68.0	1.63	66.80	25.14
CAMO34	MALE	69.0	1.80	85.10	26.18
CAMS01	MALE	50.0	1.76	102.70	33.15
CAMS02	FEMALE	75.0	1.52	66.30	28.70
CAMS05	MALE	80.0	1.74	93.00	30.72
CAMS06	MALE	62.0	1.69	77.90	27.27
CAMS08	MALE	60.0	1.75	75.40	24.76
CAMS09	MALE	52.0	1.63	69.70	26.23
CAMS10	MALE	65.0	1.79	114.10	35.61
CAMS11	FEMALE	56.0	1.58	94.70	37.93
CAMS12	MALE	61.0	1.81	87.40	26.68
CAMS13	MALE	75.0	1.76	99.70	32.19
CAMS14	MALE	70.0	1.74	111.00	36.66
CAMS15	FEMALE	55.0	1.58	74.80	29.96
CAD01	MALE	49.0	1.75	113.20	37.20
CAD02	MALE	69.0	1.81	110.60	33.80
CAD03	MALE	64.0	1.68	84.30	30.00
CAD04	MALE	59.0	1.81	81.20	24.80
CAD05	MALE	60.0	1.75	83.90	27.60
CAD06	MALE	70.0	1.68	76.90	27.20
CAD07	MALE	77.0	1.87	99.50	28.60
CAD08	MALE	64.0	1.65	58.90	21.60
CAD09	MALE	61.0	1.69	79.80	27.90
CAD10	MALE	81.0	1.66	71.40	26.10
CAD13	MALE	66.0	1.83	104.60	31.20
CAD14	FEMALE	68.0	1.54	57.50	24.20
CAD16	MALE	66.0	1.70	87.50	30.50
CAD18	MALE	71.0	1.70	97.60	33.80
CAD19	MALE	77.0	1.83	72.50	21.60
CAD20	MALE	54.0	1.90	103.40	28.60
CAD21	MALE	73.0	1.74	74.60	24.60
CAD22	MALE	57.0	1.72	86.40	29.20
CAD23	MALE	70.0	1.74	56.80	18.80
CAD24	MALE	76.0	1.77	84.40	26.90
CAD25	MALE	67.0	1.74	89.90	29.90
CAD26	MALE	54.0	1.76	91.10	29.40
CAD27	MALE	48.0	1.90	118.90	32.90

CAD28	MALE	62.0	1.66	74.50	27.20
CAD29	FEMALE	55.0	1.81	70.90	21.60
CAD30	MALE	50.0	1.56	65.20	27.00
RAM01 V1	MALE	21.0	1.84	86.80	25.64
RAM02 V1	MALE	21.0	1.82	88.90	26.84
RAM03 V1	MALE	22.0	1.76	67.00	21.63
RAM04 V1	MALE	21.0	1.87	82.10	23.48
RAM05 V1	MALE	21.0	1.65	63.00	23.14
RAM06 V1	MALE	21.0	1.82	73.60	22.22
RAM07 V1	MALE	21.0	1.68	72.00	25.51
RAM08 V1	MALE	24.0	1.79	67.00	20.91
RAM09 V1	MALE	21.0	1.81	62.70	19.14
RAM10 V1	MALE	23.0	1.76	86.20	27.83
RAM11 V1	MALE	19.0	1.74	74.40	24.57
RAM12 V1	MALE	20.0	1.89	76.50	21.42
RAM13 V1	MALE	21.0	1.89	98.20	27.49
RAM14 V1	MALE	21.0	1.76	74.50	24.05
RAM15 V1	MALE	19.0	1.79	85.70	27.49
RAM16 V1	MALE	21.0	1.83	73.40	21.92
RAM17 V1	MALE	20.0	1.79	71.60	22.35
RAM18 V1	MALE	21.0	1.78	86.00	27.14
RAM19 V1	MALE	21.0	1.86	81.10	23.44
RAM20 V1	MALE	21.0	1.67	71.50	25.64
RAM21 V1	FEMALE	20.0	1.54	46.30	19.52
RAM22 V1	FEMALE	20.0	1.58	46.40	18.70
RAM23 V1	FEMALE	26.0	1.55	43.90	18.27
RAM24 V1	FEMALE	19.0	1.59	56.40	22.31
RAM25 V1	FEMALE	22.0	1.61	52.20	20.14
RAM26 V1	FEMALE	21.0	1.64	62.10	23.09
RAM31 V1	FEMALE	23.0	1.55	48.30	20.10
RAM32 V1	FEMALE	24.0	1.60	66.70	26.05
RAM34 V1	FEMALE	18.0	1.56	54.00	22.19
RAM35 V1	FEMALE	32.0	1.63	60.00	22.58
RAM36 V1	FEMALE	20.0	1.57	57.40	23.29
RAM38 V1	FEMALE	22.0	1.58	46.50	18.63
V1RAM41	FEMALE	20.0	1.74	66.20	21.87
V1RAM43	FEMALE	26.0	1.65	60.50	22.22

V1RAM44	FEMALE	24.0	1.58	56.80	22.75
V1RAM46	FEMALE	20.0	1.65	60.50	22.22
V1RAM47	FEMALE	23.0	1.54	54.00	22.77
V1RAM48	FEMALE	19.0	1.67	103.80	37.22
V1RAM49	FEMALE	27.0	1.64	58.70	21.82
V1RAM50	FEMALE	18.0	1.58	47.20	18.91
V1RAM51	FEMALE	21.0	1.67	62.40	22.37
V1RAM52	FEMALE	18.0	1.62	51.70	19.70
V1RAM53	FEMALE	20.0	1.74	65.80	21.73
V1RAM54	FEMALE	21.0	1.69	59.20	20.73
V1RAM55	FEMALE	23.0	1.68	70.50	24.98
V1RAM56	FEMALE	19.0	1.65	47.20	17.34
V1RAM58	FEMALE	21.0	1.73	73.00	24.39
V1RAM59	FEMALE	20.0	1.58	64.40	25.80
V1RAM60	FEMALE	20.0	1.76	58.30	18.82
V1RAM61	FEMALE	27.0	1.66	59.60	21.63
ASPEN 1	MALE	22.0	1.84	98.00	28.95
ASPEN 2	MALE	23.0	1.68	60.50	21.44
ASPEN 3	MALE	23.0	1.84	103.00	30.42
ASPEN 4	MALE	21.0	1.81	80.50	24.57
ASPEN 5	MALE	18.0	1.75	80.20	26.19
ASPEN 6	MALE	20.0	1.73	77.00	25.73
ASPEN 7	MALE	20.0	1.78	73.00	23.04
ASPEN 8	MALE	22.0	1.80	74.00	22.84
ASPEN 9	MALE	21.0	1.78	110.00	34.72
ASPEN 10	MALE	30.0	1.80	65.50	20.22
NESTLE S6	MALE	68.0	1.80	92.20	28.46
NESTLE S8	MALE	79.0	1.75	82.30	26.87
NESTLE S10	MALE	76.0	1.68	86.10	30.51
NESTLE S11	MALE	65.0	1.60	59.50	23.24
NESTLE S12	MALE	70.0	1.78	83.70	26.42
NESTLE S13	MALE	71.0	1.70	84.80	29.34
NESTLE S14	MALE	65.0	1.71	80.60	27.56
NESTLE S15	MALE	66.0	1.70	78.00	26.99
NESTLE S16	MALE	66.0	1.73	82.10	27.43
NESTLE S17	MALE	70.0	1.60	62.40	24.38
NESTLE S18	MALE	68.0	1.82	99.70	30.10

NESTLE S19	MALE	71.0	1.83	108.40	32.37
NESTLE S21	MALE	67.0	1.83	82.10	24.52
NESTLE S23	MALE	65.0	1.70	62.10	21.49
NESTLE S25	MALE	70.0	1.80	92.50	28.55
NESTLE S27	MALE	69.0	1.85	94.80	27.70
NESTLE S28	MALE	67.0	1.73	89.00	29.74
NESTLE S31	MALE	78.0	1.80	74.00	22.84
ACM1	MALE	23.0	1.83	99.90	29.83
ACM2	MALE	22.0	1.60	58.90	23.01
ACM3	MALE	25.0	1.80	123.42	38.09
ACM4	MALE	18.0	1.81	91.10	27.81
ACM5	MALE	20.0	1.76	62.20	20.08
ACM6	MALE	20.0	1.86	69.90	20.20
ACM8	MALE	30.0	1.83	92.30	27.56
ACM10	MALE	21.0	1.68	77.10	27.32
ACF1	FEMALE	19.0	1.78	107.50	33.93
ACF4	FEMALE	19.0	1.60	52.90	20.66
ACF5	FEMALE	21.0	1.63	43.80	16.49
ACF6	FEMALE	20.0	1.61	68.30	26.35
ACF7	FEMALE	20.0	1.70	57.80	20.00
ACF8	FEMALE	23.0	1.61	58.40	22.53
ACF9	FEMALE	21.0	1.63	58.00	21.83
ACF10	FEMALE	27.0	1.75	102.90	33.60
V1 ACUTEENDO 1	MALE	25.0	1.85	91.00	26.60
V1 ACUTEENDO 2	MALE	22.0	1.81	91.50	27.90
V1 ACUTEENDO 3	MALE	25.0	1.79	67.50	21.10
V1 ACUTEENDO 4	MALE	22.0	1.63	71.50	26.90
V1 ACUTEENDO 5	MALE	21.0	1.69	65.50	22.90
V1 ACUTEENDO 6	MALE	21.0	1.83	84.50	25.20
V1 ACUTEENDO 7	MALE	25.0	1.83	75.00	22.40
AB-SCI04 NC	MALE	40.0	1.86	94.40	27.29
AB-SCI06 NC	MALE	42.0	1.84	96.90	28.62
AB-SCI07 NC	MALE	32.0	1.78	85.40	27.11
AB-SCI11 NC	MALE	51.0	1.86	77.00	22.26
AB-SCI12 NC	MALE	43.0	1.84	80.60	23.94
AB-SCI14 NC	MALE	43.0	1.74	60.20	20.00
AB-SCI19 NC	MALE	37.0	1.92	92.00	25.09

AB-SCI24 NC	MALE	52.0	1.80	103.00	31.97
SCI01	MALE	31.0	1.88	81.82	23.27
SCI02	MALE	53.0	1.62	77.27	29.44
SCI03	MALE	28.0	1.87	56.82	16.25
SCI04	MALE	41.0	1.91	76.70	21.14
SCI05	MALE	47.0	1.75	67.16	22.06
SCI06	MALE	40.0	1.78	88.70	28.00
SCI07	MALE	31.0	1.74	82.00	27.24
SCI08	MALE	32.0	1.78	76.70	24.21
SCI09	MALE	51.0	1.67	86.40	30.98
SCI10	MALE	58.0	1.77	120.45	38.45
SCI11	MALE	53.0	1.86	111.40	32.20
SCI12	MALE	43.0	1.80	86.60	26.88
SCI13	MALE	27.0	1.82	75.00	22.64
SCI14	MALE	44.0	1.59	51.30	20.42
SCI15	MALE	41.0	1.75	80.00	26.12
SCI16	MALE	34.0	1.73	73.80	24.66
SCI17	MALE	55.0	1.88	123.90	35.06
SCI18	MALE	37.0	1.74	67.30	22.23
SCI19	MALE	38.0	1.72	71.00	24.00
SCI20	MALE	65.0	1.68	87.80	31.29
SCI21	MALE	36.0	1.72	93.50	31.60
SCI22	FEMALE	48.0	1.66	76.70	28.00
SCI23	MALE	30.0	1.64	65.80	24.46
SCI24	MALE	52.0	1.73	62.70	20.95
SCI25	MALE	25.0	1.74	85.80	28.34
SCI26	MALE	53.0	1.66	86.40	31.35
SCI27	MALE	38.0	1.71	65.50	22.40
SCI28	MALE	26.0	1.75	86.60	28.28
SCI29	FEMALE	26.0	1.76	98.90	31.93
SCI30	MALE	30.0	1.86	96.80	27.98
SCI31	MALE	40.0	1.74	73.50	24.42
SCI32	MALE	36.0	1.85	96.10	28.23
SCI33	MALE	50.0	1.89	98.00	27.43
SCI34	MALE	23.0	1.73	61.60	20.70
EDS01	MALE	22.0	1.76	72.00	23.24
EDS02	MALE	20.0	1.80	59.70	18.43

EDS03	MALE	20.0	1.87	89.30	25.54
EDS04	MALE	24.0	1.82	91.10	27.50
TVR1	FEMALE	49.0	1.76	74.10	23.92
TVR2	FEMALE	53.0	1.68	65.50	23.21
TVR3	MALE	79.0	1.84	80.74	23.85
TVR4	MALE	54.0	1.73	103.64	34.63
TVR5	MALE	38.0	1.92	86.36	23.43
TVR6	FEMALE	71.0	1.63	74.84	28.17
TVR7	MALE	71.0	1.75	74.80	24.42
TVR8	FEMALE	55.0	1.62	93.89	35.78
TVR9	MALE	55.0	1.76	107.50	34.70
TVR10	FEMALE	62.0	1.63	61.24	23.05
TVR11	FEMALE	60.0	1.61	60.09	23.18
TVR12	FEMALE	67.0	1.60	64.54	25.21
TVR13	FEMALE	80.0	1.64	75.28	27.99
TVR14	FEMALE	58.0	1.77	87.98	28.08
TVR15	FEMALE	62.0	1.68	73.60	26.08
TVR16	FEMALE	60.0	1.66	58.86	21.36
TVR17	MALE	62.0	1.79	84.50	26.37
TVR18	FEMALE	73.0	1.54	107.16	45.18
TVR19	FEMALE	65.0	1.61	78.60	30.32
TVR20	FEMALE	67.0	1.63	72.50	27.29
PFA02	FEMALE	8.9			17.78
PFA03	FEMALE	8.7			17.64
PFA10	FEMALE	8.6			17.32
PFA11	FEMALE	8.5			19.56
PFA12	FEMALE	8.0			15.68
PFA14	FEMALE	8.5			14.80
PFA17	FEMALE	8.2			17.30
PFA30	FEMALE	7.6			21.79
PFA34	FEMALE	8.0			16.39
PFA36	FEMALE	7.5			16.51
PFA40	FEMALE	7.4			16.85
PFA55	FEMALE	7.4			15.53
PFA56	FEMALE	7.2			18.09
PFA59	FEMALE	7.3			15.17
PFA69	FEMALE	6.4			16.84
PFB03	FEMALE	9.4			18.00
PFB04	FEMALE	9.1			17.05

PFB14	FEMALE	9.9			17.67
PFB19	FEMALE	8.2			15.76
PFB24	FEMALE	9.2			15.95
PMA10	MALE	7.5			16.28
PMA15	MALE	7.4			15.01
PMA16	MALE	7.2			14.88
PMB05	MALE	10.0			21.63
PMA22	MALE	7.4			16.45
PMA24	MALE	7.9			14.89
PMB04	MALE	9.5			16.63
PMA27	MALE	7.6			15.79
PMA28	MALE	7.5			15.04
PMA32	MALE	7.6			17.34
PMA33	MALE	7.6			16.95
PMA38	MALE	7.7			15.60
PMA42	MALE	7.3			15.32
PMA67	MALE	7.4			13.88
PMA68	MALE	6.5			15.56
PMA73	MALE	6.3			15.88
PMA74	MALE	7.2			14.82
PMA77	MALE	6.6			15.99
PMB06	MALE	9.9			15.35
PMB01	MALE	9.5			15.08

Hemodynamics

Study ID	**HR**	**SBP**	**DBP**	**MAP**
SPEC02	64	106	44	60
SPEC03	63	131	61	79
SPEC04	63	126	56	73
SPEC05	58	134	68	85
SPEC06	60	102	52	65
SPEC07	53	125	56	72
SPEC08	55	105	46	60
SPEC09	50	128	59	74
SPEC10	65	135	63	78
COS01	50	101	64	81

COS02	60	120	87	97
COS03	60	107	66	83
SFCP01	81	130	79	97
SFCP02	87	140	94	109
SFCP03	79	116	59	84
SFCP04	70	125	78	95
SFCP05	68	134	72	94
SFCP06	76	129	76	95
SFCP07	64	100	67	81
SFCP08	64	113	74	88
SFCP09	86	108	65	83
SFCP10	60	118	69	88
SFCP11	60	107	57	78
SFCP12	74	114	67	86
SFCP13	92	121	74	91
SFCP14	72	117	78	91
SFCP15	60	182	85	123
SFCP16	95	140	92	110
SFCP17	83	137	86	104
SFCP18	66	113	71	88
SFCP19	56	109	71	86
SFCP21	67	122	69	89
SFCP22	88	130	73	93
SFCP23	75	130	65	90
SFCP24	84	91	63	75
SFCP26	71	120	67	88
SFCP28	79	121	86	98
SFCP29	65	121	65	87
SFCP30	95	132	83	100
SFCP31	66	115	74	88
SFCP32	66	115	74	88
SFCP33	95	156	78	111
SFCP34	81	142	90	109
SFCP35	81	121	69	89
SFCP36	81	112	68	86
SFCP42	85	149	86	109
SFCP43	103	110	71	89

SFCP45	103	124	72	91
SFCP46	85	113	68	89
SFCP47	60	112	69	86
SFCP48	67	139	73	97
AMCP1	62	112	56	82
AMCP2	57	111	64	84
AMCP3	76	96	66	79
AMCP4	74	130	69	91
AMCP5	75	83	66	87
AMCP6	91	111	66	84
AMCP7	85	101	62	79
AMCP8	80	109	59	82
AMCP9	61	103	57	77
AMCP11	94	109	51	67
AMCON1	62	107	66	83
AMCON2	60	122	69	89
AMCON3	70	111	68	85
AMCON4	54	117	65	86
AMCON5	86	104	69	83
AMCON6	84	121	66	88
AMCON7	64	126	55	86
AMCON8	71	109	67	84
AMCON10	62	109	66	84
AMCON11	65	107	64	81
TR02	57	99	59	76
TR03	62	108	66	84
TR04	47	113	69	86
TR05	54	112	67	85
TR06	55	112	72	87
TR07	80	122	67	88
TR08	67	115	74	88
TR09	82	114	74	89
TR10	66	108	64	83
TR11	52	129	68	91
TR12	72	122	68	89
TR13	75	94	59	74
TR14	67	113	69	87

TR15	61	112	71	86
TR17	55	113	71	88
TR18	58	99	62	78
TR19	69	117	74	89
TR20	81	115	65	85
TR21	76	116	64	85
TR22	63	113	66	85
TR23	59	128	70	91
TR24	60	115	63	84
TR25	50	111	65	84
TR26	43	94	66	78
TR27	67	126	75	94
CAMO01	54	123	67	85
CAMO02	60	134	73	93
CAMO03	75	130	68	89
CAMO04	71	135	70	92
CAMO05	52	126	66	86
CAMO06	60	106	69	81
CAMO07	59	114	66	82
CAMO08	58	140	83	102
CAMO09	62	150	72	98
CAMO10	79	130	74	93
CAMO11	55	128	76	93
CAMO12	68	133	67	89
CAMO13	61	115	55	75
CAMO14	72	125	63	84
CAMO15	80	143	87	106
CAMO16	68	128	64	86
CAMO17	69	101	62	75
CAMO18	64	103	62	76
CAMO19	55	141	82	102
CAMO20	53	144	80	101
CAMO21	63	122	79	93
CAMO22				
CAMO23	54	119	66	84
CAMO24	58	138	78	98

CAMO25	63	132	74	93
CAMO26	67	124	77	93
CAMO27	56	128	70	89
CAMO28	91	139	89	106
CAMO29	71	118	53	
CAMO30	48	138	78	
CAMO31	63	104	66	
CAMO32	45	140	84	
CAMO33	54	120	69	
CAMO34	63	156	97	
CAMS01	47.6	123.2	72.6	
CAMS02	57	128.4	65.6	
CAMS05	83.6	158.6	76.6	
CAMS06	87.4	116.6	72	
CAMS08	63	137.2	86	
CAMS09	61.2	113.6	69.8	
CAMS10	73	135	100	
CAMS11				
CAMS12	63.8	122	70.4	
CAMS13	68.4	151.8	84.2	
CAMS14	56.4	148.8	92.4	
CAMS15	47.8	138	74.4	
CAD01	54	143	70	94
CAD02	53	137	62	87
CAD03	48	136	76	96
CAD04	62	134	70	91
CAD05	60	133	63	86
CAD06	53	110	59	76
CAD07	64	130	64	86
CAD08	55	123	58	80
CAD09	58	123	63	83
CAD10	79	134	60	85
CAD13	61	136	58	84
CAD14	47	97	54	69
CAD16	61	111	54	73
CAD18	53	113	55	75
CAD19	45	147	59	88

CAD20	54	116	60	78
CAD21	74	127	69	88
CAD22	49	117	58	77
CAD23	72	129	66	87
CAD24	56	149	63	92
CAD25	59	105	58	74
CAD26	51	119	61	80
CAD27	52	145	71	96
CAD28	52	102	55	71
CAD29	72	180	93	122
CAD30	64	113	69	84
RAM01 V1	58	118	68	88
RAM02 V1	59	116	63	85
RAM03 V1	55	121	69	88
RAM04 V1	73	124	77	93
RAM05 V1	65	105	62	82
RAM06 V1	63	119	60	85
RAM07 V1	77	134	70	93
RAM08 V1	64	126	67	89
RAM09 V1	67	111	65	85
RAM10 V1	72	132	71	93
RAM11 V1	47	117	68	88
RAM12 V1	83	128	68	91
RAM13 V1	75	129	70	92
RAM14 V1	74	123	76	92
RAM15 V1	55	127	67	90
RAM16 V1	71	127	64	89
RAM17 V1	72	113	66	85
RAM18 V1	55	125	65	89
RAM19 V1	73	126	66	88
RAM20 V1	72	113	65	85
RAM21 V1	68	109	76	87
RAM22 V1	54	96	62	77
RAM23 V1	60	92	64	76
RAM24 V1	53	103	65	82
RAM25 V1	61	107	69	85
RAM26 V1	53	117	78	90

RAM31 V1	59	102	66	82
RAM32 V1	79	113	73	88
RAM34 V1	64	106	66	83
RAM35 V1	45	114	70	87
RAM36 V1	58	103	68	83
RAM38 V1	66	94	64	77
V1RAM41	57	107	74	86
V1RAM43	68	101	70	83
V1RAM44	61	100	67	82
V1RAM46	60	102	69	83
V1RAM47	58	95	58	74
V1RAM48	60	114	66	86
V1RAM49	60	116	78	90
V1RAM50	72	101	71	84
V1RAM51	79	111	68	85
V1RAM52	63	103	62	80
V1RAM53	52	105	66	83
V1RAM54	75	104	67	83
V1RAM55	60	105	66	83
V1RAM56	67	98	66	80
V1RAM58	51	112	65	85
V1RAM59	64	105	77	86
V1RAM60	64	103	68	83
V1RAM61	70	100	73	83
ASPEN 1	55	112	58	80
ASPEN 2	63	115	60	81
ASPEN 3	62	148	79	106
ASPEN 4	74	123	60	85
ASPEN 5	69	121	63	86
ASPEN 6	62	122	61	85
ASPEN 7	59	127	72	93
ASPEN 8	60	127	60	86
ASPEN 9	51	128	75	94
ASPEN 10	53	103	70	82
NESTLE S6	83	125	69	88
NESTLE S8	62	160	73	102
NESTLE S10	53	83	52	62

NESTLE S11	53	83	51	62
NESTLE S12	58	112	40	64
NESTLE S13	74	112	40	64
NESTLE S14	54	101	50	67
NESTLE S15	52	109	44	66
NESTLE S16	79	113	30	58
NESTLE S17	54	120	49	73
NESTLE S18	61	133	71	91
NESTLE S19	51	110	39	63
NESTLE S21	50	93	57	69
NESTLE S23	72	106	32	57
NESTLE S25	52	108	52	71
NESTLE S27	54	152	68	96
NESTLE S28	74	120	57	78
NESTLE S31	47	112	36	61
ACM1	69	124	64	86
ACM2	71	72	56	64
ACM3	60	111	64	80
ACM4	72	123	69	88
ACM5	73	114	73	90
ACM6	72	114	65	80
ACM8	69	115	68	85
ACM10	80	115	70	87
ACF1	54	131	70	91
ACF4	80	110	65	82
ACF5	77	88	74	73
ACF6	80	104	65	80
ACF7	58	64	54	60
ACF8	67	134	92	105
ACF9	55	95	52	70
ACF10	54	127	76	97
V1 ACUTEENDO 1	58	124	73	90
V1 ACUTEENDO 2	56	126	73	91
V1 ACUTEENDO 3	48	133	78	96
V1 ACUTEENDO 4	50	122	70	87
V1 ACUTEENDO 5	54	131	77	95
V1 ACUTEENDO 6	75	131	69	90

V1 ACUTEENDO 7	59	106	57	73
AB-SCI04 NC				
AB-SCI06 NC				
AB-SCI07 NC				
AB-SCI11 NC				
AB-SCI12 NC				
AB-SCI14 NC				
AB-SCI19 NC				
AB-SCI24 NC				
SCI01				
SCI02				
SCI03	69	90	52	65
SCI04	58	129	84	99
SCI05				
SCI06	68	130	70	90
SCI07	84	133	88	103
SCI08	68	79	48	58
SCI09	70	93	68	76
SCI10	60	97	52	67
SCI11	61	149	81	104
SCI12	90	131	90	104
SCI13	77	102	55	71
SCI14	74	105	74	84
SCI15	65	96	74	81
SCI16	68	83	52	62
SCI17	77	146	85	105
SCI18	67	103	63	76
SCI19	80	119	70	86
SCI20	78	129	69	89
SCI21	66	114	69	84
SCI22	70	102	66	78
SCI23	66	128	69	89
SCI24	70	131	79	96
SCI25	62	121	68	86
SCI26	67	111	73	86
SCI27	87	111	67	82
SCI28	62	153	101	118

SCI29	64	108	64	79
SCI30	98	117	67	84
SCI31	87	96	63	74
SCI32	64	118	71	87
SCI33	60	82	46	58
SCI34	70	108	67	81
EDS01	88.5	114.5	77.5	89
EDS02	72	114	68.5	87
EDS03	56	131	72	93
EDS04	67	123.7	70.3	89.3
TVR1	49	106	70	84
TVR2	61	108	70	85
TVR3	59	142	80	105
TVR4	92	126	77	94
TVR5	49	116	71	89
TVR6	57	138	86	108
TVR7	65	127	74	95
TVR8	73	125	79	97
TVR9	64	115	70	85
TVR10	62	102	58	78
TVR11	59	123	78	97
TVR12	61	118	75	92
TVR13	70	134	72	98
TVR14	55	113	76	76
TVR15	66	129	80	101
TVR16	52	93	59	72
TVR17	42	126	77	97
TVR18	60	140	70	99
TVR19	55	119	70	89
TVR20	73	140	76	101
PFA02		102	62	
PFA03		95	62	
PFA10		104	65	
PFA11		93	63	
PFA12		103	64	
PFA14		112	69	
PFA17		102	66	
PFA30		107	75	

PFA34		99	65	
PFA36		107	67	
PFA40		103	68	
PFA55		95	65	
PFA56		95	60	
PFA59		88	62	
PFA69		99	54	
PFB03		95	60	
PFB04		102	65	
PFB14		107	62	
PFB19		94	63	
PFB24		91	57	
PMA10		100	63	
PMA15		89	49	
PMA16		102	61	
PMB05		111	66	
PMA22		98	45	
PMA24		85	59	
PMB04		107	71	
PMA27		95	56	
PMA28		93	63	
PMA32		105	64	
PMA33		105	61	
PMA38		94	59	
PMA42		101	63	
PMA67		95	60	
PMA68		88	61	
PMA73		105	55	
PMA74		99	62	
PMA77		101	63	
PMB06		104	66	
PMB01		87	57	

Vascular Variables

Study ID	BL Diameter	Peak Diameter	Time Peak	Abs FMD	% FMD	4 min Diameter	Abs L-FMC	%L-FMC	TVR	ABS(FMD+LFMC)	LOW FLOW RESPONSE	AUC to peak
SPEC02	3.43	3.83	29.23	0.40	11.62	3.36	-0.07	-2.17	14.10	13.79	Constrict	10437
SPEC03	4.16	4.27	34.04	0.10	2.47	4.06	-0.11	-2.58	5.19	5.06	Constrict	6113
SPEC04	4.39	4.76	38.66	0.37	8.45	4.34	-0.05	-1.12	9.67	9.57	Constrict	7757
SPEC05	3.26	3.51	53.30	0.25	7.77	3.19	-0.06	-1.95	9.91	9.72	Constrict	37834
SPEC06	3.67	4.01	50.50	0.33	9.08	3.61	-0.07	-1.79	11.07	10.87	Constrict	16943
SPEC07	3.43	3.65		0.22	6.45	3.79	0.36	10.53	-3.69	16.98	Dilate	
SPEC08	4.82	5.18		0.35	7.26	4.75	-0.07	-1.52	8.92	8.79	Constrict	
SPEC09	4.75	4.97		0.21	4.44	4.75	-0.01	-0.14	4.59	4.58	Constrict	
SPEC10	4.13	4.20	55.73	0.07	1.77	3.83	-0.29	-7.10	9.55	8.87	Constrict	27498
COS01	3.78	3.81	135.00	0.03	0.70	3.79	0.01	0.26	0.44	1.05	Dilate	26986
COS02	4.83	5.05	72.00	0.22	4.54	4.83	-0.01	-0.12	4.67	4.66	Constrict	14113
COS03	3.63	3.63	28.00	0.00	0.00	3.51	-0.13	-3.49	3.61	3.49	Constrict	5989
SFCP01	3.98	4.21	69.23	0.24	5.91	3.95	-0.02	-0.62	6.57	6.53	Constrict	
SFCP02	3.51	4.14	45.41	0.64	18.13	4.04	0.54	15.27	2.49	33.40	Dilate	23848
SFCP03	2.84	3.25	125.97	0.41	14.52	2.77	-0.07	-2.37	17.30	16.89	Constrict	
SFCP04	2.98	3.15	31.55	0.17	5.63	2.92	-0.06	-1.96	7.74	7.59	Constrict	
SFCP05	4.86	5.13	15.66	0.27	5.47	5.07	0.21	4.22	1.20	9.68	Dilate	6558
SFCP06	3.90	4.20		0.30	7.77	3.53	-0.37	-9.49	19.07	17.26	Constrict	
SFCP07	2.98	3.51	99.65	0.53	17.83	2.89	-0.09	-2.93	21.38	20.76	Constrict	
SFCP08	2.67	3.09	32.01	0.42	15.75	2.75	0.08	2.88	12.51	18.63	Dilate	
SFCP09	2.95	3.26	66.99	0.31	10.58	2.80	-0.15	-5.08	16.49	15.65	Constrict	157889
SFCP10	3.23	3.49	41.06	0.26	8.17	3.26	0.03	0.97	7.13	9.14	Dilate	39619
SFCP11	3.50	3.65	52.66	0.15	4.24	3.46	-0.05	-1.36	5.67	5.59	Constrict	
SFCP12	3.63	3.79	45.07	0.17	4.62	3.76	0.13	3.69	0.89	8.31	Dilate	

SFCP13	3.72	3.97	98.40	0.25	6.85	3.49	-0.23	-6.17	13.89	13.03	Constrict	
SFCP14	3.05	3.48	144.16	0.43	14.06	3.07	0.02	0.57	13.41	14.63	Dilate	27513
SFCP15	4.10	4.25	168.58	0.15	3.68	3.77	-0.33	-8.16	12.90	11.85	Constrict	
SFCP16	3.61	4.04	56.83	0.43	11.89	3.64	0.03	0.87	10.93	12.76	Dilate	28969
SFCP17	4.81	5.17	55.33	0.36	7.45	4.81	0.00	-0.10	7.55	7.54	Constrict	29123
SFCP18	3.30	3.62	98.03	0.32	9.59	3.55	0.25	7.43	2.01	17.03	Dilate	19488
SFCP19	3.90	4.17	158.37	0.28	7.10	3.94	0.04	1.04	6.00	8.13	Dilate	19921
SFCP21	2.93	3.35	100.38	0.43	14.68	2.77	-0.16	-5.32	21.13	20.00	Constrict	
SFCP22	3.59	3.85	56.31	0.26	7.31	3.47	-0.12	-3.33	11.01	10.64	Constrict	41907
SFCP23	3.07	3.36	52.64	0.29	9.33	3.12	0.05	1.49	7.73	10.82	Dilate	
SFCP24	2.14	2.41	38.37	0.27	12.76	2.13	-0.01	-0.40	13.22	13.16	Constrict	
SFCP26	3.68	3.83	55.95	0.15	4.13	3.65	-0.03	-0.72	4.88	4.85	Constrict	
SFCP28	3.43	3.61	41.00	0.17	5.05	3.35	-0.08	-2.31	7.53	7.36	Constrict	
SFCP29	3.42	3.69	60.76	0.27	7.94	3.37	-0.05	-1.36	9.42	9.29	Constrict	
SFCP30	2.98	3.15	8.72	0.17	5.80	3.03	0.05	1.68	4.05	7.48	Dilate	
SFCP31	3.85	4.20	53.21	0.35	9.09	3.75	-0.09	-2.46	11.84	11.55	Constrict	
SFCP32	4.21	4.61	77.60	0.40	9.38	3.95	-0.27	-6.38	16.83	15.76	Constrict	
SFCP33	3.40	3.51	47.91	0.11	3.29	3.23	-0.17	-4.88	8.59	8.17	Constrict	
SFCP34	3.83	3.93	105.52	0.09	2.46	3.53	-0.30	-7.74	11.05	10.20	Constrict	
SFCP35	3.84	3.99	17.95	0.15	3.83	4.19	0.35	9.13	-4.85	12.96	Dilate	
SFCP36	3.81	3.83	38.81	0.02	0.48	3.75	-0.06	-1.57	2.09	2.06	Constrict	
SFCP42	3.56	3.97	162.63	0.41	11.47	3.78	0.22	6.26	4.89	17.73	Dilate	
SFCP43	3.92	3.95	71.12	0.03	0.79	3.70	-0.22	-5.61	6.78	6.40	Constrict	
SFCP45	3.36	3.71	37.05	0.35	10.44	3.59	0.23	6.81	3.40	17.24	Dilate	
SFCP46	2.44	2.99	109.13	0.55	22.67	2.23	-0.21	-8.53	34.11	31.20	Constrict	
SFCP47	2.65	3.06	81.08	0.40	15.25	2.46	-0.19	-7.09	24.04	22.34	Constrict	

SFCP48	3.79	4.09	47.97	0.30	8.04	4.00	0.21	5.58	2.33	13.63	Dilate	
AMCP1	3.66	3.70	75	0.04	1.11	3.45	-0.21	-5.83	7.37	6.94	Constrict	
AMCP2	3.27	3.59	45	0.32	9.77	3.28	0.01	0.22	9.53	10.00	Dilate	
AMCP3	2.77	3.42	180	0.65	23.38	2.93	0.16	5.95	16.45	29.33	Dilate	
AMCP4	3.81	4.15	60	0.33	8.75	3.78	-0.03	-0.80	9.63	9.56	Constrict	
AMCP5	3.02	3.04	135	0.02	0.55	2.82	-0.21	-6.80	7.89	7.35	Constrict	
AMCP6	3.30	3.64	120	0.34	10.34	3.26	-0.04	-1.16	11.63	11.50	Constrict	
AMCP7	3.50	3.75	105	0.25	7.06	3.47	-0.03	-0.89	8.01	7.94	Constrict	
AMCP8	2.95	3.53	105	0.58	19.76	2.96	0.01	0.49	19.18	20.24	Dilate	
AMCP9	2.82	3.10	150	0.28	9.86	2.99	0.17	5.99	3.65	15.85	Dilate	
AMCP11	2.41	2.91	45	0.50	20.65	2.47	0.06	2.53	17.67	23.18	Dilate	
AMCON1	3.14	3.48	120.00	0.33	10.57	3.17	0.03	0.88	9.61	11.45	Dilate	
AMCON2	3.23	3.27	180.00	0.04	1.27	3.10	-0.13	-3.99	5.48	5.26	Constrict	
AMCON3	3.14	3.36	45.00	0.21	6.77	3.25	0.10	3.32	3.35	10.09	Dilate	
AMCON4	4.13	4.26	150.00	0.13	3.15	4.21	0.09	2.09	1.04	5.24	Dilate	
AMCON5	3.07	3.29	90.00	0.22	7.24	2.96	-0.11	-3.47	11.10	10.71	Constrict	
AMCON6	3.40	3.66	120.00	0.26	7.66	3.46	0.06	1.73	5.82	9.39	Dilate	
AMCON7	3.37	3.60	75.00	0.23	6.73	3.51	0.14	4.09	2.54	10.83	Dilate	
AMCON8	2.69	2.83	90.00	0.14	5.29	2.64	-0.05	-1.82	7.24	7.11	Constrict	
AMCON10	2.86	3.18	60.00	0.32	11.35	2.91	0.05	1.78	9.40	13.14	Dilate	
AMCON11	3.08	3.10	165.00	0.02	0.54	2.74	-0.35	-11.19	13.20	11.73	Constrict	
TR02	4.06	4.27	49.86	0.21	5.25	3.96	-0.09	-2.32	7.74	7.57	Constrict	28978
TR03	4.93	5.33	43.13	0.40	8.01	4.95	0.02	0.32	7.68	8.33	Dilate	15130
TR04	3.79	4.06	34.58	0.27	7.21	3.71	-0.07	-1.96	9.38	9.17	Constrict	21763
TR05	3.69	4.00	49.87	0.31	8.32	3.59	-0.10	-2.80	11.43	11.11	Constrict	23428
TR06	4.53	5.07	48.81	0.54	11.97	4.60	0.07	1.54	10.27	13.50	Dilate	25564

TR07	4.20	4.57	62.55	0.36	8.62	4.31	0.11	2.61	5.87	11.23	Dilate	61360
TR08	3.94	4.13	41.33	0.18	4.57	3.84	-0.11	-2.67	7.45	7.23	Constrict	21132
TR09	4.34	4.60	33.54	0.26	6.06	4.29	-0.05	-1.07	7.20	7.12	Constrict	26333
TR10	3.47	3.91	54.51	0.44	12.74	3.49	0.03	0.85	11.79	13.56	Dilate	59603
TR11	3.78	3.88	35.51	0.10	2.69	3.71	-0.07	-1.91	4.67	4.61	Constrict	16101
TR12	3.87	4.38	55.18	0.52	13.33	3.86	-0.01	-0.18	13.52	13.52	Constrict	50855
TR13	3.32	3.66	44.92	0.35	10.40	3.34	0.02	0.52	9.84	10.91	Dilate	26553
TR14	3.90	4.17	47.48	0.26	6.71	3.93	0.03	0.64	6.03	7.35	Dilate	22191
TR15	4.02	4.43	45.05	0.41	10.29	4.04	0.03	0.63	9.60	10.90	Dilate	21002
TR17	4.78	5.01	40.97	0.22	4.66	4.76	-0.03	-0.56	5.26	5.23	Constrict	21549
TR18	4.30	4.71	29.53	0.42	9.72	4.35	0.05	1.19	8.42	10.90	Dilate	14921
TR19	3.29	3.48	53.86	0.19	5.77	3.28	-0.01	-0.35	6.13	6.11	Constrict	30287
TR20	4.00	4.45	43.59	0.46	11.39	3.91	-0.09	-2.34	14.06	13.75	Constrict	32891
TR21	3.98	4.52	117.72	0.54	13.67	4.08	0.10	2.57	10.81	16.25	Dilate	14330
TR22	4.03	4.46	40.68	0.43	10.72	4.10	0.07	1.70	8.84	12.39	Dilate	18326
TR23	4.11	4.37	40.78	0.26	6.31	4.07	-0.04	-0.92	7.33	7.23	Constrict	29772
TR24	4.52	4.72	52.68	0.20	4.31	4.41	-0.12	-2.54	7.03	6.85	Constrict	18356
TR25	4.08	4.31	45.82	0.23	5.64	4.05	-0.04	-0.87	6.57	6.49	Constrict	30925
TR26	3.33	3.61	40.02	0.28	8.53	3.26	-0.07	-2.00	10.77	10.55	Constrict	25868
TR27	3.97	4.39	35.62	0.42	10.60	4.02	0.05	1.33	9.15	11.92	Dilate	39121
CAMO01	6.08	6.30		0.22	3.60	6.27	0.19	3.19	0.39	6.79	Dilate	
CAMO02	4.24	4.37		0.13	2.97	4.24	0.00	-0.05	3.02	3.02	Constrict	
CAMO03	3.58	3.83		0.25	7.05	3.74	0.16	4.38	2.56	11.44	Dilate	
CAMO04	5.31	6.09		0.77	14.56	5.78	0.46	8.70	5.38	23.26	Dilate	
CAMO05	3.39	3.64		0.25	7.28	3.58	0.18	5.43	1.76	12.71	Dilate	
CAMO06	3.74	3.61		-0.13	-3.34	3.81	0.07	2.00	-5.24	5.35	Dilate	

CAMO07	3.69	3.85		0.17	4.54	3.52	-0.16	-4.42	9.37	8.96	Constrict	
CAMO08	5.07	5.27		0.20	3.94	5.16	0.09	1.85	2.06	5.79	Dilate	
CAMO09	4.00	3.79		-0.21	-5.30	3.65	-0.35	-8.84	3.88	14.15	Constrict	
CAMO10	3.22	3.38		0.16	5.00	3.21	0.00	-0.13	5.13	5.12	Constrict	
CAMO11	3.75	4.17		0.42	11.30	3.88	0.13	3.40	7.64	14.69	Dilate	
CAMO12	3.35	3.61		0.26	7.86	3.29	-0.06	-1.72	9.75	9.58	Constrict	
CAMO13	3.16	3.33		0.17	5.26	3.10	-0.06	-1.91	7.31	7.16	Constrict	
CAMO14	2.68	2.91		0.23	8.63	2.79	0.11	4.01	4.44	12.64	Dilate	
CAMO15	3.44	3.80		0.35	10.20	3.58	0.13	3.91	6.06	14.11	Dilate	
CAMO16	2.87	2.95		0.09	3.01	2.90	0.03	1.05	1.94	4.06	Dilate	
CAMO17	3.65	3.86		0.20	5.60	3.51	-0.14	-3.82	9.79	9.42	Constrict	
CAMO18	2.78	3.17		0.40	14.32	2.97	0.20	7.05	6.79	21.37	Dilate	
CAMO19	3.60	3.89		0.29	8.04	3.66	0.06	1.68	6.25	9.71	Dilate	
CAMO20	4.76	4.99		0.23	4.73	4.94	0.18	3.71	0.98	8.44	Dilate	
CAMO21	4.39	4.55		0.16	3.59	4.47	0.08	1.81	1.75	5.40	Dilate	
CAMO22	3.69	3.53		-0.16	-4.29	3.36	-0.33	-9.02	5.20	13.30	Constrict	
CAMO23	3.97	4.09		0.11	2.78	3.87	-0.11	-2.71	5.65	5.49	Constrict	
CAMO24	3.88	4.03		0.14	3.69	3.83	-0.05	-1.39	5.15	5.08	Constrict	
CAMO25	5.31	5.49		0.18	3.45	5.70	0.39	7.30	-3.59	10.76	Dilate	
CAMO26	3.01	3.21		0.20	6.79	3.00	-0.01	-0.32	7.13	7.10	Constrict	
CAMO27	2.10	2.26		0.15	7.31	2.33	0.23	10.88	-3.22	18.19	Dilate	
CAMO28	4.74	5.00		0.26	5.53	4.78	0.04	0.81	4.69	6.34	Dilate	
CAMO29	3.64	3.77		0.13	3.52	3.60	-0.03	-0.94	4.50	4.46	Constrict	
CAMO30	3.85	4.10		0.25	6.39	3.74	-0.12	-3.00	9.68	9.39	Constrict	
CAMO31	4.00	4.30		0.30	7.50	4.05	0.05	1.23	6.20	8.73	Dilate	
CAMO32	4.52	4.69		0.17	3.73	4.50	-0.02	-0.40	4.15	4.13	Constrict	

CAMO33	3.69	3.77		0.08	2.07	3.68	-0.01	-0.40	2.47	2.46	Constrict	
CAMO34	5.20	5.34		0.14	2.67	5.21	0.01	0.19	2.48	2.86	Dilate	
CAMS01	4.26	4.34		0.09	2.06	4.16	-0.09	-2.13	4.28	4.18	Constrict	
CAMS02	2.80	2.76		-0.04	-1.35	2.61	-0.19	-6.75	5.79	8.11	Constrict	
CAMS05	5.13	5.76		0.63	12.19	5.32	0.19	3.71	8.18	15.91	Dilate	
CAMS06	4.33	4.52		0.19	4.27	4.40	0.07	1.52	2.71	5.79	Dilate	
CAMS08	4.21	4.36		0.15	3.53	4.10	-0.11	-2.51	6.19	6.02	Constrict	
CAMS09	3.30	3.41		0.11	3.44	3.25	-0.05	-1.45	4.96	4.90	Constrict	
CAMS10	5.66	5.83		0.18	3.09	5.68	0.02	0.34	2.74	3.44	Dilate	
CAMS11	2.28	2.59		0.31	13.60	2.32	0.04	1.76	11.64	15.36	Dilate	
CAMS12	3.81	3.78		-0.03	-0.82	3.79	-0.02	-0.56	-0.27	1.38	Constrict	
CAMS13	3.55	3.84		0.29	8.23	3.58	0.03	0.86	7.30	9.10	Dilate	
CAMS14	4.62	4.82		0.20	4.32	4.75	0.13	2.75	1.53	7.06	Dilate	
CAMS15	2.67	2.81		0.14	5.16	2.60	-0.07	-2.60	7.96	7.77	Constrict	
CAD01	4.77	5.08	25.2	0.32	6.60	4.80	0.03	0.67	5.88	7.38	Dilate	3446
CAD02	4.19	4.40	52.2	0.21	5.00	4.27	0.08	1.86	3.03	6.87	Dilate	12580
CAD03	3.16	3.30	24	0.15	4.70	3.13	-0.02	-0.70	5.50	5.45	Constrict	2667
CAD04	5.06	5.31	64.9	0.26	5.10	5.03	-0.02	-0.48	5.65	5.62	Constrict	22890
CAD05	4.64	4.79	56.5	0.15	3.20	4.63	-0.01	-0.28	3.49	3.51	Constrict	9956
CAD06	3.31	3.47	24.8	0.16	4.70	3.37	0.05	1.64	2.90	6.48	Dilate	3815
CAD07	4.44	4.81	54.8	0.37	8.30	4.66	0.21	4.74	3.31	13.07	Dilate	5139
CAD08	3.8	4.00	100.9	0.19	5.10	3.87	0.07	1.91	3.24	6.91	Dilate	41301
CAD09	4.84	5.17	76	0.33	6.80	4.94	0.10	2.12	4.55	8.94	Dilate	20461
CAD10	4.58	4.60	16.8	0.02	0.30	4.55	-0.03	-0.75	1.03	1.18	Constrict	1137
CAD13	3.85	4.02	10.9	0.17	4.50	3.83	-0.02	-0.40	4.97	4.84	Constrict	457.7
CAD14	3.06	3.36	29.2	0.3	9.70	3.14	0.08	2.50	7.11	12.26	Dilate	3933

CAD16	4.35	4.52	59.8	0.17	4.00	4.35	0.00	0.11	3.88	4.02	Dilate	10126
CAD18	5.44	5.55	77.5	0.11	2.00	5.45	0.00	0.06	1.96	2.08	Dilate	33967
CAD19	4.55	4.83	88.3	0.28	6.20	4.67	0.12	2.57	3.52	8.73	Dilate	13705
CAD20	5.75	6.03	49.9	0.28	4.90	5.75	0.00	0.01	4.88	4.88	Dilate	5473
CAD21	4.6	4.74	67.2	0.13	2.90	4.68	0.07	1.58	1.30	4.40	Dilate	17775
CAD22	5.44	5.50	61.4	0.06	1.20	5.46	0.03	0.50	0.65	1.61	Dilate	15666
CAD23	4.26	4.43	96.3	0.17	4.10	4.35	0.10	2.26	1.81	6.25	Dilate	25117
CAD24	4.84	5.25	112.4	0.41	8.50	4.90	0.06	1.32	7.05	9.79	Dilate	18584
CAD25	3.54	3.92	91.7	0.39	10.90	3.58	0.04	1.13	9.67	12.15	Dilate	46264
CAD26	4.06	4.18	61.4	0.12	3.00	4.05	-0.01	-0.18	3.23	3.14	Constrict	9835
CAD27	5.26	5.28	38.8	0.02	0.30	5.27	0.01	0.22	0.10	0.60	Dilate	5387
CAD28	5.07	5.20	87.2	0.13	2.60	5.05	-0.02	-0.36	3.00	2.92	Constrict	19490
CAD29	5.26	5.42	14.5	0.16	3.00	5.30	0.04	0.77	2.17	3.81	Dilate	885.4
CAD30	4.00	4.00	69	0	0.00	4.05	0.05	1.35	-1.34	1.35	Dilate	12662
RAM01 V1	4.27	4.61	34.28	0.34	8.03	4.31	0.04	0.90	7.07	8.86	Dilate	26313
RAM02 V1	5.08	5.33	59.16	0.25	4.98	5.08	0.00	0.08	4.90	5.00	Dilate	21702
RAM03 V1	4.15	4.32	48.36	0.17	4.11	4.16	0.01	0.30	3.80	4.40	Dilate	31848
RAM04 V1	4.17	4.28	34.28	0.11	2.68	4.22	0.05	1.20	1.46	3.84	Dilate	26000
RAM05 V1	3.62	3.95	46.37	0.33	9.02	3.83	0.22	5.95	2.90	15.07	Dilate	40507
RAM06 V1	4.01	4.28	56.97	0.27	6.75	4.08	0.07	1.83	4.83	8.56	Dilate	33673
RAM07 V1	4.29	4.64	25.18	0.35	8.23	4.35	0.06	1.41	6.72	9.57	Dilate	20951
RAM08 V1	4.14	4.49	75.90	0.35	8.33	4.06	-0.09	-2.16	10.72	10.61	Constrict	64839
RAM09 V1	4.09	4.24	35.20	0.15	3.61	4.13	0.04	0.87	2.71	4.54	Dilate	24747
RAM10 V1	4.54	4.76	73.94	0.21	4.71	4.63	0.08	1.83	2.83	6.46	Dilate	36583
RAM11 V1	3.83	4.02	44.99	0.19	4.88	3.81	-0.02	-0.45	5.36	5.41	Constrict	30365
RAM12 V1	4.48	4.87	35.51	0.39	8.61	4.40	-0.08	-1.85	10.66	10.56	Constrict	45575

RAM13 V1	4.09	4.51	49.62	0.42	10.23	4.12	0.03	0.72	9.44	10.99	Dilate	36736
RAM14 V1	3.81	4.08	28.05	0.27	7.10	3.81	0.00	-0.10	7.21	7.19	Constrict	28433
RAM15 V1	4.65	4.93	29.96	0.28	5.93	4.68	0.02	0.53	5.37	6.55	Dilate	10567
RAM16 V1	3.81	4.39	70.66	0.57	15.06	3.92	0.11	2.87	11.85	17.83	Dilate	43616
RAM17 V1	4.25	4.53	60.57	0.28	6.61	4.33	0.08	1.90	4.62	8.49	Dilate	42759
RAM18 V1	4.78	4.96	62.25	0.17	3.63	4.75	-0.03	-0.66	4.32	4.22	Constrict	28529
RAM19 V1	4.35	4.64	57.97	0.3	6.80	4.36	0.01	0.19	6.59	7.09	Dilate	35560
RAM20 V1	4.21	4.56	78.44	0.34	8.16	4.27	0.06	1.38	6.69	9.45	Dilate	53811
RAM21 V1	2.47	2.76	39.77	0.29	11.76	2.42	-0.06	-2.26	14.35	14.00	Constrict	46156
RAM22 V1	2.82	3.13	99.21	0.32	11.19	2.77	-0.04	-1.52	12.90	12.69	Constrict	41918
RAM23 V1	2.74	2.94	25.18	0.2	7.35	2.74	0.00	-0.08	7.49	7.38	Constrict	44567
RAM24 V1	3.55	3.63	45.39	0.08	2.16	3.54	-0.01	-0.36	2.58	2.61	Constrict	39764
RAM25 V1	3.05	3.22	41.04	0.17	5.64	3.03	-0.02	-0.59	6.27	6.17	Constrict	21873
RAM26 V1	2.83	3.20	34.77	0.37	13.00	2.91	0.08	2.75	9.97	15.83	Dilate	34650
RAM31 V1	3.30	3.41	145.69	0.1	3.15	3.31	0.01	0.35	2.78	3.38	Dilate	21379
RAM32 V1	3.07	3.28	76.00	0.21	6.78	3.05	-0.02	-0.69	7.53	7.53	Constrict	62147
RAM34 V1	2.72	2.98	47.97	0.26	9.54	2.74	0.02	0.81	8.66	10.37	Dilate	41281
RAM35 V1	3.47	3.66	58.98	0.18	5.25	3.50	0.03	0.76	4.45	5.95	Dilate	21835
RAM36 V1	3.35	3.47	41.90	0.13	3.77	3.30	-0.05	-1.40	5.24	5.28	Constrict	24498
RAM38 V1	3.18	3.31	41.86	0.13	4.07	3.17	-0.01	-0.40	4.50	4.49	Constrict	28373
V1RAM41	3.34	3.65	25.38	0.31	9.27	3.49	0.15	4.44	4.62	13.75	Dilate	18514
V1RAM43	3.12	3.24	31.98	0.12	3.91	3.11	-0.01	-0.28	4.20	4.23	Constrict	16445
V1RAM44	3.00	3.22		0.22	7.25	3.13	0.13	4.46	2.68	11.59	Dilate	
V1RAM46	2.99	3.24	31.37	0.26	8.57	3.00	0.01	0.39	8.15	8.91	Dilate	20867
V1RAM47	3.27	3.64	47.53	0.37	11.33	3.36	0.09	2.62	8.49	14.08	Dilate	17773
V1RAM48	3.41	3.87	48.58	0.46	13.44	3.40	-0.01	-0.27	13.74	13.73	Constrict	25023

V1RAM49	3.22	3.48	59.80	0.26	8.04	3.19	-0.03	-0.94	9.06	8.97	Constrict	30561
V1RAM50	3.25	3.48	45.03	0.23	7.21	3.21	-0.03	-1.06	8.36	8.13	Constrict	60765
V1RAM51	3.57	3.73	37.43	0.15	4.33	3.52	-0.05	-1.39	5.80	5.73	Constrict	20599
V1RAM52	3.70	3.88	32.18	0.18	4.82	3.71	0.01	0.20	4.61	5.09	Dilate	20826
V1RAM53	3.75	4.06	20.70	0.30	8.12	3.85	0.10	2.57	5.40	10.67	Dilate	8253
V1RAM54	2.96	3.17	63.09	0.21	7.24	2.94	-0.01	-0.43	7.70	7.43	Constrict	47522
V1RAM55	3.29	3.59	35.00	0.31	9.31	3.24	-0.04	-1.36	10.82	10.67	Constrict	22386
V1RAM56	3.08	3.35	30.15	0.27	8.86	2.98	-0.09	-3.05	12.29	11.79	Constrict	33363
V1RAM58	3.15	3.42	34.00	0.26	8.39	3.14	-0.01	-0.24	8.65	8.70	Constrict	65945
V1RAM59	3.49	3.68	44.01	0.19	5.51	3.43	-0.06	-1.67	7.30	7.23	Constrict	16276
V1RAM60	3.57	3.79	35.76	0.22	6.04	3.53	-0.04	-1.20	7.32	7.15	Constrict	18043
V1RAM61	3.39	3.70	29.98	0.31	9.13	3.41	0.03	0.81	8.25	10.01	Dilate	33883
ASPEN 1	5.04	5.29		0.25	4.98	5.08	0.04	0.80	4.14	5.76	Dilate	
ASPEN 2	4.05	4.29		0.24	5.81	4.13	0.07	1.77	3.97	7.70	Dilate	
ASPEN 3	5.29	5.42		0.14	2.55	5.27	-0.02	-0.39	2.96	2.95	Constrict	
ASPEN 4	4.34	4.66		0.32	7.39	4.45	0.11	2.47	4.80	9.84	Dilate	
ASPEN 5	4.47	4.66		0.19	4.43	4.53	0.06	1.43	2.96	5.68	Dilate	
ASPEN 6	4.55	4.71		0.16	3.41	4.43	-0.13	-2.79	6.38	6.31	Constrict	
ASPEN 7	4.09	4.39		0.3	7.23	4.23	0.13	3.26	3.85	10.59	Dilate	
ASPEN 8	3.4	3.63		0.23	6.72	3.46	0.07	1.96	4.67	8.73	Dilate	
ASPEN 9	4.88	5.14		0.26	5.25	4.99	0.11	2.22	2.97	7.54	Dilate	
ASPEN 10	4.17	4.57		0.4	9.65	4.22	0.05	1.16	8.40	10.75	Dilate	
NESTLE S6	4.68	4.85	53.63	0.17	3.63	4.66	-0.01	-0.30	3.95	3.94	Constrict	16002
NESTLE S8	4.93	5.06	44.84	0.13	2.71	4.92	-0.01	-0.11	2.83	2.82	Constrict	13141
NESTLE S10	4.54	4.79	67.12	0.25	5.45	4.51	-0.03	-0.73	6.22	6.18	Constrict	12626

NESTLE S11	4.47	4.83	77.28	0.36	7.95	4.32	-0.15	-3.44	11.80	11.39	Constrict	27373
NESTLE S12	4.45	4.53	50.90	0.07	1.68	4.36	-0.09	-2.01	3.76	3.69	Constrict	17166
NESTLE S13	3.28	3.51	49.58	0.23	7.01	3.21	-0.07	-2.12	9.32	9.13	Constrict	26080
NESTLE S14	4.58	4.85	51.57	0.27	5.93	4.51	-0.06	-1.34	7.37	7.27	Constrict	19751
NESTLE S15	4.94	5.07	88.76	0.13	2.53	4.90	-0.05	-0.96	3.53	3.50	Constrict	19092
NESTLE S16	4.73	4.90	62.19	0.16	3.44	4.67	-0.07	-1.39	4.90	4.83	Constrict	14150
NESTLE S17	4.18	4.48	44.24	0.30	7.11	4.15	-0.03	-0.77	7.94	7.88	Constrict	12278
NESTLE S18	3.49	3.80	48.89	0.31	8.82	3.43	-0.06	-1.77	10.78	10.59	Constrict	15251
NESTLE S19	4.76	5.14	36.18	0.39	8.16	4.72	-0.04	-0.82	9.06	8.98	Constrict	11553
NESTLE S21	5.71	5.74	39.85	0.03	0.55	5.52	-0.18	-3.16	3.84	3.72	Constrict	3036
NESTLE S23	4.74	4.83	63.14	0.09	1.94	4.48	-0.26	-5.50	7.88	7.44	Constrict	22715
NESTLE S25	4.95	5.05	41.97	0.10	2.07	4.90	-0.04	-0.83	2.92	2.90	Constrict	10453
NESTLE S27	5.91	6.23	41.54	0.32	5.45	5.90	-0.01	-0.17	5.63	5.62	Constrict	7976
NESTLE S28	5.11	5.41	34.96	0.30	5.97	5.36	0.26	5.06	0.86	11.03	Dilate	4980
NESTLE S31	4.19	4.25	41.05	0.05	1.30	4.13	-0.07	-1.59	2.94	2.90	Constrict	10978
ACM1	4.22	4.43	41.00	0.21	5.00	4.38	0.16	3.80	1.18	8.77	Dilate	11732
ACM2	3.1	3.43	50.00	0.33	10.80	3.16	0.07	2.12	8.48	12.77	Dilate	38241
ACM3	4.86	5.25	46.00	0.39	8.00	4.99	0.13	2.63	5.23	10.66	Dilate	9196
ACM4	4.28	4.51	48.00	0.22	5.20	4.30	0.02	0.48	4.72	5.62	Dilate	22593

ACM5	3.42	3.65	35.00	0.23	6.80	3.30	-0.12	-3.62	10.78	10.35	Constrict	11556
ACM6	4.32	4.43	66.00	0.11	2.50	4.26	-0.07	-1.51	4.08	4.05	Constrict	23099
ACM8	3.28	3.78	73.00	0.5	15.20	3.30	0.01	0.42	14.67	15.67	Dilate	32042
ACM10	4.03	4.31	42.00	0.28	7.00	3.96	-0.07	-1.81	8.92	8.75	Constrict	14537
ACF1	3.98	4.19	34.00	0.21	5.30	3.92	-0.06	-1.59	7.05	6.87	Constrict	11153
ACF4	3.26	3.37	23.00	0.11	3.50	3.26	0.00	-0.04	3.53	3.41	Constrict	4215
ACF5	3.26	3.48	58.00	0.22	6.60	3.14	-0.12	-3.62	10.61	10.37	Constrict	22090
ACF6	2.9	3.24	41.00	0.34	11.70	2.99	0.09	3.06	8.42	14.79	Dilate	22742
ACF7	3.42	3.64	42.00	0.22	6.50	3.41	0.00	-0.06	6.59	6.49	Constrict	14775
ACF8	3.77	4.15	41.00	0.38	10.10	3.73	-0.04	-1.08	11.26	11.16	Constrict	12465
ACF9	4.04	4.06	68.70	0.02	0.40	3.75	-0.29	-7.27	8.31	7.77	Constrict	61073
ACF10	3.65	3.79	53.00	0.14	3.80	3.60	-0.04	-1.19	5.10	5.03	Constrict	28778
V1ACUTE ENDO 1	3.97	4.26	37.05	0.29	7.19	4.11	0.13	3.29	3.77	10.47	Dilate	12269.00
V1ACUTE ENDO 2	3.91	4.07	47.87	0.17	4.27	3.88	-0.03	-0.78	5.10	5.06	Constrict	13276.00
V1ACUTE ENDO 3	4.45	4.81	22.13	0.36	8.05	4.47	0.02	0.50	7.51	8.55	Dilate	3915.00
V1ACUTE ENDO 4	3.27	3.38	60.60	0.11	3.25	3.20	-0.07	-2.21	5.71	5.57	Constrict	37694.00
V1ACUTE ENDO 5	4.17	4.21	95.12	0.04	1.02	4.00	-0.17	-3.97	5.19	4.99	Constrict	33103.00
V1ACUTE ENDO 6	4.58	4.76	63.70	0.18	3.97	4.46	-0.11	-2.48	6.61	6.45	Constrict	25771.00
V1ACUTE ENDO 7	3.71	3.88	57.78	0.17	4.52	3.69	-0.02	-0.60	5.15	5.12	Constrict	1036.00
AB-SCI04 NC	4.39	5.08	47.22	0.69	15.70	4.20	-0.20	-4.48	21.12	20.18	Constrict	15806
AB-SCI06 NC	4.33	4.70	51.96	0.37	8.54	4.39	0.06	1.43	7.01	9.96	Dilate	15628
AB-SCI07	4.35	4.55	54.25	0.20	4.58	4.35	0.00	-0.02	4.60	4.60	Constrict	12290

NC												
AB-SCI11 NC	3.85	4.12	59.02	0.27	6.97	3.88	0.03	0.67	6.25	7.64	Dilate	22996
AB-SCI12 NC	3.92	3.97	39.03	0.05	1.30	3.85	-0.08	-1.93	3.29	3.23	Constrict	23830
AB-SCI14 NC	3.53	3.73	40.45	0.21	5.83	3.52	-0.01	-0.23	6.08	6.06	Constrict	9609
AB-SCI19 NC	4.81	5.11	53.88	0.30	6.17	4.95	0.14	2.94	3.14	9.11	Dilate	16499
AB-SCI24 NC	3.21	3.30	42.57	0.09	2.89	3.18	-0.03	-0.88	3.80	3.76	Constrict	10531
SCI01	4.23	4.55	100.83	0.32	7.54	4.04	-0.19	-4.59	12.71	12.13	Constrict	35050
SCI02	3.83	4.11	83.49	0.27	7.09	3.60	-0.24	-6.20	14.16	13.29	Constrict	74550
SCI03	3.83	4.05	76.43	0.22	5.66	3.85	0.02	0.45	5.19	6.12	Dilate	7275
SCI04	4.51	4.74	17.14	0.22	4.91	4.39	-0.12	-2.67	7.80	7.59	Constrict	3329
SCI05	4.04	4.21	49.38	0.17	4.30	3.90	-0.13	-3.33	7.90	7.63	Constrict	8632
SCI06	4.63	4.77	105.38	0.14	3.00	4.48	-0.15	-3.23	6.44	6.23	Constrict	7190
SCI07	4.83	5.27	139.85	0.43	8.99	4.84	0.00	0.06	8.93	9.05	Dilate	76663
SCI08	4.08	4.41	58.47	0.33	8.05	3.80	-0.29	-7.04	16.23	15.08	Constrict	11195
SCI09	4.28	4.56	46.98	0.28	6.54	4.48	0.19	4.55	1.90	11.09	Dilate	13856
SCI10	4.19	4.28	58.21	0.09	2.13	3.71	-0.47	-11.33	15.18	13.46	Constrict	9375
SCI11	5.47	5.69	44.26	0.22	4.03	5.00	-0.47	-8.65	13.88	12.68	Constrict	10018
SCI12	5.37	5.70	12.10	0.33	6.11	5.36	-0.01	-0.26	6.39	6.37	Constrict	933
SCI13	4.24	4.79	70.17	0.55	12.95	4.21	-0.02	-0.53	13.55	13.48	Constrict	30008
SCI14	5.10	5.24	41.73	0.14	2.82	4.98	-0.12	-2.36	5.30	5.18	Constrict	6925
SCI15	4.10	4.32	30.21	0.22	5.38	4.08	-0.02	-0.55	5.96	5.93	Constrict	6253
SCI16	3.88	4.20	71.65	0.32	8.14	3.77	-0.12	-3.00	11.48	11.14	Constrict	8743
SCI17	5.82	6.39	102.67	0.57	9.84	5.86	0.04	0.73	9.05	10.57	Dilate	21736
SCI18	3.71	4.02	44.77	0.31	8.36	3.40	-0.31	-8.41	18.31	16.77	Constrict	10561

SCI19	3.68	4.03	61.20	0.35	9.43	3.58	-0.10	-2.61	12.36	12.04	Constrict	47392
SCI20	4.69	4.90	72.24	0.20	4.36	4.65	-0.04	-0.83	5.23	5.19	Constrict	27349
SCI21	4.33	4.64	53.33	0.30	6.97	4.19	-0.14	-3.23	10.54	10.20	Constrict	11354
SCI22	3.35	3.69	53.11	0.33	9.96	3.29	-0.06	-1.82	12.01	11.79	Constrict	27983
SCI23	3.45	3.84	51.83	0.39	11.23	3.53	0.08	2.31	8.71	13.54	Dilate	10542
SCI24	4.77	5.08	48.90	0.32	6.69	4.72	-0.05	-1.05	7.82	7.73	Constrict	22166
SCI25	3.97	4.18	47.52	0.22	5.42	3.94	-0.02	-0.59	6.05	6.02	Constrict	8898
SCI26	3.45	3.75	48.42	0.29	8.53	3.41	-0.04	-1.13	9.78	9.67	Constrict	9338
SCI27	4.39	4.70	13.52	0.31	6.95	4.39	0.00	0.04	6.91	7.00	Dilate	408.9
SCI28	4.53	4.80	70.42	0.27	6.03	4.56	0.03	0.71	5.29	6.74	Dilate	38099
SCI29	3.52	3.94	25.45	0.41	11.70	3.50	-0.02	-0.69	12.47	12.39	Constrict	3185
SCI30	4.30	4.94	47.52	0.64	14.80	4.43	0.12	2.88	11.59	17.68	Dilate	16664
SCI31	4.26	4.69	50.94	0.43	10.08	4.07	-0.19	-4.41	15.17	14.50	Constrict	19907
SCI32	3.93	4.32	55.81	0.38	9.79	3.88	-0.05	-1.38	11.32	11.17	Constrict	5916
SCI33	5.17	5.39	88.04	0.22	4.32	5.18	0.02	0.31	4.00	4.63	Dilate	29922
SCI34	4.28	4.65	83.97	0.37	8.63	4.27	-0.02	-0.41	9.08	9.04	Constrict	21528
EDS01	2.94	3.20	33.49	0.25	8.62	2.96	0.02	0.62	7.95	9.24	Dilate	22189.00
EDS02	3.45	3.87	58.66	0.42	12.21	3.67	0.22	6.33	5.53	18.53	Dilate	30252.00
EDS03	3.95	4.16	71.32	0.21	5.41	4.00	0.05	1.27	4.09	6.67	Dilate	12384.00
EDS04	4.65	5.05		0.40	8.52	4.67	0.01	0.32	8.18	8.84	Dilate	
TVR1	3.99	4.21		0.23	5.67	3.95	-0.04	-0.88	6.61	6.77	Constrict	
TVR2	4.00	4.09	58.77	0.09	2.28	4.00	0.00	0.10	2.18	2.25	Dilate	
TVR3	5.71	5.78		0.07	1.23	5.67	-0.04	-0.70	1.94	1.93	Constrict	
TVR4	5.69	5.84	61.46	0.15	2.64	5.75	0.06	1.05	1.57	3.68	Dilate	
TVR5	5.45	5.53	40.27	0.08	1.52	5.49	0.04	0.77	0.75	2.29	Dilate	
TVR6	4.73	4.92	132.43	0.19	3.95	4.77	0.04	0.80	3.12	4.75	Dilate	

TVR7	4.69	4.87	80.43	0.18	3.75	4.74	0.05	1.14	2.58	4.90	Dilate	
TVR8	4.39	4.65	59.35	0.26	6.03	4.46	0.07	1.59	4.37	7.52	Dilate	
TVR9	4.45	4.64	55.30	0.19	4.30	4.46	0.01	0.16	4.14	4.49	Dilate	
TVR10	3.35	3.59	29.46	0.25	7.35	3.52	0.18	5.30	1.95	12.84	Dilate	
TVR11	4.78	4.98	64.34	0.21	4.32	4.77	-0.01	-0.22	4.56	4.55	Constrict	
TVR12	3.62	3.81	71.54	0.19	5.30	3.60	-0.02	-0.59	5.93	5.80	Constrict	
TVR13	3.74	3.88	41.30	0.14	3.69	3.72	-0.02	-0.53	4.24	4.28	Constrict	
TVR14	3.36	3.51	48.34	0.15	4.32	3.37	0.01	0.41	3.90	4.76	Dilate	
TVR15	4.00	4.11	74.18	0.11	2.63	4.00	-0.01	-0.17	2.80	3.00	Constrict	
TVR16	3.72	3.96	57.19	0.24	6.55	3.76	0.05	1.23	5.26	7.89	Dilate	
TVR17	5.46	5.72	65.52	0.26	4.81	5.53	0.08	1.39	3.37	6.27	Dilate	
TVR18	3.76	3.89	63.85	0.12	3.29	3.80	0.04	1.04	2.23	4.26	Dilate	
TVR19	3.16	3.23	33.97	0.07	2.09	3.14	-0.02	-0.67	2.78	2.76	Constrict	
TVR20	3.99	4.09	146.58	0.09	2.33	3.97	-0.02	-0.59	2.94	2.76	Constrict	
PFA02	2.74	2.90		0.16	5.7	2.89	0.15	5.5	0.35	11.31	Dilate	
PFA03	2.84	3.00		0.16	5.7	2.97	0.13	4.6	1.01	10.21	Dilate	
PFA10	2.29	2.42		0.12	5.3	2.32	0.03	1.2	4.31	6.55	Dilate	
PFA11	2.7	2.92		0.22	8	2.71	0.01	0.3	7.75	8.52	Dilate	
PFA12	2.62	2.84		0.22	8.3	2.65	0.03	1.3	7.17	9.54	Dilate	
PFA14	2.42	2.66		0.24	9.9	2.39	-0.03	-1	11.30	11.16	Constrict	
PFA17	2.71	2.88		0.17	6.2	2.71	0	-0.1	6.27	6.27	Constrict	
PFA30	2.84	3.16		0.31	11.1	3	0.16	5.7	5.33	16.55	Dilate	
PFA34	2.68	2.83		0.15	5.7	2.66	-0.01	-0.4	6.39	5.97	Constrict	
PFA36	2.78	2.92		0.14	5	2.79	0.01	0.3	4.66	5.40	Dilate	
PFA40	2.56	2.69		0.13	4.9	2.62	0.06	2.2	2.67	7.42	Dilate	
PFA55	2.46	2.68		0.22	8.9	2.52	0.06	2.4	6.35	11.38	Dilate	
PFA56	2.67	2.99		0.32	12	2.68	0.01	0.4	11.57	12.36	Dilate	

PFA59	2.24	2.44		0.21	9.2	2.31	0.08	3.4	5.63	12.95	Dilate	
PFA69	2.29	2.38		0.09	3.9	2.54	0.25	10.9	-6.30	14.85	Dilate	
PFB03	2.71	2.86		0.15	5.5	2.85	0.14	5	0.35	10.70	Dilate	
PFB04	2.58	2.69		0.1	3.9	2.62	0.04	1.4	2.67	5.43	Dilate	
PFB14	2.56	2.69		0.13	5.1	2.59	0.03	1.1	3.86	6.25	Dilate	
PFB19	2.31	2.39		0.08	3.5	2.41	0.1	4.3	-0.83	7.79	Dilate	
PFB24	2.78	2.87		0.09	3.1	2.81	0.03	1.2	2.14	4.32	Dilate	
PMA10	3.05	3.21		0.16	5.2	3.16	0.11	3.6	1.58	8.85	Dilate	
PMA15	2.37	2.53		0.16	6.6	2.42	0.05	2	4.55	8.86	Dilate	
PMA16	2.43	2.58		0.15	6.4	2.49	0.06	2.5	3.61	8.64	Dilate	
PMB05	3.1856	3.28		0.10	3.01	3.21	0.03	0.83	2.17	3.84	Dilate	
PMA22	2.35	2.65		0.29	12.5	2.53	0.18	7.5	4.74	20.00	Dilate	
PMA24	2.56	2.69		0.13	4.9	2.43	-0.14	-5.3	10.70	10.55	Constrict	
PMB04	2.49	2.65		0.15	6.17	2.56	0.07	2.76	3.32	8.92	Dilate	
PMA27	2.44	2.77		0.33	13.6	2.55	0.11	4.6	8.63	18.03	Dilate	
PMA28	2.59	2.77		0.18	7.1	2.61	0.03	1	6.13	8.11	Dilate	
PMA32	2.56	2.73		0.17	6.6	2.48	-0.08	-3.3	10.08	9.77	Constrict	
PMA33	2.47	2.67		0.2	8	2.53	0.05	2.1	5.53	10.12	Dilate	
PMA38	2.67	2.94		0.27	10.2	2.69	0.02	0.6	9.29	10.86	Dilate	
PMA42	2.07	2.14		0.07	3.5	2.08	0.01	0.4	2.88	3.86	Dilate	
PMA67	2.67	2.79		0.13	4.8	2.67	0.01	0.2	4.49	5.24	Dilate	
PMA68	2.44	2.53		0.09	3.7	2.44	0	-0.2	3.69	3.69	Constrict	
PMA73	2.84	2.90		0.06	2.3	2.73	-0.11	-3.8	6.23	5.99	Constrict	
PMA74	2.37	2.41		0.04	1.6	2.34	-0.04	-1.6	2.99	3.38	Constrict	
PMA77	2.9	3.28		0.38	13.1	2.98	0.08	2.8	10.07	15.86	Dilate	
PMB06	2.71	2.89		0.18	6.64	2.74	0.03	1.11	5.47	7.75	Dilate	
PMB01	2.76	2.87		0.11	3.9	2.75	-0.02	-0.6	4.36	4.71	Constrict	

Nitroglycerin Challenge Test Data

Study ID	BL NTG	PEAK NTG	Abs NTG	%NTG	TTP
SPEC02					
SPEC03					
SPEC04					
SPEC05					
SPEC06					
SPEC07					
SPEC08					
SPEC09					
SPEC10					
COS01					
COS02					
COS03					
SFCP01					
SFCP02					
SFCP03					
SFCP04					
SFCP05					
SFCP06					
SFCP07					
SFCP08					
SFCP09					
SFCP10					
SFCP11					
SFCP12					
SFCP13					
SFCP14					
SFCP15					
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SFCP36					
SFCP42					
SFCP43					
SFCP45					
SFCP46					
SFCP47					
SFCP48					
AMCP1					
AMCP2					
AMCP3					
AMCP4					
AMCP5					
AMCP6					
AMCP7					
AMCP8					
AMCP9					
AMCP11					
AMCON1					
AMCON2					
AMCON3					
AMCON4					
AMCON5					
AMCON6					
AMCON7					
AMCON8					

AMCON10					
AMCON11					
TR02	3.97	4.56	0.59	14.86	5.00
TR03	4.95	5.71	0.76	15.35	5.00
TR04	4.1	4.98	0.88	21.46	10.00
TR05	3.58	4.42	0.84	23.46	8.00
TR06	4.49	5.58	1.09	24.28	7.00
TR07	4.19	4.95	0.76	18.14	5.00
TR08	3.82	4.70	0.88	23.04	6.00
TR09	4.42	5.45	1.03	23.30	9.00
TR10	3.25	3.92	0.67	20.62	6.00
TR11	3.98	4.32	0.34	8.54	6.00
TR12	4.13	4.56	0.43	10.41	5.00
TR13	3.55	4.09	0.54	15.21	5.00
TR14	3.82	4.64	0.82	21.47	6.00
TR15	4.16	5.12	0.96	23.08	10.00
TR17	4.5	5.25	0.76	16.86	9.00
TR18	4.31	4.94	0.63	14.62	10.00
TR19	3.24	3.80	0.56	17.28	8.00
TR20	3.75	4.88	1.13	30.13	9.00
TR21					
TR22	4.02	4.68	0.66	16.42	7.00
TR23	4.05	4.74	0.69	17.04	10.00
TR24	4.27	5.39	1.12	26.23	9.00
TR25	4.04	4.52	0.48	11.88	10.00
TR26	3.28	4.34	1.06	32.32	6.00
TR27	3.97	4.92	0.95	23.93	8.00
CAMO01	5.76	6.27	0.51	8.80	8.00
CAMO02	4.16	4.89	0.73	17.43	9.00
CAMO03					
CAMO04	4.53	5.15	0.62	13.79	7.00
CAMO05	2.97	3.76	0.79	26.57	10.00
CAMO06	3.47	3.88	0.41	11.92	7.00
CAMO07	3.90	4.23	0.33	8.45	9.00
CAMO08	4.90	5.88	0.98	20.02	7.00
CAMO09	3.84	4.45	0.61	15.81	9.00

CAMO10	3.08	3.59	0.51	16.59	2.00
CAMO11	4.04	4.48	0.44	10.92	8.00
CAMO12	3.38	3.70	0.32	9.35	2.00
CAMO13	3.17	4.06	0.89	28.02	7.00
CAMO14	2.51	3.06	0.55	21.88	9.00
CAMO15	3.20	4.01	0.81	25.18	9.00
CAMO16					
CAMO17	3.48	4.28	0.80	22.90	7.00
CAMO18	2.85	3.23	0.38	13.21	9.00
CAMO19	3.56	4.29	0.73	20.54	7.00
CAMO20	4.79	5.56	0.77	15.97	6.00
CAMO21	4.03	4.90	0.87	21.49	9.00
CAMO22	3.24	3.80	0.55	17.03	8.00
CAMO23	3.34	3.71	0.36	10.79	5.00
CAMO24	3.65	4.32	0.67	18.33	8.00
CAMO25	5.37	5.64	0.27	5.08	5.00
CAMO26	3.25	3.65	0.40	12.20	10.00
CAMO27	1.91	2.40	0.48	25.27	8.00
CAMO28					
CAMO29	3.81	4.15	0.33	8.69	5.00
CAMO30					
CAMO31	3.79	4.75	0.96	25.31	10.00
CAMO32	4.39	4.94	0.55	12.42	10.00
CAMO33	3.61	4.34	0.73	20.19	10.00
CAMO34	4.90	5.98	1.08	22.12	8.00
CAMS01					
CAMS02	2.82	3.18	0.36	12.71	9.00
CAMS05					
CAMS06	4.29	4.71	0.43	9.93	9.00
CAMS08	4.22	4.80	0.58	13.75	10.00
CAMS09					
CAMS10	5.65	6.11	0.46	8.17	7.00
CAMS11	2.16	2.83	0.68	31.33	7.00
CAMS12	3.93	4.33	0.40	10.28	10.00
CAMS13	3.49	4.10	0.60	17.21	10.00
CAMS14					

CAMS15	2.50	3.11	0.61	24.60	8.00
CAD01	4.80	5.92	1.12	23.30	4.00
CAD02	4.14	4.95	0.81	19.57	9.00
CAD03	3.84	4.96	1.12	29.29	5.00
CAD04	5.12	5.75	0.62	12.14	6.00
CAD05	4.68	5.77	1.09	23.30	5.00
CAD06	3.44	4.27	0.83	24.16	8.00
CAD07	4.88	5.53	0.65	13.31	8.00
CAD08	3.88	4.92	1.04	26.76	7.00
CAD09	4.81	6.24	1.43	29.68	8.00
CAD10	4.52	5.47	0.95	21.07	9.00
CAD13	3.60	4.28	0.68	18.86	10.00
CAD14	3.14	3.99	0.85	27.13	5.00
CAD16	4.35	5.37	1.01	23.28	8.00
CAD18	5.43	6.26	0.83	15.36	8.00
CAD19	4.50	5.60	1.09	24.25	10.00
CAD20	5.74	6.86	1.13	19.62	4.00
CAD21	4.65	6.00	1.35	29.15	6.00
CAD22	4.68	5.86	1.18	25.21	8.00
CAD23	4.26	5.50	1.24	29.06	8.00
CAD24	4.83	5.42	0.60	12.36	7.00
CAD25	3.94	4.83	0.89	22.71	8.00
CAD26	4.23	5.21	0.98	23.12	6.00
CAD27	5.22	5.99	0.77	14.81	8.00
CAD28	4.98	5.93	0.96	19.19	10.00
CAD29					
CAD30	4.05	4.93	0.88	21.70	7.00
RAM01 V1	4.20	4.80	0.60	14.34	8.00
RAM02 V1	4.69	5.48	0.79	16.91	10.00
RAM03 V1	4.29	4.92	0.63	14.65	7.00
RAM04 V1	4.01	4.91	0.90	22.43	7.00
RAM05 V1	3.67	4.47	0.80	21.78	9.00
RAM06 V1	3.93	4.72	0.79	20.24	10.00
RAM07 V1	4.17	5.17	1.00	23.88	7.00
RAM08 V1	4.00	4.99	0.99	24.74	8.00
RAM09 V1	3.80	4.65	0.85	22.44	9.00

RAM10 V1	4.22	4.96	0.74	17.61	8.00
RAM11 V1	3.78	4.45	0.67	17.59	9.00
RAM12 V1	4.41	5.50	1.09	24.69	8.00
RAM13 V1	4.23	4.66	0.43	10.19	6.00
RAM14 V1	3.87	4.37	0.50	13.05	6.00
RAM15 V1	4.96	5.63	0.67	13.59	8.00
RAM16 V1	4.06	4.78	0.72	17.74	5.00
RAM17 V1	4.21	5.16	0.95	22.53	7.00
RAM18 V1	4.58	5.39	0.81	17.58	7.00
RAM19 V1	4.42	5.37	0.95	21.57	5.00
RAM20 V1	3.92	5.13	1.21	30.83	10.00
RAM21 V1	2.57	3.34	0.77	29.88	6.00
RAM22 V1	2.79	3.38	0.59	21.36	10.00
RAM23 V1	2.63	3.38	0.75	28.63	10.00
RAM24 V1	3.53	4.53	1.00	28.33	10.00
RAM25 V1	3.06	3.48	0.42	13.87	10.00
RAM26 V1	2.74	3.44	0.70	25.46	5.00
RAM31 V1	3.10	3.92	0.82	26.47	6.00
RAM32 V1	3.04	3.54	0.50	16.62	4.00
RAM34 V1	2.89	3.62	0.73	25.21	10.00
RAM35 V1	3.55	4.35	0.80	22.39	4.00
RAM36 V1	3.31	4.17	0.86	26.15	4.00
RAM38 V1	3.09	3.78	0.69	22.42	8.00
V1RAM41	3.58	4.45	0.88	24.50	6.00
V1RAM43	3.29	3.97	0.68	20.50	6.00
V1RAM44	3.02	3.94	0.91	30.30	5.00
V1RAM46	3.02	3.87	0.84	27.90	5.00
V1RAM47	3.68	4.57	0.89	24.30	6.00
V1RAM48	3.63	4.39	0.76	21.00	4.00
V1RAM49	3.18	4.06	0.88	27.50	
V1RAM50	3.26	4.20	0.93	28.60	8.00
V1RAM51	3.59	4.51	0.91	25.50	8.00
V1RAM52	3.80	4.69	0.90	23.70	5.00
V1RAM53	3.72	4.73	1.02	27.30	4.00
V1RAM54	3.04	3.68	0.64	21.00	4.00
V1RAM55	3.42	4.42	1.01	29.50	

V1RAM56	3.25	4.45	1.20	36.70	4.00
V1RAM58	3.36	4.23	0.87	25.80	
V1RAM59	3.46	4.28	0.82	23.70	
V1RAM60	3.67	4.53	0.86	23.40	4.00
V1RAM61	3.56	4.51	0.95	26.50	4.00
ASPEN 1					
ASPEN 2					
ASPEN 3					
ASPEN 4					
ASPEN 5					
ASPEN 6					
ASPEN 7					
ASPEN 8					
ASPEN 9					
ASPEN 10					
NESTLE S6					
NESTLE S8					
NESTLE S10					
NESTLE S11					
NESTLE S12					
NESTLE S13					
NESTLE S14					
NESTLE S15					
NESTLE S16					
NESTLE S17					
NESTLE S18					
NESTLE S19					
NESTLE S21					
NESTLE S23					
NESTLE S25					
NESTLE S27					
NESTLE S28					
NESTLE S31					
ACM1					
ACM2					
ACM3					

ACM4					
ACM5					
ACM6					
ACM8					
ACM10					
ACF1					
ACF4					
ACF5					
ACF6					
ACF7					
ACF8					
ACF9					
ACF10					
V1 ACUTEENDO 1	4.16	4.92	0.76	18.31	6.00
V2 ACUTEENDO 2	3.98	4.99	1.01	25.25	10.00
V1 ACUTEENDO 3	4.21	4.96	0.75	17.71	9.00
V2 ACUTEENDO 4	3.35	4.13	0.79	23.58	8.00
V1 ACUTEENDO 5	4.34	4.84	0.50	11.44	8.00
V2 ACUTEENDO 6	4.89	5.45	0.56	11.48	5.00
V2 ACUTEENDO 7	3.88	4.69	0.81	20.77	6.00
AB-SCI04 NC					
AB-SCI06 NC					
AB-SCI07 NC					
AB-SCI11 NC					
AB-SCI12 NC					
AB-SCI14 NC					
AB-SCI19 NC					
AB-SCI24 NC					
SCI01	4.29	5.17	0.88	20.55	5.00
SCI02	3.67	4.25	0.58	15.71	8.00
SCI03	3.98	4.14	0.16	3.93	8.00
SCI04	4.55	5.37	0.82	17.93	8.00
SCI05	4.00	4.55	0.55	13.69	11.00
SCI06	5.29	6.20	0.91	17.12	10.00
SCI07	4.82	5.17	0.35	7.33	10.00
SCI08	4.05	4.69	0.64	15.94	4.00

SCI09	4.35	5.21	0.86	19.75	8.00
SCI10	4.00	4.70	0.69	17.31	8.00
SCI11	5.18	5.60	0.41	7.99	4.00
SCI12	5.39	6.23	0.85	15.73	8.00
SCI13	4.24	4.78	0.55	12.88	6.00
SCI14	5.22	6.17	0.95	18.10	10.00
SCI15	4.13	4.68	0.55	13.20	8.00
SCI16	3.79	4.60	0.80	21.15	6.00
SCI17	5.71	6.60	0.89	15.56	8.00
SCI18	3.37	4.27	0.90	26.82	4.00
SCI19	3.83	4.73	0.90	23.44	8.00
SCI20	4.59	5.58	0.99	21.62	8.00
SCI21	4.21	4.92	0.72	17.01	6.00
SCI22	3.29	4.07	0.78	23.77	4.00
SCI23	3.64	4.36	0.72	19.86	6.00
SCI24	4.73	5.80	1.07	22.72	6.00
SCI25	3.94	4.76	0.82	20.89	4.00
SCI26	3.60	4.44	0.85	23.49	8.00
SCI27	4.82	5.88	1.06	22.06	4.00
SCI28	4.56	5.31	0.76	16.61	4.00
SCI29	4.01	4.84	0.83	20.72	6.00
SCI30	4.41	5.38	0.96	21.86	10.00
SCI31	4.23	5.46	1.23	29.11	8.00
SCI32	3.73	4.65	0.92	24.53	4.00
SCI33	4.93	5.70	0.76	15.50	6.00
SCI34	4.08	5.21	1.12	27.43	6.00
EDS01	3.14	3.89	0.75	23.89	8.00
EDS02	3.48	4.40	0.92	26.44	9.00
EDS03	4.01	4.74	0.73	18.20	9.00
EDS04	4.73	5.58	0.85	17.97	5.00
TVR1	3.84	4.67	0.83	21.72	9.00
TVR2	3.56	4.86	1.30	36.63	7.00
TVR3					
TVR4					
TVR5	5.50	6.43	0.93	16.91	9.00
TVR6					

TVR7					
TVR8					
TVR9					
TVR10					
TVR11	4.59	5.80	1.22	26.50	7.00
TVR12	4.62	5.22	0.60	12.91	9.00
TVR13	3.56	4.29	0.73	20.37	5.00
TVR14	3.19	3.90	0.71	22.26	5.00
TVR15	3.80	4.46	0.66	17.45	5.00
TVR16	3.82	4.72	0.90	23.51	6.00
TVR17	5.44	6.35	0.91	16.67	6.00
TVR18					
TVR19	3.24	3.81	0.57	17.70	6.00
TVR20	3.87	4.75	0.88	22.74	8.00
PFA02					
PFA03					
PFA10					
PFA11					
PFA12					
PFA14					
PFA17					
PFA30					
PFA34					
PFA36					
PFA40					
PFA55					
PFA56					
PFA59					
PFA69					
PFB03					
PFB04					
PFB14					
PFB19					
PFB24					
PMA10					
PMA15					
PMA16					
PMB05					

PMA22					
PMA24					
PMB04					
PMA27					
PMA28					
PMA32					
PMA33					
PMA38					
PMA42					
PMA67					
PMA68					
PMA73					
PMA74					
PMA77					
PMB06					
PMB01					

Blood flow and Shear Rate

Study ID	**Mean BL Blood Flow**	**Peak RH Blood Flow**	**Peak RH Shear Rate**
SPEC02	43.03	431.26	1686.41
SPEC03	44.38	327.52	753.05
SPEC04	78.25	456.99	890.56
SPEC05	21.00	361.83	1862.33
SPEC06	30.95	324.55	1072.32
SPEC07			
SPEC08			
SPEC09			
SPEC10	37.35	621.20	1500.51
COS01	26.14	121.39	400.39
COS02	95.01	432.67	600.30
COS03	19.44	213.72	824.11
SFCP01	19.66	440.10	1319.91
SFCP02	18.93	369.85	1197.77
SFCP03	12.39	256.27	2427.67
SFCP04	22.11	738.05	5499.38
SFCP05	56.73	351.54	500.04

SFCP06			
SFCP07	19.74	253.31	1637.46
SFCP08	10.74	127.11	1408.99
SFCP09	62.83	474.71	3097.47
SFCP10	20.44	295.27	1694.12
SFCP11	16.63	84.89	345.31
SFCP12	36.38	344.17	1134.81
SFCP13	67.07	137.76	534.68
SFCP14	13.71	142.05	742.03
SFCP15	25.05	40.81	122.89
SFCP16	31.16	258.56	875.57
SFCP17	57.15	568.57	926.59
SFCP18	14.68	157.21	735.13
SFCP19	22.10	142.32	429.94
SFCP21	16.52	146.71	1062.48
SFCP22	49.08	453.23	1766.26
SFCP23	29.63		782.63
SFCP24	9.28		
SFCP26	64.52		
SFCP28	36.91	284.81	1267.39
SFCP29	26.97	422.72	1786.44
SFCP30	63.40	130.57	741.74
SFCP31	50.99	270.17	783.70
SFCP32	51.62	461.58	1074.07
SFCP33	19.85	315.58	1304.61
SFCP34	50.01	175.50	754.34
SFCP35	39.34	52.35	173.86
SFCP36	45.38	239.68	851.65
SFCP42	77.86	342.89	1036.09
SFCP43	122.73	424.67	1614.21
SFCP45	22.60	84.25	303.73
SFCP46	48.13	167.28	1836.71
SFCP47	17.07	283.21	2329.73
SFCP48	60.29	446.78	1212.40
AMCP1			
AMCP2			

AMCP3			
AMCP4			
AMCP5			
AMCP6			
AMCP7			
AMCP8			
AMCP9			
AMCP11			
AMCON1			
AMCON2			
AMCON3			
AMCON4			
AMCON5			
AMCON6			
AMCON7			
AMCON8			
AMCON10			
AMCON11			
TR02	35.06	493.31	1312.27
TR03	61.74	421.00	584.22
TR04	63.14	380.14	1271.57
TR05	38.16	276.81	886.00
TR06	108.27	559.30	1019.79
TR07	84.33	627.02	1320.88
TR08	27.29	280.18	873.90
TR09	53.66	453.06	1013.62
TR10	50.44	392.95	1479.25
TR11	16.91	289.02	920.96
TR12	77.40	526.70	1580.87
TR13	31.80	149.58	656.32
TR14	30.81	226.82	638.77
TR15	43.87	346.84	869.00
TR17	73.82	441.92	702.24
TR18	44.06	337.98	703.16
TR19	18.81	216.72	1042.73
TR20	42.02	288.32	834.90

TR21	33.20	294.66	645.32
TR22	46.10	376.81	376.81
TR23	44.39	409.35	1050.78
TR24	42.14	353.00	620.56
TR25	195.43	533.62	1328.79
TR26	40.90	261.26	1320.11
TR27	103.83	700.59	1790.38
CAMO01			
CAMO02			
CAMO03			
CAMO04			
CAMO05			
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CAMO30			
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CAMO34			
CAMS01			
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CAMS10			
CAMS11			
CAMS12			
CAMS13			
CAMS14			
CAMS15			
CAD01	38.12	518.54	734.22
CAD02	37.29	264.98	587.66
CAD03	7.18	52.54	317.46
CAD04	55.35	565.73	757.55
CAD05	48.24	440.16	773.43
CAD06	24.33	122.72	573.05
CAD07	69.33	268.52	472.02
CAD08	27.48	202.61	680.63
CAD09	70.62	477.00	687.71
CAD10	62.53	303.40	546.37
CAD13	40.69	223.78	613.44
CAD14	35.63	117.50	610.46
CAD16	69.95	282.40	584.05
CAD18	75.09	959.41	1014.39
CAD19	22.47	210.27	355.72
CAD20	177.23	554.13	485.30
CAD21	23.48	271.86	508.15
CAD22	49.73	496.38	522.30
CAD23	24.03	262.04	538.64

CAD24	40.49	313.16	428.75
CAD25	35.72	199.58	772.74
CAD26	36.58	205.12	519.32
CAD27	54.77	349.80	409.35
CAD28	61.02	399.66	513.71
CAD29	46.09	379.18	409.66
CAD30	17.78	189.23	548.46
RAM01 V1	140.85	548.22	1033.65
RAM02 V1	122.50	823.68	1104.81
RAM03 V1	42.24	415.92	974.11
RAM04 V1	110.87	476.94	1108.30
RAM05 V1	88.41	347.20	1210.34
RAM06 V1	36.34	323.33	
RAM07 V1	36.41	468.31	1042.26
RAM08 V1	134.65	639.96	1582.98
RAM09 V1	35.55	383.05	988.10
RAM10 V1	65.59	560.75	1030.59
RAM11 V1	14.72	460.64	1405.08
RAM12 V1	127.71	663.90	1206.06
RAM13 V1	81.92	451.15	1000.33
RAM14 V1	46.28	346.76	1062.79
RAM15 V1	26.02	427.71	641.84
RAM16 V1	55.99	498.53	1285.41
RAM17 V1	46.62	474.56	1170.30
RAM18 V1	116.60	640.41	1097.93
RAM19 V1	77.49	466.32	878.66
RAM20 V1	85.94	470.82	1334.50
RAM21 V1	10.49	198.20	1908.81
RAM22 V1	13.17	198.85	1534.21
RAM23 V1	39.31	264.84	2253.86
RAM24 V1	49.20	424.38	1806.46
RAM25 V1		183.05	1061.55
RAM26 V1	15.71	323.11	2187.82
RAM31 V1	14.21	158.57	867.92
RAM32 V1	19.89	289.80	
RAM34 V1	20.88	170.77	1298.72

RAM35 V1	10.24	251.55	989.28
RAM36 V1	18.60	244.87	1139.95
RAM38 V1	10.86	181.35	991.84
V1RAM41			
V1RAM43			
V1RAM44			
V1RAM46			
V1RAM47			
V1RAM48			
V1RAM49			
V1RAM50			
V1RAM51			
V1RAM52			
V1RAM53			
V1RAM54			
V1RAM55			
V1RAM56			
V1RAM58			
V1RAM59			
V1RAM60			
V1RAM61			
ASPEN 1			
ASPEN 2			
ASPEN 3			
ASPEN 4			
ASPEN 5			
ASPEN 6			
ASPEN 7			
ASPEN 8			
ASPEN 9			
ASPEN 10			
NESTLE S6	35.59	280.60	486.69
NESTLE S8	60.19	581.51	823.89
NESTLE S10	99.81	315.87	571.24
NESTLE S11	39.47	450.82	800.00
NESTLE S12	72.15	713.21	1420.17

NESTLE S13	56.09	374.23	1717.39
NESTLE S14	45.39	574.96	961.22
NESTLE S15	35.69	337.99	496.79
NESTLE S16	59.24	478.61	776.64
NESTLE S17	29.88	332.20	691.90
NESTLE S18	27.86	301.20	1040.89
NESTLE S19	82.90	665.07	1014.53
NESTLE S21	40.97	324.31	314.38
NESTLE S23	50.05	503.31	910.45
NESTLE S25	54.53	439.23	664.40
NESTLE S27	69.69	569.68	454.02
NESTLE S28	50.41	603.37	672.62
NESTLE S31	23.76	228.36	602.23
ACM1	40.20	346.00	743.50
ACM2	49.40	371.10	2182.00
ACM3	117.10	573.40	717.30
ACM4	134.70	534.20	1162.10
ACM5	107.90	277.80	1219.50
ACM6	14.70	349.74	748.34
ACM8	55.50	254.60	1350.80
ACM10	82.10	346.30	891.80
ACF1	33.70	407.90	1164.30
ACF4	22.10	154.60	752.70
ACF5	25.90	144.30	747.10
ACF6	37.90	240.90	1630.30
ACF7	30.60	216.90	1003.10
ACF8	79.60	383.70	1169.30
ACF9	191.85	333.60	1040.72
ACF10	63.90	451.50	1787.40
V1 ACUTEENDO 1			
V2 ACUTEENDO 2			
V1 ACUTEENDO 3			
V2 ACUTEENDO 4			
V1 ACUTEENDO 5			
V2 ACUTEENDO 6			
V2 ACUTEENDO 7			

AB-SCI04 NC			1161.18
AB-SCI06 NC			1111.36
AB-SCI07 NC			583.87
AB-SCI11 NC			929.55
AB-SCI12 NC			1708.35
AB-SCI14 NC			938.17
AB-SCI19 NC			668.52
AB-SCI24 NC			668.12
SCI01	23.30	257.68	690.85
SCI02	52.17	404.18	1426.95
SCI03	72.43	212.68	757.23
SCI04	59.44	440.55	838.27
SCI05	60.52	203.40	550.04
SCI06	40.94	490.11	965.77
SCI07	128.06	575.57	862.25
SCI08	108.36	409.30	938.95
SCI09	52.97	366.91	751.85
SCI10	48.10	169.64	501.90
SCI11	62.52	467.73	500.51
SCI12	55.85	848.44	802.58
SCI13	59.83	494.41	1149.19
SCI14	32.45	415.22	563.05
SCI15	57.94	298.46	748.83
SCI16	47.92	227.72	646.76
SCI17	168.02	588.81	451.82
SCI18	59.92	226.39	885.97
SCI19	38.89	437.03	1518.72
SCI20	46.25	26.78	335.14
SCI21	85.59	22.13	379.50
SCI22	25.02	8.29	233.65
SCI23	12.59		140.67
SCI24	62.60	570.24	823.15
SCI25	50.88	297.96	840.13
SCI26	22.66	167.82	588.02
SCI27	40.93	271.28	539.53
SCI28	30.24	481.46	857.84

SCI29	22.15	291.71	995.40
SCI30	144.36	673.14	1356.10
SCI31	38.31	413.56	795.11
SCI32	45.11	144.15	415.81
SCI33	108.52	728.22	935.81
SCI34	67.47	445.06	930.43
EDS01	28.70	104.97	657.26
EDS02	33.85	207.88	778.12
EDS03	24.01	166.91	421.06
EDS04			
TVR1			
TVR2	20.39	223.28	592.44
TVR3			
TVR4	67.85	618.52	635.97
TVR5	17.32	561.22	582.96
TVR6	41.20	472.45	710.49
TVR7	68.77	456.48	727.98
TVR8		356.67	717.31
TVR9	42.50	376.38	740.46
TVR10	9.79	210.59	785.61
TVR11	41.05	426.62	631.52
TVR12	37.46	241.75	834.91
TVR13	37.80	322.92	1055.19
TVR14	32.47	276.92	1205.96
TVR15		521.37	1424.51
TVR16	21.70	329.06	990.23
TVR17		487.57	469.61
TVR18	54.32	330.30	1065.22
TVR19	8.90	128.06	727.62
TVR20	41.59	446.76	1185.95
PFA02			
PFA03			
PFA10			
PFA11			
PFA12			
PFA14			
PFA17			

PFA30			
PFA34			
PFA36			
PFA40			
PFA55			
PFA56			
PFA59			
PFA69			
PFB03			
PFB04			
PFB14			
PFB19			
PFB24			
PMA10			
PMA15			
PMA16			
PMB05			
PMA22			
PMA24			
PMB04			
PMA27			
PMA28			
PMA32			
PMA33			
PMA38			
PMA42			
PMA67			
PMA68			
PMA73			
PMA74			
PMA77			
PMB06			
PMB01			

APPENDIX 2: STATISTICS

Hemodynamics - Repeatability

Heart Rate (HR)

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The median of differences between HR_V1 and HR_V2 equals 0.	Related-Samples Sign Test	.826	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Median

HR_V1	HR_V2	diiference_HR
62.00	62.00	.0000

Systolic Blood Pressure (SBP)

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The median of differences between SBP_V1 and SBP_V2 equals 0.	Related-Samples Sign Test	.000	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Median

SBP_V1	SBP_V2	diiference_SBP
116.00	113.00	-2.0000

Diastolic Blood Pressure (DBP)

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The median of differences between DBP_V1 and DBP_V2 equals 0.	Related-Samples Sign Test	.010	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Median

DBP_V1	DBP_V2	diiference_DBP
69.00	67.00	-1.0000

Mean Arterial Pressure (MAP)

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The median of differences between MAP_V1 and MAP_V2 equals 0.	Related-Samples Sign Test	.002	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Median

MAP_V1	MAP_V2	diiference_MAP
87.00	85.00	-1.0000

ICCs

FMD Repeatability

	Intraclass Correlation[b]	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound	F Test with True Value 0 Value	df1	df2	Sig
Single Measures	.681[a]	.559	.774	5.274	97	97	.000
Average Measures	.810[c]	.717	.873	5.274	97	97	.000

Two-way mixed effects model where people effects are random and measures effects are fixed.
a. The estimator is the same, whether the interaction effect is present or not.
b. Type A intraclass correlation coefficients using an absolute agreement definition.
c. This estimate is computed assuming the interaction effect is absent, because it is not estimable otherwise.

L-FMC Repeatability

	Intraclass Correlation[b]	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound	F Test with True Value 0 Value	df1	df2	Sig
Single Measures	.013[a]	-.182	.207	1.026	97	97	.450
Average Measures	.025[c]	-.444	.343	1.026	97	97	.450

TVR Repeatability

	Intraclass Correlation[b]	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound	F Test with True Value 0 Value	df1	df2	Sig
Single Measures	.498[a]	.334	.633	2.986	97	97	.000
Average Measures	.665[c]	.501	.775	2.986	97	97	.000

Baseline Diameter Repeatability

	Intraclass Correlation[b]	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound	F Test with True Value 0 Value	df1	df2	Sig

Single Measures	.966[a]	.949	.977	56.938	97	97	.000
Average Measures	.983[c]	.974	.988	56.938	97	97	.000

Peak diameter Repeatability

		95% Confidence Interval		F Test with True Value 0			
	Intraclass Correlation[b]	Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.967[a]	.952	.978	60.626	97	97	.000
Average Measures	.983[c]	.975	.989	60.626	97	97	.000

Four-minute Diameter Repeatability

		95% Confidence Interval		F Test with True Value 0			
	Intraclass Correlation[b]	Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.961[a]	.943	.974	51.454	97	97	.000
Average Measures	.980[c]	.971	.987	51.454	97	97	.000

Absolute FMD Repeatability

		95% Confidence Interval		F Test with True Value 0			
	Intraclass Correlation[b]	Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.628[a]	.493	.735	4.393	97	97	.000
Average Measures	.772[c]	.660	.847	4.393	97	97	.000

Absolute L-FMC Repeatability

	Intraclass	95% Confidence Interval		F Test with True Value 0			

	Correlation[b]	Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.007[a]	-.187	.202	1.015	97	97	.472
Average Measures	.014[c]	-.461	.336	1.015	97	97	.472

TVR (absolute value of FMD+L-FMC) Repeatability

		95% Confidence Interval		F Test with True Value 0			
	Intraclass Correlation[b]	Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.522[a]	.363	.652	3.210	97	97	.000
Average Measures	.686[c]	.533	.789	3.210	97	97	.000

Cohen's Kappa for L-FMC

		V2LOWFLOWRESPONSEKAPPA			
		Constrict	Dilate	No change	Total
V1LOWFLOWRESPONSEKAPPA	Constrict	19	21	0	40
	Dilate	20	37	1	58
Total		39	58	1	98

Symmetric Measures

	Value	Asymptotic Standard Error[a]	Approximate T[b]	Approximate Significance

Measure of Agreement	Kappa	.121	.100	1.212	.225
N of Valid Cases		98			

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

Frequency of Low Flow Response

V1_LOWFLOW_RESPONSE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Constrict	40	40.8	40.8	40.8
	Dilate	58	59.2	59.2	100.0
	Total	98	100.0	100.0	

V2_LOWFLOW_RESPONSE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Constrict	39	39.8	39.8	39.8
	Dilate	58	59.2	59.2	99.0
	Nochange	1	1.0	1.0	100.0
	Total	98	100.0	100.0	

Nitroglycerin Challenge Test (NTG)

Relative NTG

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	V1REL_NTG	21.9219	77	6.26037	.71343
	V2REL_NTG	21.4629	77	6.44187	.73412

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	V1REL_NTG & V2REL_NTG	77	.766	.000

Paired Samples Test

		Paired Differences					
					95% Confidence Interval of the Difference		
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t
Pair 1	V1REL_NTG - V2REL_NTG	.45909	4.34886	.49560	-.52798	1.44616	.926

Paired Samples Test

		df	Sig. (2-tailed)
Pair 1	V1REL_NTG - V2REL_NTG	76	.357

Absolute NTG

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	V1ABS_NTG	.7886	77	.19159	.02183
	V2ABS_NTG	.7731	77	.20243	.02307

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	V1ABS_NTG & V2ABS_NTG	77	.739	.000

Paired Samples Test

		Paired Differences					t
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper	
Pair 1	V1ABS_NTG - V2ABS_NTG	.01545	.14261	.01625	-.01691	.04782	.951

Paired Samples Test

		df	Sig. (2-tailed)
Pair 1	V1ABS_NTG - V2ABS_NTG	76	.345

Baseline NTG Diameter

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	V1BL_NTG	3.7123	77	.71199	.08114
	V2BL_NTG	3.7074	77	.69836	.07959

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	V1BL_NTG & V2BL_NTG	77	.972	.000

Paired Samples Test

		Paired Differences					t
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		

					Lower	Upper	
Pair 1	V1BL_NTG - V2BL_NTG	.00494	.16870	.01923	-.03336	.04323	.257

Paired Samples Test

		df	Sig. (2-tailed)
Pair 1	V1BL_NTG - V2BL_NTG	76	.798

Peak NTG Diameter

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	V1PEAK_NTG	4.5004	77	.74627	.08505
	V2PEAK_NTG	4.4808	77	.74650	.08507

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	V1PEAK_NTG & V2PEAK_NTG	77	.968	.000

Paired Samples Test

		Paired Differences					
					95% Confidence Interval of the Difference		
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t
Pair 1	V1PEAK_NTG - V2PEAK_NTG	.01961	.18903	.02154	-.02329	.06252	.910

Paired Samples Test

		df	Sig. (2-tailed)
Pair 1	V1PEAK_NTG - V2PEAK_NTG	76	.366

Time to peak (TTP)

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	V1TTP	6.8947	76	2.13903	.24536
	V2TTP	7.0526	76	2.18415	.25054

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	V1TTP & V2TTP	76	.609	.000

Paired Samples Test

		Paired Differences					t	df
					95% Confidence Interval of the Difference			
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper		
Pair 1	V1TTP - V2TTP	-.15789	1.91174	.21929	-.59475	.27896	-.720	75

Paired Samples Test

		Sig. (2-tailed)
Pair 1	V1TTP - V2TTP	.474

OBSERVATIONAL ANALYSIS

Frequency of Low Flow Response

LOWFLOWRESPONSE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Constrict	190	50.7	50.7	50.7
	Dilate	185	49.3	49.3	100.0
	Total	375	100.0	100.0	

Correlations
Age x FMD

			AGE	RELFMD
Spearman's rho	AGE	Correlation Coefficient	1.000	-.238**
		Sig. (2-tailed)	.	.000
		N	375	375
	RELFMD	Correlation Coefficient	-.238**	1.000
		Sig. (2-tailed)	.000	.
		N	375	375

**. Correlation is significant at the 0.01 level (2-tailed).

Age x L-FMC

Correlations

			AGE	RELLFMC
Spearman's rho	AGE	Correlation Coefficient	1.000	-.064
		Sig. (2-tailed)	.	.220
		N	375	375
	RELLFMC	Correlation Coefficient	-.064	1.000
		Sig. (2-tailed)	.220	.
		N	375	375

Age x TVR

Correlations

	AGE	TVR

Spearman's rho	AGE	Correlation Coefficient	1.000	-.191**
		Sig. (2-tailed)	.	.000
		N	375	375
	TVR	Correlation Coefficient	-.191**	1.000
		Sig. (2-tailed)	.000	.
		N	375	375

**. Correlation is significant at the 0.01 level (2-tailed).

Moderator Analysis

Age x FMD, Sex as a moderator variable

Variables Entered/Removed[a]

Model	Variables Entered	Variables Removed	Method
1	Males, Age[b]	.	Enter
2	agexmale[b]	.	Enter

a. Dependent Variable: RelFMD

b. All requested variables entered.

Model Summary[c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics			
					R Square Change	F Change	df1	df2
1	.279[a]	.078	.073	3.76836	.078	15.757	2	372
2	.280[b]	.078	.071	3.77296	.000	.093	1	371

Model Summary[c]

Model	Change Statistics	
		Sig. F Change
1		.000
2		.760

a. Predictors: (Constant), Males, Age

b. Predictors: (Constant), Males, Age, agexmale

c. Dependent Variable: RelFMD

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	447.512	2	223.756	15.757	.000[b]
	Residual	5282.604	372	14.201		
	Total	5730.115	374			
2	Regression	448.839	3	149.613	10.510	.000[c]
	Residual	5281.276	371	14.235		
	Total	5730.115	374			

a. Dependent Variable: RelFMD

b. Predictors: (Constant), Males, Age

c. Predictors: (Constant), Males, Age, agexmale

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1	(Constant)	8.689	.455		19.107	.000	7.795	9.583
	Age	-.046	.009	-.261	-5.231	.000	-.063	-.028
	Males	-.694	.416	-.083	-1.667	.096	-1.513	.125
2	(Constant)	8.818	.620		14.218	.000	7.598	10.037
	Age	-.049	.015	-.282	-3.287	.001	-.079	-.020
	Males	-.895	.778	-.107	-1.150	.251	-2.425	.636
	agexmale	.006	.018	.037	.305	.760	-.031	.042

Coefficients[a]

Model		Collinearity Statistics	
		Tolerance	VIF
1	(Constant)		
	Age	.995	1.005
	Males	.995	1.005
2	(Constant)		
	Age	.337	2.971
	Males	.286	3.502
	agexmale	.173	5.773

a. Dependent Variable: RelFMD

Excluded Variables[a]

Model		Beta In	t	Sig.	Partial Correlation	Collinearity Statistics: Tolerance	Collinearity Statistics: VIF	Collinearity Statistics: Minimum Tolerance
1	agexmale	.037[b]	.305	.760	.016	.173	5.773	.173

a. Dependent Variable: RelFMD

b. Predictors in the Model: (Constant), Males, Age

Age x L-FMC, Sex as a moderator variable

Variables Entered/Removed[a]

Model	Variables Entered	Variables Removed	Method
1	Male, Age[b]	.	Enter
2	agexmale[b]	.	Enter

a. Dependent Variable: RelLFMC

b. All requested variables entered.

Model Summary[c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics: R Square Change	Change Statistics: F Change	Change Statistics: df1	Change Statistics: df2
1	.030[a]	.001	-.004	3.31665	.001	.164	2	372
2	.063[b]	.004	-.004	3.31608	.003	1.128	1	371

Model Summary[c]

Model	Change Statistics	
		Sig. F Change
1		.849
2		.289

a. Predictors: (Constant), Male, Age

b. Predictors: (Constant), Male, Age, agexmale

c. Dependent Variable: RelLFMC

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	3.599	2	1.800	.164	.849[b]
	Residual	4092.061	372	11.000		
	Total	4095.661	374			
2	Regression	16.002	3	5.334	.485	.693[c]
	Residual	4079.659	371	10.996		
	Total	4095.661	374			

a. Dependent Variable: RelLFMC

b. Predictors: (Constant), Male, Age

c. Predictors: (Constant), Male, Age, agexmale

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1	(Consta	.214	.400		.535	.593	-.573	1.001
	Age	-.004	.008	-.026	-.505	.614	-.019	.011
	Male	-.085	.366	-.012	-.233	.816	-.806	.635
2	(Consta	.607	.545		1.114	.266	-.465	1.679
	Age	-.015	.013	-.103	-1.158	.248	-.041	.011
	Male	-.699	.684	-.099	-1.021	.308	-2.044	.646
	agexmal	.017	.016	.132	1.062	.289	-.015	.049

Coefficients[a]

Model		Collinearity Statistics	
		Tolerance	VIF
1	(Constant)		
	Age	.995	1.005
	Male	.995	1.005
2	(Constant)		
	Age	.337	2.971
	Male	.286	3.502

agexmale	.173	5.773

a. Dependent Variable: RelLFMC

Excluded Variables[a]

Model		Beta In	t	Sig.	Partial Correlation	Collinearity Statistics: Tolerance	Collinearity Statistics: VIF	Collinearity Statistics: Minimum Tolerance
1	agexmale	.132[b]	1.062	.289	.055	.173	5.773	.173

a. Dependent Variable: RelLFMC

b. Predictors in the Model: (Constant), Male, Age

Age x TVR with Sex as a moderator variable

Variables Entered/Removed[a]

Model	Variables Entered	Variables Removed	Method
1	Male, Age[b]	.	Enter
2	agexmale[b]	.	Enter

a. Dependent Variable: TVR

b. All requested variables entered.

Model Summary[c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics			
					R Square Change	F Change	df1	df2
1	.222[a]	.049	.044	4.44631	.049	9.620	2	372
2	.223[b]	.050	.042	4.45116	.000	.190	1	371

Model Summary[c]

Model	Change Statistics
	Sig. F Change
1	.000
2	.663

a. Predictors: (Constant), Male, Age

b. Predictors: (Constant), Male, Age, agexmale

c. Dependent Variable: TVR

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	380.370	2	190.185	9.620	.000[b]
	Residual	7354.315	372	19.770		
	Total	7734.685	374			
2	Regression	384.142	3	128.047	6.463	.000[c]
	Residual	7350.543	371	19.813		

Total	7734.685	374			

a. Dependent Variable: TVR

b. Predictors: (Constant), Male, Age

c. Predictors: (Constant), Male, Age, agexmale

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1	(Consta	8.596	.537		16.020	.000	7.541	9.651
	Age	-.042	.010	-.206	-4.073	.000	-.062	-.022
	Male	-.658	.491	-.068	-1.339	.181	-1.624	.308
2	(Consta	8.379	.732		11.453	.000	6.941	9.818
	Age	-.036	.018	-.175	-2.011	.045	-.070	-.001
	Male	-.320	.918	-.033	-.348	.728	-2.125	1.486
	agexmal	-.009	.022	-.053	-.436	.663	-.052	.033

Coefficients[a]

Model	Collinearity Statistics	
	Tolerance	VIF

1	(Constant)		
	Age	.995	1.005
	Male	.995	1.005
2	(Constant)		
	Age	.337	2.971
	Male	.286	3.502
	agexmale	.173	5.773

a. Dependent Variable: TVR

Excluded Variables[a]

Model		Beta In	t	Sig.	Partial Correlation	Collinearity Statistics: Tolerance	Collinearity Statistics: VIF	Collinearity Statistics: Minimum Tolerance
1	agexmale	-.053[b]	-.436	.663	-.023	.173	5.773	.173

a. Dependent Variable: TVR

b. Predictors in the Model: (Constant), Male, Age

Correlation FMD and L-FMC

Correlations

			RELFMD	RELLFMC
Spearman's rho	RELFMD	Correlation Coefficient	1.000	.267**
		Sig. (2-tailed)	.	.000
		N	375	375
	RELLFMC	Correlation Coefficient	.267**	1.000
		Sig. (2-tailed)	.000	.

		N	375	375

**. Correlation is significant at the 0.01 level (2-tailed).

Correlation between age and vascular measures – CVD and CVD Cohort only

Correlations

			AGE	RELFMD
Spearman's rho	AGE	Correlation Coefficient	1.000	-.408**
		Sig. (2-tailed)	.	.000
		N	124	124
	RELFMD	Correlation Coefficient	-.408**	1.000
		Sig. (2-tailed)	.000	.
		N	124	124

Correlations

			AGE	RELLFMC
Spearman's rho	AGE	Correlation Coefficient	1.000	.163
		Sig. (2-tailed)	.	.071
		N	124	124
	RELLFMC	Correlation Coefficient	.163	1.000
		Sig. (2-tailed)	.071	.
		N	124	124

Correlations

			AGE	TVR
Spearman's rho	AGE	Correlation Coefficient	1.000	-.427**
		Sig. (2-tailed)	.	.000
		N	124	124
	TVR	Correlation Coefficient	-.427**	1.000
		Sig. (2-tailed)	.000	.
		N	124	124