INFORMED CONSENT FORM

1. Study Information

Protocol Title:
Phacoemulsification versus phacoemulsification with micro-bypass stent implantation in primary angle closure and primary angle closure glaucoma: Randomized double-masked clinical trial (NCT03647033)

Principal Investigator & Contact Details:
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Singapore

66023272, 91752883

Study Sponsor:

Funded by the Translational and Applied Research (STAR) Award

2. Purpose of the Research Study

You are invited to participate in a research study. It is important to us that you first take time to read through and understand the information provided in this sheet. Nevertheless, before you take part in this research study, the study will be explained to you and you will be given the chance to ask questions. After you are properly satisfied that you understand this study, and that you wish to take part in the study, you must sign this informed consent form. You will be given a copy of this consent form to take home with you.

You are invited because you have a type of glaucoma called primary angle closure or primary angle closure glaucoma. This means there is damage or potential damage to your eye nerve from high pressure in the eye. You are already receiving eye drops for your eye pressure.

This study is carried out to find out if phacoemulsification and lens implantation (cataract surgery) and phacoemulsification and lens implantation with iStent implant (cataract surgery with an iStent implant) can help control your eye pressure.

The iStent is FDA and HSA approved, which means it has been approved by the regulatory bodies in Singapore and the USA as safe and effective to use commercially.

It is a very small titanium implant that is inserted into the canal that drains fluid out of the eye at the end of cataract surgery to help reduce the eye pressure. The implant stays in the eye and does not need to be removed in the future. The implant will take an extra 10-15 mintues extra time at the end of the cataract operation.

This study will recruit *32* subjects Khoo Tech Puat Hospital over a period of 1 year. There will be 16 subjects receiving cataract surgery alone, and 16 subjects receiving the combined cataract surgery with iStent implant.

3. What procedures will be followed in this study

If you take part in this study, you will be randomized to ***"phacoemulsification and lens implantation"*** (cataract surgery) OR ***"phacoemulsification and lens implantation with iStent implant"*** (cataract surgery with an iStent implant). Randomization means assigning you to one of *2* groups by chance, like tossing a coin or rolling dice.

If you take part in this study, you will be asked to attend our eye operation follow up which would be very similar to what you would have if you were not to participate in our study. We will see you at the following time after your operation: Day 1, Week 1, Week 2, Month 1, 3, 6 and 12.

As part of the study you will not know if you received just the cataract surgery or if you received the cataract surgery with the iStent implant. This is called masking, and it is to ensure that the knowledge of your surgical status does not make your or the person checking your eye pressure biased in any way. At the end of the study at 1 year, we will inform you of the operation. Though out the study your surgeon will know which operation you received and will be responsible for the eye health.

Your participation in the study will last *1 year*. You will *have the surgery with or without the iStent implant once* and be followed up for *1 year.* You will need to visit the doctor's office *7* times in the course of the study plus the day of the surgery.

If you agree to take part in this study, the following will happen to you:

Visit 1 (Week 0) – Day of operation. You will attend the day surgery centre and have your eye operation. You will not need to stay over night for both of these procedures.

Visit 2 (Day 1) visit the eye clinic

Visit 3 (week 1) visit the eye clinic

Visit 4 (week 2) visit the eye clinic

Visit 5 (month 1) visit the eye clinic

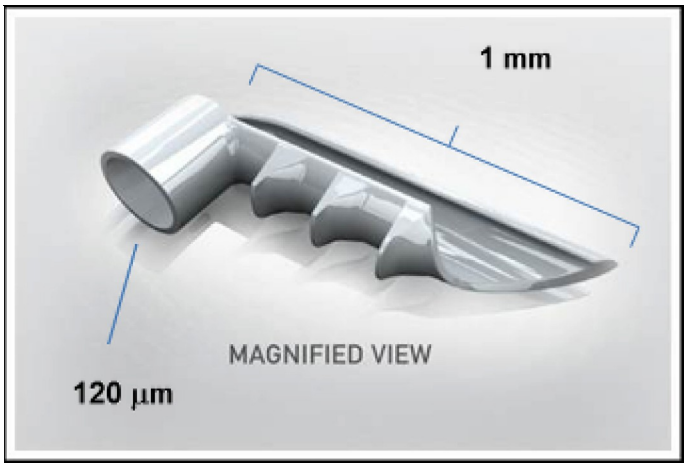
Visit 6 (month 3) visit the eye clinic

Visit 7 (month 6) visit the eye clinic

Final Visit (month 12) visit the eye clinic

When you attend our clinic, you will be asked to have your vision checked by reading letters on a chart, then having your eye pressure checked by two people. You will be examined by your surgeon to check your eye.

Please note that the effects of the iStent may not be permanent, your eye pressure may increase again after months or years, at which point you may need to restart your glaucoma medication.



Magnified diagram of the iStent implant which is around 1 mm long

4. Your Responsibilities in This Study

If you agree to participate in this study, you should follow the advice given to you by the study team. You should be prepared to visit the hospital *7 times* and undergo all the procedures that are outlined above.

5. What Is Not Standard Care or is Experimental in This Study

The study is being conducted because ***"phacoemulsification and lens implantation"*** (cataract surgery) OR ***"phacoemulsification and lens implantation with iStent implant"*** (cataract surgery with an iStent implant) is not yet proven to be a standard *Treatment* in subjects with Primary angle closure glaucoma or primary angle closure. We hope that your participation will help us to determine whether *primary angle closure with iStent implant* is equal or superior to existing *phacoemulsification alone.*

Use of a masking (one or more parties unaware of the treatment assignment), and randomization (study drug selection by chance) are only done for research studies.

Although ***"phacoemulsification and lens implantation"*** (cataract surgery) OR ***"phacoemulsification and lens implantation with iStent implant"*** may be part of standard medical care, in this study this/these procedure(s) are only being performed for the purposes of the research, and are not part of your routine care.

6. Possible Risks and Side Effects

As part of the study you will be randomly allocated to either **"phacoemulsification and lens implantation"** *(cataract surgery) OR* **"phacoemulsification and lens implantation with iStent implant"** *(cataract surgery with an iStent implant)*

Phacoemulsification with lens implantation (cataract surgery)

Cataract surgery is routinely performed to remove the lens in the eye to improve vision. In your condition of primary angle closure or primary angle closure glaucoma, the operation also helps to treat the eye pressure and glaucoma.

There are possible risks involved in cataract surgery which includes:

Infection, bleeding, reduced vision, inflammation, posterior capsular rupture (the lens bag is broken, if this happens you will need a vitrectomy and the lens may need to be placed in a

different chamber of the eye), vitreous loss (related to the posterior capsular rupture and again the vitreous will need to be removed), retinal detachment, endophthalmitis (infection inside the eye which can cause blindness and may sometimes need surgery), suprachoroidal haemorrhage (a large bleed inside the eye that can sometimes cause blindness) and intraocular lens dislocation (where the new implant lens is dislodged and sometimes needs surgery to be repositioned)

Phacoemulsification and lens implantation with iStent implant" ***(cataract surgery with an iStent implant)***

This operation combines the cataract operation with the iStent implant. The iStent implant is designed to lower the eye pressure by placing a stent to open up the eye fluid drainage outflow channel, and to bypass the blockage point in the outflow system called the trabecular meshwork (the area where the fluid exits the eye).

Potential Risks of this procedure is the same as the cataract surgery but in addition includes:

Eye pressure spikes – the eye pressure can be higher than normal after surgery and may need additional medication initially.

Bleeding in the anterior chamber (the front chamber of the eye) is common after the insertion of the iStent, but is usually minor volume and resolves after a few days.

iStent dislocation – the iStent may shift in position and may need to be retrieved in a second operation if found to be dislocated.

Infection: - There is a risk of infection inside the eye. You may need antibiotic medication or an second operation to treat this.

Failure – the iStent may not work or may stop working after months or years, at which point you will need to restart your glaucoma medication. The implant remains in the eye and does not need to be removed.

7. Possible Benefits from Participating in the Study

If you participate in this trial you may reasonably expect to benefit from the trial *of having the phacoemulsification or phacoemulsification with iStent* in the following way:

The procedures will not incur any additional cost to you.
Your participation in this study may add to the medical knowledge about the use of the iStent in your condition, - angle closure.
Your vision will improve after the surgery

8. Important Information for Women Subjects

NA

9. Alternatives to Participation

If you choose not to take part in this study, you will receive standard care for your condition. In our institution this would be to stay on medications, to have phacoemulsification with trabeculectomy.

The potential benefits of staying on medications are:

There is a lower risk of complications compared to the surgical options.

There is a lower cost compared to phacoemulsification with trabeculectomy

Medications have the following potential risks:

Allergy, rash, infection, eye irritation.

Phacoemulsification with trabeculectomy has the following potential benefit:

It has a proven record of providing good long term eye pressure control

It will improve your vision if you have a cataract

Phacoemulsification with trabeculectomy has the following risks:

Infection, bleeding, reduced vision, inflammation, posterior capsular rupture (the lens bag is broken, if this happens you will need a vitrectomy and the lens may need to be placed in a different chamber of the eye), vitreous loss (related to the posterior capsular rupture and again the vitreous will need to be removed), retinal detachment, endophthalmitis (infection inside the eye which can cause blindness and may sometimes need surgery), suprachoroidal haemorrhage (a large bleed inside the eye that can sometimes cause blindness) and intraocular lens dislocation (where the new implant lens is dislodged and sometimes needs surgery to be repositioned)

Hypotony – eye pressure becoming too low, failure – eye pressure remains high, bleb infection – infection of the elevated conjunctiva, loss of vision.

This operation has a higher risk compared to all other options mentioned on this form.

10. Costs & Payments if Participating in the Study

If you take part in this study, the following will be performed at no charge to you:

The basic operation cost which will be randomized to either: “phacoemulsification with lens implantation” OR “phacoemulsification with lens implantation plus an iStent implant”
These costs will be borne by the NMRC research grant.

If a complication arises related to the iStent implant that requires a second operation, this operation will not be charged to the patient.

If you take part in this study, you will have to pay for the following:
Any glaucoma or post-operative medications as part of your standard care.
Any complications or additional surgery as part of your standard care.
Any clinic visits as part of your standard care or follow up.

11. Voluntary Participation

Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to stop your participation will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the Principal Investigator.

If you withdraw from the study, you will be required to inform the principal investigator.

However, the data that have been collected until the time of your withdrawal will be kept and analysed. The reason is to enable a complete and comprehensive evaluation of the study.

Your doctor, the Investigator and/or the Sponsor of this study may stop your participation in the study at any time if they decide that it is in your best interests. They may also do this if you do not follow instructions required to complete the study adequately. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in

the research study.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you *(or your legally acceptable representative, if relevant*) will be informed in a timely manner by the Principal Investigator or his/her representative.

12. Compensation for Injury

If you follow the directions of the doctors in charge of this study and you are physically injured due to the trial substance or procedure given under the plan for this study, Khoo Teck Puat Hospital will pay the medical expenses for the treatment of that injury.

Payment for management of the normally expected consequences of your treatment will not be provided by the Khoo Teck Puat Hospital

Khoo Teck Puat Hospital without legal commitment will compensate you for the injuries arising from your participation in the study without you having to prove Khoo Teck Puat Hospital is at fault. There are however conditions and limitations to the extent of compensation provided. You may wish to discuss this with your Principal Investigator

By signing this consent form, you will not waive any of your legal rights or release the parties involved in this study from liability for negligence.

13. Confidentiality of Study and Medical Records

Information collected for this study will be kept confidential. Your records, to the extent of the applicable laws and regulations, will not be made publicly available.

However, Regulatory Agencies and NHG Domain-Specific Review Board and Ministry of Health will be granted direct access to your original medical records to check study procedures and data, without making any of your information public. By signing the Informed Consent Form attached, you (*or your legally acceptable representative, if relevant*) are authorizing (i) collection, access to, use and storage of your "Personal Data, and (ii) disclosure to authorised service providers and relevant third parties.

"Personal Data" means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. This includes medical conditions, medications, investigations and treatment history.

Research arising in the future, based on this Personal Data, will be subject to review by the relevant institutional review board.

By participating in this research study, you are confirming that you have read, understood and consent to the Personal Data Protection Notification

Data collected and entered into the Case Report Forms are the property of *Khoo Teck Puat Hospital.* In the event of any publication regarding this study, your identity will remain confidential.

14. Who To Contact if You Have Questions

If you have questions about this research study, you may contact the Principal Investigator,

Jason Cheng
Ophthalmology and Visual Sciences Department
Khoo Tech Puat Hospital
Singapore

66023272, 91752883

In case of any injuries during the course of this study, you may contact the Principal Investigator,

Jason Cheng
Ophthalmology and Visual Sciences Department
Khoo Tech Puat Hospital
Singapore

66023272, 91752883

The study has been reviewed by the NHG Domain Specific Review Board (the central ethics committee) for ethics approval.

If you want an independent opinion to discuss problems and questions, obtain information and offer inputs on your rights as a research subject, you may contact the NHG Domain Specific Review Board Secretariat at 6471-3266. You can also find more information about the NHG Domain Specific Review Board at www.research.nhg.com.sg.

If you have any complaints or feedback about this research study, you may contact the Principal Investigator or the NHG Domain Specific Review Board Secretariat.

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I voluntarily consent to take part in this research study. I have fully discussed and understood the purpose and procedures of this study. This study has been explained to me in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction.

By participating in this research study, I confirm that I have read, understood and consent to Khoo Tech Puat Hospital Personal Data Protection Notification. I also consent to the use of my Personal Data for the purposes of engaging in related research arising the future.

_____	_____	_____
Name of Participant	Signature	Date

<Consent should be taken from the subject, unless consent from Legally Acceptable Representative has been specifically approved for the study by DSRB>

< Please include "Translator Information" if the participant / legally acceptable representative is unable to understand English and read any of the translated consent document or short form consent forms available>

Translator Information
The study has been explained to the participant / legally acceptable representative in

_____*<insert language>*_____ by _____*<insert name of translator >* _____

Impartial Witness Statement
I, the undersigned, certify to the best of my knowledge that the participant signing this informed consent form had the study fully explained in a language understood by him / her and clearly understands the nature, risks and benefits of his / her participation in the study.

_____	_____	_____
Name of Impartial Witness	Signature	Date

Investigator Statement
I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his / her participation in the study.

_____	_____	_____
Name of Investigator / Person administering consent	Signature	Date