

Online Supplementary Appendix 1

Pre-EDIT Study: Survey of Patient Treatment Preferences for Symptomatic Malignant Pleural Effusion

Introduction

Thank you for agreeing to take part in this survey of treatment preferences. Please read the treatment summary below before answering the questions on the following page. If there is anything you do not understand, please ask the research doctor or nurse for more information.

Treatment Information Summary

There are currently 2 main ways to treat breathlessness caused by a Malignant Pleural Effusion. These are called 'talc pleurodesis' and 'IPC insertion'. IPC stands for Indwelling Pleural Catheter. Both are effective treatments and your doctors will have discussed these options with you. We have provided some written information about the advantages and disadvantages of each and are keen to learn more about the factors involved in the treatment decision you have made.

Talc Pleurodesis

Talc pleurodesis involves draining all of the fluid out of your chest using a small plastic tube called a chest drain. X-rays are used to assess whether the lung has re-expanded and made contact with the ribcage. Once this happens, sterile medical talcum powder (talc) is flushed down the chest drain and acts as a glue to fuse the lung surface to the ribcage. The drain is then removed. This process takes several days and requires an admission to hospital (for an average of 4-7 days). Talc Pleurodesis is successful in about 70% of people, in that it prevents the fluid from building up again and further procedures are not required.

One of the main problems with talc pleurodesis is that the lung does not fully inflate after fluid is drained in about 1 in 4 patients. This means that lung cannot be glued to the ribcage and in many patients the fluid will come back and a further drain will be required. Importantly, we cannot currently tell you before draining the fluid whether your lung will reinflate or not. This means 1 in 4 patients spend several days in hospital but do not get any talc put into their chest.

IPC Insertion

An IPC, or Indwelling Pleural Catheter, is a type of soft plastic drain which is tunnelled under the skin and can be drained at home by district nurses or a family member. Between drainages it is covered by a discrete dressing and is not attached to anything. IPCs can help your breathing even if your lung does not re-inflate after fluid is removed. They can be inserted as a day case under local anaesthetic, meaning a stay in hospital is not required.

Table summarising the pros and cons of Talc Pleurodesis vs IPC Insertion

	Talc Pleurodesis	IPC Insertion
FOR	Lower risk of infection	Can be inserted as day case (or 1 night stay)
	If it works, there is no need for long term drain	May improve breathlessness if your lung doesn't re-expand after fluid drainage
AGAINST	Requires 4-7 day stay in hospital	Higher risk of infection (5-10%)
	The lung needs to reinflate for it to work (will not happen in around 1 in 4 patients)	Care of drain site required and a 'reminder' of illness

The main drawback is that the drain needs to stay in for a long time, often indefinitely. Although in about 4 out of 10 patients, their IPC can be removed at some point as the fluid dries up. Some patients find an IPC inconvenient as it can interfere with daily activities such as swimming or bathing. Others do not like the hassle of a tube, or having a daily reminder of their illness. IPCs can also get infected. Because the drain is in for longer this risk is higher than for talc pleurodesis drains. Usually, infection can be treated without removing the IPC but this may require a lengthy hospital admission and prolonged antibiotics.

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SURVEY QUESTIONS

- 1. Having discussed the options with your doctor, read the attached information and had the opportunity to ask questions, do you think you have enough information to make a decision about your treatment?**

Please tick one box

Yes

No

- 2. Which of the following would you prefer to treat your malignant pleural effusion?**

Please tick one box

Talc Pleurodesis

IPC Insertion

} **go to question 3**

I would be happy to have either

I'm still not sure

} **go to question 4**

- 3. What was the main reason for choosing this treatment?**

Please circle the single most important reason in the table below

	Talc Pleurodesis	IPC Insertion
FOR	Lower risk of infection	Can be inserted as day case (or 1 night stay)
	If it works, there is no need for long term drain	May improve breathlessness if your lung doesn't re-expand after fluid drainage
AGAINST	Requires 4-7 day stay in hospital	Higher risk of infection (5-10%)
	The lung needs to reinflate for it to work (will not happen in around 1 in 4 patients)	Care of drain site required and a 'reminder' of illness

Or if there is another reason for your answer not in the table, please write this in the box below:

- 4. If you would be happy to have either treatment or still aren't sure which to choose, please write down which advantage or disadvantage you think is most important.**

Please write in the box below

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- 5. In the future, doctors may be able to routinely put talc 'glue' down an IPC. Research suggests that this would probably mean that about 5 out of 10 patients would be able to have their IPC removed after 10 weeks and not require any more procedures. If you answered 'Talc Pleurodesis' for question 1.a), would having this option available make you more likely to choose an IPC?**

Please tick one box

Yes, I would change my mind and choose IPC Insertion

No, I would still prefer Talc Pleurodesis

Not applicable, IPC Insertion is already my first choice

- 6. In the Pre-EDIT study we are researching the possibility of performing an extra fluid drainage procedure to take some pressure measurements from the chest before deciding which treatment (either Talc Pleurodesis or IPC) might be best. The reason for this is that if the pressure measurements show the lung will not re-expand then we think Talc Pleurodesis is far less likely to be successful and we would not recommend trying it. If the pressure measurements suggest the lung will re-expand, then we think we will be able to offer Talc Pleurodesis with a greater chance of success.**

How would you feel about having an additional procedure to remove some fluid and take pressure measurements before deciding which treatment might be best?

Please tick one box

Yes, I would not mind having another procedure if it provided useful information to help me make a decision

No, I am already happy with my decision and would rather not have another procedure

Not sure

- 7. If you have any comments you would like to make about your treatment or the process of deciding what treatment to have, please write these in the box below.**

Thank you for completing this survey, please return your completed survey to the research doctor or nurse



Acute Services Division

Regional Services Directorate

INFORMATION SHEET FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH PROJECT

Title of Project:

Pre-EDIT: A randomised, feasibility trial of Elastance-Directed Intra-pleural catheter or Talc Pleurodesis (EDIT) in the management of symptomatic Malignant Pleural Effusion without obvious non-expansile lung

Invitation Paragraph

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

A pleural effusion is a collection of fluid inside the chest. The fluid gathers in space called the pleural space which lies between the lung and the rib-cage. This often causes breathlessness and may unfortunately be caused by cancers affecting the pleural lining. This is called a 'Malignant Pleural Effusion'. The current standard treatment for this involves admitting the patient to hospital and draining the fluid over several days using a small chest tube (or 'drain'). Ideally, this allows the lung to re-expand into its normal position against the rib-cage. We can then put medical talc powder into the chest by flushing it down the chest drain which was used to empty the fluid. This talc acts like a glue and sticks the lung against the rib-cage, preventing any fluid from coming back – this process known as talc pleurodesis. In about 1 in 5 patients, talc pleurodesis fails because the lung does not re-inflate fully after fluid has been drained. This is called 'non-expansile lung'. In this situation the fluid almost always comes back.

If doctors could identify which patients had non-expansile lung at the start, they could avoid these failures and use a different method to treat these patients. IPCs (indwelling pleural catheters) are very effective at improving breathlessness in patients with non-expansile lung. However they require a different kind of chest drain and this needs to be left in the chest, often for many months. Via the IPC, fluid can be drained at home by the patient's district nurse, who needs to be trained in the technique. Insertion of an IPC therefore requires some planning and they are not suitable for all patients. Currently, doctors find it very difficult to predict which patients will have non-expansile lung and a significant number of patients will therefore have an attempt at talc pleurodesis without success. These patients are therefore exposed to the risks of the procedure and several days in hospital without any benefit.

We plan to test a new approach which involves measuring something called 'elastance' inside pleural space before a decision is made to try Talc Pleurodesis. Elastance reflects the ability of the lung to re-expand after fluid is withdrawn. Based on previous studies we think measuring elastance will allow us to accurately identify patients with non-

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expansile lung who should not be offered talc pleurodesis. We can then offer these patients insertion of an IPC instead and avoid a week in hospital and the small risks of Talc Pleurodesis. This new approach is called 'EDIT management'.

As part of EDIT management we will perform an additional local anaesthetic procedure to drain off some pleural fluid and measure elastance before making a decision between talc pleurodesis and insertion of an IPC. The device we will use to measure elastance has been fully safety tested and approved for use in people. It has therefore been given a 'CE mark' for this purpose; however it has not been used to direct management of patients before. For us to prove whether EDIT management using this new device improves the management of patients with malignant pleural effusion we will need to perform a large study, involving several hundred patients. The purpose of this study (called the pre-EDIT study) is to assess whether our proposed study methods are acceptable to patients and to gather information which will help us design the future EDIT study properly.

Ultimately, we hope EDIT treatment will mean patients will get the most useful procedure first time and avoid the risks and time in hospital caused by procedures which were not successful.

Why have I been invited to take part?

You have been invited to take part in this study because you have a collection of fluid in the chest (pleural effusion). Your doctors will have already explained that this has unfortunately been caused by cancer (a malignant pleural effusion). Your doctors will also have explained that your breathing is likely to be improved by drainage of the fluid, but that fluid will likely reaccumulate unless an additional procedure is performed to stop this. As mentioned earlier the standard approach in this situation is to attempt a talc pleurodesis and you are therefore eligible for this study.

Do I have to take part?

No, it is up to you to decide whether or not to take part. We will talk you through the study and go through this information sheet, which we will then give to you to keep. If you decide to take part, you will be asked to sign a consent form to show you have agreed to take part. If you decide to take part, you are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive or your future treatment.

What will happen to me if I decide to take part?

If you are interested in taking part in the study, we will first arrange a 'screening visit'. The purpose of this visit is to check that the study would definitely be suitable for you. We will ask you to sign a consent form before arranging this appointment, which does not commit you to anything else.

If you are an inpatient one of the team will come to see you in your ward. During the screening visit, the research doctor will perform an ultrasound scan of your chest to estimate how much fluid you have around your lung. This is a scan you will have had before as part of your normal care; it is painless and does not involve any risk. To be in the study, there needs to be a certain amount of fluid in your chest. The doctor will also run through a short list of questions to be sure you can be included. If you are eligible, the process of the study will be described to you in detail and you will have the opportunity to ask questions and think about whether you wish to be involved. If you want to go ahead, the doctor will ask you to sign a second consent form for enrolment into the study.

We will then arrange for you to be admitted to ward 7B at the Queen Elizabeth University Hospital. This ward specialises in treating patients with problems relating to fluid around the lungs. If you are in hospital in another ward, we can easily make

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arrangements for you to be transferred to ward 7B. On the ward, one of the research doctors or nurses will go through a questionnaire with you to collect details about your symptoms. They will also record some details about your medical history and test results from your hospital notes.

The pre-EDIT study (and the EDIT study which will follow it) is a 'randomised' study. This allows the research team to compare what happens to patients treated in two different ways. In this case the comparison is between 'EDIT management' and 'standard care'. The next step in the study process is therefore to randomise you between the two approaches (known as 'arms'). At this point it is important to remember that the treatment in both 'arms' will be carried out by the same people, i.e. the clinical team you already know. 'Standard Care' is the normal approach used in all patients not in the study and is the current best way to do things. 'EDIT management' is the new method, which we think may be better, but have no proof of this at present. The fact that there is genuine uncertainty about which is better makes 'randomisation' between the two approaches the right thing to do.

To perform the randomisation we will use a simple computer system. This ensures that half of the people in the study will have their effusion treated in the usual way (Standard Care) and the other half will be treated using the new method (EDIT treatment). All patients in the study will have their treatment delivered by the same team of doctors and nurses, all of whom specialise in these problems.

What happens next will depend on whether you have been allocated to 'Standard Care' or 'EDIT treatment'

- In patients receiving 'Standard Care' a chest drain will be inserted using local anaesthetic to ensure you are comfortable throughout this. All of the fluid will be drained over the next few days on the ward. If the lung re-expands then medical talc will be flushed down the chest drain to prevent the fluid from coming back (i.e. a talc pleurodesis will be performed if possible). If the lung does not fully re-expand after the fluid has been drained the drain will be removed and you will be able to go home. You will then be followed up carefully in the clinic.
- In patients receiving 'EDIT treatment', pleural elastance will be measured before any decision is made to try a talc pleurodesis. This will be done during an additional fluid drainage procedure using local anaesthetic to ensure you are comfortable. After this, the doctor will use the elastance measurements to work out whether or not your lung is likely to re-expand after fluid is drained. If it is likely to re-expand, they will then insert a standard chest drain and attempt a talc pleurodesis (like all of the patients receiving 'Standard Care'). However, if your lung is not likely to re-expand based on the elastance measurements, they will insert an indwelling pleural catheter (IPC) as described earlier. If you have an IPC inserted you will go home as soon as you are comfortable with this device (usually the next day).

Patients receiving 'EDIT treatment' will also have an MRI scan before and after elastance measurements are made. This is to allow us to check that the ultrasound measurements made during the screening visit are accurate and the elastance measurements made were correctly calculated using the new device.

For patients receiving 'Standard Care' we would expect you to stay in hospital for 5-7 days. We expect that most patients receiving 'EDIT treatment' will stay in for a similar length of time, but those treated with an IPC will probably go home much sooner, probably the following day.

We would like to see all patients back for a follow-up visit to see how they are doing. We will collect details on your symptoms and whether or not you have needed any further

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treatment for pleural effusion. Wherever possible, we will arrange this to fit in with one of your routine hospital follow-up appointments. You will also be asked to record some pain and breathlessness questionnaires once per week for 4 weeks once you have gone home.

What do the MRI scans involve?

The MRI scans will be performed at the Glasgow Research Imaging Facility at the Queen Elizabeth University Hospital. The first scan should take no more than 45 minutes and the second one will be much shorter, approximately 20 minutes.

On arrival at the MRI department a radiographer will go through a safety checklist and make sure that all magnetic objects (e.g. jewellery and bankcards) have been removed. Following this you will be asked to complete and sign a safety questionnaire. If there is felt to be a risk of small metal fragments in your eyes based on previous work or hobbies you may also need to have an xray to exclude these prior to having the MRI scan. The amount of radiation involved in this xray is minimal and considered completely safe.

You will be given a hospital gown to change into and then asked to lie flat on an electric bed that will move you into the scanner. The scanner is basically long and tunnel shaped. You are gently slid into the centre of the tunnel on a moving bed and the scan pictures are taken. Some people find it a little enclosing, but you can come out at any time. If you are claustrophobic please tell staff.

When you are in the scanner you will need to wear a pair of headphones, allowing you to listen to music of your choice (you are welcome to bring your own CD) and allowing us to communicate with you. The headphones are also necessary because of the loud knocking noise that occurs when the pictures are being taken. You will be given an emergency buzzer and can very quickly be taken out of the scanner should you feel uncomfortable or if it is felt necessary. During the scan you will be asked to hold your breath at times (to give a crisp picture) and to take some deep breaths in and out (so we can see how much your lung moves whilst the fluid is still there). A doctor will be in the control room throughout this procedure.

What are the possible benefits of taking part?

It is possible that those patients who receive EDIT treatment will be less likely to have failed treatment and need further procedures. However, it is important to stress that this is not yet proven and will need tested in a larger study (the EDIT study) if the current study (pre-EDIT) shows promising results.

Even if we don't find that the EDIT treatment works well, it will give researchers extremely useful information which may help guide future treatments and help us to know how they should be tested. This may be of benefit to other patients in the future.

What are the potential risks in taking part?

There are risks with all medical procedures, including those given as part of 'Standard Care', but the chances of a serious complication are low. National guidelines will be followed to minimise risk. All procedures will be performed by a suitably trained and experienced doctor.

The particular risks will be explained to you before each procedure and you will have chance to ask as many questions as you wish before proceeding. All chest drainage procedures carry small risks including discomfort (although once local anaesthetic is given, we expect all patients to be comfortable during these procedures), bleeding, infection, damage to the lung or other structures in the body, failure to complete the procedure and risk of any drain inserted becoming dislodged before the talc is given. IPCs carry the same risks, although the risk of infection is higher (5-10%, over the time

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in which the IPC is kept in). This higher infection risk is worth it because an IPC is the only effective treatment for patients in whom a talc pleurodesis fails.

It is important for you to understand that patients who receive EDIT treatment will have an additional fluid drainage procedure to allow elastance measurements to be taken. In order to get these measurements, this procedure might involve removal of a larger volume of fluid that is normally recommended in 'routine practice'. However, 'routine practice' does not involve use of pressure monitoring during fluid drainage, which we plan to do in this study. This is important because drainage of large volumes has been shown to be safe when pressure monitoring is used. Therefore, we do not believe this will involve any significant additional risk. Having two procedures rather than just one may increase the risk of a complication since each procedure has its own risks, but as mentioned before, the size of these risks are very low.

EDIT treatment patients will also have less fluid in their chest when their chest drain or IPC is inserted (after making this decision based on elastance results). This may mean that a slightly different technique is needed to put the drain in safely without causing damage to the lung underneath. This would involve use of blunt needle to let a small amount of air into the chest before the drain goes in. This ensures that the lung is not close to the rib cage when the drain is inserted. This technique is used every week to perform similar procedures in our unit and across the country. It is considered a safe way to perform procedures in this setting and we do not think this significantly increases any risks. However this will be carefully recorded during the study.

Are there any risks related to the MRI scans?

The MRI scanner is very safe as long as you have no metal implants in your body. Staff who are experienced in MRI scans will be present during your MRI scan and you will be asked a series of safety questions to ensure you have no metal implants/fragment in your body. If you do have a metal implant/fragment an MRI scan may not be safe and you would not be eligible for this study.

During the MRI scan a dye (contrast agent) will be injected into a vein in your arm. This makes any abnormal tissue appear brighter on the scan and easier to measure. The dye is called Gadolinium DTPA and is generally very safe. There are however some potential side effects although these are uncommon and generally mild. The most frequent side effects are a brief headache and nausea (feeling sick). This occurs in 1 to 3 patients out of every hundred who have the injection. Sometimes there is a sensation of heat, cold and/or pain at the injection site. An extremely rare (affecting less than 1 in 10000 people receiving Gadolinium), but serious, side effect is an allergic reaction to the dye therefore please inform the doctor if you have a history of allergies. This type of reaction may involve difficulty breathing and swelling of the lips or face but generally responds very well to emergency drug treatment.

Gadolinium contrast can also very rarely cause a serious condition called nephrogenic systemic fibrosis (NSF) in patients who have very poor kidney function. Your doctor will check blood tests to measure your kidney function as part of your routine care and will inform you if your kidney function is not good enough for the Gadolinium to be given safely with regards to this rare complication. In patients with normal kidney function the Gadolinium is cleared from the body in the urine within 24 hours and NSF is not a concern.

Are there risks from the X-rays in the study?

During the course of the study you will need to have approximately 8 chest x-rays. As mentioned above, you may also need to have 2 x-rays of the eyes to exclude metal objects before having an MRI scan. X-rays involve exposing the body to radiation which can be harmful at high levels but the total dose of radiation involved in this study is extremely low. It is equivalent to the same amount of radiation a typical person would

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receive from their normal surroundings over a period of 16 days and is therefore considered to be trivial by radiation experts.

What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak with the research doctor/nurse who will do their best to answer your questions.

If taking part in this research study harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay your legal costs. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism is available to you.

If you have private medical insurance, you may wish to check with your company before agreeing to take part in the study to ensure that participation in the study will not affect your insurance cover.

Will my taking part in the study be kept confidential?

You can be assured that any data collected during the course of this study and any of the results published will not identify you personally. Your medical records will only be available to the research doctors, your hospital consultant, trial sponsor (NHS Greater Glasgow & Clyde) and regulatory authorities.

We will inform your general practitioner (GP) of your participation in this study.

We would like to use your NHS number to follow-up on your health.

Who is organising and funding the research?

The research is being carried out by Dr. Kevin Blyth from the Department of Respiratory Medicine at the Queen Elizabeth University Hospital, Glasgow.

The costs of running and organising this study have been met by a grant from the NHS Greater Glasgow & Clyde Endowment Fund and Rocket Medical. None of the doctors or other staff conducting the research are being paid for recruiting patients into the study.

Who has reviewed the study?

This study was reviewed by a number of medical specialists during its development. All research in the NHS is also looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. The West of Scotland Research Ethics Committee has reviewed and approved this study to confirm that the 'rights and protection of patients' health have been considered. In addition, the study has been reviewed by the Research and Development Department of your local hospital.

Contact for further information

If you have further questions about your illness or clinical studies, please discuss them with your doctor. If you would like independent advice or further information you may also find it useful to contact British Lung Foundation, website: www.blf.org.uk, telephone 03000 030 555 and address: British Lung Foundation, 73-75 Goswell Road, London, EC1V 7ER

If during the course of the study you have any questions regarding your participation or would like further study specific information before making your decision please contact:

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Name
Telephone Number

Dr Kevin Blyth
0141 451 6099

If you find the wording difficult to understand or would like us to explain things to you once more, please feel free to ask your doctor, or nurse.

Thank you for taking the time to read this information sheet. If you wish to take part you will be given a copy of this information sheet and a signed consent form to keep

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CONSENT FORM FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH

PROJECT:

CONSENT TO PRE-EDIT STUDY SCREENING VISIT

Title of Project: Pre-EDIT: A randomised, feasibility trial of Elastance-Directed Intra-pleural catheter or Talc Pleurodesis (EDIT) in the management of symptomatic Malignant Pleural Effusion without obvious non-expansile lung

**Please initial
EACH BOX**

1. I confirm that I have read and understand the information sheet dated (Version) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I agree to attend for a study screening visit, including chest ultrasound scan, as described in the Patient Information Sheet.

Please sign and date below:

Name of Participant

Date

Signature

Name of Researcher

Date

Signature

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CONSENT FORM FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH

PROJECT:

CONSENT TO **PARTICIPATION IN PRE-EDIT STUDY**

Title of Project: Pre-EDIT: A randomised, feasibility trial of Elastance-Directed Intra-pleural catheter or Talc Pleurodesis (EDIT) in the management of symptomatic Malignant Pleural Effusion without obvious non-expansile lung

**Please initial
EACH BOX**

1. I confirm that I have read and understand the information sheet dated (Version) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand the study involves random allocation of treatment which neither myself nor the researchers can influence.
4. I understand I may be asked to have two MRI scans for research purposes and understand and accept the possible risks from these.
5. I agree to the recording of my measurements, including elastance measurements, volume of fluid removed and MRI scan findings as described in the Patient Information Sheet.
6. I agree to the recording of my pain and breathlessness scores as described in the Patient Information Sheet
7. I give permission for my initials, date of birth and NHS or Community Health Index (CHI) number to be collected for follow-up purposes.
8. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from NHS Greater Glasgow and Clyde (study sponsor) or regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
9. I consent to my GP being informed of my participation in this study.
10. I agree to take part in the above study.

Please sign and date below:

Name of Participant

Date

Signature

Name of Researcher

Date

Signature

Acute Services Division

Regional Services Directorate

PATIENT TREATMENT PREFERENCE SURVEY FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH PROJECT

Title of Project:

Pre-EDIT study: Survey of Patient Treatment Preferences for Symptomatic Malignant Pleural Effusion

Invitation Paragraph

We would like to invite you to take part in a short treatment preference survey which is connected to a research study called Pre-EDIT. It should take less than 5 minutes to complete. Your answers to this survey will be anonymised and will have no bearing on your medical care. Participating in this survey is separate to the Pre-EDIT study and does not commit you to any other research activity.

Please take time to read the following information carefully. Talk to others about the survey if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of this survey?

A pleural effusion is a collection of fluid inside the chest. The fluid gathers in an area called the pleural space which lies between the lung and the rib-cage. This often causes breathlessness and may unfortunately be caused by cancers affecting the pleural lining. This is called a 'Malignant Pleural Effusion'.

There are currently 2 main ways for doctors to treat Malignant Pleural Effusion. These are called 'talc pleurodesis' or 'IPC insertion' and are described in more detail at the beginning of the survey. Both are effective treatments but both have their own advantages and disadvantages. Individual patient preference is therefore essential in deciding the best treatment but at the moment, little research has been done to understand how patients make this decision.

We would like to better understand the views of patients in making a decision between talc pleurodesis and IPC insertion. In particular, we would like to know which pros and cons of the two treatments are deemed most important. This will allow us to direct our research efforts to focus on improvements to these treatments which are most relevant to our patients.

Why have I been invited to take part?

You have been invited to take part in this study because you have a pleural effusion causing breathlessness and your doctors have recommended either talc pleurodesis or IPC insertion.

Do I have to take part?

No, it is entirely up to you to decide whether or not to take part. We will talk you through the survey and go through this information sheet, which we will then give to you to keep. If you decide to take part, you will be asked to sign a consent form to show you

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have agreed to take part. If you decide to take part, you are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive or your future treatment.

What are the possible benefits of taking part?

Completing this survey will not have any direct benefits to your own medical care but we hope this information will be of benefit to patients in the future by directing our research towards improving our treatments in a way that matters to patients. We also hope the results will better inform the way in which doctors discuss these treatments with patients.

What are the potential risks in taking part?

There are no risks associated with completing this survey. Your answers will have no bearing on your medical care.

Will my taking part in the study be kept confidential?

You can be assured that any data collected during the course of this survey and any of the results published will not identify you personally. We may use anonymised quotes from your responses in our report of the survey results and any possible publications that arise from this.

Who is organising and funding the research?

The research is being carried out by Dr Kevin Blyth from the Department of Respiratory Medicine at the Queen Elizabeth University Hospital, Glasgow.

The costs of running and organising the Pre-EDIT study, which this survey is part of, have been met by a grant from the NHS Greater Glasgow & Clyde Endowment Fund and Rocket Medical. None of the doctors or other staff conducting the research are being paid for recruiting patients into the survey.

Who has reviewed the study?

This study was reviewed by a number of medical specialists during its development. All research in the NHS is also looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. The West of Scotland Research Ethics Committee has reviewed and approved this study and survey to confirm that the 'rights and protection of patients' health have been considered. In addition, the study has been reviewed by the Research and Development Department of your local hospital.

Contact for further information

If you have further questions about your illness or clinical studies, please discuss them with your doctor. If you would like independent advice or further information you may also find it useful to contact British Lung Foundation, website: www.blf.org.uk, telephone 03000 030 555 and address: British Lung Foundation, 73-75 Goswell Road, London, EC1V 7ER

If during the course of the study you have any questions regarding your participation or would like further study specific information before making your decision please contact:

Name	Dr Kevin Blyth
Telephone Number	0141 451 6099

If you find the wording difficult to understand or would like us to explain things to you once more, please feel free to ask your doctor, or nurse.

Thank you for taking the time to read this information sheet. If you wish to take part you will be given a copy of this information sheet and a signed consent form to keep.

Online Supplementary Appendix 3

CONSENT FORM FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH

PROJECT:

CONSENT TO PRE-EDIT TREATMENT PREFERENCE SURVEY

Title of Project: Pre-EDIT study: Survey of Patient Treatment Preferences for Symptomatic Malignant Pleural Effusion

**Please initial
EACH BOX**

- 4. I confirm that I have read and understand the information sheet dated (Version) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

- 5. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

- 6. I understand my responses will be anonymised for the purpose of analysing the survey and reporting its findings but that anonymised quotes may be used in publications.

- 4. I agree to my anonymised responses being stored on secure NHS computer systems.

- 5. I agree to participate in the above survey.

Please sign and date below:

Name of Participant

Date

Signature

Name of Researcher

Date

Signatu

Online Supplementary Appendix 4

Pre-EDIT Trial Specific Instruction (TSI): **Management of Talc Pleurodesis (TP)**

Introduction

TP will be attempted in patients receiving standard care and those receiving EDIT management who have been directed to chest drain insertion (**not** those undergoing indwelling pleural catheter insertion). The timing of the decision to attempt TP is described in detail in section 7.5 of the trial protocol. As described, TP should only be attempted where sufficient pleural apposition exists and there is a recent chest radiograph to demonstrate that the drain side holes are all located within the pleural cavity.

1. Preparation:

- a) Obtain informed written consent for talc pleurodesis.
- b) Ensure that the required equipment and assistant are available:
 - a. Dressing pack
 - b. 2x pair of sterile gloves
 - c. 0.9% saline 100ml sterile bag
 - d. 4g Sterile Talc
 - e. 1% lidocaine (3mg/kg)
 - f. 10ml leur lock syringe
 - g. 2x 20ml leur lock syringe
 - h. 50ml syringe
 - i. 4x 21g needles
 - j. Alcohol swabs
- c) Administer pre-medication, drug and dose at clinician's discretion (for example Oramorph 10mg).
- d) Position patient so they are sitting comfortably with the drain site and 3-way tap easily accessible.
- e) Wash hands and unpack sterile items onto opened sterile dressing pack.
- f) Wash hands and put on sterile gloves.
- g) Use the 21g needles and syringes to draw up the following:
 - a. 10ml syringe with 10ml 0.9% saline
 - b. 20ml syringe with 1% lidocaine (volume / dose dependent on patient's weight)
 - c. 50ml syringe with 50ml 0.9% saline and 4g sterile talc
 - d. 20ml syringe with 20ml 0.9% saline

2. Talc instillation:

- a) Apply sterile drape from dressing pack between 3-way tap and its surroundings.
- b) Ensure 3-way tap is 'turned off' to side access port.
- c) Remove bung from access port and clean both port and bung thoroughly with an alcohol swab and allow to dry for at least 30 seconds.
- d) Attach 10ml syringe with 0.9% saline and flush the drain to ensure patency – if the patient find this manoeuvre painful then TP should not be attempted and another CXR obtained to reassess the drain position.
- e) Remove 10ml syringe and attach 20ml syringe with lidocaine.

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- f) Instil this into the pleural cavity and turn 3-way tap rapidly to occlude drain and contain the lidocaine.
- g) Reapply bung and allow 10 minutes for the lidocaine to take effect.
- h) Wash hands and don new pair of sterile gloves.
- i) Repeat step 2. c)
- j) Attach 50ml syringe containing talc slurry, instil into pleural cavity and turn 3-way tap rapidly to occlude drain.
- k) Remove 50ml syringe and attach 20ml syringe containing 0.9% saline.
- l) Flush 0.9% saline into pleural cavity, taking care to avoid loss of talc slurry into drainage tubing.
- m) Occlude drain by turning 3-way tap.

3. Post-talc:

- a) Open 3-way tap 2 hours after talc instillation.
- b) Attach drain to thoracic suction at -10 cm H₂O and titrate up to -20 cm H₂O, if tolerated.
- c) Record pleural drainage values at least 8 hourly.
- d) A daily CXR will be performed.
- e) The drain should be removed once the following conditions are met:
 - a. At least 24 hours have elapsed since talc instillation
 - b. Drainage volumes have fallen below 250ml in the preceding 24 hours
 - c. There remains adequate pleural apposition on that day's CXR with no suggestion of fluid re-accumulation due to drain blockage
- f) Where loss of drain patency is suspected following talc instillation, the chest drain should be flushed with 20ml of sterile 0.9% saline following local guidance.
- g) Once the chest drain is removed, a further CXR should be performed.

If drain output does not fall below 250ml in the preceding 24 hours by 96 hours post talc instillation, then the ongoing drain management will be at the discretion of the primary physician.

Online Supplementary Appendix 5

Pre-EDIT – GN17ON084	
Contrast Lung Study	
Radiologist: Gordon Cowell (gordoncowell@nhs.net) Doctor: Geoff Martin (geoffreymartin@nhs.net)	
History	Malignant pleural effusion
Patient Prep	No Prep – Patients will attend from Respiratory ward – 7B
Equipment	Spine coil and body coil
IV Contrast	Type: Single dose of Gadovist
Check patient ID, complete Safety Checklist and exclude chance of pregnancy	
<u>Scan Technique:</u>	
<u>PRE-ASPIRATION</u>	
<ul style="list-style-type: none"> ▪ Localisers ▪ HASTE localiser – Axial and Coronal ▪ T1 VIBE Cor Pre Gd – Keep voxels isotropic, increase slice thickness if patients struggling to hold breath ▪ 4D TWIST acquisition during tidal free-breathing and maximal inspiratory/expiratory efforts ▪ Dual phase T1 VIBE post Gd @ 40sec followed by 20 sec delay (Each scan is manually triggered) ▪ VIBE at: <ul style="list-style-type: none"> ▪ 3 mins ▪ 4.5 mins ▪ 9 mins ▪ 13.5 mins (All Manually triggered) ▪ Axial Diffusion – cover mid-section of lungs, unless there is an identifiable mass, then centre block here ▪ Remove patient, transferred to Level 5 CRF for pleural aspiration and Digital Pleural Manometry 	
<u>POST-ASPIRATION</u>	
<ul style="list-style-type: none"> ▪ Localisers ▪ T1 VIBE ▪ 4D TWIST acquisition during tidal free-breathing and maximal inspiratory/expiratory efforts 	
Images to PACS	Everything
Archiving	Anonymise and send everything to archive

Online Supplementary Appendix 6

Pre-EDIT Trial Specific Instruction: **Digital Pleural Manometry (DPM) including Ultrasound Estimation of Pleural Effusion Volume, M-mode atelectatic lung assessment and Large Volume Thoracentesis**

PRE-ASPIRATION THORACIC ULTRASOUND (TUS) ASSESSMENT

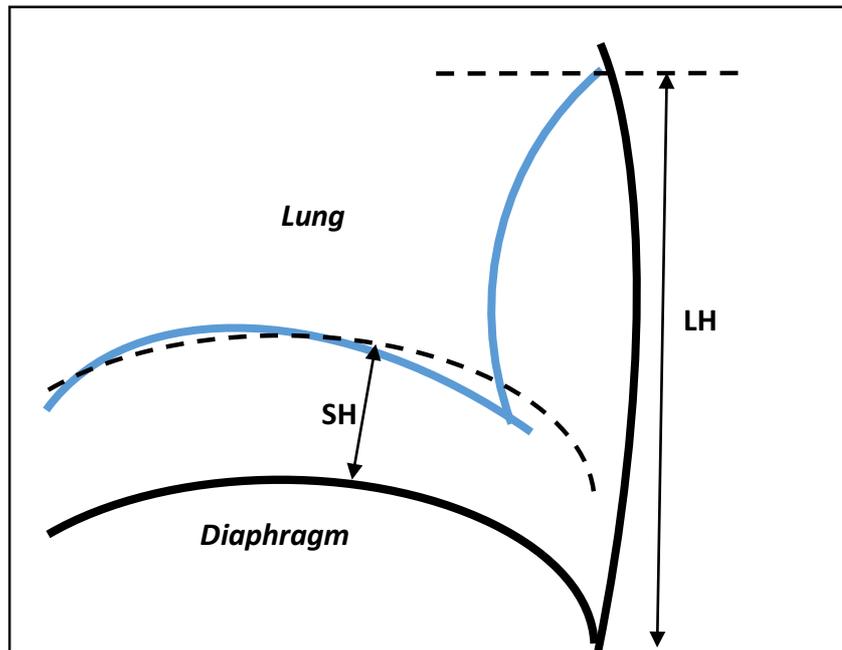
1. Record start time for TUS.
2. Position patient comfortably sitting upright at 90°.
3. Set ultrasound machine to B mode (2D).
4. Identify effusion and ipsilateral hemidiaphragm with the probe in a vertical alignment.
5. Optimise image with appropriate depth and gain settings.
6. Freeze screen at a representative lateral chest wall site in the posterior axillary line and use digital calipers to measure and record (in centimetres) the lateral height (LH), posterior height (PH) and median sub-pulmonary height of the effusion (SH) in centimetres, as shown in figure 1 overleaf.
7. Where LH or PH is greater than the maximum dimensions of a single ultrasound image and therefore cannot be measured digitally, the probe and disposable skin marker should be used to mark the extent of the effusion on the chest wall. A tape measure should then be used to measure LH or PH from these markings.
8. Calculate estimated pleural effusion volume (E) as follows:

$$E \text{ (ml)} = (\text{LH} + \text{SH}) \times 70$$

9. Identify effusion and ipsilateral hemidiaphragm with the probe placed on the posterior chest wall.
10. Progressively move the probe superiorly until the first image of atelectatic lung is achieved.
11. Hold the probe in this position and switch to M-mode recording.
12. Ensure M-mode region of interest is focused on atelectatic lung edge.
13. Record cine loops of this assessment over at least 3 cardiac cycles.
14. Return to B mode sonography.
15. Identify a safe catheter insertion site – where possible this should be in the posterior axillary line in the second rib space above the costophrenic angle.
16. Mark safe insertion site with disposable marker pen.
17. Record completion time for ultrasound scan, including calculation of E and TMAV.
18. M mode analysis will be performed offline – the mean atelectatic lung edge displacement over 3 consecutive cardiac cycles will be recorded.

Online Supplementary Appendix 6

Figure 1.
Schematic representation of the Thoracic Ultrasound measurements required to estimate pleural effusion volume (E) using the Goecke model



LH

measurements should be taken in the posterior axillary line.

PH measurements should be taken immediately lateral to the tip of the spinous processes.

LARGE VOLUME THORACENTESIS WITH DPM

1. Preparation:

- a) Ensure no contraindication to thoracentesis (e.g. coagulopathy defined by INR >1.5 or platelet count <50)
- b) Obtain informed written consent from the patient.
- c) Ensure that the required equipment and assistant are available:
 - a. Sterile gloves and gown
 - b. Skin marker pen
 - c. Antiseptic solution (chlorhexidine/alcohol or povidone iodine solution)
 - d. Sterile drape and dressing pack/table cover
 - e. Sterile dressing to hold catheter (eg peripheral venous cannula dressing)
 - f. Rocket Medical DPM compatible pleural aspiration catheter and associated equipment:
 - i. Scalpel blade
 - ii. 3-way tap
 - iii. 50ml leur lock syringe
 - iv. 2L drainage bag
 - g. 2x green (21g) and 1x orange (25g) needles
 - h. 20ml syringe
 - i. 1% lidocaine up to 3mg/kg, dose at discretion of operator
 - j. Bio-occlusive dressing
 - k. Sterile US probe cover
 - l. Sterile US gel

Online Supplementary Appendix 6

- d) Position the patient so they are sitting upright and leaning forwards against a cushioned table. Unpack equipment on to sterile field.

2. *Catheter insertion:*

- a) Record procedure start time.
- b) Wash hands and put on gown and gloves.
- c) Clean the skin using anti-septic solution and create a sterile field using sterile drapes.
- d) Infiltrate the skin with lidocaine using 25g needle initially to raise a bleb and then 21g needle to infiltrate intercostal muscles and costal pleura.
- e) Wait 2 minutes for lidocaine to take full effect.
- f) Attach transducer cable to DPM display unit and turn power on without compromising sterility of gloves/gown with help from assistant.
- g) The display unit will automatically 'zero' and then display pressure (IPP)/time graph; subsequent changes in IPP the transducer experiences at the catheter sleeve will now be recorded.
- h) Use scalpel blade to make a 4-5mm superficial horizontal incision at marked site.
- i) Insert aspiration catheter via incision aiming to pass the catheter over superior border of lower rib of marked intercostal space; indicator mark at hilt of insertion needle will change from green to red during insertion and return to green once pleural space successfully reached.
- j) Once indicator green, confirm position by free aspiration of pleural fluid using 10ml syringe then advance catheter a further 1cm before twisting and disconnecting insertion needle at one-way valve.
- k) Hold needle in fixed position relative to the patient and advance catheter over needle until catheter fully inserted into pleural space then withdraw needle completely.
- l) Attach clamped drainage line with 3-way tap to catheter and also to drainage bag.
- m) Rotate catheter to ensure that pressure transducer is level with insertion site.
- n) Apply sterile dressing to hold catheter and pressure transducer in position.

3. *Pleural aspiration and manometry*

- a) Ensure 3-way tap turned off to catheter.
- b) Attach 50ml leur lock syringe to 3rd port on 3-way tap then unclamp drainage line taking care to maintain a closed system and avoid the introduction of air to the pleural space or aspiration equipment.
- c) Ask assistant to document opening pleural pressure.
- d) Aspirate pleural fluid in 50ml aliquots and discard into drainage bag via 3-way tap. The assistant should record end-expiratory IPP, the cumulative fluid volume removed and the time of each IPP reading at 50ml intervals. A dedicated data collection table in the CRF is provided for this purpose.

NOTE: Care should be taken to ensure an end-expiratory IPP measurement is recorded. Since the DPM equipment records a mean IPP over the preceding 5 seconds, the patient should be coached to perform a 5 second breath hold at the end of a tidal breath at each 50ml interval.

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- e) At the point in time when 200, 500 and 1000ml have been aspirated, the patient will be coached to perform maximal inspiratory and expiratory manoeuvres. The patient should perform a 5 second breath hold at full inspiration and also at full expiration. The IPP associated with each breath hold should be recorded in addition to the end-expiratory IPP.
- f) At operator selected intervals, the ultrasound probe, within a sterile cover, should be placed on the patient's chest wall at a site adjacent to the aspiration catheter which would be suitable for subsequent ICD or IPC insertion and a horizontal measurement of the distance between costal pleura and atelectatic lung edge should be made.
- g) Continue sequential aspiration until one of the following criteria is met;
 - i. Horizontal distance between costal pleura and lung edge $\leq 30\text{mm}$
 - ii. Patient develops chest discomfort
 - iii. Patient develops excessive coughing which they find uncomfortable
 - iv. Pleural pressure $\leq -20\text{cmH}_2\text{O}$
- h) Record reason for termination and document closing pleural pressure.
- i) With the patient holding their breath at maximal inspiration, remove the aspiration catheter and apply bio-occlusive dressing to wound.
- j) Weigh filled drainage bag and subtract weight of unfilled drainage bag to obtain accurate pleural fluid volume (ΔV_{OUT}).
- k) Record completion time for procedure. Calculate and record total time taken for the procedure.
- l) Calculations mean pleural elastance (P_{EL}) and rolling average of P_{EL} ($P_{\text{EL}250}$) should then be completed whilst the patient undergoes post-procedure MRI scanning.

POST-ASPIRATION TUS ASSESSMENT

1. Position patient comfortably sitting upright at 90°
2. Set ultrasound machine to B mode (2D).
3. Identify effusion and optimize image with appropriate depth and gain settings.
4. Repeat measurement of LH and SH as described in the pre-aspiration TUS assessment.
5. Identify potential lateral insertion site for chest drain (ICD); ideally in mid- or posterior-axillary line 2 rib spaces above the costophrenic angle.
6. Freeze image in this position and use digital calipers to measure depth of fluid between costal pleura and lung edge (D_{90}).
7. The patient should then be positioned in a lateral decubitus position and TUS should be performed along the mid-axillary line.
8. The diaphragm should be identified and the probe then moved superiorly until a potentially suitable indwelling pleural catheter (IPC) insertion site is identified; ideally in 2 rib spaces above the costophrenic angle in the mid- to anterior-axillary line.
9. Freeze image in this position and use digital calipers to measure depth of fluid between costal pleura and lung edge (D_{LAT}).

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A standard Seldinger technique should be used for:

- ICD insertion where D_{90} is $> 20\text{mm}$
- IPC insertion where D_{LAT} is $> 20\text{mm}$

Where the minimum depth requirement is not met, a Boutin needle should be used for pleural cavity access. Details are given in Appendix 7

Online Supplementary Appendix 7

Pre-EDIT Trial Specific Instruction (TSI): **Pneumothorax induction using Boutin needle**

Introduction

This TSI describes the method which should be used for the insertion of a guide wire into the pleural cavity for patients receiving EDIT management where post-DPM TUS (see Appendix 4) demonstrates insufficient residual pleural fluid for safe insertion or either intercostal chest drain (ICD) or indwelling pleural catheter (IPC) using a standard Seldinger technique.

1. Preparation:

- a) Identify appropriate clinical area for procedure – either large single room or in endoscopy suite.
- b) Operators should change into ‘theatre blues’.
- c) Written informed consent will be taken. This process should take into account the potential increased risk associated with use of Boutin needle access of the pleural space.
- d) Ensure that the required equipment and assistant are available. Equipment lists are given in the procedure specific TSIs (see Appendices 1 and 3). In addition to the other listed equipment, a sterile Boutin needle will also be required. Furthermore, lidocaine with adrenaline will be used in all cases undergoing Boutin needle access irrespective of whether ICD or IPC is being placed.
- e) Consider pre-medication, eg Oramorph 20mg.
- f) Position the patient so they are lying in a comfortable lateral decubitus position with their head and arms adequately supported.
- g) Use thoracic ultrasound to assess the effusion and apply relevant skin markings as described in the ICD and IPC TSIs. Ensure lung sliding is present in the area adjacent to the planned drain insertion site.
- h) Wash hands.
- i) Unpack required equipment on to sterile field.

2. Guide wire insertion:

- a) Wash hands and put on gown and gloves.
- b) Clean the skin using anti-septic solution and create a large sterile field using drapes.
- c) Draw up lidocaine with adrenaline into a 20ml syringe.
- d) Palpate the superior border of the lower rib of the intercostal space where ICD/IPC insertion is planned. Infiltrate the skin at this point with lidocaine / adrenaline using a 25g needle to raise a bleb.
- e) Use a 21g needle to cautiously infiltrate lidocaine / adrenaline up to, and including, the periosteum of the previously palpated superior border of the lower rib of the chosen intercostal space.
- f) The limit of the rib edge should be identified with the 21g needle and further lidocaine / adrenaline applied immediately superior to the rib such that adequate anesthesia of the underlying costal pleura is achieved, ideally without breaching the pleura with the sharp tip of the 21g needle.
- g) Allow 2 minutes for the lidocaine to take full effect.

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- h) Use a scalpel blade to make a 4mm (ICD planned) or 7mm (IPC planned) superficial horizontal incision at the ICD/IPC entry site.
- i) Assemble the Boutin needle with the cutting trocar.
- j) Recheck the path / angle required to access the intercostal space immediately superior to the lower rib border using the 21g needle.
- k) Using the same approach, place the Boutin needle into the incision and using carefully controlled pressure, push the tip of the needle into the intercostal muscles taking care not to advance the sharp needle tip beyond the muscle layer.
- l) Hold the outer portion of the Boutin needle in position.
- m) Twist the sharp trocar to remove this and replace it with the blunt introducer.
- n) Using further controlled pressure, advance the now blunt Boutin apparatus until a 'give' is felt as the blunt needle punctures the costal pleura.
- o) Hold the needle outer, remove the central blunt needle to leave an open lumen and allow the patient to take 10 complete breaths to introduce an iatrogenic pneumothorax.
- p) Replace blunt Boutin trocar and remove apparatus from pleural cavity.
- q) Proceed to guidewire insertion at same site using standard Seldinger introducer needle.

3. Completion of insertion procedure:

- For ICD insertion, the procedure should continue following the relevant TSI (Appendix 1) from point 2. i).
- For IPC insertion, the procedure should continue following the relevant TSI (Appendix 3) from point 3. k)

Online Supplementary Appendix 8

Pre-EDIT Trial Specific Instruction (TSI): Intercostal Chest Drain (ICD) Insertion

Introduction

This TSI describes the method which should be used for ICD insertion using a Seldinger technique for patients within the Pre-EDIT study. This will include:

- Patients receiving Standard Care
- Patients receiving EDIT Management where $\text{MaxP}_{\text{EL250}} < 14.5 \text{ cm H}_2\text{O/L}$ **AND** post-DPM TUS demonstrates sufficient residual pleural fluid for safe insertion (see Appendix 4)

Where there is insufficient residual fluid for safe insertion using a Seldinger technique, the TSI in Appendix 6 should be followed.

1. *Preparation:*

- a) Ensure no contraindication to chest drain insertion (e.g. coagulopathy defined by INR >1.5 or platelet count <50)
- b) Obtain informed written consent from the patient.
- c) Ensure that the required equipment and assistant are available:
 - a. Sterile gloves
 - b. Skin marker pen
 - c. Antiseptic solution (chlorhexidine/alcohol or povidone iodine solution)
 - d. Chest drain dressing
 - e. 1-0 (or thicker) silk suture
 - f. Rocket Medical 12Fr Seldinger technique chest drain insertion kit
 - g. 1% lidocaine up to 3mg/kg, dose at discretion of operator
 - h. Chest drain bottle
 - i. Chest drain tubing
 - j. Sterile water for chest drain bottle
- d) Position the patient so they are sitting upright and leaning forwards against a cushioned table.
- e) Use thoracic ultrasound to assess the effusion and identify safe chest drain insertion site on lateral chest wall and mark with skin marker pen.
- f) Wash hands.
- g) Unpack equipment on to sterile field.
- h) Unpack chest drain bottle and add sterile water to 'fill line'.
- i) Attach chest drain tubing to drain bottle whilst maintaining the sterility of the tubing and 'fir cone' tip.

2. *Chest drain insertion:*

- a) Wash hands and put on gown and gloves.
- b) Clean the skin using anti-septic solution and create a sterile field using sterile drapes.
- c) Infiltrate the skin with lidocaine using 25g needle initially to raise a bleb and then 21g needle to infiltrate intercostal muscles and costal pleura.
- d) Wait 2 minutes for lidocaine to take full effect.

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- e) Attach 10ml syringe to introducer needle and cautiously advance this within the marked rib space at an angle perpendicular to the chest wall until pleural fluid can be freely aspirated.
- f) Remove the 10ml syringe from the introducer needle and pass approximately half the length of the guide wire into the pleural cavity via the lumen of the introducer needle.
- g) Remove the introducer needle over the guide wire whilst taking care to keep the guide wire in position within the pleural cavity.
- h) Use the scalpel blade to make a 4mm superficial horizontal incision at the site of guide wire entry on the chest wall.
- i) Thread the dilator onto the guide wire and use a firm, controlled pushing and twisting motion to advance this into the pleural cavity. The dilator safety guard should only be removed if essential for access to the costal pleura.
- j) Whilst advancing the dilator, ensure it follows the same tract as the guide wire and that the wire does not become kinked or twisted.
- k) Remove the dilator and hold sterile swab over wound.
- l) Thread chest drain onto guide wire and advance drain the required distance into pleural cavity; this will depend upon the size of the patient's hemithorax and chest wall thickness.
- m) Remove guide wire and central stiffening 'core' from chest drain whilst leaving the drain in position.
- n) Attach closed 3-way tap to distal end of chest drain.
- o) Suture drain in position.
- p) Attach chest drain tubing to chest drain via 3-way tap and 'fir cone' connector.
- q) Apply drain site dressing then remove drapes.
- r) Apply tape to chest drain and 3-way tap connections.
- s) Apply 40-50cm length of tape to form an 'omentum' between chest wall and the drain.

3. *Post-insertion ICD management*

- a) Allow up to 1000ml to drain within the first hour following insertion then occlude drain output using 3-way tap for at least 1 hour before further drainage. Drainage should also be stopped if the patient develops chest discomfort during drainage.
- b) A chest radiograph should be performed to assess the drain position.
- c) Thereafter, aim to drain up to 500ml / hour and minimise the time spent with the drain occluded.
- d) Drain output should be documented on a chest drain chart at least 4 times per day.
- e) The drain should be flushed twice daily with 20ml of sterile 0.9% saline following local protocols.

Online Supplementary Appendix 9

Pre-EDIT Trial Specific Instruction (TSI): **Insertion and drainage of Indwelling Pleural Catheter (IPC)**

Introduction

This TSI describes the method which should be used for IPC insertion using a Seldinger technique for patients within the Pre-EDIT study. These patients will be receiving EDIT management where $\text{MaxP}_{\text{EL250}} \geq 14.5 \text{ cm H}_2\text{O/L}$ **AND** post-DPM TUS demonstrates sufficient residual pleural fluid for safe insertion (see Appendix 4)

Where there is insufficient residual fluid for safe insertion using a Seldinger technique, the TSI in Appendix 6 should be followed.

1. Preparation:

- a) Ensure no contraindication to IPC insertion (e.g. coagulopathy defined by INR >1.5 or platelet count <50)
- b) Obtain informed written consent from the patient.
- c) Operator should change into 'theatre blues'.
- d) Ensure that the required equipment and assistant are available:
 - Sterile gloves and gown
 - Skin marker pen
 - Sterile foil bowel
 - Bottle of sterile 0.9% saline
 - Antiseptic solution (chlorhexidine/alcohol or povidone iodine solution)
 - 2x 2-0 silk sutures
 - Rocket Medical IPC insertion kit
 - 1% lidocaine with 1:200,000 adrenaline, up to 6mg/kg, dose at discretion of operator
 - 20ml leuc lock syringe
 - Additional 21g needle
 - Rocket Medical IPC drainage bottle pack
- e) Consider pre-medication, eg Oramorph 20mg.
- f) Position the patient so they are lying in a comfortable lateral decubitus position with their head and arms adequately supported.
- g) Use thoracic ultrasound to assess the effusion and identify safe IPC pleural cavity access site on lateral chest wall ('entry site') and mark with skin marker pen.
- h) Use tape measure to plan IPC exit site which should be 5cm anterior and inferior of the entry site and within the same intercostal space. Mark exit site and planned subcutaneous path of IPC.
- i) Wash hands.
- j) Unpack equipment on to sterile field.
- k) Pour 0.9% saline into foil bowel without compromising sterility.

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2. *IPC insertion:*

- a) Wash hands and put on gown and gloves.
- b) Clean the skin using anti-septic solution and create a large sterile field using drapes.
- c) Draw up lidocaine with adrenaline into two 20ml syringes.
- d) Infiltrate the skin with lidocaine using 25g needle initially to raise a bleb at the IPC entry site and then 21g needle to infiltrate intercostal muscles and costal pleura.
- e) Using the other lidocaine-filled syringe, infiltrate the skin and subcutaneous tissues from the entry site, along the intended IPC tunneling site, to the exit site.
- f) Wait 2 minutes for lidocaine to take full effect.
- g) Attach 10ml syringe to introducer needle and cautiously advance this at the entry site at an angle perpendicular to the chest wall until pleural fluid can be freely aspirated.
- h) Remove the 10ml syringe from the introducer needle and pass approximately half the length of the guide wire into the pleural cavity via the lumen of the introducer needle.
- i) Remove the introducer needle over the guide wire whilst taking care to keep the guide wire in position within the pleural cavity. Anchor the distal tip of the guide wire using the weight of damp sterile swabs.
- j) Use the scalpel blade to make an approximately 7mm superficial horizontal incision at the site of guide wire entry on the chest wall and also at the planned IPC exit site.
- k) Use the forceps and blunt dissection to create a subcutaneous IPC tunnel between the entry and exit sites.
- l) Moisten the drainage catheter using sterile saline.
- m) Using the plastic trocar, place the drainage catheter in the subcutaneous tunnel such that the distal end of the catheter is closest to the exit site and the Dacron cuff is approximately 1 cm from the entry site.
- n) Remove the plastic trocar from the drain tip and clean drain with a moistened swab.
- o) Thread the dilator onto the guide wire and use a firm, controlled pushing and twisting motion to advance this into the pleural cavity.
- p) Whilst advancing the dilator, ensure it follows the same tract as the guide wire and that the wire does not become kinked or twisted.
- q) Remove the dilator leaving the dark grey cuff in situ.
- r) Pass the drainage catheter into the pleural space via the dark grey cuff which should be split and removed to allow complete subcutaneous passage of the catheter.
- s) Check position of Dacron cuff – this should now be approximately 1cm from exit site. If required, the catheter may be pulled back to optimise its position.
- t) Close entry site wound with 2 sutures.
- u) Close exit site wound and secure IPC with a further 2 sutures.
- v) Clean and dry wounds and surrounding skin.
- w) Attach IPC drainage bottle and drain up to 600ml if the patient is comfortable during drainage.
- x) Remove drainage bottle and apply cap to IPC valve.
- y) Apply IPC dressing, ensuring both wounds are covered and the IPC is neatly coiled between the top dressing and the foam pad.

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3. *Post-insertion IPC management*

- a) A chest radiograph should be performed to assess and document the IPC position.
- b) Patient should be admitted to ward 7B.
- c) A further drainage of up to 600ml should take place on the evening of insertion. This will be performed by suitably trained staff on the ward. Drainage will be stopped at the onset of any chest pain, 'tugging' or discomfort.
- d) The following morning a further drainage of up to 600ml should be attempted.
- e) Following discharge, domiciliary IPC drainage will take place by suitably trained district nursing staff. All patients will initially undergo daily drainage.
- f) Drainage frequency will be reduced sequentially each time < 400ml is aspirated on 2 consecutive occasions following the intervals below:
 - Initially daily
 - Three times per week
 - Twice per week
 - Once weekly
 - Once fortnightly
- g) Where < 400ml is regularly aspirated fortnightly, consideration will be given to IPC removal which will be at the discretion of the primary physician.