Biopsy Manual
Meso-ORIGINS

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When contacting, please include the following information:

- Study name (Meso-ORIGINS)
- Your name, email address and telephone number
- Your centre details
- Patient study number (if applicable)

2 Introduction

This document provides a framework for the technical procedures related to histological sampling (biopsy) in the Meso-ORIGINS study. This allows study outcomes, including adverse event data, to be reported in the context of methodological homogeneity, but is not meant to replace existing protocols in participating units and it is acknowledged that practices vary considerably. Nevertheless, the following are minimum requirements that should apply to all study participants. Areas expected to vary to a greater or lesser degree between sites are *italicised.*

3 Scope

This manual covers Local Anaesthetic Thoracoscopy (LAT), Video Assisted Thoracoscopic Surgery (VATS or 'Surgical') Thoracoscopy, Ultrasound (US)-guided Biopsy and Computed Tomography (CT)-guided biopsy.

Different biopsy techniques are deployed in the two arms of the study. In Arm A, if there is CLINICAL SUSPICION OF MESOTHELIOMA, any biopsy procedure may be used as directed by the clinician in charge/site PI. The biopsy samples acquired are done so as part of routine care, with later retrieval of FFPE tumour blocks for research purposes.

In Arm A, if there is NO CLINICAL SUSPICION OF MESOTHELIOMA after at least 18-months of reassuring clinical follow-up (Visit A5 onwards), participants may be invited to have dedicated research re-biopsy (at Visit A8). At this timepoint, only LAT, US-guided and CT-guided biopsies may be used. VATS is not deemed acceptable due the additional risks related to general anaesthesia.

In Arm B, only LAT or VATS may be used for acquisition of dedicated multi-region pleural biopsies alongside diagnostic sampling for suspected mesothelioma. The selection between LAT and VATS is at the discretion of the clinician in charge/site PI.

Site activities should be confirmed during site set-up and can be clarified at any time via the local PI or the PREDICT-Meso Project Manager: Alexandrea.Macpherson@glasgow.ac.uk

4 Responsibilities

The site PI and delegated clinical members of the research team are responsible for ensuring that biopsy procedures at their centre are performed in accordance with these instructions. Please read this manual carefully and contact the Project Manager with any questions. Please ensure that you complete and return the declaration at the end of this document (Section 16) stating that you have received, read and understood this manual.

5 Related Documents

- Clinical Study Protocol: Meso-ORIGINS
- Meso-ORIGINS Sample Handling Manual
- Meso-ORIGINS US Manual
- Meso-ORIGINS MRI Manual
- Meso-ORIGINS Exhaled Breath Sampling Manual

6 Arm A

In Arm A, repeat pleural biopsies may be performed at any time following consent and registration if there is CLINICAL SUSPICION OF MESOTHELIOMA. At CLINICAL SUSPICION OF MESOTHELIOMA, the re-biopsy procedure occurs within clinical care and any biopsy method may be used. This selection is at the discretion of the clinician in charge/site PI, but thoracoscopic (LAT or VATS) sampling is preferred when feasible. **Dedicated research biopsies are not acquired at this time point but routine care FFPE tumour blocks must be retrieved and sent to the PREDICT-Meso RTB as soon as possible after sampling and diagnostic testing has been completed**.

7 Arm B

7.1 Local Anaesthetic Thoracoscopy (LAT)

7.1.1 Pre-LAT Assessment and Safety Procedures

Assessment regarding the safety and feasibility of LAT should be performed. This will include an ultrasound scan and appropriate blood tests occurring as part of routine care at Visit B1. The following guide is not meant to replace existing pre-LAT checklists in participating units, but should serve as a minimum standard:

- Review blood results, including full blood count, coagulation screen, renal function and Group and Save (G&S). Ensure the G&S is valid and in date. *Note that a second G&S may be required in some centres*
- Update ECG as appropriate
- Review the patient's medication list. Note:
    - Warfarin should have been stopped at least 3 days pre-procedure and a normalised INR must be confirmed before LAT
    - Clopidogrel must be stopped at least 7 days pre-procedure
    - All DOACs must be stopped at least 2 days pre-procedure
    - Aspirin can be continued
- Ensure the patient has been appropriately fasted (at least 6 hrs prior to procedure time)
- Review the patient's understanding of procedure, answer any questions and complete procedural consent form *(this may be done pre-admission if this is local policy)*
- Secure IV access
- *Prescribe appropriate medications, according to local policies,* including pre-medication, post-procedure analgesia and VTE prophylaxis
- Nursing staff should record routine observations pre-procedure (HR, BP, RR, SaO_2, Temp)

7.1.2 Location and Staffing

LAT should be performed in a suitable location *as per local arrangements* (ideally an endoscopy suite or theatre) to ensure sterile conditions can be maintained throughout. Minimum staffing should include:

- Primary operator: Suitably trained, independent operator, with experience in Level II LAT, including use of a Boutin needle for pneumothorax induction
- Scrub nurse: One suitably trained nurse to assist the first operator during the procedure
- A third adequately trained member of the team to administer IV sedation and analgesia where necessary is also required. This member of staff may be medical or nursing
- A *second nurse* acting as a 'runner' is also recommended. This team member can assist with non-sterile duties, e.g. performing observations, changing fluids, opening equipment packs

7.1.3 Instruments and Equipment

All LAT procedures in Meso-ORIGINS should be carried using *existing instruments and equipment at each site.* Minimum requirements should include:

- Sterile gowns and gloves
- Sterile needles and syringe for local anaesthetic administration
- Surgical cut down kit including, scalpel and blunt forceps
- Rigid or semi-rigid thoracoscope
- Boutin-type needle
- Port with Conical tip trocar and cannula
- Cold light source
- Optical biopsy forceps (double spoon) for use with rigid thoracoscope or appropriate disposable biopsy forceps for use with semi-rigid kit
- De-mister - either via thoracoscope warmer or suitable sterile de-misting solution
- Chest drain (at least 20F), tubing and bottle
- Sutures
- Chest drain dressing
- Sterile Talc or Indwelling Pleural Catheter (IPC)

7.1.4 Positioning, Ultrasound & Site Preparation

The patient should be positioned in the lateral decubitus position with the affected side lying superiorly. The patient should be made as comfortable as possible. It is recommended that at least one pillow is placed under the head and a further pillow placed underneath the dependant ribcage to avoid unhelpful rib crowding on the affected side. The patient's arms should be flexed and rested in front of their face or extended straight using an arm support.

On-table ultrasound should be performed after position and before access. This is to ensure the anatomy, including the extent of loculation has not changed since screening and to facilitating surface marking, including marking of the optimal site of safe access.

On-table US should be focused in the safe triangle. If no fluid is visible, lung sliding in at least one position should be confirmed by a suitably trained operator before proceeding. The diaphragm should then be identified, and its position marked. On the left side, the cardio-pleural angle should also be identified by a surface marking. Finally, a suitable entry site within the safe triangle should be marked.

A sterile field should then be created. The operator performing the LAT must wash their hands using a standard surgical scrub technique before donning sterile gloves and gown. The patient's skin at the access site should be thoroughly cleaned using an *iodine-based solution or equivalent* as per local protocol. The site should be dressed using sterile drapes applied.

7.1.5 Anaesthesia and Access

1-2% lidocaine (+/- adrenaline) should be used to anaesthetise the skin and subcutaneous tissues down to the parietal pleura. The quoted maximum dose of 3mg/kg should not be exceeded. Once the skin and underlying tissue have been adequately anaesthetised, an incision in the same plane as the underlying rib should be made. This should be just deep enough to expose underlying subcutaneous fat and just long enough to allow blunt dissection and subsequent entry of the thoracoscopy port.

Pneumothorax induction may be required in the context of small or minimal pleural effusion, and should not dissuade proceeding with LAT. This can be *+/- direct ultrasound guidance* (as per Corcoran et al, Thorax 2015), based on the primary operator's current practice.

Placement of a Boutin-type needle for pneumothorax induction should include initial shallow penetration using the sharp obturator. Prior to insertion into the intercostal space, the blunt obturator should be swapped in, allowing safe access to the pleural cavity. Once the parietal pleural has been punctured, the blunt obturator should be removed to allow entrainment of air into the pleural cavity. Ten breaths should be counted to allow a sufficient volume of air to enter the space before replacing the blunt obturator, screwing it in place and removing the needle.

Blunt dissection should then be performed to create a tract suitable for placement of the thoracoscopy port. This should be done with blunt forceps as per standard practice. Following blunt dissection, it should be possible to insert the port with no (or minimal) resistance.

7.1.6 Inspection & Pleural Fluid Sampling

Insertion of the thoracoscope should be preceded by removal of any pleural effusion using a flexible suction catheter. At Visit B2, samples of this pleural fluid should be collected and processed as Section 7.1.10. Systematic visual inspection of the pleural cavity (including costal surface, diaphragm, apex, lung surface) should then be performed.

Any abnormalities should be documented on the corresponding Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3). If the lung fails to deflate sufficiently to allow full inspection, operators are advised to:

a) ensure any fluid sitting on the mediastinal surface has been completely removed by reinserted the suction catheter around the posterior and anterior borders of the lung

b) Remove the thoracoscope and allow a larger volume of air to enter the pleural cavity during free breathing: to facilitate this the tip of the port should be directed upwards

7.1.7 Biopsy Sampling

At Visit B2, **4-6 dedicated research biopsies** should be taken from different sites of **visible parietal pleural abnormality**, in addition to clinical biopsies. The number of clinical biopsies taken should be at the discretion of the primary operator. Clinical biopsies should be placed into standard clinical pots and processed as per local policies. IV analgesia should be given pre-biopsy.

Research biopsies should ideally be taken from a range of pleural anatomical zones, as defined on the Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3). These should not include areas of visceral pleura. The sampling of diaphragmatic sites is permitted, but caution is advised unless large, polypoid and easily sampleable disease is identified. Research biopsies should be collected and handled as per the Meso-ORIGINS Sampling Handling Manual.

Specific Guidance for Arm B LAT Research Biopsies:

- Six formalin-filled research biopsy pots are provided in the Visit B2 pack.
- Label these pots #1, #2, #3, #4, #5, #6 prior to use
- **Samples from a single site must be put in a single numbered research biopsy pot**
- Biopsies from different sites should **neve**r go in the same pot
- **Note:** Multiple biopsies might be taken from the same site, e.g., to get deeper biopsies. 'Re-biopsying the biopsy site' is a standard approach and samples acquired in this way should be considered as a single site - i.e these multiple samples should go in the same pot.
- If biopsies are taken from a different site, even if this is in the same pleural zone - a new biopsy pot must be used.
- The six research biopsy pots provided in the visit pack are not sterile, and should only be introduced into the sterile field in a sterile container, e.g., a gallipot
- Research Biopsy Pot #1 should be opened and placed inside this gallipot (or other suitable vessel) within reach of the operator acquiring the biopsies

- Tissue samples should be removed from biopsy forceps using a sterile needle, tweezers or other suitable method, before placement into Research Biopsy Pot #1
- The biopsy forceps should not be dipped into the biopsy pot, unless they are rinsed to remove formalin before the scope is inserted back into the patient
- Once sampling at the first research site has been completed, the lid on Research Biopsy Pot #1 should be secured tightly.
- The pot can then be lifted out of the sterile gallipot by a non-sterile assistant and replaced with Research Biopsy Pot #2, which should be opened, ready to accept samples
- The process should be repeated until up to 6 research sites have been sampling, filling up to 6 research biopsy pots
- The Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3 of the Meso-ORIGINS Biopsy Manual) must be completed. For each biopsy site record: the pot number, the corresponding zone, and any visible pleural abnormalities. The form also records the number of clinical biopsies taken.
- All biopsy pots containing research samples (up to 6) should be placed back inside the sealable plastic bag provided in the visit pack, alongside a local pathology department request form **highlighting that these are research biopsies, and NO DIAGNOSTIC ANALYSES ARE TO BE PERFORMED – ONLY FFPE BLOCK CREATION.**
- The FFPE blocks generated should be stored at room temperature in local pathology, before shipping to the PREDICT-Meso Research Tissue Bank (RTB) as soon as possible after collection. This retrieval activity is part of Visit B3. See Meso-ORIGINS Sample Handling Manual section 13 for shipping details.

7.1.8 Drain Placement and Pleurodesis

Once the operator is satisfied that all necessary biopsies have been taken, a final visual inspection of the pleural cavity should be performed, to ensure haemostasis at each biopsy site and to plan drain placement. Talc poudrage or IPC placement can be considered at the discretion of the primary operator.

Care should be taken to minimise the time between removal of the thoracoscope and associated port and insertion of the chest drain, given the potential for the lung to re-expand during this interval. An intercostal drain (at least 20F is recommended but can be as per local policy) should be inserted via the port access site and directed to the lung apex, if possible. Operators may also choose to direct the drain using a guidewire inserted via the port prior to its removal, e.g., in cases where blunt dissection was technically challenging.

Once the drain is in place, it should be connected to an underwater seal or electronic drainage system (e.g., Thopaz®) depending on local policies. The drain should be secured, ideally by 2 sutures, which should also tighten the wound around the tube. The site should be cleaned of any blood before the application of a suitable dressing.

7.1.9 LAT Report

All LATs should be *documented as per local policy* in patient notes +/- electronic systems. In addition, the Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3) must be completed.

This worksheet should be uploaded onto local electronic health records to act as source data for the procedure that will be common to all sites. The completed worksheet data must also be inputted to the Meso-ORIGINS MACRO® database.

7.1.10 LAT Pleural Fluid Sample Processing and Storage

A total of 200 ml of pleural fluid should be collected and processed as described in the Meso-ORIGINS Sample Handling Manual. These samples should be split into 4 x 50 ml aliquots, generating the following:

- 1 x Unprocessed 50 ml sample for generation of cell lines (participating sites only)
- 1 x Unprocessed 50 ml sample for banking
- 2 x Processed 50 ml sample for Cell Pellet and Supernatant Banking

7.1.11 Electronic transfer system

Linked anonymised LAT reports should be transferred as .pdf files, annotated by the participant's unique study ID and the date of LAT using the University of Glasgow Transfer Service (https://transfer.gla.ac.uk/).

This is a secure system with all files transferred in an encrypted format and access strictly controlled and logged. Data files will be uploaded to the service in a password-protected encrypted archive format. See Appendix 4 for full instructions on the labelling transfer process.

7.1.12 Drain Removal, Discharge and Follow-up

The intercostal drain should be removed once maximum lung re-expansion has been achieved on a chest radiograph acquired 1-12 hours after LAT. Ideally, discharge should occur on the same day as the procedure. Where clinically indicated, or for logistical reasons, patients may be admitted to hospital overnight after LAT. Patients should be provided with written details of their follow-up appointment (venue, date, time) to discuss LAT results (Visit B3) prior to discharge home.

7.2 Video-Assisted Thoracoscopy Surgery (VATS) Thoracoscopy

7.2.1 Location and Staffing

VATS should be performed in an operating theatre to ensure sterile conditions can be maintained throughout the procedure. Minimum staffing should include:

- Primary operator: Suitably trained, independent operator should be present at all times.
- Anaesthetist: Responsible for induction and maintenance of general anaesthesia.
- Scrub nurse: One suitably trained nurse to assist the first operator during the procedure
- A *second nurse* acting as a 'runner'; available to assist with any non-sterile duties, e.g., performing regular observations, changing fluids, opening equipment packs

7.2.2 Instruments and Equipment

All VATS procedures in Meso-ORIGINS should be carried using *existing instruments and equipment at each site*. Minimum Instrument and Equipment requirements should include:

- Sterile gowns and gloves
- Sterile needles and syringe for local anaesthetic administration
- Surgical cut down kit including, scalpel and blunt forceps
- Rigid or semi-rigid thoracoscope and appropriate biopsy forceps
- Port with Conical tip trocar and cannula
- Cold light source
- Chest drain (at least 20F), tubing and bottle, dressings
- Sutures

7.2.3 Positioning and Site Preparation

The patient should be positioned in the lateral decubitus position with the affected side lying superiorly. A sterile field must be created, including use of an *iodine-based solution or equivalent* as per local protocol. The site should be dressed using sterile drapes applied.

7.2.4 Access

Access should use standard VATS methodology. One or two ports may be inserted depending on local policy.

7.2.5 Inspection & Pleural Fluid Sampling

Insertion of the thoracoscope should be preceded by removal of any pleural effusion using a flexible suction catheter. Samples of pleural fluid should be collected and processed as per Section 7.2.9. Systematic visual inspection of the pleural cavity (including costal surface, diaphragm, apex, lung surface) should then be performed. Any abnormalities should be documented on the corresponding Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3).

7.2.6 Biopsy Sampling

At Visit B2, **4-6 dedicated research biopsies** should be taken from different sites of **visible pleural abnormality,** in addition to clinical biopsies. The number of clinical biopsies taken should be at the discretion of the primary operator. Clinical biopsies should be placed into standard clinical pots and processed as per local policies.

Research biopsies should ideally be taken from a range of pleural anatomical zones, as defined on the Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3). These **may include areas of visceral pleura** at the discretion of the primary operator**.** Research biopsies should be collected and handled as per as per the Meso-ORIGINS Sampling Handling Manual.

Specific Guidance for Arm B VATS Research Biopsies:

- **Six formalin-filled research biopsy pots are provided in the Visit B2 pack**
- Samples from a single site **must** be put in a **single numbered research biopsy pot**
- Biopsies from different sites should **neve**r go in the same pot
- **Note:** multiple biopsies might be taken from the same site, e.g., to get deeper biopsies. 'Re-biopsying the biopsy site' is a standard approach and samples acquired in this way should be considered as a single site – these multiple samples should go in the same pot.
- If biopsies are taken from a different site, even if this is in the same pleural zone – a new biopsy pot must be used.
- The six research biopsy pots provided in the visit pack are not sterile, and should only be introduced into the sterile field in a sterile container, e.g., a gallipot
- Research biopsy pot #1 should be opened and placed inside this gallipot (or other suitable vessel) within reach of the operator acquiring the biopsies
- Tissue samples should be removed from biopsy forceps using a sterile needle, tweezers or other suitable method, before placement into research biopsy pot #1
- The biopsy forceps should not be dipped into the biopsy pot, unless they are rinsed to remove formalin before the scope is inserted back into the patient
- Once sampling at the first research site has been completed, the lid on research biopsy pot #1 should be secured tightly.
- The pot can then be lifted out of the sterile gallipot by a non-sterile assistant and replaced with Research Biopsy Pot #2, which should be opened, ready to accept samples

- The process should be repeated until up to 6 research sites have been sampling, filling up to 6 research biopsy pots
- The Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3 of the Meso-ORIGINS Biopsy Manual) must be completed, including any visible pleural abnormalities, the sites that research biopsies were taken from and the pots used for each site. The form also records the number of clinical biopsies taken
- All biopsy pots containing samples (up to 6) should be placed back inside the sealable plastic bag provided in the visit pack, alongside a local pathology department request form **highlighting that these are research biopsies, and NO DIAGNOSTIC ANALYSES ARE TO BE PERFORMED – ONLY FFPE BLOCK CREATION.**
- The FFPE blocks generated should be stored at room temperature in local pathology, before shipping to the PREDICT-Meso Research Tissue Bank (RTB) as soon as possible after collection. This retrieval activity is part of Visit B3. See Meso-ORIGINS Sample Handling Manual section 13 for shipping details.

7.2.7 Drain Placement and Pleurodesis

Once the operator is satisfied that all necessary biopsies have been taken, a final visual inspection of the pleural cavity should be performed, to ensure haemostasis at each biopsy site and to plan drain placement. Talc poudrage or IPC placement can be considered at the discretion of the primary operator.

An intercostal drain (at least 20F is recommended but can be as per local policy) should be inserted via the port access site and directed to the lung apex, if possible.

Once the drain is in place, it should be connected to an underwater seal or electronic drainage system (e.g., Thopaz®) depending on local policies. The drain should be secured, ideally by 2 sutures, which should also tighten the wound around the tube. The site should be cleaned of any blood before the application of a suitable dressing.

7.2.8 VATS Thoracoscopy Report

All VATS Thoracoscopies should be *documented as per local policy* in patient notes +/- electronic systems. In addition, the Meso-ORIGINS Arm B Thoracoscopy Worksheet (Appendix 3) must be completed.

This worksheet should be uploaded onto local electronic health records to act as source data for the procedure that will be common to all sites. The completed worksheet data must also be inputted to the Meso-ORIGINS MACRO® database.

7.2.9 VATS Pleural Fluid Processing and Storage

A total of 200 ml of pleural fluid should be collected and processed as described in the Meso-ORIGINS Sample Handling Manual. These samples should be split into 4 x 50 ml aliquots, generating the following:

- 1 x Unprocessed 50 ml sample for generation of cell lines (participating sites only)
- 1 x Unprocessed 50 ml sample for banking
- 2 x Processed 50 ml sample for Cell Pellet and Supernatant Banking

7.2.10 Electronic transfer system

Linked anonymised VATS reports should be transferred as .pdf files, annotated by the participant's unique study ID and the date of LAT using the University of Glasgow Transfer Service (https://transfer.gla.ac.uk/).

This is a secure system with all files transferred in an encrypted format and access strictly controlled and logged. Data files will be uploaded to the service in a password-protected encrypted archive format. See Appendix 4 for full instructions on the labelling and transfer process.

7.2.11 Drain Removal, Discharge and Follow-up

The intercostal drain should be removed once maximum lung re-expansion has been achieved on a chest radiograph acquired 1-12 hours after VATS Thoracoscopy. Ideally drain removal and discharge should occur on the same day as the procedure. However, it is acknowledged that overnight admission may be standard practice in some centres after VATS. Patients should be provided with written details of their follow-up appointment (venue, date, time) to discuss LAT results (Visit A9) prior to discharge home.

8 Declaration

I confirm that I have received, read and understood this manual (insert version number)

Site:_____

Site PI Name:_____

Signature: _____

Date: _____

Please return this declaration to the Project Manager Alexandrea.macpherson@glasgow.ac.uk

Appendix 1 – Arm B Thoracoscopy Worksheet

MESO-ORIGINS
THORACOSCOPY WORKSHEET: Arm B, Visit B2

ISRCTN22929761

Meso-ORIGINS: **Meso**thelioma **O**bservational study of **RI**sk prediction and **G**eneration of paired benign-meso tissue samples, **I**ncluding a **N**ested MRI **S**ub-study

Patient Initials: (F) ____ (S) ____	**Date of Birth:** *DD* / *MON* / *YYYY*	**Study Number:**

GENERAL

Side: o Right o Left **Procedure Type** o LAT o VATS

Septations: o Yes o No

Volume drained:_____ ml

PROCEDURE DETAILS

DRUG	**OPTION (please ü)**	**DOSE**
Pre-medication	o **Oramorph**	**_____mg**
	o **Atropine**	**_____mg**
	☐ **Sevredol**	**_____mg**
	☐ **Other, specify *(incl unit)*: _____**	**_____**
Sedation	☐ **Midazolam**	**_____mg**
	☐ **Propofol**	**_____mg**
	☐ **Other, specify *(incl unit)*: _____**	
	☐ **General Anesthesia**	
Local anaesthetic	☐ **Lidocaine** ☐ **1%** ☐ **2%** **_____ml** ☐ **Adrenaline inclusion**	
	☐ **Other, specify *(incl unit)*: _____**	**_____**
Analgesia	☐ **Alfentanyl**	**_____micrograms**
	☐ **Fentanyl**	**_____micrograms**
	☐ **Morphine**	**_____mg**
	☐ **Other, specify *(incl unit)*: _____**	**_____**

US on table: ☐ Yes ☐ No **Boutin with US:** ☐ Yes ☐ No

Fluid on US: ☐ Yes ☐ No ☐ N/A **Talc:** ☐ Yes ☐ No **If yes, dose given:**_____ g

Boutin induction: ☐ Yes ☐ No **Drain size:** _____**F**

IMMEDIATE COMPLICATIONS: IF NONE TICK HERE ☐

Haemorrhage requiring transfusion: ☐ Yes ☐ No **Failure of procedure:** ☐ Yes ☐ No

Hypotension requiring intervention: ☐ Yes ☐ No **Other** ☐ **Yes specify:**_____

BIOPSY DETAILS

RESEARCH BIOPSIES Ideally 4-6 from different zones				CLINICAL BIOPSIES	
POT	**ZONE**	**APPEARANCE**		**ZONE**	**APPEARANCE**
#1					
#2					
#3					
#4					
#5					
#6					

RECORD APPEARANCE IN ZONES AS:

- MACRO - macroscopic nodules
- MICRO - microscopic nodules
- THICK - pleural thickening
- PLAQUE – calcified pleural plaque
- NORMAL – no abnormality seen

BIOPSY SAMPLING

- See Biopsy Manual Section 7.1.7

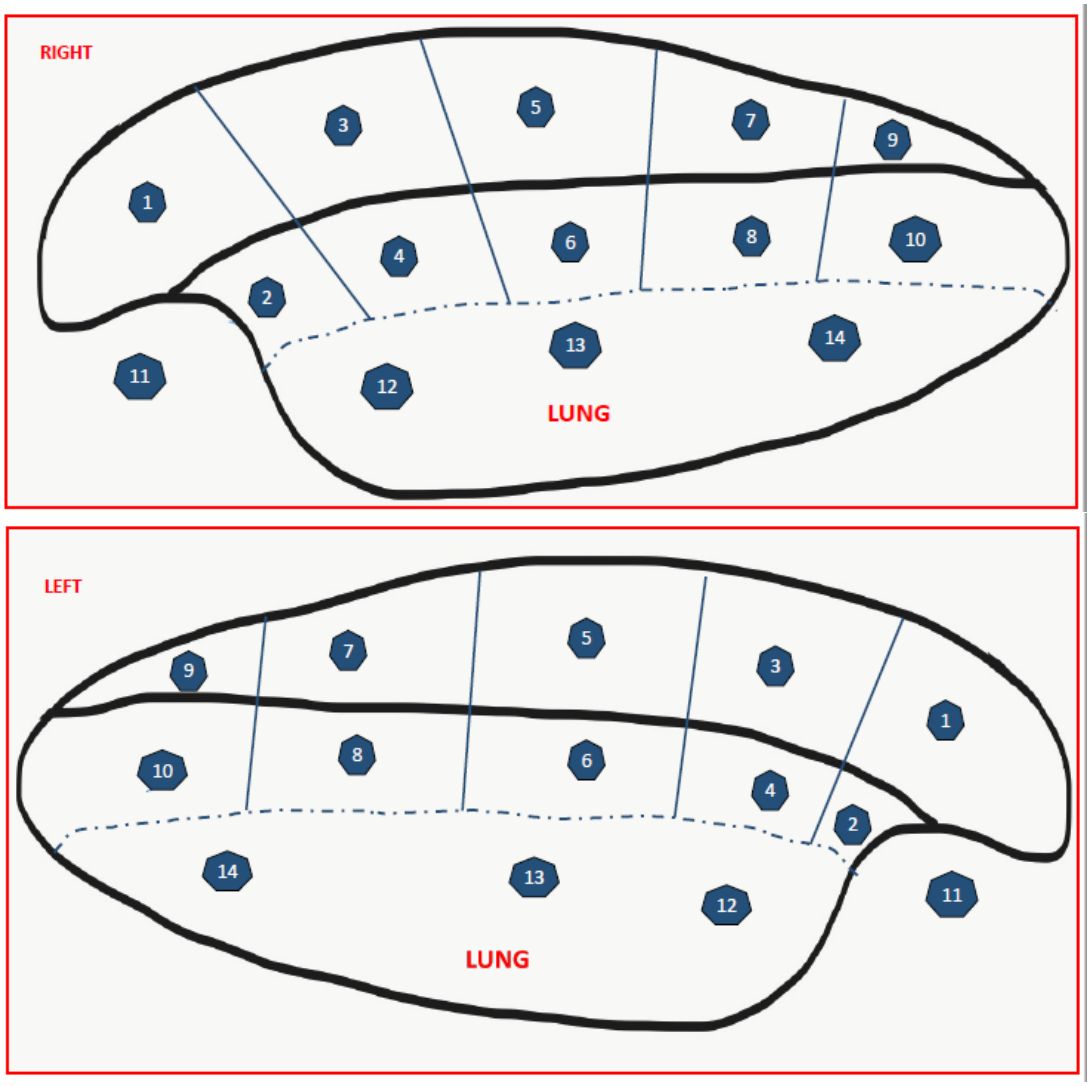
RESEARCH BIOPSIES:

- Six pots are provided in the visit pack.
- Label the biopsy pots #1, #2, #3, #4, #5, #6. Along with Study ID and Visit (e.g. MO-001, B2, #4)
- **Samples from a single biopsy site must be put in a single numbered biopsy pot.**
- Multiple biopsies might be taken from the **same site** to get deeper biopsies - use the **same pot**.
- If biopsies are taken from a **different site** in the same zone - use a **different pot**.
- **Biopsies from different sites should NEVER GO IN THE SAME POT.**
- Record the zone and appearance of each biopsy site

CLINICAL BIOPSIES:

- Clinical biopsies should be sent in a **separate biopsy pot** (not provided) for **normal diagnostic processing**
- Number of clinical biopsies at operator discretion.

NOTES ON PLEURAL ZONE MAP BELOW: Odd-numbered parietal zones correspond to upper half of field of view. The dashed line = the visceral surface of the lung. Zone 11=Diaphragm. Zones 12-14=RLL, RML & RUL on right; LLL, Lingula & LUL on left



INVESTIGATOR SIGNATURE: _____ **DATE:** *DD* / *MON* / *YYYY*

Appendix 2 - Glasgow University Transfer Service User Instructions

Data export and secure transfer

Electronic transfer system

Linked anonymised data in the agreed format will be transferred using the University of Glasgow Transfer Service (https://transfer.gla.ac.uk/). This is a secure system with all files transferred in an encrypted format and access strictly controlled and logged.

Drop off requests will be sent to the nominated site contact by email from the PREDICT-Meso Project Manager Alexandrea.MacPherson@glasgow.ac.uk

To request a drop off request, please contact Alexandrea.MacPherson@glasgow.ac.uk

Data upload format

Files should be labelled as follows:
MO Patient study ID number. Visit (eg A1). Procedure (eg LAT or VATS)
Example: MO-001.A1.LAT or MO-123.B2.VATS

All files for a single participant should be packaged into a folder labelled with the appropriate Participant Study ID (e.g MO-001, MO-002). Given the large size of this folder, for transfer purposes each folder should be compressed and sent as a zipped file (e.g. using *WinZip* or *7-Zip*).

Virus checking

Please note that the uploaded files are scanned for viruses but the recipient should still exercise as much caution in downloading and opening them as is appropriate.

Confidential information

Whilst the transfer service has features that make it more secure than email, any information that is confidential should be encrypted.

The request will be set up so that data files uploaded to the service will be in a password-protected encrypted archive format. The password will be set by the requestor and sites do not have to action this.

Glasgow transfer service user instructions

You will receive an email from [UofG Transfer] that contains details of the request and a link to the transfer platform for file drop off. Example below:

[UofG Transfer] Meso-ORIGINS Image files transfer request

University of Glasgow File Transfer <filetransfer@gla.ac.uk>
Mon 06/09/2021 16:40
To: You

This is a request from Alexandrea MacPherson of University of Glasgow.
Please click on the link below and drop off the file or files I have requested.The link is only valid for 7 days from the time of this email.More information is in the note below.
https://transfer.gla.ac.uk/req?req=144974529

If you wish to contact Alexandrea MacPherson, just reply to this email.
* Note *
Please upload the study images for Meso-ORIGINS. Files should be transferred as DICOM files and labelled as follows:
Patient trial ID number. Site registration number. Visit (eg A1). Image type (eg CT or X-ray) Example: 1234.002.A1.CT
Please use this naming convention in the description request also.

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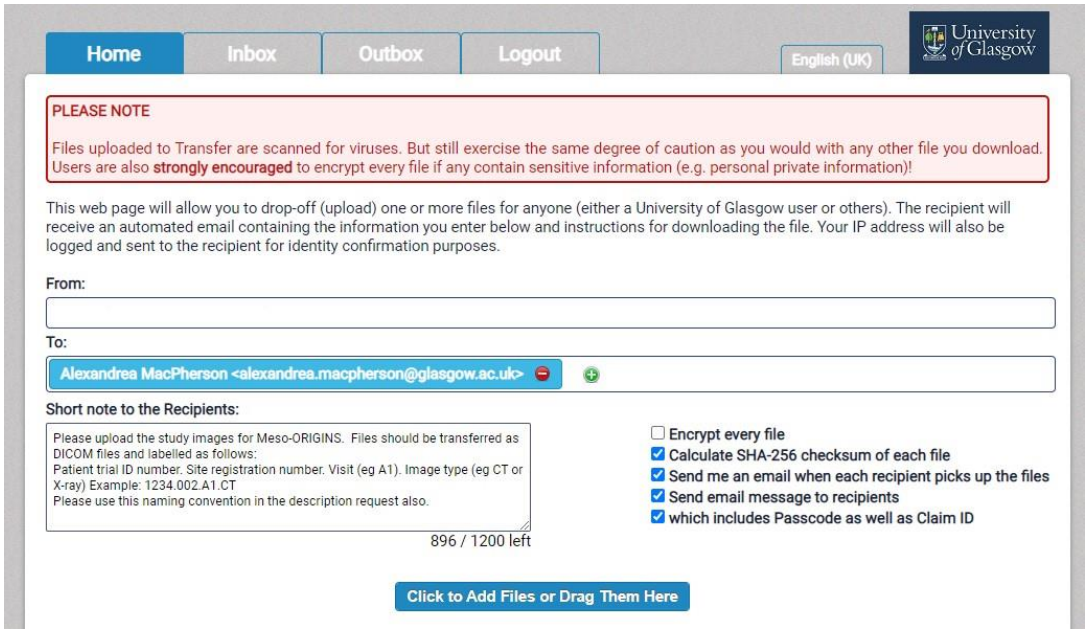
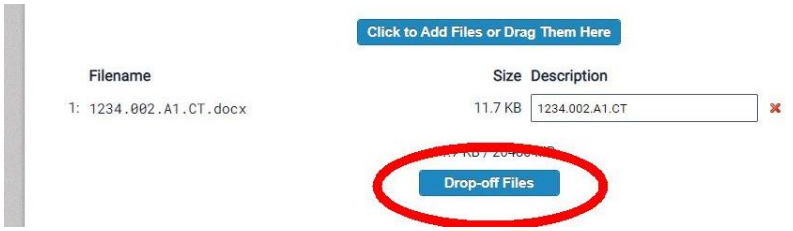
Alexandrea MacPherson
alexandrea.macpherson@glasgow.ac.uk
University of Glasgow

Requests are valid for 7 days, please complete in this window.

Upon clicking the link, you will be taken to the following page:



1. Click the blue button to add your files, or drag them over the button.
2. A file description is requested- please use the file name using the naming convention above.
3. Once complete a new blue ‘drop off files’ button will appear. Press this to drop-off files.



If the files are successfully uploaded, an email is sent to the recipient explaining that a drop-off has been made with a link to access the drop-off.

Other information (the internet address and/or hostname from which the drop-off was created, for example) is retained, so that the recipient can verify the identity of the sender.

Once the recipient has collected the files, you will be sent an automated email to let you know your drop off has been collected.