RESEARCH PROTOCOL

1. **Study Title**
   Perioperative haemostasis, Procedure-related Pain after Physiological or Pharmacological modifications of Local anaesthesia around the Eyes (P4LE) – a double-masked, split-face, active-controlled, pilot randomised clinical trial

2. **Principal Investigator**
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This protocol complies with the Declaration of Helsinki and ICH-GCP.

3. **Background**
   Eyelid procedures including blepharoplasties and correction of eyelid malposition including ptosis, entropion and ectropion are amongst the commonest outpatient or ambulatory procedures worldwide.[1] While cataract operation has turned to become suture-less, needle-less and rather painless,[2] periocular anaesthesia by subcutaneous and/or subconjunctival injection of local anaesthetic agents, e.g. Xylocaine and Marcaine, are necessary preoperatively for eyelid surgeries. However, injection of local anaesthesia (LA) is often the most painful and feared part of the surgery. Various approaches have been investigated to minimise pain during periocular injection of LA and improve haemostasis, including buffering with sodium bicarbonate, warming to body temperature, dilution, adding hyaluronidase and tranexamic acid, using smaller needle sizes, and physical distraction by tapping or vibration.

   Lignocaine is a weak basic amide that is available commercially as salts of strong acids. The cation salt form of lignocaine is in equilibrium with its uncharged base form in aqueous solution. Alkalinisation by adding sodium bicarbonate promotes dissociation of lignocaine to its uncharged base form, which is able to penetrate cell membranes to exhibit their actions on nerve blockade.[3] Similarly, temperature increases the equilibrium constant of the dissociation of local anaesthetic such that there is increased concentration of the uncharged base form to improve nerve penetration.[3] Additionally, skin nociceptors are sensitive to both the acidic nature of the local anaesthetic agent and cold sensation, so acidic and cold solutions will stimulate nociceptors to generate pain.[3] Hyaluronidase, a common adjuvant, improves the spread and absorption of lignocaine by breaking down hyaluronic acid in connective tissues.[4] It also alkalinises the local anaesthetic solution due to its phosphate buffers.[4] Tranexamic acid is an anti-fibrinolytic that decreases bleeding by inhibiting the conversion of plasminogen to plasmin to prevent degradation of fibrin.

In a recent review, buffering of LA has been shown to significantly reduce injection-related pain during periocular anaesthesia in a meta-analysis of five randomised controlled trials (RCT), while one RCT evaluating the warming of local anaesthetic agent to body temperature of 36.5-38°C did not show statistically significant benefit.[5] However, most published studies randomised patients into two groups, with one group receiving either a buffered or warmed solution and another group receiving a control solution on the study eyelids. Such inter-personal comparison remains subjective and confounded by individual pain tolerance. Other studies adopted a split-face approach by injecting a study LA agent to one eyelid then a control LA agent to another eyelid,[6] but the sequence of injection may introduce systemic and recall bias as the second periocular injection has been shown to be more painful.[7] Others have used the upper eyelid as a control for the lower eyelid, but the difference in nerve distribution of the upper and lower eyelids makes direct comparison irrelevant.[8] Welch et al.[9] were the first and only group to date to adopt simultaneous bilateral eyelid injection with a single needle entry point to obtain real-time intra-patient comparison of the pain score of injection, and demonstrated that two-thirds of patients found buffered lignocaine to be less painful with an average difference of 0.9 units out of 10.

The addition of hyaluronidase for local anaesthetic eye blocks has been studied in a Cochrane review and meta-analysis, which concluded that there was low quality of evidence due to high heterogeneity of studies and no statistical difference on intraoperative pain.[4] However, all included studies involved retrobulbar, peribulbar or sub-Tenon blocks. The effect of hyaluronidase as an adjunct to reduce pain during periocular anaesthesia remains uncertain. However, the use of hyaluronidase may hasten the tissue absorption of local anaesthetic agent thus decrease post-injection swelling which is crucial in eyelid operations. Tranexamic acid has been used locally and topically to improve perioperative haemostasis in eyelid surgeries. Paramo et al.[10] demonstrated in a split-face study of bilateral eyelid surgeries that preoperative injection of 0.5 mL of 100 mg/mL tranexamic acid compounded with 2.25 mL of 2% lignocaine with 1:100,000 adrenaline and 2.25 mL of 0.5% bupivacaine with 1:200,000 adrenaline decreased postoperative bruising immediately after operation and at one-week post-operation. Marous et al.[11] showed that both intravenous (1 g tranexamic acid in 100 mL normal saline bolus) and subcutaneous (100 mg/mL tranexamic acid mixed with 2% lignocaine with 1:100,000 adrenaline in 1:1 ratio) tranexamic acid reduced postoperative bruising and oedema after upper eyelid blepharoplasty. Pain associated with the injection has not been reported in these two studies.

The above results were reported in mostly Caucasian patients. It has been shown that pain sensitivity and tolerance vary widely across ethnicities related to physiological and sociocultural differences. Asian subjects have been reported to exhibit higher pain sensitivity and lower pain tolerance in earlier literature.[12, 13] Therefore, research gaps exist in the safety, efficacy (effect size) and cost-effectiveness of physiological (temperature and pH) and pharmacological (hyaluronidase, tranexamic acid) modifications of a commonly used local anaesthetic agent (lignocaine) on reducing perioperative pain (injection and procedure-related), haemostasis and swelling for the most prevalent upper eyelid procedure (blepharoplasty) in Chinese. On the other hand, practice gaps on feasibility and cost-effectiveness in our overloaded health care system (Hospital Authority) remain to be evaluated.

4. Aims and Hypotheses

The aim of the project is to test the hypothesis that the following modifications during subcutaneous eyelid injection of LA, compared to 2% lignocaine with 1:200,000 adrenaline,

reduce injection pain and procedure-related pain and improve perioperative haemostasis.
1. Buffering of 2% lignocaine with 1:200,000 adrenaline by adding sodium bicarbonate;
2. Warming of 2% lignocaine with 1:200,000 adrenaline to 37°C;
3. Addition of hyaluronidase to 2% lignocaine with 1:200,000 adrenaline; and
4. Addition of tranexamic acid to 2% lignocaine with 1:200,000 adrenaline.

5. Study Design

This is a double-masked, prospective, randomised controlled trial of patients undergoing bilateral upper eyelid blepharoplasty requiring subcutaneous anaesthesia at Prince of Wales Hospital, Alice Ho Miu Ling Nethersole Hospital and CUHK Medical Centre. Inclusion criterion includes adult patients aged 18 or above scheduled for bilateral primary upper eyelid blepharoplasty. Exclusion criteria include patients aged less than 18, pregnancy, allergy to local anaesthetic agents, history of previous eyelid surgery and patients on antiplatelets or anticoagulants. The study will be performed in accordance with the regulations of the Declaration of Helsinki after approval from the Institutional Review Board. Written informed consent will be obtained from all patients. A standardised data collection sheet will be used to gather data including age, sex, ethnicity, diagnosis, surgery performed, type of LA used for each eye, injection pain score, intraoperative pain score, postoperative pain score, postoperative ecchymosis score and postoperative swelling score.

Before the trial, an experiment is conducted to standardise the preparation of the buffered and warmed solutions. The first part involves measuring the pH of the local anaesthetic solutions with a pH meter, including the buffered solution (0.9 mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 8.4% sodium bicarbonate) and unbuffered solution (0.9 mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 0.9% normal saline). The second part involves measuring the temperature of the warmed solution and room temperature solution of 2% lignocaine with 1:200,000 adrenaline. A previous study has shown that warming lignocaine to 48°C with a water bath and then drawing up 2.5 mL of warmed solution with a 5 mL syringe resulted in a solution of 36.5-38°C for 2 minutes.[8] A similar experiment will be conducted to determine the temperature of the water bath needed, the optimal timing of injection after removal from the water bath, and the final solution temperature with the aim of achieving body temperature of 37°C. The temperature of the room temperature solution will also be measured by a digital thermometer.

Patients undergoing bilateral upper eyelid blepharoplasty are equally randomised into four groups, namely (1) buffered group, (2) warmed group, (3) hyaluronidase group, and (4) tranexamic acid group.

- For the buffered group, one eye of each patient is randomised to receive the buffered solution of 0.9 mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 8.4% sodium bicarbonate, and the other eye will receive the unbuffered solution of 0.9 mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 0.9% normal saline.
- For the warmed group, one eye of each patient is randomised to receive the warmed solution of 1 mL of 2% lignocaine with 1:200,000 adrenaline warmed to 37°C, and the other eye will receive the room temperature solution of 1 mL of 2% lignocaine with 1:200,000 adrenaline.
- For the hyaluronidase group, one eye of each patient is randomised to receive a solution 0.9 mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 150 IU/mL hyaluronidase solution (prepared by mixing 10 mL 0.9% normal saline with 1500 IU hyaluronidase powder), and the other eye will receive a solution of 0.9

mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 0.9% normal saline.

- For the tranexamic acid group, one eye of each patient is randomised to receive a solution 0.9 mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 100 mg/mL tranexamic acid, and the other eye will receive a solution of 0.9 mL of 2% lignocaine with 1:200,000 adrenaline mixed with 0.1 mL of 0.9% normal saline.

Patients are not aware of the solution given to either eye.

We acknowledge that true investigator and patient masking of a warmed solution is not completely feasible because the surgeon may also detect the temperature of the syringe when injecting the solution and the patient may feel the temperature of the solution during injection, as discussed in previous studies. A warmed solution decreases injection pain because it stimulates fewer temperature-sensitive nociceptors, so it is not practical to completely mask the solution temperature from patients, although patients are not aware of the solution temperature before injection. However, we aim to preserve masking and reduce bias as much as possible by standardising the injection needle, volume and rate, and using the same pain rating visual analogue scale (VAS) for pain assessment.

5-mL syringes with 30-gauge 1-inch needles are used to prepare the anaesthetic solutions before the operation by personnel not involved in the injection of LA. The needles are inserted simultaneously to both upper eyelids by two ophthalmologists unaware of the content of the solution. 1 mL of anaesthetic solution is injected simultaneously to both eyelids at a rate of 0.1 mL/second for 10 seconds. Surgery for both eyelids are then performed as per the usual manner.

The patient is asked to rate the sensation of pain felt for each eyelid at the following timepoints using a pain rating VAS of 0 to 10, including (1) immediately after injection (sensation of pain felt during infiltration of LA but not needle entry), (2) after conclusion of the surgery (pain encountered during the surgery), and (3) one-week post-operation (postoperative pain).

Postoperative haemostasis is examined at one-week post-operation. Postoperative ecchymosis and swelling scores are rated by a masked ophthalmologist based on clinical photos using a standardised rating score of 0 to 5 adapted from previous studies.[11]

The first stage of the pilot RCT involves identifying two of the most effective modifications by comparison of modified LA versus unmodified LA. The second stage of the pilot RCT involves head-to-head comparison of the two most effective modifications (namely modification A versus B), as well as both modifications combined versus either modification alone (namely modifications A+B versus A and A+B versus B). Patients are equally randomised into three groups. For the first group, one eye is randomised to receive modification A, and the other eye will receive modification B. For the second group, one eye is randomised to receive modifications A and B combined, and the other eye will receive modification A alone. For the third group, one eye is randomised to receive modifications A and B combined, and the other eye will receive modification B alone. The effect size and potential side effects of combining the modifications will be assessed. The solution preparation, safety and chemical stability data for the combined modifications are shown in the following table.

Modification A	**Modification B**	**Modification**	**Injection**	**Safety and**

		A+B	volume and rate	chemical stability data
Warmed (1 mL of 2% lignocaine with 1:200,000 adrenaline warmed to 37°C)	**Sodium bicarbonate** (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 8.4% sodium bicarbonate)	0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 8.4% sodium bicarbonate, warmed to 37°C	1.0 mL (0.1 mL/second for 10 seconds)	Jaichandran et al.[14] have demonstrated that combined warming and buffering with sodium bicarbonate in peribulbar anaesthesia prior to cataract surgery is safe and significantly reduced injection pain compared to unbuffered control solution at room temperature.
Warmed (1 mL of 2% lignocaine with 1:200,000 adrenaline warmed to 37°C)	**Hyaluronidase** (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 150 IU/mL hyaluronidase)	0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 150 IU/mL hyaluronidase solution, warmed to 37°C	1.0 mL (0.1 mL/second for 10 seconds)	The heat stability of hyaluronidase has been investigated and one laboratory study has shown that hyaluronidase demonstrated stability and highest activity at 37°C.[15]
Warmed (1 mL of 2% lignocaine with 1:200,000 adrenaline warmed to 37°C)	**Tranexamic acid** (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 100 mg/mL tranexamic acid)	0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 100 mg/mL tranexamic acid, warmed to 37°C	1.0 mL (0.1 mL/second for 10 seconds)	The heat stability of tranexamic acid has been investigated and no chemical breakdown was demonstrated at a temperature of 50°C.[16]
Sodium bicarbonate (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 8.4% sodium bicarbonate + 0.1 mL of 0.9% normal saline)	**Hyaluronidase** (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 150 IU/mL hyaluronidase + 0.1 mL of 0.9% normal saline)	0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 8.4% sodium bicarbonate + 0.1 mL of 150 IU/mL hyaluronidase	1.1 mL (0.1 mL/second for 11 seconds)	Moharib et al.[17] have investigated the effect of combining sodium bicarbonate and hyaluronidase on providing analgesia during sub-Tenon anaesthesia for cataract surgery. 88% of patients achieved adequate analgesia with this

				drug combination.[17]
Sodium bicarbonate (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 8.4% sodium bicarbonate + 0.1 mL of 0.9% normal saline)	**Tranexamic acid** (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 100 mg/mL tranexamic acid + 0.1 mL of 0.9% normal saline)	0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 8.4% sodium bicarbonate + 0.1 mL of 100 mg/mL tranexamic acid	1.1 mL (0.1 mL/second for 11 seconds)	The combination of sodium bicarbonate and tranexamic acid in local anaesthetic solution has been reported to be safe and effective for facial cosmetic surgery by Fathimani et al.[18]
Hyaluronidase (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 150 IU/mL hyaluronidase + 0.1 mL of 0.9% normal saline)	**Tranexamic acid** (0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 100 mg/mL tranexamic acid + 0.1 mL of 0.9% normal saline)	0.9 mL of 2% lignocaine with 1:200,000 adrenaline + 0.1 mL of 150 IU/mL hyaluronidase + 0.1 mL of 100 mg/mL tranexamic acid	1.1 mL (0.1 mL/second for 11 seconds)	Both tranexamic acid and hyaluronic acid, the substrate of hyaluronidase, inhibit the activation of plasminogen to plasmin.[19] Hyaluronidase breaks down hyaluronic acid and may theoretically decrease the effect of tranexamic acid. If these two modifications are the most effective when used separately, the proposed trial will investigate whether their interaction is clinically significant when used in combination.

In the event of allergic or other adverse reactions after the injection of local anaesthesia, an unblinding mechanism is in place with a 24-hour emergency contact number available to allow identification of the injected solution and provision of necessary medical care.

6. Eligibility Criteria

Inclusion criteria

- Patients undergoing bilateral upper eyelid blepharoplasty requiring subcutaneous anaesthesia at Prince of Wales Hospital, Alice Ho Miu Ling Nethersole Hospital and CUHK Medical Centre; and
- Adult patients aged 18 or above.

Exclusion criteria

- Patients aged less than 18;
- Pregnancy;
- Allergy to local anaesthetic agents;
- History of previous eyelid surgery; and
- Patients on antiplatelets or anticoagulants.

7. Study Outcomes

Primary Outcome
Pain of injection of LA, measured by a pain rating VAS of 0 to 10.

Secondary Outcomes
1. Pain encountered during the surgery, measured by a pain rating VAS of 0 to 10.
2. Pain encountered one week after surgery, measured by a pain rating VAS of 0 to 10.
3. Postoperative ecchymosis at one week after surgery, rated based on clinical photos using a standardised rating score of 0 to 5 adapted from previous studies.[11]
4. Postoperative swelling at one week after surgery, rated based on clinical photos using a standardised rating score of 0 to 5 adapted from previous studies.[11]

8. Statistical Considerations and Data Analysis

Sample Size
This pilot RCT aims to assess the effect size of the use of buffering, warming, hyaluronidase and tranexamic acid as adjuncts to LA on reducing injection and procedure-related pain and improving perioperative haemostasis for bilateral upper eyelid blepharoplasty in a Chinese population.

The addition of sodium bicarbonate is the most studied method for reducing pain during the local injection of lignocaine solution for ophthalmologic surgeries, while the results of other methods are less readily available. Therefore, the sample size calculation is based on four previous publications that studied the effect of adding sodium bicarbonate to a local anaesthetic solution of lignocaine with or without adrenaline on pain reduction.[6, 8, 14, 20] Two of these four studies investigated transcutaneous local anaesthesia for blepharoplasty, one study investigated transcutaneous local anaesthesia for cataract surgery, while one study investigated peribulbar local anaesthesia for cataract surgery. The pooled mean difference in pain score is 2.32 (on a scale of 0-10), and the pooled standard deviation is 1.55, based on the results of these four studies.

We determined that, with a level of significance of 0.05 and a power of 0.8, in order to detect a clinically meaningful difference in pain score of 2.0, assuming a standard deviation of 1.55, the calculated sample size is 9.4 (rounded up to 10) eyelids per intervention arm.[21]

Therefore, for the first stage of the pilot RCT, the target sample size is set at 10 eyelids for each treatment arm. The sample size of the first stage is 40 patients involving 80 eyelids, with 10 patients in each of the four groups (10 eyelids of 10 patients receiving modified lignocaine solution and 10 fellow eyelids of these 10 patients receiving control lignocaine solution for each group).

For the second stage of the pilot RCT, the target sample size is set at 13-14 eyelids for each treatment arm. Therefore, the sample size is 40 patients involving 80 eyelids, with 13-14 patients in each of the three groups.

We acknowledge that the available studies were conducted in non-Chinese subjects, so the effect size may differ in our local population. We also understand that the effect sizes of warming and the addition of hyaluronidase or tranexamic acid are not available. Therefore, if none of the four modifications are found to be effective in reducing pain or improving haemostasis, the first stage of the pilot RCT (40 patients) will be duplicated in the second stage of the pilot RCT (another 40 patients) to increase the sample size and improve the power in detecting a meaningful difference. If effective modifications are identified only after duplication of the first stage (80 patients in total), future RCTs may investigate the combined effects of these modifications. For the current study, no additional patients will be recruited beyond the originally planned 80 patients.

The results of this pilot RCT study will be used to scale up the project into a full-scale RCT, by informing the effect size of buffering, warming, adjuvant hyaluronidase and tranexamic acid to LA on reducing injection and procedure-related pain and improving perioperative swelling and haemostasis in a Chinese population undergoing bilateral upper eyelid blepharoplasty to guide sample size calculation.

Regarding the feasibility of subject recruitment, upper lid blepharoplasty is one of the most common oculoplastic procedures. In the year 2024, 80 surgeries involving upper lid blepharoplasties were performed by our department at the Prince of Wales Hospital and Alice Ho Miu Ling Nethersole Hospital, including 14 bilateral upper lid blepharoplasties alone, 7 unilateral upper lid blepharoplasties alone, 14 bilateral upper lid blepharoplasties combined with other procedures, and 45 unilateral upper lid blepharoplasties combined with other procedures. Most patients who underwent unilateral upper lid blepharoplasty eventually required sequential upper lid blepharoplasty for the contralateral eye within the same year. Reviewing the current surgery waiting list (as of 26th Sept 2025), 30 patients are on the waiting list for bilateral upper lid blepharoplasty alone, and 20 patients are on the waiting list for bilateral upper lid blepharoplasty combined with other procedures. We expect that approximately 80% of these patients will be eligible and consent to the proposed RCT after considering the inclusion and exclusion criteria. We plan to regularly discuss the current study in monthly departmental meetings and at grand rounds to promote patient recruitment at the Prince of Wales Hospital and Alice Ho Miu Ling Nethersole Hospital. Co-applicant Prof Kelvin Chong, head of the orbital and oculoplastic (OOP) team of the study sites, has approved the study team to approach each patient during his/her pre-operative visit for upcoming upper lid blepharoplasties. To further expand the recruitment network, Prof Chong, director of the Eye Centre at CUHK Medical Centre, has also approved the study team to do the same. The study team also has a backup plan to extend the invitation to oculoplastic teams of all other six clusters within the Hospital Authority, in case the recruitment is slower than expected. We believe that subject recruitment is feasible after considering the above factors.

Statistical Methods

The Wilcoxon signed rank test is used to analyse the difference between the modified lignocaine solution and control lignocaine solution because the above outcome measures are considered non-parametric variables and the data is considered to be paired as one eyelid of each patient acts as the control of the other eyelid. The significance level is set at $\alpha = 0.05$.

Pain during local anaesthetic injection is the most clinically relevant, patient-centred outcome and thus proposed it as the primary outcome. Postoperative ecchymosis and

swelling are also clinically important outcomes, because they affect the postoperative recovery, including wound healing, early cosmetic and functional outcome, and patients' satisfaction and quality of life. We acknowledge that certain secondary outcomes, e.g., postoperative pain, may be confounded by the presence or degree of intraoperative bleeding, postoperative ecchymosis, and swelling. Therefore, we shall take precautions to analyse and interpret each outcome both with and without adjusting for potential confounders, including intraoperative bleeding, postoperative ecchymosis, and swelling, using various models of multivariate analysis.

9. Ethical Considerations

The study will be conducted in full conformance with principles of the Declaration of Helsinki and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP), and within the laws and regulations of Hong Kong SAR.

Patients' data privacy is protected according to the data storage criteria set by the Hospital Authority. Patients' data will be kept safely in the study period and will be destroyed 5 years after the study according to the protocol set by the Hospital Authority to protect patient's data confidentiality.

10. Significance

Buffering or warming lignocaine and the additions of hyaluronidase and tranexamic acid are useful adjuncts to reduce injection and procedure-related pain and may also improve perioperative haemostasis and postoperative swelling with minimal cost, complexity and complications. However, there has been no RCT comparing head-to-head or combining these adjuvants. There is also lack of level 1 evidence from RCT conducted in non-Caucasian populations. Their use in a Chinese population has not been investigated previously. Reducing perioperative pain, bleeding and swelling are keys to enhancing the outcome, safety, efficiency and ultimately cost-effectiveness of ophthalmic surgeries carried out under local anaesthesia. Our proposal, if supported, will immediately impact on local clinical practice, and directly inform health service management on the evolving landscape of ambulatory surgery centre development in Hong Kong. Our results may shift the current paradigm of carrying out many ophthalmic and other head and neck operations under general and/or monitored anaesthetic care and extend the use of local anaesthesia to patients who would otherwise require general anaesthesia due to fear of pain. Converting general anaesthesia to local anaesthesia would ultimately reduce healthcare costs.

11. Institutional affiliations

This study is led by the Department of Ophthalmology and Visual Sciences at The Chinese University of Hong Kong.

12. Sponsors and Sources of Fundings

The Health and Medical Research Fund, which is a non-commercial local research grant, has been applied and is recommended for support subject to clarifications/amendments.

13. Potential Conflicts of Interest

All investigators declared that they are not aware of any conflicting interests that may affect their unbiased performance of their responsibilities in the study.

14. Incentives for Subjects

HK$100 (equivalent to about USD 13) cash incentive is provided to each participant at the end of the study as a courtesy for their voluntary effort in joining the study, which involves additional time spent for the assessment of pain scores and postoperative bruising and swelling and potentially longer operation time.

15. Provisions for Treating and Compensating Subjects

If subjects are injured during their participation in this study, the investigator will provide medical treatment to them or refer them to other treatment. They are not giving up any of their legal rights by signing this informed consent form. An insurance policy will be arranged for the study.

16. References

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