Participant Information Sheet

Interventional Study - *Adult providing own consent*

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Adult providing own consent

Liverpool Hospital

Title	**PROMPT: PROcedural sedation vs Methoxyflurane a Prospective cohorT Study.**
Short Title	**PROMPT**
Protocol Number	2021/ETH00822
Project Sponsor	None
Coordinating Principal Investigator	Dr Ross Copping
Associate Investigators	Dr Paul Balamon, Dr Louise Wei, Dr Jules Catt
Location	Liverpool Hospital

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you are undergoing a procedure with interventional radiology. The research project is evaluating a well-known medication called Methoxyflurane (Penthrox) and comparing it to traditional procedural sedation in the form of intravenous midazolam and fentanyl. The "green whistle" is widely used by ambulance and surf lifesavers in the community; this study is to see its role in Interventional Radiology.

This participant information sheet tells you about the research project, explaining the process and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you do not have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests and treatments that are described
• Consent to the use of your personal and health information as described.

You will be given a copy of this participant information sheet to keep for your own records.

2 What is the purpose of this research?

Procedures performed in interventional radiology are often quick and minimally invasive, however some procedures traditionally require increased pain relief and sedation than local anaesthetic alone. For these procedures, we have previously used intravenous medications (midazolam and fentanyl) for sedation and pain relief; however, dosing of these medications is controlled by your nurse or doctor which can lead to under or over dosing of medications, or delayed pain relief due to delays in administration of medication. We believe that letting the patient control how much medication and how often can be effective.

Methoxyflurane (Penthrox) is a safe inhaled pain relief medication traditionally used in the community, ambulance and emergency department settings. It is administered via a hand-held "green whistle" that you can use yourself, and safely use as much as you want or need during the procedure. The device delivers the medication very quickly but limits the amount of medication inhaled to safe levels and serious adverse reactions are rare. In our experience so far, patients have reported reduced levels of pain and anxiety when using the "green whistle", which has been supported by other research papers looking at various procedures.

The purpose of this study is to determine whether use of Methoxyflurane (Penthrox) plus local anaesthesia for interventional radiology procedures provides better patient experience and procedural outcomes than traditional intravenous medications (midazolam and fentanyl). Improvement in patient experience and procedural outcomes have already been shown in other procedures in the hospital and community setting. We hope that showing the benefit of Methoxyflurane (Penthrox) will lead to improved outcomes and patient experiences in the future.

Medications, drugs and devices have to be approved for use by the Australian Federal Government. Methoxyflurane (Penthrox) has been approved in Australia for over 30 years, and is specifically validated in Australia to treat:
(1) pain in the emergency setting in stable conscious patients presenting after trauma, under the supervision of trained personnel
(2) pain in monitored conscious patients who require pain relief (analgesia) for surgical procedures such as the change of dressings.

This research is being conducted by the Liverpool Hospital Interventional Radiology Department.

This research has been initiated by the study doctor, Dr Ross Copping.

There is no funding or grant for this procedure.

There is no commercial sponsorship for the study.

3 What does participation in this research involve?

You will be assessed to see if you meet the inclusion criteria for this project. If deemed eligible, a consent form and thorough discussion will occur regarding the project, and what is involved.

At the time of enrolment into the study, you will be asked some questions regarding your general health and function, as well as pre-procedural pain and anxiety.

You will be participating in a Prospective randomised control study comparing methoxyflurane vs intravenous fentanyl and midazolam. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). Participants will be allocated into one of two study groups: one group will receive local anaesthesia and intermittent dosing of intravenous fentanyl and midazolam throughout the procedure; the other group will receive local anaesthesia plus and the "green whistle" with medication (Methoxyflurane). Participants are allocated to one of these 2 groups by randomisation to ensure there is no bias, giving you a 50/50 chance of being allocated into each group. We will closely monitor the experience between these 2 groups, including levels of pain and anxiety, and compare to see if Methoxyflurane (Penthrox) is of benefit when compared to intravenous fentanyl and midazolam.

This study is not blinded, which means you will be told which analgesia plan will be used for your procedure. Throughout the procedure, you will be asked regarding your pain and anxiety levels at regular intervals. After the procedure you will be interviewed prior to discharge home regarding your experience with the procedure and anaesthesia you received.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

4 What do I have to do?

There are no restrictions in participating in this study. You will be monitored in the interventional radiology department for a minimum of one hour post procedure as is routine to ensure you are well. You should follow the post procedure instructions provided which may vary depending on the individual procedure.

5 Other relevant information about the research project

This project will have two different groups – those receiving the methoxyflurane medication loaded in the "green whistle" and those receiving intermittent dosing of intravenous midazolam and fentanyl. You will still be given local anaesthetic regardless of which group you are allocated to, which is the current standard practice.

For this study we will be aiming to recruit over a hundred participants over the duration of the data collection period. This study is being run at a single site; in the Liverpool Hospital Interventional Radiology department.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage without compromising your treatment in any way.

If you do decide to take part, you will be given a consent form to sign and you will be given a copy of this sheet to keep for your own records.

Your decision whether or not to take part or to take part and then withdraw, will not affect your planned treatment, your relationship with your treating team or your relationship with Liverpool Hospital.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. There are other options available, including receiving the same treatment under intravenous sedation with midazolam and fentanyl if you do not participate in the study. Intravenous midazolam and fentanyl is the current standard practise for these procedures.

The use of the green whistle will be explained to you on enrolment to the study and can be reiterated throughout the duration of the procedure. If at any stage you believe your pain is not under control you can elect to be removed from either arm of the study. Importantly, methoxyflurane should offer patients better, more immediate control of their pain. It also wears off fastener than intravenous sedation medications meaning you will recover from sedation faster.

Potential benefits of participating in this study include the possibility of better control of your pain relief and alleviation of your anxiety. If this medication is of benefit, this will help make patients more comfortable for these procedures in the future.

Potential downsides would include the possibility of you not receiving enough analgesia from the use of the green whistle. Your pain levels will be monitored regularly throughout the procedure. The green whistle containing methoxyflurane contains a dilution hole which upon covering with your fingers can deliver an increased dose of methoxyflurane to achieve optimal analgesia.

Other downsides would include the possibility of an adverse reaction or allergy to the medications with either arms of the study which is rare and a risk that would exist outside participation in the study.

Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include reduced pain and anxiety for you during the procedure (and possibly other patients going through the same procedure in the future).

9 What are the possible risks and disadvantages of taking part?

Medical treatments often cause side effects. Generally, Methoxyflurane (Penthrox) is safe. You may have none, some or all of the effects listed below, and they can range from mild to moderate or severe. If you are concerned or experience any of these side effects, please talk with your study doctor. Your study doctor will closely monitor for any potential side effects. There may be side-effects that the researchers do not expect or do not know about which can be serious. Please tell your study doctor immediately about any new or unusual symptoms that you experience.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

Methoxyflurane can accumulate in the body if administered to patients with significant kidney impairment. These patients may experience more intense effects and side effects of methoxyflurane. For this reason, recent blood tests will be reviewed for all potential participants to screen for renal impairment, and participants with renal impairment will be ineligible for this study.

Side Effect	How often is it likely to occur?	How severe might it be?	How long might it last?
Dizziness	8.2%	Mild	Minutes to hours
Euphoria	4.1%	Mild	Minutes to hours
Nausea	2%	Mild	Minutes to hours
Decreased level of consciousness/somnolence	4.1%	Mild	Up to 48 hours
Diaphoresis (sweating)	2%	Mild	Minutes to hours
Dysgeusia (altered taste)	2%	Mild	Minutes to hours
Flushing	2%	Mild	Minutes to hours
Hypertension (high blood pressure	2%	Mild	Minutes to hours
Anxiety and depression	2%	Mild	Minutes to hours
Confusion	2%	mild	Up to 48 hours

In the event that participation in this research uncovers a medical condition which you were unaware, optimal care will be taken to disclose the condition to you and manage according to best practice guidelines. We will refer to your GP and refer you to a relevant specialist.

The effects of methoxyflurane on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant, trying to become pregnant or breast-feeding. Women will have to take a pregnancy test prior to enrolment if there is a possibility that they are pregnant. Men should avoid unprotected sex and should not donate sperm for at least 24 hours after the procedure. Both male and female participants are strongly advised to use effective contraception around the time of the procedure. You should discuss methods of effective contraception with your local doctor or study doctor.

If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant. For men, you should advise your study doctor if you make someone pregnant within 24 hours after receiving medication for the procedure. Your study doctor will advise on medical attention for your partner should this be necessary.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

10 What will happen to my test samples?

Blood tests are already performed as part of the work-up for these procedures and these be reviewed prior to enrolment in the study as per standard practise. This is important to ensure your safety and appropriateness to be enrolled in the study.

Blood will be collected, primarily to assess kidney and liver function, prior to your procedure as part of routine care. The results of these blood tests will be used to assess your eligibility to participate in this study. The blood tests are sent to NSW health pathology after collection for processing and storage. Like any other blood test, the blood will be stored for a period of 7 days before being discarded. The blood samples will not be stored for future research.

Samples of your blood obtained for the purpose of this research project *will* be transferred to *NSW health pathology service*. Similarly, tissue samples obtained from deep tissue biopsies will also be sent to the pathology service for storage and analysis. Your blood or tissue will not be sold by Liverpool Hospital, however NSW may charge study doctors a fee to recover some of the costs of storing and administering the tissue samples.

Once your blood samples are transferred to *NSW health pathology*, Liverpool Hospital will not be able to control whether the *NSW health pathology* transfers or sells your samples at some future date, however *Liverpool hospital* will not knowingly transfer your samples to anyone who has expressed intent to sell the samples.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

It may also be necessary for you to take medication during or after the research project to address side effects or symptoms that you may have. You may need to pay for these medications and so it is important that you ask your doctor about this possibility.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The drug/treatment/device being shown not to be effective
- The drug/treatment/device being shown to work and not need further testing
- Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities.

15 What happens when the research project ends?

At the end of the research project, the information and data will be processed and reviewed. If the data indicates that use of methoxyflurane provides improved patient experience and/or procedural outcome in patients undergoing procedures in interventional radiology when compared to intravenous midazolam and fentanyl, then methoxyflurane will be offered to patients undergoing interventional radiology procedures as part of standard care in the future.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Your information will remain coded into the data and can be re-identifiable, access to the data will be limited to the researchers listed in the study and the files will be stored electronically with password encryption at Liverpool Hospital. Your information will be stored for 15 years (minimum length for clinical trial research) and after this period, will be discarded. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Specific names or birth dates will not be presented in any research presentation forms, data access will only be limited to the researchers listed and the information will be password encrypted in order to maintain confidentiality.

Information about your participation in this research project may be recorded in your health records.

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

If there are complaints regarding your treatment by members of staff, you may contact the clinical trials coordinator in order to lodge a complaint. This will ensure that a formal system of review is conducted in order to prevent further instances from arising.

There are two avenues that may be available to you for seeking compensation if you suffer an injury as a result of your participation in this research project:

- The pharmaceutical industry has set up a compensation process, with which the Sponsor of this research project has agreed to comply. Details of the process and conditions are set out in the *Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial*. In accordance with these Guidelines, the sponsor will determine whether to pay compensation to you, and, if so, how much. A copy of the Guidelines is available to you from the research staff on request. If you have any questions about the Guidelines, please contact Dr Ross Copping.
- You may be able to seek compensation through the courts.

18 Who is organising and funding the research?

This research project is being conducted by the Liverpool Interventional Radiology Department, including Dr Ross Copping, Dr Paul Balamon, Dr Louise Wei and Dr Jules Catt.

There is no sponsorship or funding for this study.

Liverpool Hospital and the interventional radiology department will not benefit financially from this research project. Similarly, you will not benefit financially from your involvement in this research project.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of South West Sydney Local Health District (SWS LHD).

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on 8738 7056 or any of the following people:

Clinical contact person

Name	Ross Copping
Position	Interventional Radiology Fellow
Telephone	8738 7056
Email	ross.copping@health.nsw.gov.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Reviewing HREC approving this research and HREC Executive Officer details

This study has been approved by the South Western Sydney Local Health District Human Research Ethics Committee. Any person with concerns or complaints about the conduct of this study should contact the Research and Ethics Office, Locked Bag 7103, LIVERPOOL BC NSW 1871 on 02 8738 8304 / fax 02 8738 8310 / email SWSLHD-ethics@health.nsw.gov.au, website: http://www.swslhd.nsw.gov.au/ethics/default.html and quote 2021/ETH00822.

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.