Using artificial intelligence to predict the risk for posterior capsule opacification after phacoemulsification

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PURPOSE: To apply artificial intelligence models to predict the occurrence of posterior capsule opacification (PCO) after phacoemulsification.

SETTING: Farabi Eye Hospital, Tehran, Iran.

DESIGN: Clinical-based cross-sectional study.

METHODS: The posterior capsule status of eyes operated on for age-related cataract and the need for laser capsulotomy were determined. After a literature review, data polishing, and expert consultation, 10 input variables were selected. The QUEST algorithm was used to develop a decision tree. Three back-propagation artificial neural networks were constructed with 4, 20, and 40 neurons in 2 hidden layers and trained with the same transfer functions (log-sigmoid and linear transfer) and training protocol with randomly selected eyes. They were then tested on the remaining eyes and the networks compared for their performance. Performance indices were used to compare resultant models with the results of logistic regression analysis.

RESULTS: The models were trained using 282 randomly selected eyes and then tested using 70 eyes. Laser capsulotomy for clinically significant PCO was indicated or had been performed 2 years postoperatively in 40 eyes. A sample decision tree was produced with accuracy of 50% (likelihood ratio 0.8). The best artificial neural network, which showed 87% accuracy and a positive likelihood ratio of 8, was achieved with 40 neurons. The area under the receiver-operating-characteristic curve was 0.71. In comparison, logistic regression reached accuracy of 80%; however, the likelihood ratio was not measurable because the sensitivity was zero.

CONCLUSION: A prototype artificial neural network was developed that predicted posterior capsule status (requiring capsulotomy) with reasonable accuracy.

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Posterior capsule opacification (PCO) is the most common complication of cataract surgery.[1,2] It is caused by the growth and transdifferentiation of retained lens epithelial cells.[3,4] Posterior capsule opacification causes secondary visual loss that necessitates laser capsulotomy in more than 20% of patients. Several factors affect the occurrence of PCO,[5–7] including patient age at the time of surgery,[8] sex,[9] pseudoexfoliation (PXF) syndrome,[10] diabetes mellitus,[11] ocular anatomy (ie, axial hyperopia),[7] intraocular lens (IOL) material[9] and design (haptic angulation and edge features),[12] surgical technique,[7] and surgeon experience.[13,14]

Because of the complex nature of PCO pathogenesis, machine-learning algorithms are expected to be useful in modeling and predicting its occurrence. Decision trees are formed through recursive partitioning and dividing the data based on the values of a selected attribute. The model is transparent in a way that allows the decision maker to follow a specific path of classification, prediction, and decision making. Artificial neural networks are computational models that consist of nodes (neurons) arranged in layers interconnected with transfer functions (synapses). After input information at a layer is processed, neurons of the next layer are provided with new inputs. These formations

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can be trained, refined, tested, and evaluated by datasets.[15,16]

These models have been used in different medical fields to predict breast cancer survival,[17] trauma mortality,[18] and liver disease diagnosis.[19] The reported applications in ophthalmology are glaucoma diagnosis[20] and risk prediction,[21] survival prediction in choroidal melanoma,[22,23] and classification of corneal topography.[24]

In this study, we used the aforementioned artificial intelligence models for PCO prediction.

PATIENTS AND METHODS

Dataset

The dataset comprised patients randomly selected from a pool who had phacoemulsification for age-related cataract from 2006 to 2007 at Farabi Eye Hospital, Tehran. Selected patients were reexamined 2 years after surgery, at which time their posterior capsule status was determined. A new diagnosis of clinically significant PCO was made when the estimated visual acuity in the pseudophakic eye by red reflex (with a dilated pupil) was worse than 20/30. In cases of significant corneal opacity, the examiner directly judged the density of PCO during biomicroscopy.

Data Polishing and Feature Selection

Data were screened for missing values and outliers. Outliers were double checked with the registered information in the original records. A literature review was the basis for including potential determinants of PCO incidence; the following were identified: age,[8] sex,[9] PXF,[10] axial length,[7] diabetes mellitus,[11] surgeon experience,[13,14] IOL type,[9] and cataract type.[25] Expert opinion and statistical feature selection were used to further validate the choices; corneal opacity and surgically challenging eye variables were added. As a result, 10 of 35 registered variables were selected for entry in the models. Binary logistic regression was used for multivariate modeling.

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Decision-Tree Development

The QUEST algorithm (Clementine 12.0, Integral Solutions, Ltd.) was used for decision-tree development. QUEST is a classification algorithm that generates a binary decision tree for independent and simultaneous pruning and splitting of data. For each part, the correlation between each predictor variable and the target was found by using the analysis-of-variance F test, Levene test (for ordinal and continuous predictors), and Pearson chi-square test (for nominal predictors). The predictor with the highest association with PCO was selected for splitting. Quadratic discriminant analysis was used to find the optimum splitting point for the predictor variable. The process was repeated recursively until 1 stopping rule was triggered.

Artificial Neural Network Development

Three back-propagation artificial neural networks were constructed with 4, 20, and 40 neurons in 2 hidden layers and trained with the Levenberg-Marquardt protocol using log-sigmoid and linear transfer functions (Matlab, version 7.10.0.499, Mathworks, Inc.). The neurons in each layer of the artificial neural network were not connected to neurons of the same layer but were connected to all neurons in the preceding and following layers. In the training phase, data were fed into a particular neuron of the input layer. Each neuron input was multiplied by a weight. The neuron would transmit the result to all the neurons of the next layer as long as it exceeded a threshold specified by a predefined transfer function. The result would be achieved when the data approached the output layer. The algorithm would measure the deviation of the produced answer from the actual observation and pass it backward through the network. The weight of each neuron would be adjusted to minimize the error for every eye in the training set. The receiver-operating-characteristic (ROC) curve was used to compare the efficiency of the 3 artificial neural networks. For each class—that is, eyes with PCO and eyes without PCO—threshold values would be applied to outputs between 0 and 1. The sensitivity and 1-specificity were calculated for each threshold. The ROC curve shows to what extent the probabilities of randomly selected true positive cases of artificial neural network scores are significantly different from the probability of randomly selected true negative scores. To further illuminate the artificial neural network black box, relevance of each input variable for PCO prediction was measured by dividing the sum square of its weight for the neurons in the second layer to the sum square of whole weights; this was performed for the 40-neuron artificial neural network.[26]

To develop models, the examined eyes were randomly assigned to a training dataset and a test dataset (using the Matlab software randomization function "dividerand"). The total network parameters for the largest artificial neural network (40-neuron network = 4 neurons in the first hidden layer, 35 neurons in the second hidden layer, and 1 neuron as output layer) with 10 inputs equaled 255. Thus, to have a generalizable network with the abovementioned architecture, it had to be fed with a training dataset of at least 255 data points.[27] The proportion of 80:20 was used for the training and the test dataset, respectively, providing the minimum training sample size needed and enough samples for the test group.

The statistical parameters of sensitivity, specificity, accuracy, and the likelihood ratio were measured to evaluate the performance of the derived models. The performance parameters were compared with those obtained from binary logistic regression using SPSS software (version 15.0, SPSS, Inc.).

RESULTS

The dataset comprised 352 eyes of 284 patients randomly selected from a pool of 5478 phacoemulsified patients. The mean age of the patients was 66.1 years $\pm$ 8.8 (SD); 138 patients (48.6%) were women. Thirty-four patients had bilateral surgery; 184 (52.2%) were right eyes. Nine eyes had a history of laser capsulotomy. In 31 eyes, a laser capsulotomy was indicated at the time of the follow-up visit (PCO cumulative incidence 11.4%).

There were 282 eyes in the training dataset and 70 eyes (8 with PCO) in the test dataset. The training and test datasets were comparable in demographic characteristics (all $P > 0.05$).

Table 1 shows associations with laser-treated PCO in conventional univariate analysis. Female sex, having corneal opacity at the time of surgery, and being operated on by a novice surgeon were significantly associated with laser-treated PCO. In binary logistic modeling, the latter 2 factors remained significant ($R^2 = 0.09$, $P = .004$). The model accuracy was high (88%); however, its likelihood ratio was nonsense because the sensitivity of the model was close to zero.

Figure 1 shows 1 of the optimum decision trees. Laser capsulotomy was indicated for 30 eyes (11.3%) of 282 in the training dataset. In cases with a clear cornea, the cumulative incidence of clinically significant PCO was 9.5%. This was about one fourth of the PCO incidence in eyes with an opaque cornea. It was also higher in eyes that had mature cataract (22.7% versus 8.2%). Posterior capsule opacification was more common in women than in men (11.8% versus 5.5%). The accuracy, specificity, and sensitivity of the presented decision tree were 50%, 50%, and 40% respectively, and the likelihood ratio was 0.8.

The artificial neural network with 40 neurons provided the best prediction (area under curve [AUC] approximately 0.71) (Figure 2). The specificity and sensitivity of the artificial neural network were 97% (1 false positive) and 25% (2 true positives), respectively, with a positive likelihood ratio of 8 and an accuracy of 89%. Age at the time of surgery, IOL type, and surgically challenging eye contributed more (17.0%, 12%, and 10%, respectively) in predicting the outcome (relevance assessment of the input variables).

Table 1. Univariate analysis of visually significant PCO by input variables.

Input Variable	Distribution (n)	PCO Frequency % (n)	*P* Value (χ^2 test for PCO)
Age*	—	—	.42
Sex			<.001
Male	181	6.6 (12)	
Female	171	16.4 (28)	
Pseudoexfoliation			
Positive	30	13.3 (4)	.72
Negative	322	11.2 (36)	
Axial length			.21
<22.0 mm	39	17.9 (7)	
≥22.0 to <24.5 mm	272	10.6 (29)	
≥24.5 mm	41	9.7 (4)	
Diabetic status			.75
Diabetic	81	12.3 (10)	
Not diabetic	271	11.1 (30)	
Surgeon experience			.05
Beginner	51	21.5 (11)	
Not beginner	301	9.6 (29)	
IOL material			.26
Hydrophobic	46	6.5 (3)	
Hydrophilic	306	12.1 (37)	
Cataract severity			.47
Mature	33	15.1 (5)	
Not mature	319	10.9 (35)	
Surgically challenging†			.15
Positive	75	16.0 (12)	
Negative	277	10.1 (28)	
Corneal opacity‡			<.001
Positive	20	30.0 (6)	
Negative	332	10.2 (34)	

IOL = intraocular lens; PCO = posterior capsule opacification
*For this continuous variable, K-independent-sample test was used.
†Eyes with a small pupil, PXF syndrome, phacodonesis, remarkable corneal opacity, or shallow anterior chamber (eg, intumescent cataract).
‡An axial or paraxial opacity necessitating use of capsule dye during capsulorhexis and the one hampering visualization during nucleotomy.

DISCUSSION

Several risk factors for PCO have been identified.[5,7] Previous studies mainly focused on finding univariate associations, and linear models were used in most cases. To address the complexity of the pathobiology of PCO, we aimed to apply artificial intelligence systems to predict clinically significant PCO.

The QUEST algorithm was used for decision-tree modeling because it is fast and less prone to biases than other exhaustive search methods, such as classification and regression trees (Figure 1).[28] The low accuracy of our decision tree (approximately 50%) can be attributed to training the model with a small dataset. In addition, the model was trained mostly with negative cases (eyes that did not require laser capsulotomy), which led to low sensitivity for a positive status; that is, the need for capsulotomy. Also,

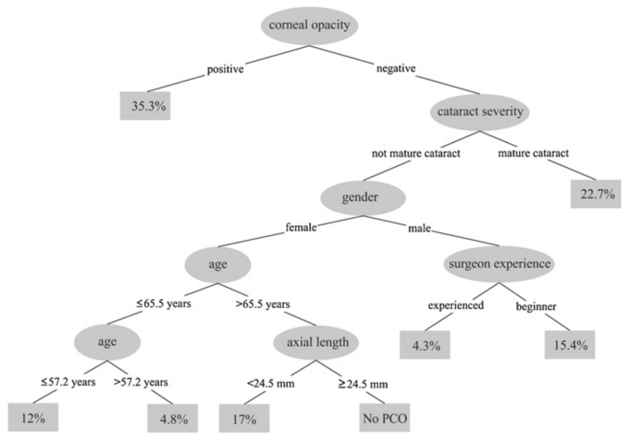

Figure 1. Decision tree for PCO after phacoemulsification. Percentages refer to the probability of developing clinically significant PCO in the respective branch (PCO = posterior capsule opacification).

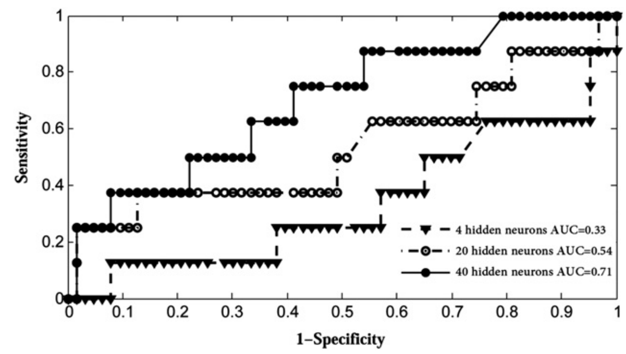

Figure 2. The ROC curves of 3 artificial neural networks with 4, 20, and 40 neurons in 2 hidden layers trained with the batch Levenberg-Marquardt training protocol and containing log-sigmoid and linear transfer functions (AUC = areas under the curve).

some branches of the developed decision tree were inconsistent; for example, age (Figure 1). This instability in the model is probably also the result of the sample size. Alternatively, one might suggest a U-shaped association for age and PCO rather than a linear association. For instance, we know that PCO is quite common in the young; however, a higher prevalence of diabetes mellitus and PXF in advanced age may also cause more PCO in the elderly. As mentioned, the interactions are complex, which supports the suitability of artificial intelligence for disclosing the pathways. The decision tree we present is illustrative only; decision-tree benchmarks can be developed with huge prospective datasets of known and probable risk factors.

Decision-tree models are popular because of their transparency. This facilitates their application by clinicians.[15] For instance, based on our decision tree, we do not expect a 70-year-old woman with a nonmature cataract, a clear cornea, and an axial length of over 24.5 mm to develop visually significant PCO necessitating laser capsulotomy in the first 2 years after phacoemulsification.

Although it is not valid to break down the decision tree in a univariate fashion,[29] the finding that corneal opacity was chosen as the first branching criterion may underscore the importance of appropriate capsulorhexis and complete lens material cleanup in PCO prevention.[8,14] Consistent with previous reports,[13,14] in 1 branch of our decision tree, surgery by a novice surgeon was linked to a 3 times higher incidence of PCO.

Neural networks are neither transparent nor do they allow univariate interpretations; that is, one cannot observe the association of a single determinant with the outcome.[15] However, a combination of factors with certain scenarios may be linked to the outcome. But, as mentioned, age, IOL material, and a surgically challenging eye had a greater contribution in the prediction process regardless of giving a correct or wrong answer.

Our 40-neuron 3-layered artificial neural network reached a forecasting accuracy of 89% with a positive likelihood ratio of 8 in 1 of its runs (Figure 2). In other words, a positive result in that model added at least 40% to the pretest probability that an eye will develop PCO necessitating capsulotomy. Binary regression analysis had a comparable accuracy (88%); however, the likelihood ratio was incalculable because of the instability of its predictions.

Artificial neural networks have the utmost plasticity. This means that their implicit functions and coefficients are constantly modified in response to input data to be consistent with the observed event (training). Then, they are tested using a subsample of the same reference population for optimization. This minimizes the "residual" in the developed model and ensures a high internal validity. This perfect-fit approach has its own downside, however; it threatens generalizability. On the contrary, classic regression models provide the best fit along with a residual. This leads to lower internal validity but broader applicability and higher external validity. Modern regression models, with the aid of computer software, allow application of versatile fits beyond simple linear (eg, logarithmic), and this gives flexibility (pseudoplasticity) to regression analysis as well.

Ideally, we should have a huge multisource dataset (such as that of the European Registry of Cataract Surgery Outcomes) with inputs of known risk factors plus possible determinants to develop a generalizable artificial neural network. This model predicts the outcome when a certain level of stability is achieved and will carry on training by continual inputs and reinforcements on its own predictions, right or wrong.

Ideally, the network should be fed by cases whose characteristics cover the whole range of possible combinations in terms of the definite and probable risk factors. In fact, the sample should be several times bigger than the number of possible combinations because the event probability is not always the same for any combination.

We uploaded a digital module of our prototype artificial neural network for PCO prediction.[A] There, with free access, clinicians are provided with the opportunity to test the probability of significant PCO development in their hypothetical or real cases. Alternatively, they can test the predictive performance of the model by entering data from known cases. Although our model is far from perfect, it exemplifies the use of such tools in ophthalmology and reminds us of the great potential of artificial intelligence to improve patient care in terms of diagnosis, prognostication, and planning.

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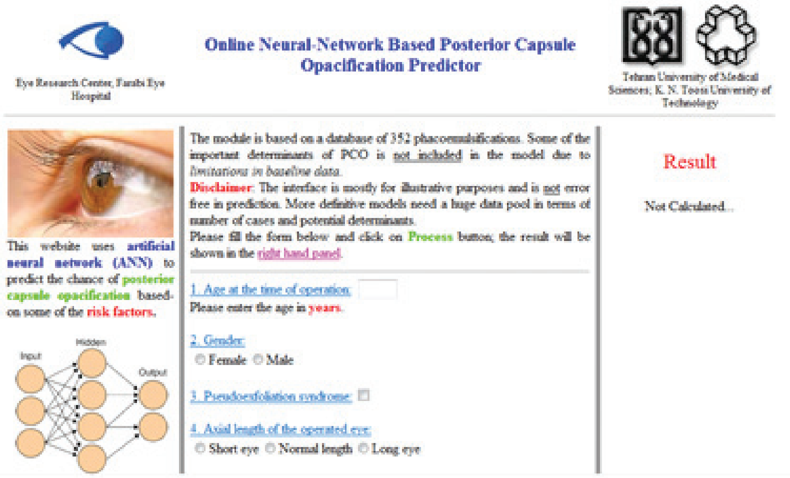
نمایه شده در کتاب اولین‌ها دانشگاه علوم پزشکی تهران

محاسبه‌گر پیش‌بینی کننده عارضه کدورت کپسول خلفی به‌دنبال عمل جراحی آب‌مروارید با استفاده از هوش مصنوعی

اهداف

امکان پیش‌بینی احتمال بروز عارضه کدورت کپسول خلفی پس از عمل جراحی آب‌مروارید به عنوان راهنمایی جهت بیمار و تنظیم پیگیری پس از عمل

به کارگیری فرآیندهای جدید در ارایه خدمات

خلق فناوری های جدید یا توسعه فناوری های موجود

میان رشته ای بودن

نام واحد یا گروه آموزشی که نوآوری در آن انجام شده است: مرکز تحقیقات چشم، بیمارستان فارابی

نام واحدها یا سازمان های همکار: دانشگاه خواجه نصیر طوسی

حوزه تمرکز اولیه نوآوری:

هوش مصنوعی، هوش بالینی، پیش‌بینی عارضه عمل جراحی

حوزه مرتبط با موضوع نوآوری در مرحله اولیه

- جراحی
- سلامت الکترونیک
- کاربردی نمودن دانش

پیش‌زمینه: (شامل موارد موثر در ارائه ایده و توسعه نوآوری می‌باشد. از جمله تشخیص شکاف در ارائه خدمات یا محصول موجود، سوال مطرح شده برای فرد یا گروه و پیش‌بینی تقاضا در آینده)

۱- ناشناخته بودن نسبی عوامل خطر برای بروز عارضه کدورت کپسول خلفی

۲- امکان پذیر نبودن پیش‌بینی احتمال بروز عارضه در شرایط فعلی

۳- تمرین به کارگیری داده‌کاوی در یک بانک اطلاعاتی

حیطه: (در چه حوزه‌ای این ابتکار عمل انجام شد؟ آیا منشاء شکل گیری این ابتکار از فعالیت های مشابه یا نتیجه طرح‌های دیگر بوده است؟)

هوش مصنوعی و داده‌کاوی در پزشکی و چشم‌پزشکی

این رویکرد سال‌هاست که در پزشکی جهت پیش بینی و پیش‌آگهی و تسهیل تصمیم‌گیری بالینی مورد استفاده قرار گرفته است و از جمله درباره ملانوم کوروئید، قوز قرنیه و آب سیاه در چشم‌پزشکی به کار گرفته شده است.

مزیت‌ها: (نوآوری چه مزایایی برای کاربران در پی داشته است؟ آیا این ابتکار عمل برای ارائه کنندگان مراقبت‌های بهداشتی، کارایی داشته یا عملکرد آنها را ارتقا داده است؟)

هوش مصنوعی ارائه شده با وجود کارایی، خطاهای تخمینی قابل توجهی دارد. اما صرف معرفی آن و ایجاد امکان دسترسی برای آن برای کاربران و مخاطبین آموزنده بوده است.

نکات آموزنده : (مثبت یا منفی، شامل هر چالشی که با آن رو به رو بوده اید.)

هوش مصنوعی را بایستی براساس و برای مجموعه داده جامع از فاکتورهای تاثیرگذار و با کیفیت بالا و حجم نمونه مناسب طراحی و آموزش داد.

منابع مورد نیاز

می‌توان این هوش مصنوعی را بهینه نمود و یا با یک بیماری جدید، شبکه عصبی (ساختار و ورودی‌ها) بهتری ساخت. به علاوه دیدگاه به کارگیری شده قابل تعمیم برای حالات بالینی دیگر می‌باشد.

نوع نوآوری

تحولی/بنیادی

تاییدیه‌ها و جایزه‌ها (مواردی که منجر به کسب نشان یا گواهی از مراجع علمی و قانونی شده است نیز درج گردد):

برای تاییدیه وزارت بهداشت اقدام شده و پروژه از ۶۰ امتیاز مورد نیاز، ۴۵ امتیاز را کسب نموده و ۱۵ امتیاز باقی‌مانده منوط به کسب رتبه علمی از جشنواره‌ها (رازی و خوارزمی) و یا پتنت بین‌المللی می‌باشد.

عناوین مقالات چاپ شده در این زمینه درج گردد

۱- ارائه به صورت پوستر در کنگره جراحی کاتاراکت- رفراکتیو ۲۰۱۱ در وین

۲- ارائه به صورت سخنرانی در سمینار هوش بیمارستانی- سال ۱۳۹۰، ایران، دانشگاه علوم‌پزشکی تهران

۳- ارائه به صورت سخنرانی در سفر و بازدید علمی از دانشگاه جانز هاپکینز، بیمارستان چشم ویلمر ۲۰۱۲

آیا این نوآوری در قالب پتنت (patent) ثبت شده است؟ (تصویر آن ضمیمه شود)

بله، به صورت پتنت ملی ثبت شده است.

گروه هدف اولیه: (گروه یا جمعیتی که خدمت یا محصول برای آنان آماده شده است)

چشم‌پزشکان (و بیماران) با مراجعه به سایت مربوطه

نوآوری انجام شده در کدامیک از حوزه های ذیل قرار دارد :

- نوآوری فناورانه
- محاسبه‌گر هوش مصنوعی

از چه زمانی ابتکار عمل تبدیل به فعالیت یا عمل شده است؟

-۱۳۹۰/۱۳۹۱

-۲۰۱۱/۲۰۱۲

زمان بندی انجام طرح نوآوری

زمان شروع پروژه: ۱۳۸۸

زمان پایان پروژه: ۱۳۹۱

مقدار بودجه: ۵۰۰۰۰۰۰۰ ریال **منبع سرمایه گذاری:** ۳۰۰۰۰۰۰۰ شخصی و ۲۰۰۰۰۰۰۰ دانشگاه

سطح تاثیر

دانشکده دانشگاه منطقه کشورهای منطقه خلیج فارس جهان ❋

معاونت پژوهشی- شورای پژوهشی (در قالب بخشی از یک طرح پژوهشی مصوب)

سازمان : دانشگاه علوم پزشکی تهران

اعضای پروژه که مایلند نام آنها ثبت شود: دکتر سید فرزاد محمدی، دکتر هادی زارع، مهندس مصطفی صباغی و دکتر فاروق طایی

اعضای درگیر در پروژه که مایلند نام آنها ثبت شود: دکتر سیدحسن هاشمی، دکتر سمیه علیزاده و دکتر مرسده مجدی‌نسب

محل یا محل‌های استفاده از نتایج نوآوری(لطفا واحدها، سازمان‌ها یا مراکزی که به هر شکل این نوآوری در آن محل کاربردی شده یا مورد استفاده قرار می گیرد را لیست نمایید)

مادول هوش مصنوعی در فضای وب بارگذاری شده و در قالب یک Spreadsheet به صورت دسترسی آزاد قابل بهره‌برداری است:
www.pco-prediction.com

1. Using artificial intelligence to predict the risk for posterior capsule opacification after phacoemulsification. J Cataract Refract Surg 2012; 38:403–408


قوه قضائیه

سازمان ثبت اسناد و املاک کشور

گواهی نامه ثبت اختراع

۰۲۰۱۲۷ الف/۸۹

مشخصات مالک: فاروق طائی - مصطفی صباغی- سیدفرزاد محمدی - سحر طباطباوکیلی

نشانی: تهران /میدان قزوین/ بیمارستان فارابی/ مرکز تحقیقات چشم فارابی

مشخصات مخترع: فاروق طائی - مصطفی صباغی- سیدفرزاد محمدی - سحر طباطباوکیلی- هادی زارع مهرجردی

عنوان اختراع: طراحی و ساخت دستگاه محاسبه گر (پیش بینی کننده) احتمال بروز کدورت کپسول خلفی با استفاده از ابزارهای یادگیری ماشینی (هوش مصنوعی) .

طبقه بندی بین المللی:

حق تقدم:

شماره و تاریخ اظهار نامه اصلی : محل ثبت:

مدت حمایت: ۲۰سال از تاریخ ۱۳۹۰/۱۲/۲۱تا۱۴۱۰/۱۲/۲۱	شماره و تاریخ ثبت اظهار نامه: ۱۳۹۰/۱۲/۲۱-۳۹۰۱۲۰۸۱۹	شماره و تاریخ ثبت اختراع: ۱۳۹۱/۰۲/۰۴-۷۴۷۵۹

اداره کل مالکیت صنعتی رئیس اداره ثبت اختراعات مهرداد الیاسی تاریخ: ۱۳۹۱/۰۲/۲۴ امضاء:

❋ ضمائم گواهی نامه: توصیف ادعا، خلاصه توصیف نقشه

❋❋ در صورت تعدد مخترعین، مالکین و یا تغییرات، مراتب بشرح مندرج در ظهر گواهی نامه می باشد