Patient Information Leaflet

The VIOLET Study

Video assisted thoracoscopic lobectomy (VATS) versus conventional Open Lobectomy for lung cancer

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<<To be presented on site-headed paper>>

The VIOLET Study

Video assisted thoracoscopic lobectomy versus conventional open lobectomy for lung cancer

You are being invited to take part in a research study. Before you decide whether to take part or not, you need to understand why the research is being done, and what it involves. Taking part in research is voluntary; it is up to you to decide to join the study. If you decide not to take part, or decide to withdraw from the study, you will not have to give a reason. Nobody will be upset, and the standard of care you receive will not be affected.

Please take time to read the following information carefully. One of our team will go through the information leaflet with you, explain the study in more detail, and answer any questions you have. If anything is not clear or you would like more information, please ask a member of the local research team (see contact details on page 1). Talk to others about the study, such as friends or relatives, and take time to decide.

What is the purpose of the study?

This study has two purposes and is made up of two parts. Firstly, in part A of the VIOLET study, we would like to know more about how people who have been diagnosed with lung cancer make decisions about whether to take part in research. To find out, we would like to audio-record all telephone and face-to-face consultations between patients and healthcare staff. This will allow us to assess how research into different treatments is discussed. We will also invite some patients to talk to one of our researchers.

Part B of the VIOLET study aims to compare two ways of performing an operation called a lobectomy. This operation aims to remove the cancer by taking away the part of the lung which contains the tumour. One way of performing this operation is by open surgery and the other is a form of keyhole surgery called video-assisted thoracoscopic surgery (VATS). At present, we do not know which way of performing the operation offers the best treatment and recovery for patients. This is the primary goal of our research.

Patients who agree to participate in Part B of the study will also be invited to take part in an **optional** sub-study where regular blood samples will be taken. We want to see if we can predict whether cancer will return after surgery (known as cancer recurrence), using a new blood test. The new test will identify tiny amounts of cancer tumour (ctDNA) in the blood after surgery, which ***may*** indicate that the cancer is more likely to return and we would like to understand more about this. To do this, we will compare the blood results of those patients whose cancer returns to the blood results of those patients who remain cancer-free. Our offering this optional sub-study does not mean we think your cancer will return and we will not know whether the blood test predicts cancer recurrence until the study has been completed.

Why have I been invited?

You have been invited to take part because you may be offered a lobectomy to treat your known or suspected lung cancer. This type of surgery is offered to patients who have been told that they have either known or suspected lung cancer. Patients with suspected lung cancer are usually offered this operation if a test (called a biopsy) confirms the presence of cancer. This study will involve around 500 patients undergoing lobectomy, across the UK.

What will happen to me if I take part?

What will happen to you if you decide to participate will depend upon which part(s) of the study you agree to. **You can agree to none, one or both parts of the study. If you choose to participate in Part B you will also be given the opportunity to take part in an optional blood sub study.**

PART A – INFORMATION STUDY

During your next appointment you will meet a surgeon and a research nurse. They will ask you some questions and explain the different ways that a lobectomy can be performed. This includes both VATS and open surgery. To evaluate the information given to you at that meeting and any future consultations, we would like your permission to audio-record your discussion.

Some patients will also be invited to attend an interview with one of our researchers. These interviews are optional, so you do not have to take part if you would prefer not to. However, if you agree to be interviewed the researcher will talk to you about your experiences since your diagnosis, the discussions with your surgeon and nurse and your views on the VIOLET study.

PART B – MAIN STUDY (VATS VS OPEN SURGERY)

If you agree to take part in the main study, you will help us to determine whether VATS or open surgery offers the best treatment and recovery from cancer. Both treatments are currently used by doctors but we do not know which is best. To compare the two treatments, we need similar groups of patients to have either open surgery or VATS. To make sure this is done fairly, the method of surgery is allocated at random – a process called randomisation.

If you agree to take part in the main study, you will have an equal chance of having open surgery or VATS and it is important that you only agree to take part if you believe you would be prepared to accept either treatment. The surgeon treating you is experienced in both techniques and you will receive the best possible care.

If you agree to participate in the optional sub-study, blood samples will be taken at different time points over five years, either at a VIOLET study visit or by your GP practice. You will also be asked to complete health questionnaires over the five years. The blood samples will be analysed at a laboratory in the United States of America.

What will I have to do?

PART A – INFORMATION STUDY

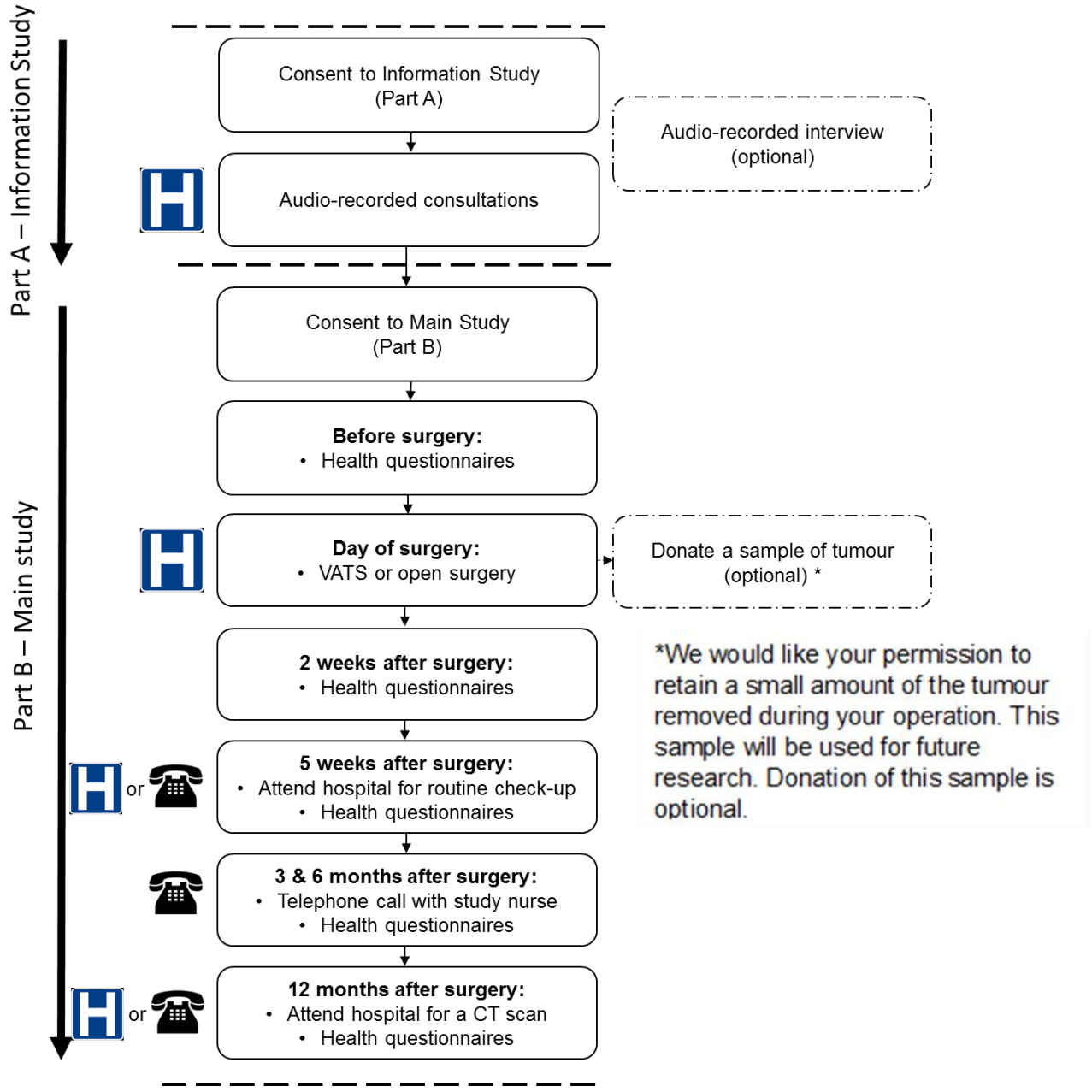
One of our researchers will contact you to find out if you are willing for your consultations to be audio-recorded. If you agree to be audio-recorded, we will ask you to sign a consent form. You will also be asked to indicate if you would be willing to be interviewed by one of our researchers – this is optional. If you agree to take part, a researcher from the University of Bristol will contact you. The interview will be arranged for a time & place convenient to you and may be in person or over the telephone.

PART B – MAIN STUDY (VATS VS OPEN SURGERY)

If you are interested in participating in the main study after talking to your surgeon, you will be asked to sign a consent form. You will then be allocated to have VATS or open surgery. To make the study fair, you will not be told which operation you will have – a process called blinding. After your surgery, your scars will be bandaged and you will be asked which operation you think you received and whether you are experiencing any pain. This will provide us with useful information about the treatments. When you are ready to leave the hospital after your operation, your nurse will tell you which operation you had – if you wish to know.

During your involvement in the study, you will be asked to complete health questionnaires at the times identified in the diagram on page 4. These questionnaires should take no more than 15 minutes to complete. You will have the option of receiving paper questionnaires and returning them in pre-paid envelopes or completing online forms via the VIOLET website: https://cteu-trials.bristol.ac.uk/violet

The diagram below shows parts A and B of the VIOLET study and what each part involves. Hospital visits and telephone calls are identified with these symbols: 🏥, ☎ Hospital visits after your operation may take place at the hospital where you have your surgery or at a local hospital – these visits are part of normal care. If these visits take place at a local hospital, you will also be contacted by a research nurse who will ask you some questions about your health & recovery.



If you would like to participate in the optional blood sub-study you will be asked to sign the 'optional' section on the consent form. Four 10mL tubes (approximately 8 teaspoons) of blood will be taken before the day of surgery and at eight further time-points after the surgery. Blood sample kits will be posted to you at 5 weeks, 6 months, 12 months, 18 months, 2 years, 3 years, 4 years and 5 years after joining the VIOLET study. The blood samples can be taken by your GP surgery or alternatively by a research nurse if you have a VIOLET study visit coming up.

From 18 months onwards we will send you health questionnaires with the blood kit. These will be a little different to the questionnaires we ask you to complete at 1, 3, 6 and 12 months and should not take more than 10 minutes to complete. As mentioned above, you will have the option of receiving paper questionnaires and

returning them in pre-paid envelopes or completing them online via the VIOLET website: https://cteu-trials.bristol.ac.uk/violet. If the questionnaires aren't returned to us, the research nurse will telephone you to check if you still want to take part and if so, to obtain the questionnaire details over the phone. **Remember, you can take part in none, one or both parts of the study.** If you choose to participate in *part A but not part B*, we will ask if you would be willing to complete health questionnaires before and 5 weeks after your operation and, if you will allow us to collect some information about the type of surgery you chose. If you agree to this you will be asked to sign a consent form.

What are the possible risks and benefits of taking part?

Private medical or life insurance may be affected by taking part in a research study so you may wish to check with your insurance company before taking part. The risks and benefits are provided below:

PART A – INFORMATION STUDY

If you agree to take part in the information study you will help us to improve how surgery and research are discussed with patients. There should also be no risks associated with participating in the information study, as this just involves talking to hospital staff and researchers. Most people find that this is comforting but some can find it uncomfortable. If this happens, you will be able to stop the consultation or interview at any time, without giving a reason.

PART B – MAIN STUDY (VATS VS OPEN SURGERY)

If you agree to take part in the main study, you will help us to determine whether VATS or open surgery offers the best treatment and recovery for patients. This information will be useful to the NHS and future patients.

There should also be no additional risk if you agree to take part in the main study as both operations are in use and neither is new or experimental. Your doctor will explain the risks and benefits of the procedures but the key facts are provided below:

Open surgery – Key facts
• The surgeon makes a single incision in the chest. • The surgeon can directly see the lungs and tissues. • The surgeon will remove the lobe of the lung containing the tumour. • Surgery typically takes 3-4 hours. • Open surgery is the most commonly used method of performing a lobectomy. • The length of your hospital stay will depend upon how well you recover after surgery.

VATS (keyhole) surgery – Key facts
• The surgeon will make between 1 and 4 small incisions in the chest • A special camera allows the surgeon to see the lungs and tissues. • The surgeon will remove the lobe of the lung containing the tumour. • Surgery typically takes 3-4 hours.

- The length of your hospital stay will depend on how well you recovery after surgery
- If there are complications, the surgeon may need to perform open surgery to complete the operation.

By taking part in this study you will have a chest x-ray before you are discharged, and a CT scan 12 months after your operation. These exams involve small doses of radiation from the x-rays used to form the images of your body. We estimate that the radiation dose for a chest x-ray is equivalent to about 3 days of natural background radiation, and the radiation dose for a CT scan is equivalent to about 5 years of natural background radiation. The total dose of radiation would increase your life-time risk of cancer by 0.1%. You will be at no greater risk if you decide to take part in the study because these scans are part of normal care at your hospital. If your scans identify any problems, your doctor will discuss these with you. If you agree to participate in the sub-study and provide blood samples, you will help us to find out whether we can predict if and when cancer could return in some patients.

There should be no additional risk if you agree to donate blood samples. The blood collected for the study is a small amount and you should not notice any effect of this. Blood will be taken by a clinically trained member of staff from a vein in your arm using a needle. Occasionally, patients experience some discomfort when the needle is inserted to draw blood. Afterwards you may develop some localised bruising and we advise contacting your GP for advice if you have any concerns.

Expenses

Travel expenses are only payable if you have to attend a visit that is *not* part of normal care. For this reason, travel expenses are only payable if you have to travel to attend a study interview or if you decide to participate in the sub study as this will involve additional visits to your GP to have blood samples taken.

What happens if the research study stops or if new information becomes available?

If the research study stops, you will continue to receive routine care at your treating hospital. If we get new information about the treatment being studied your doctor will tell you and discuss whether you should continue in the study.

What if there is a problem?

If you have any concerns or questions about this study, please contact the research team listed on the front cover of this leaflet. Alternatively, you can discuss these with a member of the research team who will come to see you before your surgical consultation. Please ask any further questions before deciding to take part in the study, or at any time during the study.

If you have concerns about the way you have been approached or treated during the course of the study, you may wish to contact the Patient Advice and Liaison Service (PALS) on:

< Insert site specific PALS details >	Or contact Patient Complaints:
< PALS Address 1 >	< Patient Complaints Address 1 >
< PALS Address 2 >	< Patient Complaints Address 2 >
< PALS Address 3 >	< Patient Complaints Address 3 >
< PALS Address 4 >	< Patient Complaints Address 4 >
< PALS Address 5 >	< Patient Complaints Address 5 >
< PALS Telephone >	Manager on < complaints telephone
< PALS email >	number >

We have no reason to believe that you will be placed at any greater risk by taking part in this research study. However, if something goes wrong and you are harmed during the research study there are no special compensation arrangements. The < insert Trust name > cannot offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm. Ex-gratia payments may be considered in the case of a claim.

If anything goes wrong as a consequence of taking part in the study because negligence has occurred, Royal Brompton & Harefield NHS Foundation Trust, who is sponsoring the study, will compensate you. Negligence would include, for example, a situation in which injury is caused by a deviation from the study protocol by the researcher. Your legal right to claim compensation for injury where you can prove negligence is not affected. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action against the < insert Trust name >, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in the study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential and stored securely. This includes details such as your name, address and NHS number, which allow us to keep in touch with you during the research.

PART A – INFORMATION STUDY

Audio-recorded data will be transferred via a secure data link to the University of Bristol. All audio-recordings (from consultation appointments and interviews) will be labelled with a unique reference number (not with your name) to hide your identity. Recordings will be transcribed (i.e. a written record of the conversation produced) by either a University of Bristol employee or by a University of Bristol approved transcribing service. These transcripts will also be anonymised so that you cannot be recognised from any of the information we collect from you. All paper copies of the transcripts will be stored securely.

We may use quotes and play parts of your audio-recordings (from interviews and appointments/meetings) as part of publications, teaching and presentations at academic meetings. If we do use any of your data, all quotes will be anonymised (and voices modified if necessary) so that you cannot be identified. We may also use the data collected (including quotes) in our future research, teaching and publications looking at common issues across studies. You will not be identified in any way in any presentation, report or publication.

PART B - MAIN STUDY (VATS VS OPEN SURGERY)

We will need access to your medical notes to record information about your health, which is essential to allow us to compare the two operations. Only authorised members of hospital staff and researchers at the coordinating centre will have access to these records.

Occasionally, other members of NHS staff or research staff may need to check your medical records. This will be done by NHS staff or by researchers who are bound by the same rules of confidentiality as all NHS staff. The confidentiality of your medical records will be respected at all times.

With your consent, your GP will be informed that you are taking part in the research study. Your GP may be asked to provide medical information where it is required for the research. After you leave the study we would like to know how you are progressing using information collected routinely in the NHS. With your permission information will be obtained from the NHS Information Centre's 'Medical Research Information Service'. Any information received in this way remains confidential.

What will happen to my data?

Your data will be stored and used in compliance with the relevant, current data protection laws; Data Protection Act 1998 and General Data Protection Regulation (GDPR) 2016.

Any data collected about you during the course of the study will be securely stored (on a NHS database) and then transferred to the VIOLET study team at the University of Bristol. The data will be transferred by a secure data link and any extracts used in the analysis will be anonymised (i.e. you cannot be identified from them).

At the end of the study your data (including transcripts of your audio-recordings) will be stored indefinitely in an online secure database, alongside the data collected on the other study participants. The database can only be accessed by authorised users ('controlled access'), and you cannot be identified by any information held. This database will be made available to researchers to use in other related research but they will only be allowed to access it if their research has been approved by a Research Ethics Committee. Sharing the study data helps to maximise the impact of the money invested into this study and can encourage new avenues of research.

What will happen if I don't want to carry on with the study?

If you decide to not carry on with the study, you can withdraw at any time and without giving a reason. A decision to withdraw will not affect the standard of care you receive. Exactly what happens if you withdraw depends on which parts of the study you have agreed to and when you withdraw.

If you have agreed to take part in the information study (Part A) and then decide not to continue with the study, your care will continue in the normal way. We will not record any of your discussions and you will not be approached for an interview. We will ask your permission to keep information collected already as this is valuable to our research.

If you have agreed to take part in the main study of VATS vs open surgery and you withdraw **before the operation**, you will be offered the usual treatment at your hospital. If you have agreed to take part but then decide not to continue with the study **after your operation**, your care will continue in the usual way. We will ask you what you would like us to do with any information, and blood and tumour samples that have already been collected. Information and any samples collected up to the point that you decide to withdraw are still valuable for our research.

What will happen to any samples I give?

The blood samples that you provide us with will be labelled with your unique study number; no other personal identifiable data will be included. Your samples will be sent by courier to a laboratory in the United States of America for processing and storage whilst the study is underway. The research staff in the laboratory will not have access to any of your personal identifiable or medical data and will be responsible solely for testing the samples. The data that are generated by the laboratory will be sent to the research team at the University of Bristol for analysis in an encrypted format. Any information received in this way remains confidential.

The purpose of the tests which will be carried out on your blood samples will be to try to detect tiny amounts of cancer tumour DNA (ctDNA). This is very different to genetic testing which will not be performed on your samples. The research carried out has no clear medical meaning (at the moment) as it is exploratory. Therefore we will not tell you about your results, as we will not be testing for specific known conditions or diseases, so the information gained would not be meaningful to you personally.

Tumour samples retained for the research will also be given a unique code, which will mean that you cannot be identified from your sample. These samples will be stored, potentially for many years, until analysed. They will be used for this study and approved future research.

If you withdraw from the study, you can ask for your samples and any information from their analysis to be destroyed.

What will happen to the results of the research study?

The results of the main study will not be known until about 5 years after the start of the study. The results of the blood sub-study will not be known until 10 years after the start of the study. The results may be reported in medical journals or presented at meetings but your identity will not be disclosed. During the course of the study, we will ask if you would like to receive a summary of the results after the research has finished.

Who is organising and funding the research?

The research is funded by the National Institute for Health Research. The Royal Brompton & Harefield NHS Foundation Trust has overall responsibility for conduct of the study. The research is being organised and run on their behalf by the Clinical Trials and Evaluation Unit, University of Bristol. Guardant Health are a laboratory in the United States of America who are providing the funding for the optional blood sub-study.

Who has looked at the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by NRES Committee London - Dulwich.

Further information

You can obtain general advice on lung cancer and its treatment from Cancer Research UK: Web: http://www.cancerresearchuk.org/ or telephone: 0808 800 4040

General information on clinical research is available from the UK Clinical Research Collaboration (UKCRC), who produce the booklet: “Understanding Clinical Trials”.

Paper copies can be requested by email (info@ukcrc.org), telephone (+44 (0)20 7395 2271) or writing to:

UK Clinical Research Collaboration, C/O Medical Research Council
One Kemble Street
London WC2B 4TS

For electronic copies see: http://www.ukcrc.org/category/publications/information-booklets/

Thank you for taking the time to read this leaflet.

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