**Study Protocol**

# Assessment of Actual Intraocular Pressure after Corneal Refractive Surgery Based on Big Data and Artificial Intelligence

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## 1. Significance, Background, and Current Status

Studies show the global average prevalence of myopia is 22%, with hyperopia incidence being similar. In China, the myopia prevalence is 31%, making it one of the countries with the highest rates of myopia. Currently, the safety and efficacy of corneal refractive surgery (CRS), such as LASIK and SMILE, for correcting myopia, hyperopia, and other refractive errors are well-established. An increasing number of patients undergo CRS to alleviate the inconveniences caused by refractive errors. While LASIK has long been regarded as a classic procedure, since the first report of Small Incision Lenticule Extraction (SMILE) for myopia correction in 2008, it has evolved into one of the mainstream surgical techniques. With the rapid advancement of refractive surgery, minimizing postoperative complications while maintaining excellent visual outcomes has become a major focus for clinicians. Postoperative intraocular pressure (IOP) monitoring is a crucial observation index.

Theoretically, IOP should not change significantly after CRS, as the surgery does not affect aqueous humor dynamics or intraocular volume. However, numerous studies indicate that alterations in corneal shape and biomechanical properties, particularly corneal thinning, lead to artificially low IOP readings with various tonometers, especially those dependent on corneal thickness. Furthermore, postoperative management often requires prolonged use of corticosteroid eye drops to suppress inflammation and promote wound healing. Extended steroid use can increase aqueous outflow resistance, elevating IOP, particularly in steroid responders, and potentially leading to steroid-induced glaucoma. Additionally, high myopia is a known risk factor for primary open-angle glaucoma. Therefore, based on preoperative and postoperative corneal parameter changes, rapidly and effectively determining the actual IOP range after CRS is of great significance for guiding clinical medication and screening for steroid-induced glaucoma.

Big Data and Artificial Intelligence (AI) are increasingly applied in medicine. AI primarily includes two technical branches: machine learning (ML) and deep learning. ML, a novel AI technology, has garnered significant interest in medical applications in recent years. It typically involves computer simulations that integrate human-like learning, refine knowledge structures, and continuously improve performance to aid diagnosis and intelligent decision-making, becoming a pivotal method in AI. Resembling neural network processes, ML systems are trained on selected input data using appropriate algorithms to produce corresponding outputs. It is now widely used to solve complex problems in engineering and science. In ophthalmology, AI/ML has gained attention for assisting in disease detection and monitoring, demonstrating advantages in fundus image diagnosis, keratoconus screening, and glaucoma

classification. In corneal refractive surgery, ML has been applied to preoperative parameter design and outcome optimization, showing good safety, efficacy, and predictability. Preliminary attempts have been made to use AI decision trees to evaluate the safety and efficacy of CRS.

Building on this advanced technology and our previous research findings—which suggest that IOPcc and Pentacam-derived correction formulas (with the Shah correction method being preferable) provide relatively reliable IOP estimates after SMILE—this study aims to establish a data-driven model. Using Shah-corrected IOP as a reference to define postoperative IOP status, we will train and iteratively optimize a model by incorporating all relevant preoperative and postoperative parameters potentially affecting IOP. The goal is to predict the true IOP after CRS, thereby guiding postoperative follow-up, facilitating early detection of IOP elevation, and identifying potential glaucomatous tendencies.

## 2. Research Plan (Objectives, Content, Methodology, Key Challenges, and Solutions)

### 2.1 Study 1: IOP Changes and Value Prediction after FS-LASIK and SMILE

A total of 350 patients undergoing SMILE and 350 undergoing FS-LASIK between October 1, 2023, and January 2, 2025, will be enrolled. Parameters including spherical equivalent (SE), central corneal thickness (CCT), mean keratometry (Km), residual stromal bed thickness (RST), percent tissue altered (PTA), and IOP values preoperatively and at 1 week, 1 month, and 2 months postoperatively will be recorded. These parameters will be included in a multiple linear regression model to analyze factors influencing postoperative IOP and derive a preliminary estimation formula for postoperative IOP measurements. Differences in IOP changes between the two surgical groups will be compared, and other influencing factors will be explored.

### 2.2 Study 2: Assessment of IOP Measurement Levels after CRS Based on Machine Learning

Data from approximately 10,300 SMILE and 11,000 FS-LASIK patients treated between October 1, 2020, and April 1, 2025, will be collected. Parameters affecting IOP, such as SE, CCT, Km, RST, and PTA, will be included to explore a predictive ML model for post-CRS IOP. The information gain algorithm will quantify the influence of various factors on postoperative IOP. Follow-up IOP measurements (preoperative, 1 week, 1 month, 2 months) and Pentacam Shah-corrected IOP will be recorded. The estimation formula from Study 1 will also be used to calculate postoperative IOP. Several different ML models will be constructed based on features with higher weights to build predictive models for judging IOP levels at follow-up timepoints. Clinical validation will be performed.

A cross-validation method will be employed to verify the model's effectiveness. Internal validation will first be conducted using the training dataset. The entire modeling dataset will be randomly divided into 10 equal folds. Nine folds will be used

for model training, and the remaining fold will serve as the test set. The trained model will predict outcomes on the test set, and prediction errors will be calculated (e.g., sum of squared errors). This process will be repeated 10 times, each time with a different fold as the test set. The average performance across all 10 iterations will be reported.

## 3. Technical Roadmap

### Detailed Protocol: 3.1 Inclusion Criteria

1. Normal preoperative IOP, no glaucoma or suspected glaucoma.
2. Corneal thickness ≥ 480 μm.
3. Discontinuation of rigid gas permeable contact lenses for ≥3 months and soft contact lenses for ≥2 weeks prior to examination.
4. Clear cornea, no corneal leukoma, no history of ocular trauma.
5. No previous ocular surgery.
6. Willingness to participate and comply with all study examinations and procedures.

### 3.2 Exclusion Criteria

1. Severe psychiatric disorders.
2. Ocular hypertension, suspected glaucoma, or glaucoma.
3. Concurrent other ocular diseases (e.g., corneal opacity, uveitis).
4. History of ocular surgery, trauma, or contact lens wear (as per inclusion criterion #3).
5. Nystagmus or inability to cooperate with examinations.
6. Presence of other ocular surface diseases, dry eye syndrome, fundus diseases, or systemic diseases affecting the study.

### 3.3 Criteria for Withdrawal, Dropout, or Study Termination

1. Inability to complete the study protocol after enrollment.
2. Poor quality of research-related ophthalmic examinations.

### 3.4 Data Collection and Other Measures 1. Data Collection:

1. Demographic data: Name, gender, age.
2. Medical history: Documented systemic diseases.
3. Comprehensive ophthalmic examinations: Visual acuity, refraction, IOP, corneal topography (Pentacam), slit-lamp examination, ocular biometry, axial length, lens status, intraoperative parameters, postoperative IOP, and postoperative refraction.
4. Ensuring Patient Compliance: The study details will be thoroughly explained to patients and their families. Informed consent will be obtained. Good communication and patient care will be maintained throughout the study to enhance trust and compliance.

3.5 Study Endpoints

Primary endpoints include preoperative and postoperative computerized IOP measurements.

3.6 Statistical Analysis

All analyses will be performed using SPSS version 29.0 (SPSS Inc.). The normality of data distribution will be assessed using the Kolmogorov-Smirnov test. Normally distributed data will be presented as mean ± standard deviation ($x \pm s$), and Pearson correlation analysis will be used for continuous variables. Non-normally distributed data will be presented as median (Q1, Q3), and Spearman correlation analysis will be employed. A P-value $< 0.05$ will be considered statistically significant.

**3.7 Key Challenges and Proposed Solutions**

1. **Study 1:** The potential confounding effects of different refractive errors and corneal thickness will be addressed. Participants will be stratified into three groups based on SE: < -3.00 D, -3.00 D to -6.00 D, and > -6.00 D. Inter-group differences will be analyzed to control for their impact on the final results.

2. **Study 2:** Using the formula from Study 1 and the Shah-corrected IOP to define IOP status may still contain judgment errors, leading to predictive bias in the ML model. This will be mitigated by validating against historical data with confirmed postoperative ocular hypertension.

3. **Overall Goal:** Establishing a deep learning-based model to predict post- refractive surgery IOP and accurately judge its level aims to resolve clinicians' difficulties in interpreting IOP readings after surgery.

**4. References**

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