

**NUFFIELD DEPARTMENT OF SURGICAL SCIENCES
 UNIVERSITY OF OXFORD**



SOP Number: JWVSU_01_V2.2
SOP Title: OxAAA JWVSU FMD, NMD and AAA video loop measurements.

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1. PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe the standard procedures to be followed when assessing flow mediated dilation (FMD), Nitroglycerine (NTG) mediated dilatation (NMD), and the process of capturing longitudinal and transverse AAA video loops in clinical studies sponsored by the Nuffield Department of Surgical Sciences, University of Oxford in conjunction with NIHR Oxford Biomedical Research Centre.

2. INTRODUCTION

This document outlines the correct procedures for recording flow mediated dilation (FMD) in the brachial artery, Nitroglycerin mediated dilatation of the brachial artery (NMD) and the recording of longitudinal and transverse AAA video loops within the Jackie Walton, Vascular Studies Unit (JWVSU) for the Oxford Abdominal Aortic Aneurysm Study (OxAAA).

3. SCOPE

This SOP applies to clinical research where the Nuffield Department of Surgical Sciences, University of Oxford has accepted the role of 'Sponsor', in the Jackie Walton Vascular Studies Unit. This SOP may or may not apply to commercially sponsored research or research sponsored by an external non-commercial organisation.

4. RESPONSIBILITIES

a. Investigator or delegate

- Ensure the subject understands the procedure as described below.
- Ensure that the subject will be continuously observed during the study.

5. SPECIFIC PROCEDURE

a. Equipment

- Arm rest with stereotactic ultrasound probe-holder
- Adjustable rolled towel in a pillow case.X2
- Tourniquet or fabric bandage.
- ECG Lead (e.g. M1669A) and electrodes
- Ultrasonic gel
- Forearm-sized blood pressure cuff
- 400 microgram and 25 microgram metered dose sub-lingual NTG spray
- Pipettes
- Vascular ultrasound machine (e.g. Philips CX50)
- Vascular linear and curvilinear array ultrasound probe (Philips L12-3 and C5-1)
- Examination couch with variable height
- Android device with FMD/NMD timing program
- Study form v2.3
- Examination table – approx. 80 cm in height and 30 cm x 40 cm top

Interventions

STANDARD OPERATING PROCEDURE

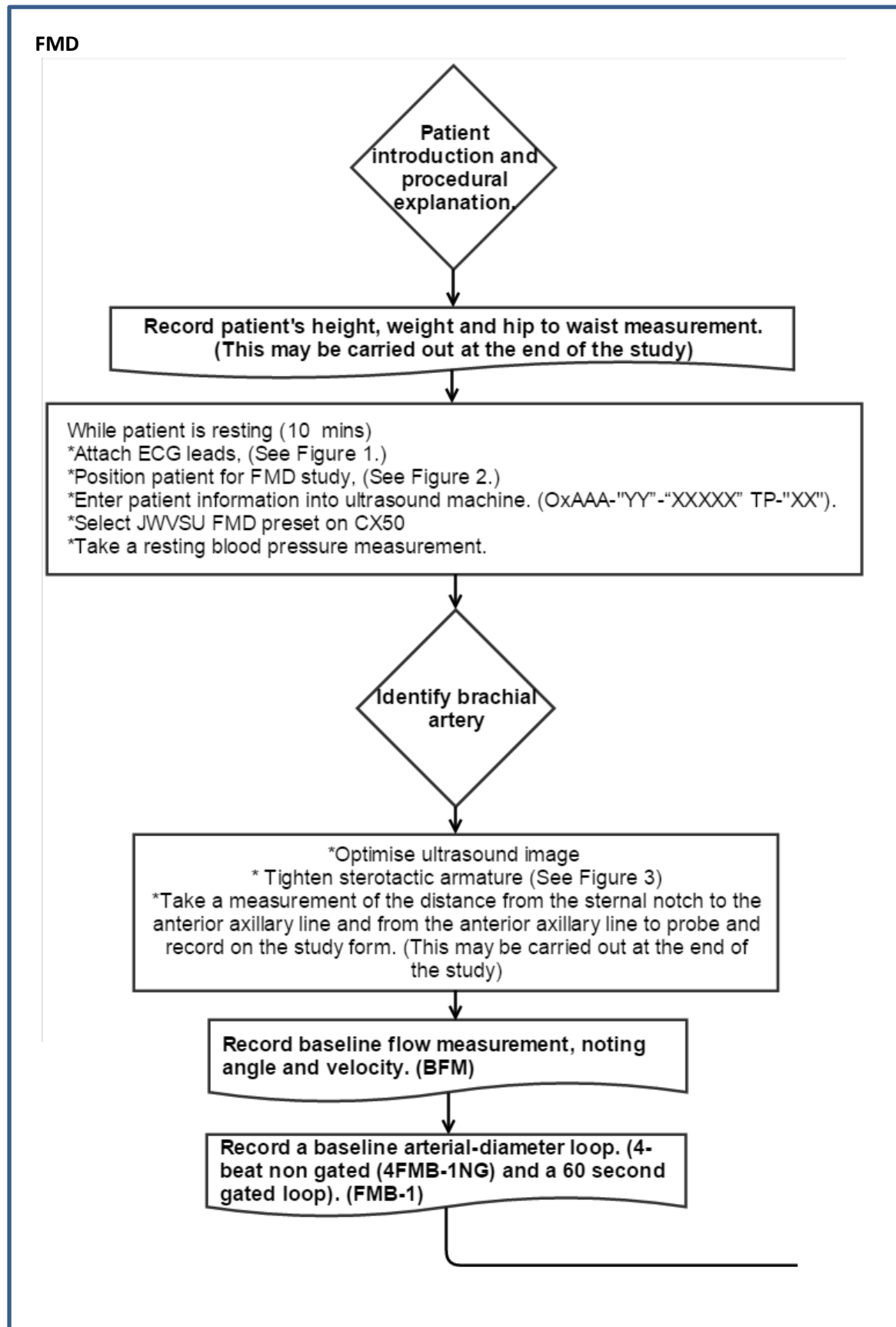
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Jackie Walton Vascular Studies Unit

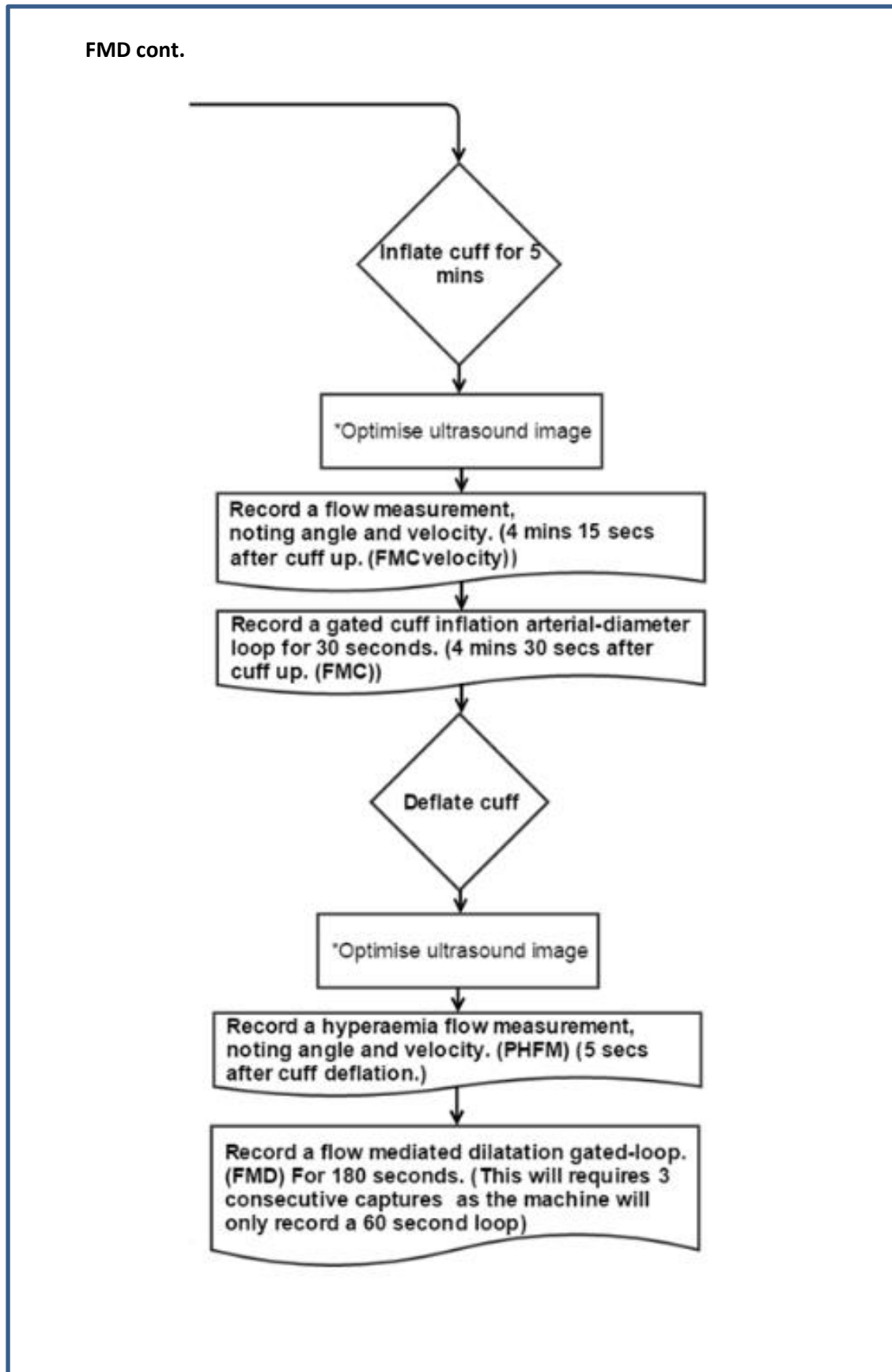
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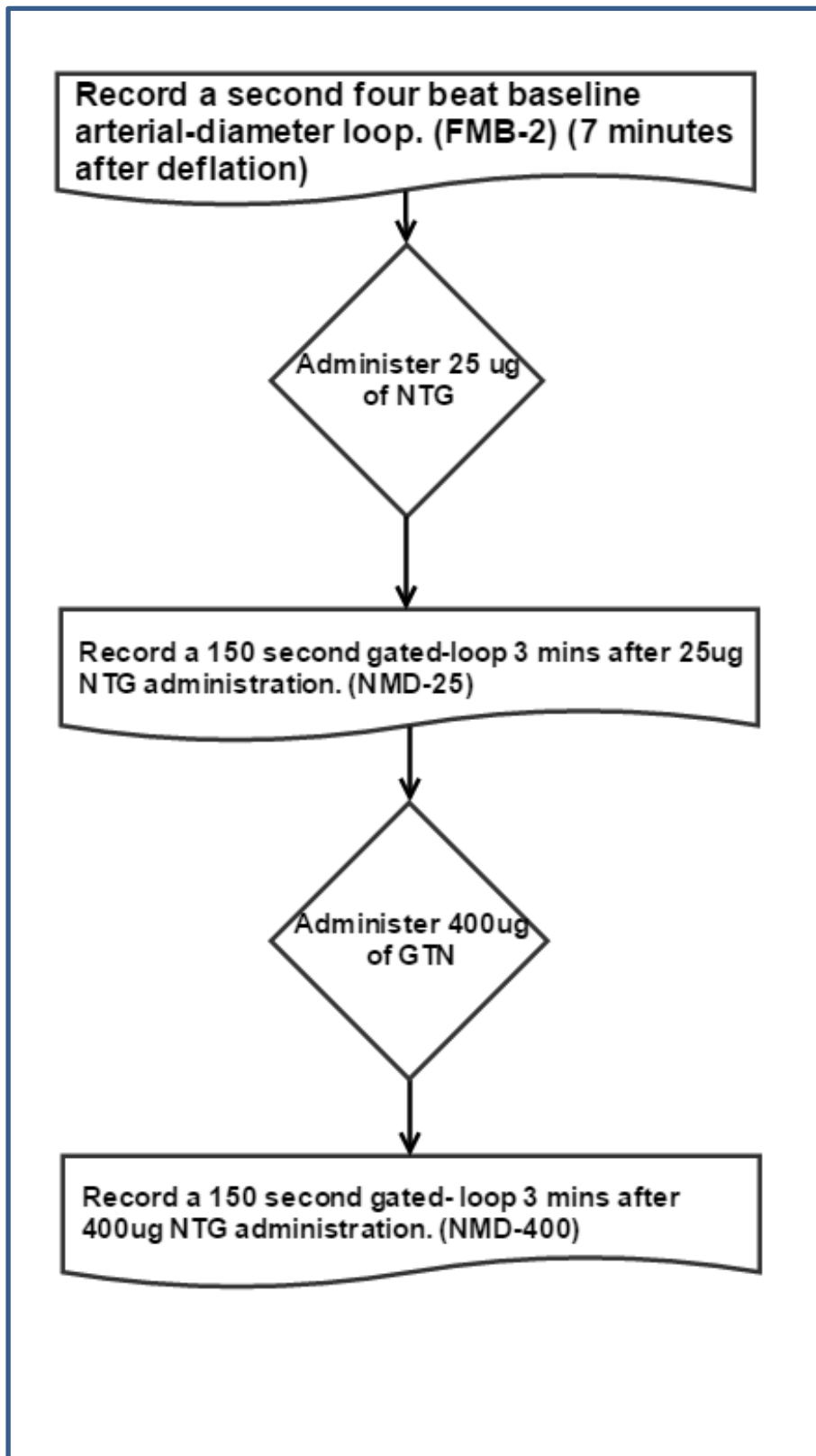
- Scales
- Electronic blood pressure machine
- Tape Measure

b. FMD and NMD flow charts



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c. **Procedure for the routine AAA surveillance scan. Before the commencement of the procedure patients should confirm they have fasted for 6 hours and have not had any stimulant drinks for at least 24hours e.g. Coffee, cigarettes**

1. Measure and record the subject height, weight, hip (at top level of hip bone) and waist (at level of naval) measurement in the patient study form. (This may be carried out at the end of the study to ensure the patient has recovered from the NMD study).
2. Ask the subject to undress from the waist up unless they have a short sleeved shirt or top before placing them in the supine position on the bed in a quiet room. (~22°C)
3. Attach ECG electrodes in conventional positions at least 20cm from the heart and connect to machine. The red electrode should be placed on the right-hand side above the level of the heart, the yellow electrode should be placed on the left-hand side above the level of the heart, and the green electrode should be placed on the left-hand side below the level of the heart. (See figure 1.)

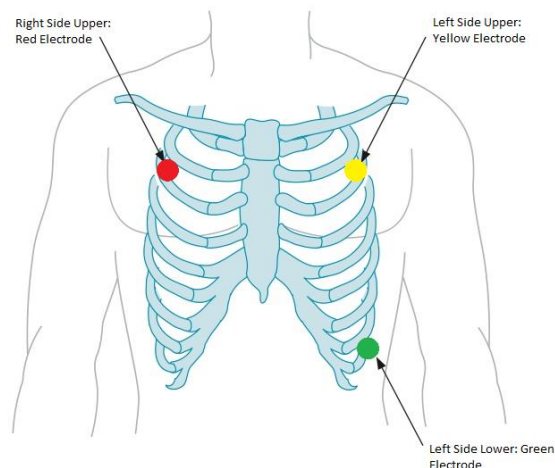


Figure 1.

4. Connect the Philips Curvilinear array ultrasound probe (C5-1) to the CX50 and lock in place on the right hand side of the machine.
5. Select **AbVasc pre-set imaging mode** on the CX50 console.
6. A routine AAA surveillance scan should be carried out in accordance with the local unit protocol and recorded on the JWVSU AAA surveillance form.
7. Under the **physio menu**, using the **'next arrow'** in the centre of the top row of the console switch between the menus and turn the ECG channel from **'off'** to **'internal'**. Then, using the next arrow again to switch menus, turn the trigger from **'off'** to **'on'**. Turn the physio menu off and then set the loop type from **time to beats (4 beats)**.
8. Ensure clear R wave tracing on ultrasound machine and record the patient's heart rate on the study form making note of irregularities.
9. A video loop recording, four beats long, should be obtained in transverse and longitudinal.

10. Wipe aqueous gel off subject and ultrasound probe with paper towel. Use specialised probe disinfectant as required.

d. Procedure for a standard FMD Study:

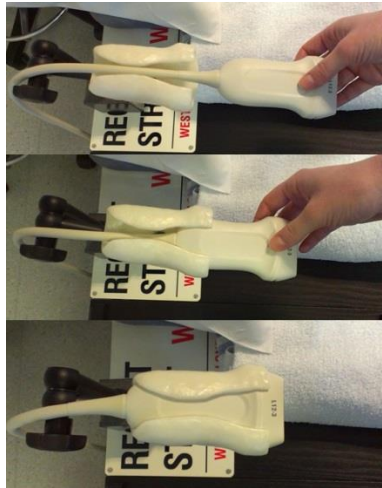
1. Take a resting blood pressure measurement and record on the study form.
2. Ask the subject to place their right arm outstretched upon the arm-rest. Ensure that the subject lies approximately horizontally, in a relaxed position with elbow and wrist completely supported by the rolled towels and a clear space underneath the forearm to ensure the blood pressure cuff does not move the arm when inflated. (See figure 2).

Figure 2.



3. Apply the correctly-sized blood pressure cuff to the forearm muscle mass, such that the top edge sits just below the cubital fossa (~3-5cm). Ensure that the cuff is wrapped snugly and evenly and is not touching either the armrest-bed or adjustable rolled towels.
4. Instruct the subject to keep as still as possible throughout the study.
5. Allow the subject to rest in supine position for **10 minutes** before commencing the rest of the procedure. In the meantime, do the following:
6. Enter subject details on ultrasound machine. Use the anonymised ID format for FMD study. This should be in the format of OxAAA-“YY”-“XXXXX” TP-“ZZ”. If you are unsure, check that an ID has been assigned.(YY is the study group, XXXXX the study number, TP ZZZ is the time point)
7. Select **JWVSU FMD pre-set imaging mode** on the CX50 console. (See appendices for the JWVSU FMD pre-set parameters)
8. Fit the ultrasound probe into the probe holder ensuring the leading edge is directed towards the subject's head (note: the probe should slide into the clip from underneath, do not press the probe in from the front or prise open the jaws of the clip). (See figure 3.)

Figure 3.



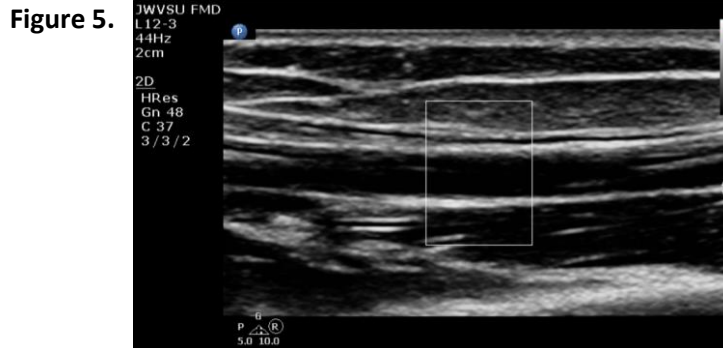
9. Apply the magnetic base of probe-holder to the armrest in line with the elbow so that the probe can comfortably reach the target artery. Ensure that the probe-holder's base does not touch the cuff, the subject's arm or the supporting towels. (See figure 4.)

Figure 4.



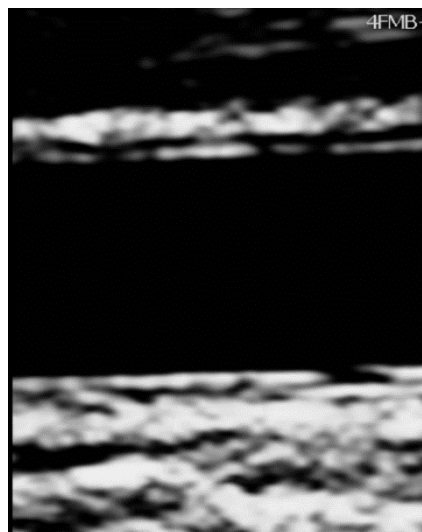
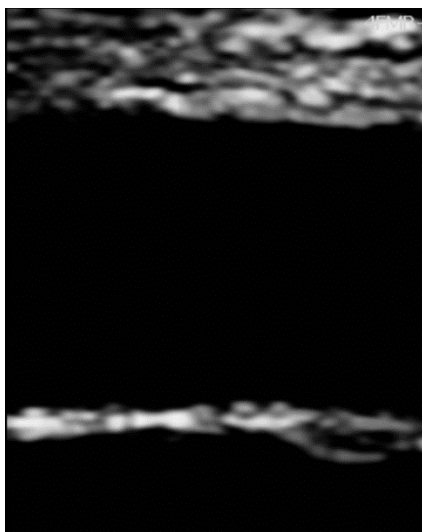
10. Apply sufficient ultrasound gel for the examination. Identify the brachial artery bifurcation through transverse views in both B mode and colour flow. Trace the brachial artery proximally to **approximately 5 cm** from the bifurcation.
11. Using the brachial artery as the axis, turn the probe $\sim 90^\circ$ so that it is in line with the longitudinal axis of the brachial artery.
12. Push down on probe slightly to ensure that vessel does not collapse, in order to confirm that the image depicts the brachial artery and not the adjacent vein.
13. Acquire an image of the brachial artery in longitudinal section using colour flow and pulse-wave Doppler to further ensure vessel is arterial.
14. Adjust the probe such that the artery appears straight, horizontal, and in the optimum focal zone of the machine.
15. Adjust the depth and optimise the image using the focus, B-mode gain (set to 96 on pre-set) and compression (set to 46 on pre-set). Ensure that only light pressure is applied to the arm by the probe, to avoid distorting the artery.
16. Tighten stereotactic armature, without moving the probe, such that the image position and quality are unaltered.
17. Take a measurement from the sternal notch to the anterior axillary line and from the anterior axillary line to the middle of the probe and record the results on the study form. (This may be carried out at the end of the study)

18. Using zoom function, enlarge the most clearly visualised and stable section of the vessel using the minimum size box of the zoom function (1.0 x 0.74 cm on CX50). (See Figure 5.)

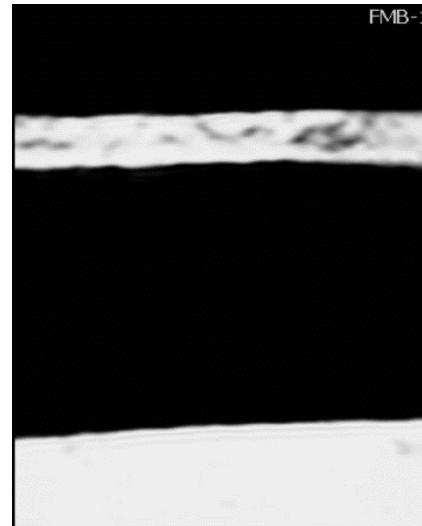
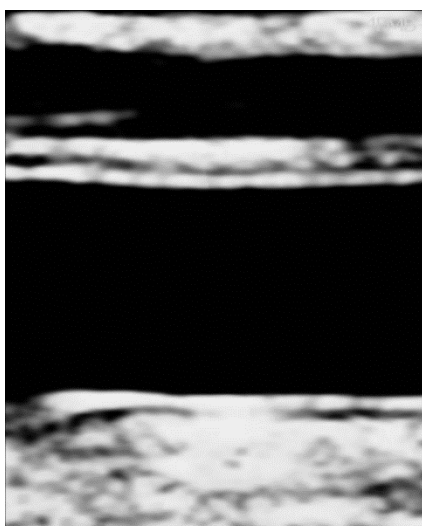


19. Optimise the image to the lowest compression and gain settings which maintain edge coherence whilst removing noise. Adjust compression before gain. See imaging guidelines below to ensure image is suitable for analysis.

IMAGING GUIDELINES FOR OPTIMAL ANALYSIS



The image on the left is not easily analysable and will not yield good results. The image on the right, while analysable, will have to be done mostly by hand as the software will pick up outer and inner walls intermittently.



The image on the left is a good example of visible vessel walls, and is sufficient for study. However, the analysis software may still intermittently pick up the outer wall. The image of the right will analyse very well, and is ideal for scans. In this situation, locate vessel walls, acquire an image that looks like the left, and then turn the gain up and conduct the study in image conditions on the right.

20. Make very fine adjustments to the probe position as required, to ensure the image is of the exact vessel diameter before fully tightening the armature.
21. Record a baseline flow measurement using pulsed wave Doppler positioned in the middle of the artery at the appropriate angle to minimise inaccuracy. (Try to keep the angle between 45-60°). **(BFM Velocity)**
22. Record a **four beat** baseline non-gated arterial-diameter loop **(4FMB-1NG)**.
23. Press the zoom button twice to return to the zoomed out image with the zoom box region indicated, press freeze, acquire a still image **(FMB Location)**, unfreeze the image, and press the zoom button once more to return to the previously selected zoom region.
24. **Under the physio menu turn the trigger from 'off' to 'on' and the loop type to time (60seconds)**. Record a 60 second gated arterial-diameter loop **(FMB-1)**.
25. **Locate the radial pulse.**
26. Inflate BP cuff to the higher of the systolic pressures i.e. BP+50mmHg or 200mmHg, for **5 minutes**. The timer should be started on the android tablet FMD program once the cuff is inflated.
27. During cuff inflation, check that the previously located radial pulse has stopped, indicating occlusion of the artery. If radial pulse persists, slightly increase the cuff pressure.
28. Do not adjust the probe position during cuff-up.
29. If the image quality is not impaired by movement associated with cuff inflation record a flow mediated constriction velocity recording 4minutes 25 seconds post inflation using pulse wave Doppler. **(FMC Velocity)**
30. Record a further 30 second gated arterial-diameter loop at 30 seconds before cuff deflation, for measuring Flow-Mediated Constriction **(FMC)**.
31. Deflate cuff
32. Adjust vascular probe (if required) to maintain image quality.
33. **It is highly important that the visualised segment of the brachial artery remains exactly the same throughout the examination** to ensure the vessel section in view has not changed from the baseline. Identification of the brachial bifurcation (step 12) is therefore highly important as it will allow for tracing of the same segment if the probe position is lost accidentally.
34. Record a peak hyperaemia flow measurement, approximately 5 seconds after the cuff is completely deflated, using pulsed wave Doppler positioned in the middle of the artery at an appropriate angle to minimise inaccuracy. (Try to keep the angle between 45-60° and aim to use the same angle as in step 22). **(PHFM Velocity)**
35. Record a 180 second gated arterial-diameter loop after cuff deflation starting 15 seconds after deflation. **(FMD)** (This will require 3 pushes of the capture button as the maximum loop time is restricted to 60 seconds. The ultrasound machine 'beeps' after each loop capture.)
36. Press the zoom button twice to return to the zoomed out image with the zoom box region indicated, press freeze, acquire a still image of the vessel following FMD **(FMD location)**, unfreeze the image, and press the zoom button once more to return to the previously selected zoom region.
37. Prepare the patient for the next stage of the investigation.

38. Adjust the vascular probe if required to maintain image quality.

e. Procedure for sub-lingual NTG mediated dilation study. To be performed after the FMD study.

Exclusion Criteria:

- Systolic BP below 100 mm Hg
 - Heart Rate below 60 bpm
 - No physicians present
 - Pharmacological contraindication, such as previous adverse reaction(s)
1. Seven minutes after cuff deflation record a second 60 second gated baseline arterial-diameter loop. **(FMB-2)**
 2. Administer 25µg of sub-lingual NTG to the patient.
 3. Wait 3 minutes for the 25µg of sub-lingual NTG to take effect.
 4. Then record a 150 second gated arterial-diameter loop. **(NMD-25)** (This will require 3 pushes of the capture button as the maximum loop time is restricted to 60 seconds. The ultrasound machine 'beeps' after each loop capture.)
 5. Administer 400µg (1 full spray) of sub-lingual NTG to the patient. Provide warning that this may cause slight headache or light-headedness in some individuals for 10 to 15 minutes, but it will be gone before the procedure finishes.
 6. Wait 3 minutes for the 400µg of sub-lingual NTG to take effect.
 7. Then record a 150 second gated arterial-diameter loop. **(NMD-400)** (This will require 3 pushes of the capture button as the maximum loop time is restricted to 60 seconds. The ultrasound machine 'beeps' after each loop capture.)
 8. Measure distance from distal edge of probe to axillary crease and from axillary crease to sternal notch. Loosen probe holder and remove transducer from patient.
 9. Remove ECG electrodes and wipe aqueous gel off subject and ultrasound probe with paper towel. Use specialised probe disinfectant as required.
 10. The FMD study equipment should be moved to the side for the next stages of the investigation.
 11. Prepare the patient for the next stage of the investigation.

Appendix

Study equipment list

Arm rest with stereotactic ultrasound probe-holder



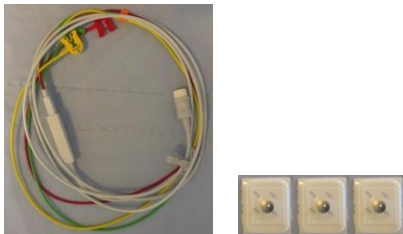
Rolled towel in pillow case



Tourniquet



ECG Lead (e.g. M1669A) and electrodes



Ultrasonic gel



Forearm-sized blood pressure cuff



Sub-lingual NTG spray



Vascular ultrasound machine (e.g. Philips CX50)



Vascular linear array ultrasound probe (e.g. Philips L12-3)



Couch



Timing data sheet

(See FMD Study form v2.4)

JWVSU FMD Pre-set parameters Philips CX50

2D settings:

- 2D Opt, HRes
- Gain, Gn 96
- Compression, C 46
- Loop type, Beats
- Loop beat, 4
- Focal Zone, 1
- Harmonics, ON
- XRES, ON
- Sono CT, ON
- Res/Speed, S1
- Grey Scale mapping, 3
- Persist, 2
- Smooth, 3
- Power, -0.03dB
- iSCAN Gain, 0.0dB
- Chroma, OFF
- Biopsy, OFF
- Trapezoid, OFF
- TGC, ON
- LGC, OFF
- Zoom, smallest box, 1cm x 0.74cm
- ECG, internal