Vascular measures

BRHS 30 year follow-up (Q30)

2010-2012

At the 30-year BRHS follow-up examination a vascular assessment was carried out of the BRHS participants who attended for examination (Appendix 1). The vascular assessment was carried out by a team of two ultrasound technicians from the Wales Heart Research Institute (WHRI), Cardiff University, under the direction of Professor Julian Halcox and Dr Libby Ellins.

The data and scanned images were processed and analysed at Cardiff University/Swansea University and a set of vascular measurements were produced. The raw data and images are held by Professor Julian Halcox and Dr Libby Ellins at Swansea University. (LE believes a copy is also with the BRHS – check).

The methodological summaries for the vascular measures are described in sections 1.1 to 1.6. The vascular assessment protocol can be found in Appendix 1.

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APPENDIX 1 BRHS Vascular Assessment protocol and data collection form

Vascular measurements - BRHS 30 year follow-up (Q30) 2010 -12

VARIABLE DESCRIPTION	Units/Category labels	BRHS VARIABLE NAME	Method section	Data access
Vascular Technician CR, EE, KS	CR, EE, KS	Q30Carotid_initials1		yes
Vascular Technician CR, EE, KS	CR, EE, KS	Q30Carotid_initials2		yes
Vascular Technician CR,KS,XX(xx=blank on file)	CR, EE, KS, XX=missing	Q30Carotid_scan_operator		yes
RIGHT SIDE Baseline Diameter	mm	Q30Mean_R_BL_DM	1.2	yes
RIGHT SIDE Peak Diameter	mm	Q30Mean_R_PK_DM	1.2	yes
RIGHT SIDE Carotid IMT - RIGHT side(unadjusted)	mm	Q30Mean_R_BLIMT	1.2	yes
RIGHT SIDE SBP	mmHg	Q30Mean_R_SBP		yes
RIGHT SIDE DBP	mmHg	Q30Mean_R_DBP		yes
RIGHT SIDE Heart Rate	Bpm	Q30Mean_R_HR		yes
RIGHT SIDE Pulse Rate	bpm	Q30Mean_R_PP		yes
RIGHT SIDE Distension	mm	Q30Mean_R_Distension	1.2	yes
RIGHT SIDE Distensibility	$x10^{-3}$ kPa^{-1}	Q30Mean_R_Distensibility	1.2	yes
LEFT SIDE Baseline Diameter	mm	Q30Mean_L_BL_DM	1.2	yes
LEFT SIDE Peak Diameter	mm	Q30Mean_L_PK_DM	1.2	yes
LEFT SIDE Carotid IMT - LEFT side(unadjusted)	mm	Q30Mean_L_BLIMT	1.2	yes
LEFT SIDE SBP	mmHg	Q30Mean_L_SBP		yes
LEFT SIDE DBP	mmHg	Q30Mean_L_DBP		yes
LEFT SIDE Heart Rate	bpm	Q30Mean_L_HR		yes
LEFT SIDE Pulse Rate	bpm	Q30Mean_L_PP		yes
LEFT SIDE Distension	mm	Q30Mean_L_Distension	1.2	yes
LEFT SIDE Distensibility	$x10^{-3}$ kPa^{-1}	Q30Mean_L_Distensibility	1.2	yes

VARIABLE DESCRIPTION /cont.	Units/Category labels	BRHS VARIABLE NAME	Method section	Data access
RIGHT SIDE Mean Brachial	mmHg	Q30Mean_R_Brachial	1.6	yes
RIGHT SIDE Mean Ankle	mmHg	Q30Mean_R_Ankle	1.6	yes
RIGHT SIDE Mean Ankle Brachial Pressure Index	ratio	Q30Mean_R_ABPI	1.6	yes
LEFT SIDE Mean Brachial	mmHg	Q30Mean_L_Brachial	1.6	yes
LEFT SIDE Mean Ankle	mmHg	Q30Mean_L_Ankle	1.6	yes
LEFT SIDE Mean Ankle Brachial Pressure Index	ratio	Q30Mean_L_ABPI	1.6	yes
Right Side Occluding	Y=Yes N=No	Q30_RSide_Occluding		yes
Right Side Data Loss	**A**=POOR QUALITY **B**=PARTICIPANT UNSUITABLE **D**=ARRHYTHMIA **E=**EQUIPMENT FAILURE **H**=REFUSED TO HAVE MEASURE **I**=STAFF SICKNESS **J**=ABORTED **MA**=Measure Accepted	Q30_RSide_Data_Loss		yes
Left Side Occluding	**Y**=yes **N**=No U=missing/blank	Q30_LSide_Occluding		yes
Left Side Data Loss	**A**=POOR QUALITY **B**=PARTICIPANT UNSUITABLE **D**=ARRHYTHMIA **E=**EQUIPMENT FAILURE **H**=REFUSED TO HAVE MEASURE **I**=STAFF SICKNESS **J**=ABORTED **MA**=Measure Accepted	Q30_LSide_Data_Loss		yes

VARIABLE DESCRIPTION /cont.	Units/Category labels	BRHS VARIABLE NAME	Method section	Data access
PWV operator = CR, KS, XX(xx=blank on file)	CR, KS, XX(xx=blank on file)	Q30PWV_operator		yes
PWV time - hour		Q30PWV_time_h		yes
PWV time - minute		Q30PWV_time_m		yes
Pulse Wave Analysis using Omron - Seated_Mean Systolic Pressure	mmHg	Q30PWA_O_SEAT_Mean_SP	1.5	yes
Pulse Wave Analysis using Omron - Seated_Mean Diastolic Pressure	mmHg	Q30PWA_O_SEAT_Mean_DP	1.5	yes
Pulse Wave Analysis using Sphygmocor - Mean Heart Rate	Bpm	Q30PWA_S_Mean_HR	1.5	yes
Pulse Wave Analysis using Sphygmocor - Mean Central Augmentation Pressure	mmHg	Q30PWA_S_Mean_C_AP	1.5	yes
Pulse Wave Analysis using Sphygmocor - Mean Augmentation Index % (pc=%)	%	Q30PWA_S_Mean_AI_pc	1.5	yes
Pulse Wave Analysis using Sphygmocor - Mean Central Systolic Pressure	mmHg	Q30PWA_S_Mean_C_SP	1.5	yes
Pulse Wave Analysis using Vicorder - Systolic Pressure	mmHg	Q30PWA_V_Seat_SP	1.5	Yes
Pulse Wave Analysis using Vicorder - Diastolic Pressure	mmHg	Q30PWA_V_Seat_DP	1.5	Yes
Pulse Wave Analysis using Vicorder - Mean Heart Rate	Bpm	Q30PWA_V_Mean_HR	1.5	yes
Pulse Wave Analysis using Vicorder - Mean Central Augmentation Pressure	mmHg	Q30PWA_V_Mean_C_AP	1.5	yes
Pulse Wave Analysis using Vicorder - Mean Augmentation Index % (pc=%)	%	Q30PWA_V_Mean_AI_pc	1.5	yes
Pulse Wave Analysis using Vicorder - Mean Central Systolic Pressure	mmHg	Q30PWA_V_Mean_C_SP	1.5	yes
Pulse Wave Velocity using Omron - Supine Systolic Pressure	mmHg	Q30PWV_O_SUP_SP	1.4	yes
Pulse Wave Velocity using Omron - Supine Diastolic Pressure	mmHg	Q30PWV_O_SUP_DP	1.4	yes
Pulse Wave Velocity using Sphygmocor - Mean Carotid Heart Rate	Bpm	Q30PWV_S_Mean_CAR_HR	1.4	yes
Pulse Wave Velocity using Sphygmocor - Mean Femoral Heart Rate	Bpm	Q30PWV_S_Mean_FEM_HR	1.4	yes
Pulse Wave Velocity using Sphygmocor - Mean Transit Time	ms	Q30PWV_S_Mean_TT	1.4	yes
Pulse Wave Velocity using Sphygmocor - PWV Distance	mm	Q30PWV_S_PWV_DIST	1.4	yes
Pulse Wave Velocity using Sphygmocor - Mean_PWV	m/s	Q30PWV_S_Mean_PWV	1.4	yes
Pulse Wave Velocity using Vicorder - Mean Heart Rate	bpm	Q30PWV_V_Mean_HR	1.4	yes
Pulse Wave Velocity using Vicorder - Mean Transit Time	ms	Q30PWV_V_Mean_TT	1.4	yes
Pulse Wave Velocity using Vicorder - Mean PWV Distance	cm	Q30PWV_V_Mean_PWV_Dist	1.4	yes
Pulse Wave Velocity using Vicorder - Mean PWV	m/s	Q30PWV_V_Mean_PWV	1.4	

VARIABLE DESCRIPTION /cont.	Units/Category labels	BRHS VARIABLE NAME	Method section	Data access
Plaque analysis Observer = BWJ,CG, KS, LH RM	BWJ, CG, KS, LH, RM	Q30US_plaque_OBS		yes
RIGHT SIDE Plaque - at least one plaque on RIGHT side	0=No Plaque 1=Plaque 2=Can't see	Q30R_Plaque	1.3	yes
RIGHT SIDE Common Carotid Artery PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30R_CCA	1.3	yes
RIGHT SIDE Bifurcation PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30R_BIF	1.3	yes
RIGHT SIDE Internal Carotid Artery PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30R_ICA	1.3	yes
RIGHT SIDE External Carotid Artery PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30R_ECA	1.3	yes
LEFT SIDE Plaque - at least one plaque on LEFT side	0=No Plaque 1=Plaque 2=Can't see	Q30L_Plaque	1.3	yes
LEFT SIDE Common Carotid Artery PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30L_CCA	1.3	yes
LEFT SIDE Bifurcation PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30L_BIF	1.3	yes
LEFT SIDE Internal Carotid Artery PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30L_ICA	1.3	yes
LEFT SIDE External Carotid Artery PLAQUE	0=No Plaque 1=Plaque 2=Can't see	Q30L_ECA	1.3	yes
				yes
Carotid IMT - RIGHT side(adjusted)	mm	Q30Mean_R_BLIMT_adj	2.0	yes
Carotid IMT - LEFT side(adjusted)	mm	Q30Mean_L_BLIMT_adj	2.0	yes

Q30 PULSE PRESSURE DATA

VARIABLE DESCRIPTION	Units/Category labels	BRHS VARIABLE NAME	Method section	Data access
Examination day		Q30SEVRExamDate_d		yes
Examination month		Q30SEVRExamDate_m		yes
Examination year		Q30SEVRExamDate_y		yes
Examination time Hour		Q30SEVRstart_timeH		yes
Examination time Minutes		Q30SEVRstart_timeM		yes
Examination time Seconds		Q30SEVRstart_timeS		yes
Vicorder mean Cardiac Output VMCO(L/min)	L/min	Q30VMCO		yes
Vicorder mean total peripheral resistance VMTPR (PRU)	Peripheral resistance units (PRU)	Q30VMTPR		yes
Vicorder mean stroke volume VMSV (ml)	ml	Q30VMSV		yes
Vicorder mean arterial pressure VMMAP(mmHg)	mmHg	Q30VMMAP		yes
Vicorder mean peripheral augmentation index VMPAIx (%)	%	Q30VMPAIx		yes
Vicorder mean end systolic pressure VMESP (mmHg)	mmHg	Q30VMESP		yes
Vicorder mean end systolic pressure index VMESPI	ratio	Q30VMESPI		yes
Vicorder mean subendocardial viability ratio VMSEVR (%)	%	Q30VMSEVR		yes

VARIABLE DESCRIPTION /cont.	**Units/Category labels**	**BRHS VARIABLE NAME**	**Method section**	**Data access**
Vicorder mean peripheral pulse pressure VMPP (mmHg)	mmHg	Q30VMPP		yes
Vicorder mean aortic pulse pressure VMAoPP (mmHg)	mmHg	Q30VMAoPP		yes
Examination day		Q30pp_xdated		yes
Examination month		Q30pp_xdatem		yes
Examination year		Q30pp_xdatey		yes
Examination time Hour		Q30pp_starttimeH		yes
Examination time Minutes		Q30pp_starttimeM		yes

1.0 Vascular Methods

Document prepared by Libby Ellins (Swansea University)

1.1 Carotid Artery Ultrasound Measurements

Carotid arteries were imaged by two experienced vascular technicians. All studies were performed using the Z.One Ultra ultrasound system (Zonare Medical Systems, Mountain View, CA) with a 5-10-mHz linear probe. All recordings were ten-second cine loops taken in DICOM format to be downloaded for offline analysis.

Initially, a cross-sectional sweep of the carotid artery was recorded starting at the clavicle and ending at the jaw bone. Images were then focused longitudinally on the posterior (far) wall of the artery, with a small section of the bifurcation visible on the left side of the image. The zoom function was then used to magnify the area and a recording was taken. The internal and external carotid arteries were assessed for the presence of plaque, and when present still images were taken. If the plaque was considered to be significant then Colourflow was used to view the blood flow after the plaque, and recordings were taken in both longitudinal and cross-sectional views.

1.2 Carotid Intima Media Thickness (cIMT) and Distensibility

Using the longitudinal images of the carotid artery, distension and cIMT (the distance between the leading edge of the intima and the media-adventitia interface) was measured with the Carotid Analyser software (Medical Imaging Applications, Iowa City, IA). A region of interest of 5-10 mm was selected in a plaque free area, at least 1cm from the bifurcation. Mean cIMT was calculated from IMT measurements taken from three end-diastolic images. Maximum and minimum carotid artery diameters were taken from three consecutive waveforms, and mean distension was calculated (equation below).

Distensibility was calculated using the methods described by Dijk et al., (2005) as follows:

((2 x Mean Distension/Baseline diameter)/Mean PP (kPa)) * 1000

Where mean distension was calculated by:

Peak Diameter – Baseline Diameter

Joke M. Dijk, Ale Algra, Yolanda van der Graaf, Diederick E. Grobbee, Michiel L. Bots Carotid stiffness and the risk of new vascular events in patients with manifest cardiovascular disease. The SMART study Eur Heart J (June 2005) 26 (12):1213-1220.

1.3 Plaque analysis

Carotid artery ultrasound scans were assessed for the presence of atherosclerotic plaques by 5 trained observers, using either the Z.One Ultra ultrasound system (Zonare Medical Systems, Mountain View, CA) or Microdicom software (Microdicom, Bulgaria). Carotid plaques were classified as an area of intima-media thickening which is ≥1.2 mm (measured using callipers on the software described above) at its thickest point, or an area with ≥50% thickness than the corresponding IMT if there was diffuse thickening. Plaques were identified as being present in the Common Carotid Artery, Bifurcation, Internal Carotid Artery or External Carotid Artery.

1.4 Pulse Wave Velocity

Pulse wave velocity (PWV) was measured at the right carotid and femoral arteries by two experienced operators using the following techniques: the Sphygmocor (Atcormedical, Australia) and the Vicorder (Skidmore Medical, Bristol UK). All participants were positioned in a semi-supine position with their torso at a 30˚angle.

Sphygmocor: Two blood pressures were taken on the right arm using an automated sphygmomanometer (Omron, Japan), averaged and entered into the Sphygmocor software (Version 8.2). PWV length was measured by subtracting the proximal length (sternal notch to carotid pulse) from the distal length (sternal notch to femoral pulse). PWV pressure waveforms were recorded at two sites sequentially; carotid and then femoral artery. The waveforms were visually assessed to ensure they were of good quality. Optimally, two recordings were taken with a difference in PWV ≤0.5 m/s and standard deviation ≤10%; and then averaged. However, if this could not be achieved 4 measures were taken, those with standard deviation >15% were rejected, and the remaining results were averaged.

Vicorder: PWV pressure waveforms were simultaneously assessed at the carotid and femoral arteries. To do this an inflatable bladder attached to a neck collar was positioned over the right carotid pulse, and a Hokanson SC10 cuff was placed around the middle of the right thigh. PWV length was measured from the sternal notch to the centre of the thigh cuff, and entered into the Vicorder software (Version 6.0.4773.18964). The cuffs were then simultaneously inflated. The waveforms were visually assessed so that a minimum of 3 good quality waveforms were taken. Two recordings were taken with a difference in PWV ≤0.5 m/s and averaged.

1.5 Pulse Wave Analysis

Pulse wave analysis (PWA) was measured by two experienced operators using two techniques: the Sphygmocor (Atcormedical, Australia) and the Vicorder (Skidmore Medical, Bristol UK). All participants were seated with their arm resting on a pillow on their lap. Optimally all measures were taken on the right arm.

Sphygmocor: Two blood pressures were taken using an automated sphygmomanometer (Omron, Japan), averaged and entered into the Sphygmocor software (Version 8.2). Measurements were taken at the radial artery. The waveforms were visually assessed such that 15 seconds of the best quality were taken, in order to minimise artefact caused by movement and arrhythmias. Two recordings were taken with differences in augmentation pressures of ≤5 mmHg and augmentation index of ≤5%. Furthermore, the following quality control measures were adhered to: Signal strength ≥75; Pulse height variation ≤ 5; Diastolic variation ≤5; Shape deviation ≤5; and Operator index ≤85. The results of the two readings were then averaged.

Vicorder: A Hokanson SC10 was positioned around the middle of the upper arm, for brachial artery PWA. Initially, an oscillatory blood pressure was taken using the Vicorder device. Following this the cuff was then inflated to diastolic pressure for PWA, during which the operator visually assessed the waveforms. The measurement was recorded when a stable waveform (without artefact from movement and arrhythmia) was shown. Two recordings were accepted when both readings of augmentation pressure and augmentation index were within ≤ 5 mmHg and ≤5% of each other. These results were then averaged.

1.6 Ankle Brachial Pressure Index

Ankle brachial pressure index (ABPI) measurements were taken using the Vicorder device (Skidmore Medical, UK), in the right and left sides sequentially by two experienced operators. To do this Hokanson SC10 cuffs were positioned on the upper arm and lower leg (above the ankle). Photoplethysmography sensors were then clipped to the end of the digitus me'dius (middle finger) and the hallux (big toe). The brachial and tibial arteries were occluded simultaneously, as the cuffs were inflated to 180mmHg. As the cuffs slowly deflated, the pulse data was visually assessed to minimise artefact from movement and to ensure that the blood pressures were taken at the point of the pulse returning at both sites. The Vicorder device provided blood pressures for both the brachial and ankle, and the ABPI ratio. Optimally, two measurements were recorded with a difference of ≤5 mmHg in either the brachial or the ankle pressures. However, if this could not be achieved three measures were taken and averaged.

****************** END ************************

2.0 Carotid IMT adjustments

Adjustment was made for those with an IMT measurement available on only one side - Right or Left

ONLY 1610 subjects had IMT measurements on both the LEFT and RIGHT carotid arteries.
IMT_diff = Mean_L_BLIMT - Mean_R_BLIMT
The mean of the IMT_diff= **0.0497081**

If there was a measurement for the Right side IMT but not for the left then
we added ½*(mean difference between the Left and Right IMT measurement)
Mean_R_BLIMT_adj=Mean_R_BLIMT +(**0.0497081**/**2)**

If there was a measurement for the LEFT side IMT but not for the RIGHT then
we subtracted ½*(mean difference between the Left and Right IMT measurement)
Mean_L_BLIMT_adj=Mean_L_BLIMT - (**0.0497081**/**2)**

SAS CODE
** avergage difference between Left and Right IMT;

Variable	N	Mean	Std Dev	Minimum	Maximum
IMT_DIFF	1610	0.0497081	0.2159540	-0.7900000	1.570
Mean_R_BLIMT	1648	0.7805340	0.1761842	0.2900000	1.640
Mean_L_BLIMT	1658	0.8278589	0.2002881	0.4300000	2.570
av_imt_unadjusted	1696	0.8065537	0.1577754	0.4400000	1.785
av_imt_adj	1696	0.8064071	0.1580441	0.4648541	1.785

```
Q30av_imt_unadjusted=mean(Mean_R_BLIMT, Mean_L_BLIMT);
imt_diff=0.0497081;
half_imtdiff=0.0497081/2;

Mean_L_BLIMT_adj=Mean_L_BLIMT;
Mean_R_BLIMT_adj=Mean_R_BLIMT;

if Mean_R_BLIMT =.    and Mean_L_BLIMT ne .  then Mean_L_BLIMT_adj=Mean_L_BLIMT-half_imtdiff;
if Mean_R_BLIMT ne .  and Mean_L_BLIMT =.    then Mean_R_BLIMT_adj=Mean_R_BLIMT+half_imtdiff;
```

APPENDIX 1

BRITISH REGIONAL HEART STUDY

Vascular Assessment protocol

30 year follow-up (Q30)

2010-2012

Vascular Assessment

carried out by

Wales Heart Research Institute(WHRI), Cardiff University

Workstations 2 and 3

Vascular assessment protocol

Written by Dr Libby Ellins

Date: May 2010

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List of abbreviations

ABI – Ankle Brachial Index

ABPI –Ankle Brachial Pressure Index

BP – Blood Pressure

BRHS – British Regional Heart Study

CCA – Common Carotid Artery

ECA – External Carotid Artery

ICA – Internal Carotid Artery

IMT – Intima-Media Thickness

m/s – Metres per Second

PPG - Photoplethysmography

PWA – Pulse Wave Analysis

PWV – Pulse Wave Velocity

Protocol for non-invasive vascular measures for the British Regional Heart Study

Introduction:

The British Regional Heart Study (BRHS) is a prospective study in middle-aged men drawn from general practices in 24 British towns, recruited in 1978-1980. It was set up to determine the factors responsible for the considerable variation in coronary heart disease, hypertension and stroke in Great Britain. It also seeks to determine the causes of these conditions in order to provide a rational basis for recommendations towards their prevention.

For this revisit the surviving study participants in this established cohort (approximately 4000 men aged 70-89 years) will undergo a final screening. The field study team will use imaging techniques to measure disease and ageing of the heart and arteries and measure a wide range of established and novel factors which may affect CVD risk at this age. The study aims to increase understanding of how health behaviours and the ageing process affect CVD in later life, and how CVD risk and cardiovascular ageing can be reduced in the elderly.

The study will involve a field team of two nurses and two ultrasound technicians staying in the 24 participating BRHS towns (based in England, Scotland and Wales) for two week periods between early 2010 and late 2011. Participants will then come to the study General Practice for re-examination; home visits will be made to a limited number of study participants who are not able to travel.

Vascular Measures

Carotid intima-media thickness (IMT) is a measure of early structural changes in the vessel wall and is related to cardiovascular risk. IMT will be measured from the far wall of the common carotid artery (CCA) with computer assisted acquisition, processing and storage. IMT will be determined as the interface between the lumen-intima and media-adventitia and will be measured 1-2 cm proximal to the carotid bifurcation. Optimal images are recorded in DICOM format as a cine loop and downloaded for later offline analysis.

Plaque presence

Presence or absence of plaque in the carotid artery has been shown to be an indicator of cardiac risk.

Arterial distensibility is a measure of vascular elastic properties of the artery and will be measured in the common carotid artery, using high-resolution ultrasound on a segment of vessel 1-2 cm proximal to the bifurcation. This can be acquired at the same time as the IMT. Stiffer arterial walls re less prone to expand during systole and related blood pressure variability, and this can be quantified by means of measuring changes in vessel diameter during the cardiac cycle. Brachial artery blood pressure will be measured using an oscillometric blood pressure device following a 10 minute supine rest, immediately after the image acquisition.

Pulse wave velocity (PWV) is a measure of arterial stiffness, measured over an extended section of the arterial circulation. Increased PWV reflects increased arterial stiffness. Carotid-femoral PWV which predominantly reflects aortic stiffness is considered the optimal measure of arterial stiffness and is now widely used as a valid non-invasive measure of arterial disease. Carotid –femoral PWV will be measured at rest using both the Vicorder and Sphygmocor systems.

Using the Vicorder, proximal and distal blood pressure cuffs are wrapped around the neck and thigh. The distance between the sternal notch and the middle of the thigh cuff is measured and recorded. The cuffs are then inflated to 65mmHg and the corresponding oscillometric signal for each cuff is analysed digitally to provide the PWV.

The Sphygmocor system uses applanation tonometry. A pressure tonometer is used to record transcutaneously the pressure pulse waveform in the underlying artery. An R-timing reference is provided by simultaneous recording of an ECG signal. Consecutive pressure pulse recordings are performed at two superficial artery sites (carotid – femoral segment).

The mean time difference between R-wave and pressure wave is calculated on a beat-to-beat basis from each set of pressure-pulse and ECG waveform data using integral software. PWV is calculated using the mean time difference and arterial path length between the two recording points.

Pulse wave analysis (PWA) measures the augmentation index (a representative surrogate of wave reflection) and generates a central blood pressure. It is measured using the Sphygmocor system. A pressure tonometer is used to record transcutaneously the pulse pressure waveform in the underlying radial artery. A transfer function is then used on the signal to generate information regarding central and augmentation pressures.

Ankle-brachial pressure index (ABPI) is the ratio of the systolic pressure at the ankle to that in the arm. This is measured using the Vicorder system to record systolic pressures in both the right brachial artery and the right and left posterior tibial arteries using oscillometric sensors.

Arrival at site:

Assess room being used for measurements. Decide on best positions for the two workstations taking into account lighting levels, privacy for the subjects using screens, sufficient room for movement around couch, flow of subjects between the two workstations.

General Comments

When the participant arrives at the workstation, Collect BRHS form from them, and confirm their ID by asking name and date of birth.The participants need to be rested prior to commencing the measurements, to allow baseline cardiovascular variables to stabalise. In addition, ensure that all procedures are described to the participant, and explain that they will be repeated.

All data should be backed up to the USB drives at the end of each day, and then to the Analysis computer at the end of each week.

Equipment /consumables:

Carotid IMT and distensibility.

- Zonare ultrasound machine and linear array probe
- Key board, printer and extra monitor
- Omron blood pressure monitor and cuffs
- Couch for participant to lie on
- Trolley with wheels to hold machine
- Adjustable stool
- Pillow
- Consumables: tissues, tissue for couch, ultrasound gel, pens

PWV/ PWA/ABPI

- Laptop
- Vicorder
- Sphygmocor
- Cuffs
- Trolley with wheels to hold equipment
- Couch
- Adjustable stool
- Thermometer for room and skin temperature
- Tape measure
- Consumables: tissue for couch, pens

Protocol for Workstation 2

Scanning procedure for Carotid IMT and distensibility.

Slide the scan engine onto the 1st shelf of the cart, until it locks into place. Attach the ultrasound probe to the side of the scan engine and place in the holder. Place the plug in the socket and switch on.

Ask the participant to lie down with their head near the top end of the couch.

Ensure the ultrasound machine is within easy reach when scanning the participant's neck and the screen is at a comfortable angle without the operator straining their neck. Adjust height of the stool to ensure a comfortable position at the head end of the couch.

When the participant is settled on the couch, place a blood pressure cuff securely onto the participant's right arm. Then request they hold a thermometer probe for a few minutes. When a relatively constant temperature is given, record the skin and room temperatures on the data sheet.

Whilst waiting for a steady temperature, input the participant details:

Press New Patient

Using the keyboard enter:

- ID
- Gender
- Date of Birth
- Operator

The exam type is always vascular and the preset Vascular Research (these should not be altered). Selecting Exit will cause the scanning screen to return. Initials and ID of participant should be in the top left corner of the screen. Label image as RCCA (right common carotid artery)

The participant will be scanned supine, with lateral, chin-up head tilt to 45^{o}. Ensure there is easy access to the participant's neck and that this is a comfortable position for the participant. Apply gel to the probe.

Starting on the right side, place the probe at the bottom of the neck in the transverse position. The notch on the probe should be pointing towards the right. Aligning the transverse image of carotid artery in the middle of the screen, slide probe up the neck until the carotid widening into bulb is visible and the common carotid bifurcates into the internal carotid artery (ICA) and external carotid artery (ECA). Two distinct vessels should be seen. Sweep up as far as possible. Repeat this upward sweep having first pressed store to record as a cine loop.

Slide back down the neck to the beginning of the bulb; turn the probe 90^{o} to image a longitudinal plane. The notch on the probe should be pointing up towards the head. Check the angle of the probe; it should be about ear to ear. Align image with beginning of the bulb at the left side of the screen, the artery should be horizontal across screen, and intima should be visible on both anterior and posterior CCA walls.

Select Zoom, position the box to the desired spot, and push select twice, (image should zoom). Adjust the image, then press store to record cine loop (see figure 2 (the perfect image). Maintain the image for the entire 10s recording, a minimum of 5 consecutive beats is required. Remove the probe, and wipe it clean and along with the participant's neck.

Take 2 blood pressure recordings on right arm, 30 seconds apart, recording the readings on the datasheet.

Repeat these measurements on the left side, then press end Exam to exit and save the data.

Image optimization:

Push Optimize or try increasing/decreasing the Gain (by turning the grey dial). This can help the picture quality and display the intima more clearly

If the artery is sitting very low on the screen, adjust the depth so that it sits closer to the middle of the screen.

If the artery is sitting very high on the screen try to lift the probe so still in contact with the gel but not so close to the skin, this can help the artery to drop towards the middle of the screen which allows a better image.

If one wall is very 'fuzzy', use the 'time gain controls' to improve the image.

If the presence of plaque is found

Record still images of the thickest point of plaque in both cross-sectional and longitudinal orientations ensure images are correctly labelled with artery location.

Record a cross-sectional scan of carotid going down to the root of the vessel and back up as far as possible beyond the bifurcation with flow.

Image the area of plaque longitudinally with flow –adjust flow box to correct angle, and record a cineloop.

If possible measure the amount of plaque in the area and record as a still image correctly labelled.

Note location of plaques on the data sheet.

Data management

Exporting data

First turn the machine off, place the USB stick into back port, and turn the machine on again. Press Archive and select the exams for export. When the USB stick is recognised, select the Drive, and press Export. Wait for data to be transferred, click OK

Press Archive to return to the main screen.

Back up of data

To be done at Cardiff after each period of field work.

Attach then ultrasound machine to the cart. Switch on both the cart and the ultrasound machine (using the on button on the cart). Press Archive, then highlight the data to be backed-up, and click Export. Select the device to be copied to i.e. Cart hard drive, and click Export. Press Archive again to close this window and return to the main screen.

Copy data from USB stick onto computers at Cardiff files labelled BRHS and town name.

Protocol for Workstation 3

Procedure for measuring PWA using Sphygmocor

Open Sphygmocor programme on laptop by double clicking on icon on desktop. Ensure that BHRS is the default database, if this is not the case, click System, Database Manager, Select BRHS. Then click Select and OK.

Select 'Create New', then insert participant details:

- patient ID
- Initials
- Date Of Birth
- Sex

Then select 'Update'.

Click PWA and Study. Take 2 blood pressure measurements with the Omron, write them on the data sheet and enter the average into the PWA screen. Check default Radial is ticked, and insert Operator initials

Click Capture Data. Record 15 seconds of good quality waveforms and press space bar/the foot pedal to capture the data.

Clicking on the Detailed screen, all numbers under Quality Control should be GREEN Operator Index should be 85 or above. If these criteria are not met the measurement should be repeated.

To repeat the measurement press F3, and then enter. Two measurements should be taken at the Radial artery, and the difference between the AIx of the two data sets should be ≤5%.

NOTE: Ensure the tonometer is always replaced and secured after each measure, as it is fragile

Procedure for measuring PWA using Vicorder

Place the SC10 cuff securely around the upper right arm with the tube positioned in line with the brachial artery. Attach this to the red pressure hose.

Click on PWA in Quick Launch. The acquire screen will appear overlaid by PWV study screen, ensure that the data will be saved in a file BRHS.pwa (this will need to be altered before and after taking the Osc BP)

Click on OSC BP. Inform the participant that the cuff will inflate and press Space to inflate the cuff for a BP reading. When completed press return to save blood pressure which is automatically entered into the study screen.

Remember to ensure that the PWA data will be saved to BRHS.pwa, then click OK. Also ensure that the data is being backed up to the CSV file, on the right side of the input box.

On the acquire screen press the Space to inflate the cuff. When there has been a run of good quality waveforms press space to freeze, then return to save the results. Repeat for a second reading – if there is a difference of >0.5 between the two Augmentation Index results take a third reading.

Procedure for measuring PWV using Sphygmocor

Equipment/consumables:

- Sphygmocor with tonometer and laptop with integral software.
- Omron BP monitor with adult cuff.
- Consumables: water based felt tip pen, 3 x ECG electrodes per participant

Scanning procedure for pulse wave velocity

In the patient details screen, ensure the correct participant is highlighted, click the ‘PWV’ icon and then ‘Study’.

Ensure that at Site A the Carotid box is ticked, and at Site B the Femoral box is ticked. Feel the pulses at the carotid and femoral, mark with a pen, and measure the distance to them from the suprasternal notch. Note: Ensure that the measurement does not follow the contours of the body. Enter the sternal notch to femoral artery measurement (mm) in the Distal box, and the sternal notch to carotid artery in the Proximal box.

Systolic and Diastolic blood pressures should remain the same.

Note: Ensure that the PWV algorithm is 3-Intersecting Tangents

Insert initials in Operator. Connect the ECG leads from the Sphygmocor to the electrodes on the chest.

Click Capture Data, and the screen will appear with the ECG in yellow.

Sit at the head of the couch, asks the participant to extend their neck backwards as far as possible, this tightens the sternocleidomastoid muscle to give you a firm structure to exert pressure against. Feel for the right carotid pulse and place the tonometer directly over the strongest pulse point on the neck. Exert gentle, steady pressure to obtain a reading. When there is 15 seconds of steady readings with uniform shape, height and rhythm; press the space bar /foot pedal to capture the data. Pay particular attention to the upstroke of each wave as the readings are taken from the intersecting tangent at the base of the upstroke.

Both the operator and the subject must be perfectly still for this recording. The operator should ensure they are in a comfortable position with their arm rested on the couch and with a straight back (couch/bed and chair at the correct height).

A message will appear, asking if a measurement will be taken at Site B, click 'Yes' to accept, and move to take a measurement at the femoral artery.

Repeat for Femoral pulse:

Feel for the femoral pulse and place the tonometer over the point where it is strongest. Repeat as for the carotid measurement.

Once both measurements have been taken, the report screen will appear with the Carotid reading at top and the Femoral reading below. In the panel at the bottom marked SD (m/s) both numbers must be GREEN, if one or both are RED repeat the measures. Under Pulse Wave Velocity (m/s) a value with a standard deviation will be given, a PWV with a SD above 10% of the PWV is not acceptable.

These measurements should be repeated, to gain to PWV values with a difference of <0.5 m/s.

The Sphygmocor software can be shut down by pressing the X in the top right hand corner, all data will be saved to the hard drive automatically.

Procedure for measuring PWV using Vicorder

Procedure for Carotid to Femoral PWV:

Click on the PWV icon in the Quick launch Tab of the main Vicorder screen. Click edit patient data and enter the patient details:

- Surname
- first name
- ID number

Ensure that the data is saved in the BRHS.pwv, which can be altered in the top left box.

Position the participant at a 30° angle, so that their head and shoulders are higher than the rest of their body. Attach the femoral cuff to the top of the participant's right leg, with the tube facing upwards towards the centre of the body. Connect the blue cable to this tube. Next attach carotid sensor around the participant's neck, making sure that the bladder of the cuff is anatomically positioned over the carotid artery, and attach the red cable to this tube.

Measure the distance from the suprasternal notch to the middle of the leg cuff, in a straight line (not following the stomach contour). Record this measurement in the Length box in the PWV study information, and on the data sheet. Following this, measure the distance from the suprasternal notch to the bottom of the neck sensor (angled towards the participant's ear). Record this measurement in the comments box in the PWV study information, and the data sheet.

Inform the participant that the cuff is going to inflate, and then click the space bar to start the cuff inflation. To change the scale of the waveforms so that they fit on the screen, use the up and down buttons on the Vicorder, or change gain icon on the screen (F5). When three waveforms of a similar shape and size are obtained click Space to stop the recording.

Click Enter/Return button to save the data. It will then be possible to repeat the measurement.

Repeat this procedure two more times, as two PWV measurements within a range of 0.5 m/s are required.

Saving Data:

Plug in USB stick.

Open:

- My computer
- Programme files
- Skidmore medical folder
- Data folder
- Highlight required data
- Right click on mouse – copy
- Open removable disk file
- Open PWV folder
- Right click on mouse – paste

Safely remove USB stick and turn off laptop.

Procedure for measuring ABPI using Vicorder

PPG

Place SC10 cuffs over the Brachial artery on both arms, and above the ankle on both legs. The red pressure hose should be used at the Brachial cuff and the blue at the ankle. With the PPG sensors inserted into the clips, attach the red sensor to the middle finger and the blue sensor to the big toe. Note that extraneous light should be excluded.

Click on the ABI icon, when the screen opens ensure that it is in the multi-channel, bilateral mode. If this is not the case, press Multi-Chan/F4.

When clear waveforms are observed, inform the participant that the cuff will be inflated and press Space. The cuff will then automatically bleed pressure, the PPG signal reappears when the cuff reaches systolic pressure. At any point after the reappearance of the signal the display may be frozen by pressing Space.

Press Enter to save the Data. This should be repeated twice for each side, the repeated measurements (each side) should be <5mmHg apart

Doppler

The pressure cuffs should remain in place from the PPG measurement. The red pressure hose should be attached at site of measurement. Click on the Pressures icon. When the screen opens, PPG will be the default measurement, to change this to Doppler click press Mode/F12 twice.

Apply ultrasound gel to the end of the Doppler probe, and place the probe over the right Brachial artery distal to the cuff. The probe should be positioned such that the direction of blood flow is towards the probe, with the probe at a 45° angle. Both the operator and the participant should remain still during the measurement.

Once an adequate signal is obtained, inform the participant that the cuff will inflate, then press Space to inflate. The cuff will then automatically bleed pressure, the Doppler signal reappears when the cuff reaches systolic pressure. At any point after the reappearance of the Doppler signal the display may be frozen by pressing Space. To save data press Enter.

This measurement should then be repeated at the Posterior Tibialis and the Dorsalis Pedis, on the right and left sides.

Return to the main screen by pressing Close/Esc

APPENDIX 1
Vascular measures
Data collection form Workstation 2

DATASHEET: CARDIFF UNIVERSITY

British Regional Heart Study 2010-2012

Batch / Study # Date
DOB:

BIOIMPEDANCE

Pacemaker? ☐ No = 2 Both Bio impedance measurements
YES = 1→ NO BIOIMPEDANCE MEASUREMENTS GO DIRECT TO BLOOD TEST

NO Pacemaker: BOTH BIOIMPEDANCE MEASUREMENTS

1. Bodystat Instrument ☐ Reading ☐☐☐☐

STATION 2: Observer ID. ☐☐ ROOM TEMP ☐☐.☐ °C SKIN TEMP ☐☐.☐ °C

RIGHT SIDE **Comments**

RCCA □ ....
RDist □ ....

PLAQUE ☐ **Y=1**

RCCA ☐ RCCB ☐ RICA ☐ RECA ☐

Cuff size (Armcirc < 22 cm = 1 (small), 22-32 cm = 2 (medium), >32 cm = 3 (large)

RBP1 Sys ☐☐☐ Dia ☐☐☐ HR ☐☐☐

RBP2 Sys ☐☐☐ Dia ☐☐☐ HR ☐☐☐

Left side **Comments**

LCCA □ ....
LDist □ ....

PLAQUE ☐ **Y=1**

LCCA ☐ LCB ☐ LICA ☐ LECA ☐

LBP1 Sys ☐☐☐ Dia ☐☐☐ HR ☐☐☐

LBP2 Sys ☐☐☐ Dia ☐☐☐ HR ☐☐☐

Observer ID ☐☐ **Comments** ☐

APBI (PPG)

1.Sys BP R brachial ☐☐☐ Sys BP R toe ☐☐☐ RABPI ☐.☐☐
2.Sys BP R brachial ☐☐☐ Sys BP R toe ☐☐☐ RABPI ☐.☐☐
3.Sys BP R brachial ☐☐☐ Sys BP R toe ☐☐☐ RABPI ☐.☐☐

1.Sys BP L brachial ☐☐☐ Sys BP L toe ☐☐☐ LABPI ☐.☐☐
2.Sys BP L brachial ☐☐☐ Sys BP L toe ☐☐☐ LABPI ☐.☐☐
3.Sys BP L brachial ☐☐☐ Sys BP L toe ☐☐☐ LABPI ☐.☐☐

APPENDIX 1
Vascular measures
Data collection form Workstation 3

STATION 3 Observer ID [ ][ ]

Comments [ ]

PWA (Sphyg)

R BP	Sys	[ ][ ][ ]	Dia	[ ][ ][ ]	HR	[ ][ ][ ]
R BP	Sys	[ ][ ][ ]	Dia	[ ][ ][ ]	HR	[ ][ ][ ]

Reading 1	Augmentation (mmHg)	[ ][ ][ ]	AIx (%)	[ ][ ][ ]
Reading 2	Augmentation (mmHg)	[ ][ ][ ]	AIx (%)	[ ][ ][ ]

PWA (Vicorder)

R BP	Sys	[ ][ ][ ]	Dia	[ ][ ][ ]	HR	[ ][ ][ ]

Reading 1	Augmentation (mmHg)	[ ][ ][ ]	AIx (%)	[ ][ ][ ]
Reading 2	Augmentation (mmHg)	[ ][ ][ ]	AIx (%)	[ ][ ][ ]

Comments [ ]

R BP1	Sys	[ ][ ][ ]	Dia	[ ][ ][ ]	HR	[ ][ ][ ]
R BP2	Sys	[ ][ ][ ]	Dia	[ ][ ][ ]	HR	[ ][ ][ ]

PWV (Sphyg)

							Accepted
1	CAR-FEM	Dis [ ][ ][ ]	Prox [ ][ ][ ]	(mm)	[ ][ ] . [ ] ± [ ] . [ ]	m/s	☐
2	CAR-FEM	Dis [ ][ ][ ]	Prox [ ][ ][ ]	(mm)	[ ][ ] . [ ] ± [ ] . [ ]	m/s	☐
3	CAR-FEM	Dis [ ][ ][ ]	Prox [ ][ ][ ]	(mm)	[ ][ ] . [ ] ± [ ] . [ ]	m/s	☐
4	CAR-FEM	Dis [ ][ ][ ]	Prox [ ][ ][ ]	(mm)	[ ][ ] . [ ] ± [ ] . [ ]	m/s	☐

PWV (Vicorder)

1	CAR-FEM	Dis [ ][ ] . [ ]	Prox [ ][ ] . [ ]	(cm)	[ ][ ] . [ ]	m/s
2	CAR-FEM	Dis [ ][ ] . [ ]	Prox [ ][ ] . [ ]	(cm)	[ ][ ] . [ ]	m/s