Participant Information Sheet

Pharmacological Regulation of Optical Properties of the Lens (PROPeL) Study

Formal study title:	*Investigating the role of mainstream pharmacological agents in the regulation of the optical properties of the in vivo human ocular lens*
Study location:	Faculty of Medical and Health Sciences, Grafton campus, University of Auckland 85 Park Road, Grafton, Auckland 1023, NZ

Lead researcher: **Dr Alyssa Lie**
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Approved by the Health and Disability Ethics Committee (HDEC), reference no.: 2023 EXP 13538

TO THE PARTICIPANT:

You are invited to take part in a research study on that uses magnetic resonance imaging (MRI) to investigate whether eye drops that are commonly used to change the size of the pupil can also change the optical properties of the crystalline lens inside the eye.

To help you decide whether you would like to take part in this study, this Participant Information Sheet explains why we are doing it, what taking part would involve for you, what the benefits and risks to you might be, and what would happen after the study ends. You do not have to decide today whether or not you want to take part in this study.

This document is 10 pages long (including a Consent Form). We highly encourage you to take your time to read and understand all of the information provided below. Please feel free to discuss it with your whānau, family, other significant support people and/or healthcare providers. We will also go through this information with you and answer any questions you may have about the study.

Whether or not you take part is entirely your choice. If you do not wish to take part, you do not have to give a reason, and it will not affect any the standard care you may receive at the Grafton Optometry Clinic or Centre for Advanced MRI in any way. If you decide to take part now, but change your mind later, you are free to withdraw from the study at any time without having to give a reason.

If you agree to take part, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

WHAT IS THE PURPOSE OF THE STUDY?

Presbyopia is the loss of the eye's near focusing ability with age. Most people begin to notice the symptoms of presbyopia at 40-50 years old, when they start experiencing difficulty reading small print. For this reason, people usually have to rely on reading glasses (or some other form of optical correction) to see near objects clearly from middle-age onwards.

Presbyopia is believed to be due to a 'stiffening' of the crystalline lens inside the eye with age. Because of this, the lens can no longer change its shape to help our eye change its focus from distance to near objects. The lens is thought to get stiffer because of failure to properly circulate water and important nutrients to protect its proteins against damage.

Recently, animal research studies have shown that it is possible to regulate the water and nutrient circulation around the lens using pharmacological agents which are found in eye drops commonly used during eye examinations to dilate or constrict the pupil. This raises the question of whether these eye drops have the potential to be used as a treatment for delaying or preventing the onset of presbyopia.

The goal of this study therefore is to use magnetic resonance imaging (MRI) to assess whether water circulation and protein distribution in the lens changes when commonly-used pupil-dilating or pupil-constricting eye drops are instilled into the eye. The results of this study will inform us on future strategies for developing new treatments for presbyopia, and alleviate our reliance on reading glasses.

WHO CAN TAKE PART IN THE STUDY?

You have been invited to take part in this study as you have healthy vision, either with or without presbyopia. You are eligible to participate if you are between 18 and 55 years old.

You will **not** be eligible to participate if you:

- Have significant refractive error that is over ±6 Dioptres (*check with us*)
- Have any eye diseases or eye conditions that affect your vision (*check with us*)
- Have had previous eye surgery (*check with us*)
- Have a personal or family history of epilepsy or seizures
- Have a history of neurological disorders or disease
- Have metal implants (e.g. a cardiac pacemaker) that prevent you from having an MRI scan
- Have experienced a serious head injury or skull fracture
- Are pregnant or breastfeeding, because safety of eye drops used in this study has not been established for use in pregnancy and lactation. If you become pregnant during the study, you will not be able to continue your participation in the study.

You will be asked to remove all eye makeup (like mascara and eyeliner) when attending your study visits, as the use of these products may affect the quality of the data obtained.

WHAT DOES TAKING PART IN THE STUDY INVOLVE?

This study involves attending a few visits throughout the duration of the study. At these visits, pupil-dilating or pupil-constricting eye drops will be instilled into your eyes, and we will compare the measurements obtained before and after use of the eye drops. You will be informed of which eye drops you will be receiving at the beginning of the study, and you will receive the same eye drops throughout the duration of the study.

All visits will take place at the University of Auckland's Faculty of Medical and Health Sciences (Grafton campus). The anticipated total amount of time you could dedicate to this study is 4 hours across 3 visits (1 optometric examination and 2 MRI scan sessions).

You are free to withdraw your participation at any point during the study period.

Pre-enrolment screening

Before being invited to attend the first study visit, you will be asked to complete some questionnaires to help us determine your overall eligibility for the study. This includes answering a few questions about your medical history, your previous eye care and any eye problems. It also includes completing a MRI safety form to ensure that it will be safe for you to undergo an MRI scan as per standard practice.

We will also ask for your permission to obtain past medical or health records from your GP or optometrist to check your eligibility to take part in the study.

Study visit #1: Optometric examination

For the first study visit, you will be asked to come to the Grafton Optometry Clinic to assess your eligibility to participate in the remainder of the study. Here, we will check your spectacle prescription, vision, near-focusing capabilities, and eye health using standard optometric tests. Common eye imaging modalities such as optical biometry, retinal and anterior segment photography, and optical coherence tomography may be also performed as part of the assessment (if a valid medical reason to perform the test arises). Once all of the baseline assessments are completed, you will be informed whether or not you are eligible to proceed with the remainder of the study.

Once your study eligibility is established, eye drops will be instilled and all clinical procedures will be repeated 30 minutes to an hour after administration of the eye drops. All optometric tests and imaging will be performed by a NZ-registered optometrist, or by optometry student(s) under the supervision of a NZ-registered optometrist. The total testing time for this study visit is anticipated to be up to 2 hours.

Study visits #2 and #3: MRI scans

After you have completed study visit #1, you will be invited to return for visits #2 and #3, each of which involves undergoing an MRI scan at the Centre for Advanced MRI (CAMRI), based at the University of Auckland's Grafton campus. The MRI protocols employed here are completely safe and non-invasive.

Before entering the scanner, you will be asked to complete a MRI safety form which will be evaluated by an MRI technologist or radiographer to ensure that it is safe for you to undergo an MRI scan. Afterwards, you will be asked to change out of all clothing containing metal, and into a dressing gown, prior to entering the MRI chamber. Once inside, you will be asked to lie on your back on a table, and your head will be stabilised by foam pads. The scanner is quite noisy when it is operating, so you will be given earplugs to wear. Throughout the scan, we will communicate with you via an intercom system regarding when each scan is starting and what to expect.

The MRI scan will be made up of a series of short sequences that range from 1 to 4 minutes long. During each sequence, you will be asked to fixate on a target presented on a screen that you will view from a mirror. For certain sequences, you may be given glasses to wear that may make your vision blurry. You will be given time to rest your eyes in between sequences. The entire duration of the MRI visit is anticipated to be one hour, including changing time and plenty of rest breaks between scans.

The same MRI protocols will be used for both study visits. The MRI scan at study visit #2 will be performed to obtain a baseline scan; the MRI scan at study visit #3 will be performed 30 minutes to an hour after the instillation of the eye drops used at the optometric examination (Study visit #1). Your eyes as well as your brain will be scanned as part of the MRI protocol, but we will not analyse any scans of your brain.

WHAT ARE THE POSSIBLE RISKS OF THE STUDY?

Risks of Eye drops

There is a small risk of side effects from the use of pupil-dilating or pupil-constricting eye drops. For this reason, you will be assessed by a NZ-registered optometrist for suitability prior to instillation of the drops.

For pupil-dilating eye drops, the potential side effects are: blurred vision, eye irritation, dry mouth, headache, nausea, sensitivity to light, and temporary burning/stinging sensation in the eyes. In very rare cases, allergic reactions, eye pain, irregular or rapid heartbeat, paleness or flushing of the skin, skin rash, constipation and abdominal pain, rigid muscles, shortness of breath, dizziness/fainting, or vomiting may occur.

For pupil-constricting eye drops, the potential side effects are: blurred vision, eye/eyelid irritation, watery eyes, browache/headache, nausea, and temporary burning/stinging sensation in the eyes. In very rare cases, allergic reactions, retinal detachments, vitreous haemorrhages, irregular or slowed heartbeat, increased salivation or sweating, shortness of breath, or vomiting may occur.

It is strongly recommended to avoid driving immediately after receiving the eye drops, so please arrange a way to get home safely (take public transport, bring a support person to drive you home, ask the study team to arrange free taxi transport). If any concerns arise after your visit(s), please contact us immediately.

Risks of using an unapproved medicine

VUITY is one of the pupil-constricting eye drops that may be used in this study. VUITY has not been approved by Medsafe in New Zealand, but has received United States Food and Drug Administration (FDA) approval as a treatment for presbyopia. However approval has been received from the Standing Committee on Therapeutic Trials (SCOTT) to use VUITY eye drops in this study.

If you wish to participate in the study, but do not wish to receive VUITY eye drops, you can opt to receive an approved pupil-constricting eye drop (Pilocarpine) instead.

Risks of MRI scan

Some people may get a claustrophobic reaction inside the MRI scanner due to the enclosed environment. If this occurs, you can press a button, and the scan will be stopped immediately. You may experience some eye fatigue as you will be required to fixate on a target through glasses that are designed to blur your vision. You may also experience some boredom as you will be viewing the same target throughout the duration of the MRI scan. You are free to stop and discontinue the MRI scan on account of any discomfort during the scan.

Incidental Findings

In the event that any incidental findings are detected during the optometric examination performed on you, the findings will be treated as they would be in standard practice. A NZ-registered optometrist will review the finding and explain the condition and its potential visual consequences (if any) to you. Where the finding requires further investigation or management, you will be referred to the appropriate healthcare professional (e.g. ophthalmologist, optometrist, or GP). If the finding is not clinically significant, you will be offered the option to have the information about the incidental findings sent to your optometrist and/or GP, to ensure the long-term continuity of care.

In the event that any incidental findings are detected through performing an MRI scan on you, a radiologist will be consulted to review the scan and generate a report on the finding. You will be informed of the finding and a copy of the radiologist's report will be sent to you. Where the finding requires further investigation or management, you will be referred to your GP. If the finding is not clinically significant, you will be offered the option to have the information about the incidental findings sent to your GP to ensure the long-term continuity of care.

A comprehensive eye examination will **not** be conducted as part of this study, and the MRI scans performed as part of this study will **not** be routinely reviewed by a radiologist. Therefore, we are unable to perform diagnostic eye tests or MRI scans for medical purposes of areas where you have known abnormalities.

If you do not consent to being informed of any incidental findings arising as part of this study, then you are not eligible to participate in this study.

WHAT ARE THE POSSIBLE BENEFITS OF THE STUDY?

There will be no direct benefits for you in this study. However, if you are receiving VUITY eye drops as the study intervention, your near vision may improve for up to 6 hours after. Regardless of what eye drops you receive, you will be offered a copy of your spectacle prescription, any images/scans obtained of your eyes, and your MRI scan on USB.

WHO IS PAYING FOR THE STUDY, AND WILL ANY COSTS BE REIMBURSED?

There is no fee involved for taking part in this study. This study is funded by grants from the National Institute of Health and the University of Auckland.

Upon the completion of each study visit, you will be given a gift voucher as a token of our appreciation for your time contribution toward the study (koha). You will receive this regardless of whether you withdraw during the study.

WHAT WILL HAPPEN TO MY INFORMATION?

During this study, the researchers will record information about you and your study participation. If needed, information from your optometrist, GP and/or hospital records may also be collected for the purposes of confirming the eligibility and safety of your participation prior to study enrolment. **You cannot take part in this study if you do not consent to the collection of this information.**

Identifiable Information

Identifiable information is any data that could identify you (e.g. your name, date of birth, or address). In addition to clinical researchers within the study team, the following groups may have access to your identifiable information:

- CAMRI MRI technologist/radiographers (to assist with the MRI scans in this study).
- Your doctors (GP and/or other specialists) and optometrist, if a study test reveals an unexpected result that could be important for your health or well-being. This allows appropriate follow-up to be arranged.
- The University of Auckland (as the organisation with responsibility for the initiation, management, and financing arrangements of the study), ethics committees, or government agencies from New Zealand or overseas, if the study or site is audited. Audits are done to make sure that participants are protected, the study is run properly, and the data collected is correct.

De-identified (Coded) Information

To make sure your personal information is kept confidential, you will not be identified in the processing and analysing of data. Instead, your data will be identified by a unique code. Only the lead researcher will keep a list linking your code with your name, so that you can be identified by your coded data if needed.

Information that personally identifies you will not be included in any report generated about this study. Results of this study may be presented at conferences, included in research theses, and published in international scientific journals, but not in any form that would reasonably be expected to identify you.

Security and Storage of Your Information

Your identifiable information is stored securely in locked cabinets and on secure computer networks at the University of Auckland during the study. After the study, it is transferred to a secure archiving site. As with all medical information, this information will be stored for at least 10 years, before being securely destroyed.

Your coded information will be entered into electronic spreadsheets and sent through a secure server to the University of Auckland. Coded study information will be kept by the University of Auckland in secure, cloud-based storage indefinitely. All storage will comply with local and/or international data security guidelines.

Risks

Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded information, there is no guarantee that you cannot be identified. The risk of people accessing and misusing your information (e.g. making it harder for you to get or keep a job or health insurance) is currently very small, but may increase in the future as people find new ways of tracing information.

Rights to Access Your Information

You have the right to request access to your information held by the study research team. Please ask if you would like to access the results of your optometric examination and/or MRI scans during the study. You also have the right to request that any information you disagree with is corrected. If you have any questions about the collection and use of information about you, you should ask a member of the study research team.

Rights to Withdraw Your Information

You may withdraw your consent for the collection and use of your information at any time, by informing a member of the study research team. If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you.

If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. Alternatively, you may ask for it to be deleted when you withdraw. **However, you will not be able to withdraw data if analyses have already been performed on it at the time of your withdrawal.**

Māori Data Sovereignty

During the study, data may be collected from participants identifying as Māori. Māori data sovereignty is about protecting information or knowledge that is about (or comes from) Māori people. We recognize personal and health information is a tāonga (treasure). To help protect this taonga:

- We have completed a formal Māori consultation with the University of Auckland (Waipapa Taumata Rau) as part of the Locality Approval Process about the collection, ownership, and use of data in this study.
- We allow Māori organisations to access de-identified study data, for uses that may benefit Māori.
- We understand that Māori consider the head tapu and the study researchers will be mindful of this and act respectfully.

Should you have any concerns regarding appropriate practice/ tikanga to address cultural issues, please let us know.

Ownership Rights

Information from this study may lead to discoveries and inventions or the development of a commercial product. The rights to these will belong to the University of Auckland. You and your family will not receive any financial benefits or compensation, nor have any rights in any developments, inventions, or other discoveries that might come from this information.

WHAT IF SOMETHING GOES WRONG?

In the unlikely event of a physical injury as a result of your participation in this study, you may be eligible **to apply** for compensation from ACC under the Injury Prevention, Rehabilitation and Compensation Act.

ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act, just as you would be if you were injured in an accident at work or at home. **This does not mean that your claim will automatically be accepted.** You will have to lodge a claim with ACC, which may take some time to assess.

If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors, such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the research investigators.

For more details, please refer to http://www.acc.co.nz. If you have any questions about ACC, please feel free to ask the researchers for more information before you agree to take part in this trial. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study will not affect your cover.

WHAT HAPPENS AFTER THE STUDY, OR IF I CHANGE MY MIND?

If you choose not to take part, this will not affect the standard of care you may receive at the Grafton Eye Clinic or Centre for Advanced MRI in any way.

If you are a student at the University of Auckland, withdrawal from the study will have no impact whatsoever on your academic assessment or teaching. If you are a student of the School of Optometry and Vision Science, the Head of School has given assurance that participation or non-participation will have no effect on your grades or standing. If you are a staff member of the University of Auckland, your non-participation will not affect your employment.

If you do agree to take part, but change your mind later, you are free to withdraw from the study at any time without having to give a reason. If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. Alternatively, you may ask for it to be deleted when you withdraw. **However, you will not be able to withdraw data if analyses have already been performed on it at the time of your withdrawal.**

WHO HAS APPROVED THE STUDY?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The Central HDEC has approved this study (ref no.: 2023 EXP 13538).

CAN I FIND OUT THE RESULTS OF THE STUDY?

If you would like a summary of the overall project findings, please indicate this on the consent form. Please contact the lead researcher and let them know you would like to also receive any publications resulting from the study. Note that this study will be run over a long period of time and there is often quite a delay between when the data is collected and when a paper is published, so there may be a gap in time between when you participate and when you receive the summary (1-2 years). This summary will not contain any identifying details for any participants.

WHO DO I CONTACT FOR MORE INFORMATION, OR IF I HAVE CONCERNS?

Thank you for giving us your time to consider participating in this study. If you would like to take part, or have any questions, concerns, or complaints about the study at any stage, you can contact:

Lead researcher:	**Dr. Alyssa Lie**
Email:	a.lie@auckland.ac.nz
Phone:	(+64)21 0266 4662

Prof. Paul Donaldson (Head of School of Medical Sciences)

Email:	p.donaldson@auckland.ac.nz
Phone:	(+64)9 373 7599 ext 84625

If you want to talk to someone who is not involved with the study, you can contact an independent health and disability advocate on:

Email:	advocacy@advocacy.org.nz
Phone:	0800 555 050
Fax:	0800 2 SUPPORT (0800 2787 7678)

If you require Māori cultural support, talk to your whānau in the first instance. Alternatively, please contact:

Name:	He Kamaka Waiora, Provider Arm Services
Phone:	(09) 307 4949
Address:	Level 15, Building 4, Auckland City Hospital, Grafton, Auckland

You can also contact the Health and Disability Ethics Committee (HDEC) that approved this study on:

Email:	hdecs@moh.govt.nz
Phone:	0800 4 ETHICS (0800 438 442)

Consent Form

Pharmacological Regulation of Optical Properties of the Lens (PROPeL)Study

Please read and tick to indicate you consent to the following.

I have read the Participant Information Sheet, or have had it read to me in a language I understand, and I fully comprehend what it says.		
I have been given sufficient time to consider whether or not to participate in this study.		
I have had the opportunity to use a legal representative, whānau/family support, or a friend to help me ask questions and understand the study.		
I am satisfied with the answers I have been given regarding the study, and I have a copy of this Consent Form and Participant Information Sheet.		
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time. I also understand that I cannot withdraw data if analyses have already been performed on it.		
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I understand that my participation, withdrawal or non-participation in the study will not affect services that may be provided to me by the Grafton Optometry Clinic or the Centre for Advanced MRI. If I am a student, it will have no effect on my grades or standing.		
I consent to the research staff collecting and processing my information, including information about my health.		
I consent to my GP and any relevant healthcare provider (specialists and/or optometrist) being informed of any significant abnormal results obtained during the study.		
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.		
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.		
I have been informed of and understand the risks involved with eye drops in this study.		
I give my consent to receive VUITY eye drops as a potential study intervention.	Yes ☐	No ☐
I understand the compensation provisions in case of injury during the study.		
I know who to contact if I have any questions about the study in general.		
I wish to receive a summary of the results from the study. If **yes**, please write your email address below:	Yes ☐	No ☐
I am happy to be contacted by researchers within the school about taking part in future research (up to a maximum of 4 times a year).	Yes ☐	No ☐

Declaration by participant:

I hereby consent to take part in this study.

Participant's name: _____

Signature: _____ Date: _____

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: _____

Signature: _____ Date: _____