ARTIFICIAL INTELLIGENCE ON GUARD OF REPRODUCTIVE HEALTH

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Abstract: According to large-scale international studies, infertility affects about 186 million people around the world. The number of infertile couples increases every year. There are chances to solve this problem by implementing assisted reproductive technologies, mainly in vitro fertilization, into clinical practice. Despite high level of modern reproductive medicine development, only about a third of interventions succeed. Artificial Intelligence technologies are being integrated to make the stages of infertility diagnosis and treatment more accurate and effective. The most progressive directions of current studies are: improvement of quality of biomaterial assessment for IVF, prediction of IVF outcome based on patient data, as well as other methods. This review presents main applications of machine learning algorithms in reproductive medicine, steps involved in creating learning models, some of limitations as well as prospects for implementing these methods into clinical practice.

Keywords: artificial intelligence, machine learning, neural networks, infertility, artificial insemination.

1 Introduction

According to prior research, infertility affects about 186 million people worldwide (Inhorn & Patrizio, 2015). Main causes of infertility in women are menstrual disorders, diseases of the endocrine system, ovulatory dysfunction, damaged fallopian tubes, etc. Main factors of male infertility are abnormal spermatogenesis, genetic factors and vascular diseases. It should be noted that in about 30% of cases, diagnostic measures are unsuccessful and the cause of infertility remains unknown (Masoumi et al., 2015).

Low IVF success rates are alarming in the context of the increasing number of infertile couples (Sun et al., 2019). Assisted reproductive technologies (ART), the most common of which is in vitro fertilization, came to the aid of infertile couples. Despite its high cost, complicated technique and rather low success rate (20-30%) (Wang & Sauer, 2006), in vitro fertilization remains the main method of infertility treatment. Result of IVF is influenced by many factors: age of woman, condition of uterus, quantity and quality of obtained biomaterial (oocytes), morphological features of sperm, etc. (Greil et al., 2010). Perhaps one of the main factors affecting the outcome is quality of embryo. Careful evaluation of this parameter is especially important for the fastest pregnancy-onset (VerMilyea et al., 2020). In modern laboratories, embryo evaluation is done manually, through visual assessment of embryo morphology through an optical microscope. However, this method has significant disadvantages. First of all, evaluation is subjective because it depends on the level of knowledge and experience of the specialist. Therefore, it is difficult to make it objective, even within the same clinic. Secondly, evaluation is not universal; this is often due to the fact that medical centers use different grading systems (Steptoe & Edwards, 1978). A possibility to select one embryo with the highest potential would increase the chances of successful fertilization outcome (Wang et al., 2019). In addition, it would eliminate the risk of multiple pregnancies due to transfer of several embryos into the womb (Saeedi et al., 2017).

ART includes other complex stages of prevention, diagnosis and treatment as well as large amounts of digital data. Thus, reproductive technologies become a vast field for Artificial Intelligence (AI) algorithms and classical statistical methods, which could play a key role in development of systems medicine and improvement of health care quality for infertile couples. This paper discusses basic principles of Artificial Intelligence algorithms in the context of ART, applications of AI as well as some limitations and disadvantages.

The term "Artificial Intelligence" was first introduced by John McCarthy in 1956, defining AI as the ability of machines to learn and exhibit intelligence different in its properties from human and animal intelligence (Patel et al., 2009). Artificial Intelligence explores potential relationships in large data sets using mathematical algorithms. Moreover, to increase the accuracy of the algorithms, AI is capable of obtaining new information from successful clinical cases. Therefore, AI has a potential to reduce the number of unavoidable errors in diagnosis and treatment, and to make predictions about the health of patients (Patel et al., 2009).

Machine learning is the most commonly used class of AI-based methods in medicine, which provides tools that allow a computer to improve the analysis of present events using previous (previously entered) data. The computer, facing a familiar task, uses prior knowledge to find the most successful solution (Ranjini et al., 2020). Thus, machine learning is a subset of AI that includes computer algorithms that are able to model the relationships between sets of observable variables (input data) and sets of known output data (Camacho et al., 2018).

There are some limitations and unsolved problems with the application of machine learning algorithms, related to both the technological side of the issue and the implementation of the algorithms in real-life settings. «Underfitting» and «overfitting» are among the main challenges.

«Overfitting» manifests itself in creation of overly complicated models. Creation of such models is associated with the necessity of using large data volumes. In cases of overfitting, the situation is created when the developed model describes a particular situation under study to a high degree of certainty, adapts to teaching examples, but later yields erroneous results with new data. Frequently, the overfitting problem is due to the use of incomplete information and overly complicated models where inputs are very similar to each other.

«Underfitting» is basically the opposite to «overfitting». Underfitting consists in creating overly simple models. “Underfitting” is a situation, when the algorithm cannot capture the main trend in the data, the relationship between input and output data. The reason may be the choice of an overly simple or unsuitable algorithm (Jenkins et al., 2020).

Both overfitting and underfitting of artificial intelligence indicate a mismatch between the model and the nature of data relationships. The underfitting problem is solved by making the model more complicated, the overfitting one – by simplifying the model.

Deep learning algorithms require the use of really large databases for training, which is not always possible. Otherwise, the results may be incorrect and, consequently, all of the work on the model could be useless (Krittanawong et al., 2017).

Even if an algorithm has already been created, tested and validated, researchers face another problem – the so-called "AI Chasm". The "chasm" means that there is a huge difference between the development of a robust algorithm and its implementation in the real work of clinical workflow. Since the model is initially tested on a sample of data from a particular population, there is no guarantee that it will be able to successfully deal with the samples from another population or with a different type of data (Keane & Topol, 2018).

Reproductive medicine can render its prediction, diagnosing, and treatment of diseases more accurate and effective, respectively; to achieve this, the use of software based on artificial intelligence technologies is expedient for medical community in their daily practices. Creation of such software products requires selecting a model and machine learning method to fit into specific features of the problem in question best, as well as creating an algorithm to help timely discover and study potential associations in big data belonging to the domain of reproductive medicine. All the above confirms relevance of the topic of this study.

2 Literature Review

The main algorithms used in reproductive medicine include Decision tree, Random forest, Support vector machine (SVM), Bayesian network (BN), Convolutional neural network (CNN), Artificial neural network (ANN) etc. (Wang et al., 2019).

Decision tree. Compared to other algorithms, Decision tree is easier to understand and interpret. The disadvantage of it is the high risk of "overfitting" (situation when the model demonstrates poor performance with examples that were not involved in its training) (Wang et al., 2019).

Decision tree can be used to identify the embryo with the highest implantation potential. Carrasco B. et al. performed a study, in which 800 embryos with known implantation data were selected. The morphological and morphokinetic parameters of the embryos were evaluated retrospectively, resulting in a hierarchical model that allows to make predictions about the success of embryo implantation using the parameters listed above (Carrasco et al., 2017).

Using such algorithms as Decision tree, Support vector method, Logistic regression, Multilayered perceptron (MLP), Sahoo A. J., Kumar Y. (2014) established the relationship between some lifestyle and environmental parameters and human sperm quality in their study. They demonstrated that age, surgical interventions, alcohol consumption, smoking, and accidents are the parameters that have the strongest impact on sperm quality. In addition, the results of the study reveal that information filtering methods increase the accuracy of algorithms.

Random forest is an algorithm consisting of an ensemble of decision trees. It corrects for the risk associated with decision trees "overfitting" and provides more accurate results than an individual model. However, Random forest requires complex maintenance.

Liao S., Pan W, Dai W., Jin L., Huang G., Wang R., Hu C., Pan W., Tu H. (2020) developed a dynamic infertility assessment system based on the parameters of patients such as age, body mass index, follicle stimulating hormone level, antral follicle count, anti-Mullerian hormone level, number of oocytes, and endometrial thickness. A Random forest algorithm was used to determine the weight of each parameter. After testing and validation, an infertility assessment system was obtained that is capable, using the above parameters, to assign a patient to one of the five categories (A, B, C, D, E), simplifying the diagnostic process.

A group of researchers led by Hafiz P. (2017) made a comparison of Random forest, Recursive partitioning (RPART), Adaptive boosting, One-nearest neighbor algorithms in the context of IVF and ICSI outcome prediction using 29 variable parameters. Data from 486 patients were chosen. According to the results of the study, RF and RPART outperform the other decision-making algorithms. It was also found that a woman's age, serum estradiol level on the day of chorionic gonadotropin administration, and the number of developed embryos were the most appropriate parameters for this type of prediction.

Support vector machine. Classifiers based on this algorithm divide the data into two classes, using the construction of one or more linear boundaries - separating hyperplanes (Jakkula, 2011). Typically, this method is used in classification and regression tasks. Its disadvantage is the complexity of model training (Wang et al., 2019).

Filho E. S., Noble J. A., Poli M., Griffiths T., Emerson G., Wells D. (2012) used the SVM algorithm to create a semi-automated system for assessing embryo viability based on the morphological features of blastocysts. Images of blastocysts obtained by microscopy were segmented using image processing and analysis technologies. Parts such as zona pellucida, trophectoderm, and inner cell mass (embryoblast) were distinguished. These data were further processed and then entered into the algorithm to assess the viability of the embryo by its morphological features. The authors are convinced that the developed system will help to avoid subjective evaluation and make the analysis of embryos more accurate.

Support vector machine can also be used to assess the quality of sperm that is used for in vitro fertilization. Mirsky S.K., Barnea I., Levi M., Greenspan H., Shaked N.T. (2017) suggested applying quantitative phase maps for automated sperm evaluation. Obtained by interferometric phase microscopy, images of spermatozoa were processed - cell structure features such as 3D morphology, contents and parameters of spermatozoa heads were extracted. Data in the form of 378 sperm images from 8 donors were used to train the SVM-based classifier. The authors point out that to obtain more correct results, it is necessary to continue searching for a suitable algorithm, as well as to use more extensive data sets for training.

Bayesian network. Multiple studies have been conducted on the Naïve Bayes classifier. This is the simplest algorithm among the many algorithms based on Bayes' theorem. The main disadvantage of BN is that the input data must be statistically independent; otherwise, there are problems with the performance of the algorithm.

Although the Bayesian classifier is a simplified classifier, it can handle complex tasks, such as predicting the probability of successful embryo implantation after IVF.

Uyar A., Bener A., Ciray H. N. (2015) conducted a retrospective survey designed to predict the outcome of embryo implantation as a result of sperm injection into the oocyte cytoplasm (ICSI). A database comprised of the information of about 2435 transplanted embryos was used to train the algorithm. As a result, they obtained a model that can predict the outcome of embryo implantation after ICSI with an accuracy of 80.4%.

In this way, the Bayesian classifier can also be used to select the best material for in vitro fertilization. In particular embryos, as demonstrated in the study of Morales D. A, Bengoetxea E., Larrañaga P., García M., Franco Y., Fresnada M., Merino M. (2008). In order to create a database, information on embryos from 63 clinical cases was selected. The variables that determine, according to the researchers, the success of implantation was highlighted: the thickness of the zona pellucida, the degree of fragmentation, multinuclearity and blastomer size. In addition, the following parameters were used: age, number of previous IVF cycles, sperm quality, cause of infertility, number of transferred embryos, whether embryo was frozen or not, and day of embryo transfer. The information was then used to train several types of Bayesian classifiers, including the Naive Bayesian classifier, which demonstrated an accuracy of 68.25%. The authors believe that this finding will not only help as a decision support system for infertility treatment, but can also serve as a training tool for young embryologists (Morales et al., 2008).

Artificial neural networks are algorithms that, to varying degrees, imitate the behavior of the human brain. Their working principle, respectively, is based on neuronal interaction. In ANN, the neuron’s role is played by Artificial neural network nodes connected hierarchically. Therefore, input data for some nodes serves as output data for other nodes. In the field of assisted reproductive technologies, ANN can be used to solve problems of classification, prediction and sample selection. Some of the disadvantages include the "black box" principle (Artificial networks have limited abilities for the user to determine causal relationships between input and output data), the significant computational load, and the tendency of these algorithms to "overfitting" (Tu, 1996).

El-Shafeiy E., El-Desouky A., El-Ghamrawy S. (2018) used the capabilities of Artificial neural networks, particularly the Multilayer perceptron, to determine sperm quality. The database included the records of 100 patients. As variables 9 lifestyle factors were chosen. The ANN's work was enhanced by another algorithm, the Sperm Whale Optimization algorithm. The result turned out to be promising: the accuracy of the analysis was 99.96%. The researchers believe that this is caused by the combined use of ANN and SWA.

Multilayer Perceptron, Support vector method, Random forest, and Decision tree were used in a study of Hassan M. et al. (2020) to predict the outcome of IVF. Data on infertility treatment of 1729 patients were used to train the algorithms. The 25 parameters that were used to assess prognosis included age, indication for IVF, method of sperm collection, endometrial wall thickness, sperm quality, number of retrieved oocytes, administration of ovulation stimulating drugs, etc. 18 parameters had numerical values and 7 had categorical values. The accuracy of the MLP method was 97.77%. The best results were using the Support vector machine (98.01% accuracy) and the Random forest method (98.83% accuracy) (Hassan et al., 2020).

Convolutional neural network successfully handles large data sets, especially data in the form of images. During their analysis, CNN acts as a mathematical operator, which, having received images and a filter as input data, produces filtered output data. In reproductive medicine, this feature of the Convolutional neural network is actively used to classify embryo images.

In the assessment of embryonic viability, Time-lapse analysis is often used. The technology involves continuous observation of the embryo's development in an Incubator environment. The device includes a microscope and a camera that takes pictures of the embryo at short intervals. The images are then edited into a film, and a specialist assesses the embryo's development using this film.

The timing of the embryo's development stages, such as the time it takes to reach the 5-cell stage, correlates with the embryo quality and viability (Khan et al., 2015).

To perform accurate time measurements, it is necessary to manually track changes in blastocyst morphology. Khan A., Gould S., Salzmann M. (2016) proposed to automate the counting of blastocyst cells from time-lapse images. Information of 256 embryos as raw 148,993 frames of time-lapse technique were analysed. As a training annotation, the developed framework used only the number of cells in the image, not requiring such parameters as the shape and size of the cells and their location. As a result, a CNN-based cell counter was obtained with an accuracy of 87.36%.

Miyagi Y., Habara T., Hirata R., Hayashi N. (2020) in their study established a possibility to predict birth in patients of several age groups based on blastocyst imaging data. 5,691 blastocyst images taken 115 (or 139) hours after insemination were collected. The images were then divided into groups based on the age of the patients. A CNN-based algorithm was developed for each of the age groups. At the same time, the data was analyzed using a Conventional embryo evaluation system. As a result, Artificial Intelligence demonstrated higher total specificity and sensitivity values than the traditional evaluation system.

One of the most commonly used embryo grading scales is the Gardner scale, which can be used to classify embryos. According to Chen T. J., Zheng W. L., Liu C. H., Huang I., Lai H. H., Liu M. (2020) the development of an automated system will reduce the subjectivity of evaluation as well as the amount of time spent on this stage of IVF. A total of 171,239 microscopy images of 16,201 embryos were selected. Authors note that this is the first study of its kind to use data from an Asian population. The images were divided into three groups: 60% for CNN training, 20% for validation, and 20% for testing. The algorithm used, based on CNN, was pre-trained on the ImageNet database (a project to build and maintain a massive database of annotated images). The same data was analyzed and assigned to groups according to the Gardner scale by three experienced embryologists. When the results were compared, the algorithm demonstrated an average analysis accuracy of 75.36%.

3 Research Methodological Framework

The objective of this research is to identify machine learning algorithms which can ensure reliable prediction, diagnosing, and treatment of diseases in reproductive medicine.

The following research tasks are outlined:

- to conduct information search for the experience of using artificial intelligence in reproductive medicine;
- to highlight the most advanced machine learning methods which can ensure a higher quality of evaluation of biological material for in vitro fertilization and prediction of the outcome of artificial insemination.

To complete the set tasks and achieve the objective, the following methods were used:

- information search through sources of scientific technical information and medical information ones on the research topic;
- analysis of the collected material with its subsequent systemization;
- the properties transfer method, in particular, transferring the properties of artificial intelligence to reproductive medicine.

4 Results and Discussion

As a result of the information search conducted in relation to the experience of using artificial intelligence in reproductive medicine, it has been found that promising lines of research are the following: a higher quality of evaluation of biological material for in vitro fertilization and prediction of the outcome of artificial insemination based on the data of the married couples.

The principal focus area of modern studies in reproductive medicine is creation of software means based on artificial intelligence; they maintain high accuracy in the work of software algorithms and obtaining results to be able subsequently to ensure reliable prediction, diagnosing, and treatment of diseases. The principal problem holding back on implementation of artificial intelligence systems is the one consisting in systems showing a good result when tested on a certain sample from the data array but yielding a not quite credible result if used on data drawn from another sample, e.g., when studying people from another population. This requires accumulation large databases, building more complex and multi-purpose algorithms, which inevitably leads to the overfitting problem arising.

When studying the opportunities of using artificial intelligence in reproductive medicine, it has been found that the main machine learning methods applied in this domain are the support vector machine, random forest and decision tree algorithms, Bayesian classifiers, and artificial neural networks.

The central problem to the use of artificial intelligence is the necessity of accumulating and systemizing large data volumes. To collect these data, a vast amount of observation of diverse groups has to be conducted, their results have to be systemized, and significant primary and secondary factors have to be identified, with the effect individual factors and various combinations of them produce on the disease course registered as well. When building work algorithms for artificial intelligence, the major challenge consists in overcoming the overfitting problem which arises inevitably out of the necessity of using large data volumes. Software products must contain algorithms which can process data collected from images, digital data obtained by medical tests, and descriptive characteristics logged during the visual inspection.

The decision tree and random forest algorithms demonstrate good results when used in reproductive medicine as classification tools and means of predicting the disease course.

Overcoming the under- and overfitting situations is the key challenge to development of artificial intelligence algorithms.

Efforts to intensify development of software using artificial intelligence in medicine are associated with rapid development of computer technologies and expansion of the sphere of their use, both leading to accumulation of increasingly larger volumes of digitized information.

Alongside clinical trials proving their success, to implement artificial intelligence technologies into medical practice, tests are required to prevent situations termed «AI Chasm».

Creation of new and improvement of current artificial intelligence models, neural network ones in particular, urges for processing increasingly larger data volumes. Quite frequently, the required data volumes turn out to be insufficient or unavailable due to the modern medicine development level and computer technologies used in it. Thus, the major prerequisites to advance of artificial intelligence methods are to increase the amount of digitized information and to expand the possibilities of sharing it among researchers studying similar problems in people of different populations.

5 Conclusion

In order to improve the quality of care for the patients, experts from the international medical community are calling for help of computer technology.

Artificial Intelligence algorithms, despite their limitations, show promising results.

Assisted reproductive technology is a vast field for the implementation of machine learning algorithms. This field of medicine has not only large databases ("Big Data") represented by electronic medical records, but also modern diagnostic and treatment methods, into which classification, prediction and clinical decision support systems based on the work of AI can be integrated.

Thus, ART is becoming not just a resource for the development of Artificial Intelligence in medicine, but also a platform for the subsequent application of algorithms in the clinical practice.

At present, the use of artificial intelligence in reproductive medicine is not yet developed sufficiently due to imperfection of software algorithms. Some factors curbing its progress are the needed large data volumes and high resource intensity of computing tools.

Analysis of the available artificial intelligence methods has shown there is no single across-the-board method to solve all problems faced by reproductive medicine. For each task, its own method has to be selected which enables one to achieve the target result at the required accuracy level. In the course of the review conducted, possibilities of various information processing methods and reproductive medicine domains where they have shown good results have been found.

Literature:

1. Camacho, D. M., Collins, K. M., Powers, R. K., Costello, J. C., Collins, J. J.: *Next-generation machine learning for biological networks.* Cell, 173(7), 2018. 1581-1592 pp. doi: 10.1016/j.cell.2018.05.015.

2. Carrasco, B., Arroyo, G., Gil, Y., Gómez, M. J., Rodríguez, I., Barri, P. N., Veiga, A., Boada, M.: *Selecting embryos with the highest implantation potential using data mining and decision tree based on classical embryo morphology and morphokinetics.* Journal of assisted reproduction and genetics, 34(8), 2017. 983-990 pp. doi: 10.1007/s10815-017-0955-x.

3. Chen, T. J., Zheng, W. L., Liu, C. H., Huang, I., Lai, H. H., Liu, M.: *Using deep learning with large dataset of microscope images to develop an automated embryo grading system.* Fertility and reproduction, 1(1), 2020. 1-6 pp. doi:10.1142/S26 61318219500051.

4. El-Shafeiy, E., El-Desouky, A., El-Ghamrawy, S.: *An optimized artificial neural network approach based on sperm whale optimization algorithm for predicting fertility quality.* Studies in Informatics and control, 27(3), 2018. 349-358 pp. doi:10.24846/v27i3y201810.

5. Filho, E. S., Noble, J. A., Poli, M., Griffiths, T., Emerson, G., Wells, D.: *A method for semi-automatic grading of human blastocyst microscope images.* Human reproduction, 27(9), 2012. 2641-2648 pp. doi: 10.1093/humrep/des219.

6. Greil, A. L., Slauson-Blevins, K., McQuillan, J.: *The experience of infertility: a review of recent literature.* Sociology of health & illness, 32(1), 2010. 140-162 pp. doi: 10.1111/j.14 67-9566.2009.01213.x.

7. Hafiz, P., Nematollahi, M., Boostani, R., Namavar Jahromi, B.: *Predicting implantation outcome of in vitro fertilization and intracytoplasmic sperm injection using data mining techniques.* International journal of fertility and sterility, 11(3), 2017. 184-190 pp. doi: 10.22074/ijfs.2017.4882.

8. Hassan, M. R., Al-Insaif, S., Hossain, M. I., Kamruzzaman, J.: *A machine learning approach for prediction of pregnancy outcome following IVF treatment.* Neural computing and applications, 32(7), 2020. 2283-2297 pp. doi: 10.1093/humr ep/dez064.

9. Inhorn, M. C., Patrizio, P.: *Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century*. Human Reproduction Update, 21(4), 2015. 411-426 pp. doi: 10.1093/humupd/dmv016.

10. Jakkula, V.: *Tutorial on support vector machine (SVM).* Sch EECS, Washington State University, 2011. Available from: https://www.semanticscholar.org/paper/Tutorial-on-Support-Vector-Machine-(-SVM-)-Jakkula/7cc83e98367721bfb908a8f703ef5379042c4bd9.

11. Jenkins, J., Sheryl van der Poel, Krüssel, J., Bosch, E., Nelson, S. M., Pinborg, A., Yao, M. *Empathetic application of machine learning may address appropriate utilization of ART.* Reproductive biomedicine online, 41(4), 2020. 573-577 pp. doi: 10.1016/j.rbmo.2020.07.005.

12. Keane, P. A., Topol, E. J.: *With an eye to AI and autonomous diagnosis*. NPJ digital medicine, 1(40), 2018. doi: 10.1038/s41746-018-0048-y. Available from: https://www.researchgate.net/publication/327271322_With_an_eye_to_AI_and_autonomous_diagnosis.

13. Khan, A., Gould, S., Salzmann, M.: *Automated monitoring of human embryonic cells up to the 5-cell stage in time-lapse microscopy images.* 12th International symposium on biomedical imaging. IEEE. 2015. 389-393 pp. doi: 10.1109/ISB I.2015.7163894.

14. Khan, A., Gould, S., Salzmann, M.: *Deep convolutional neural networks for human embryonic cell counting.* Computer vision – ECCV 2016 Workshops. 2016. 339-348 pp. doi: 10.1007/978-3-319-46604-0_25.

15. Krittanawong, C., Zhang, H., Wang, Z., Aydar, M., Kitai, T.: *Artificial intelligence in precision cardiovascular medicine.* Journal of the American college of cardiology, 69(21), 2017. 2657–2664 pp. doi: 10.1016/j.jacc.2017.03.571.

16. Liao, S., Pan, W, Dai, W., Jin, L., Huang, G., Wang, R., Hu, C., Pan, W., Tu, H. *Development of a dynamic diagnosis grading system for infertility using machine learning.* JAMA network open. 3(11), 2020. doi: 10.1001/jamanetworkopen.20 20.23654.

17. Masoumi, S. Z., Parsa, P., Darvish, N., Mokhtari, S., Yavangi, M., Roshanaei, G.: *An epidemiologic survey on the causes of infertility in patients referred to infertility center in Fatemieh Hospital in Hamadan.* Iranian journal of reproductive medicine, 13(8), 2015. 513-516 pp.

18. Mirsky, S. K., Barnea, I., Levi, M., Greenspan, H., Shaked, N. T.: *Automated analysis of individual sperm cells using stain-free interferometric phase microscopy and machine learning.* Cytometry. Part A: the journal of the international society for

analytical cytology, 91(9), 2017. 893-900 pp. doi: 10.1002/cyto.a.23189.
19. Miyagi, Y., Habara, T., Hirata, R., Hayashi, N.: *Feasibility of deep learning for predicting live birth from a blastocyst image in patients classified by age.* Reproductive medicine and biology, 18(2), 2020. 190-203 pp. doi: 10.1002/rmb2.12266.
20. Morales, D. A, Bengoetxea, E., Larrañaga, P., García, M., Franco, Y., Fresnada, M., Merino, M.: *Bayesian classification for the selection of in vitro human embryos using morphological and clinical data.* Computer methods and programs in biomedicine. 90(2), 2. 2008. 104-116 pp. doi: 10.1016/j.cmpb.2007.11.018.
21. Patel, V. L., Shortliffe, E. H., Stefanelli, M., Szolovits, P., Berthold, M. R., Bellazzi, R., Abu-Hanna, A.: *The coming of age of artificial intelligence in medicine.* Artificial intelligence in medicine, 46(1), 2009. 5-17 pp. doi: 10.1016/j.artmed.2008.07.017.
22. Ranjini, K., Suruliandi, A., Raja, S. P.: *Machine learning techniques for assisted reproductive technology: a review.* Journal of circuits, systems, and computers, 29(11), 2020. doi: 10.1142/S021812662030010X. Available from https://www.researchgate.net/publication/337599178_Machine_Learning_Techniques_for_Assisted_Reproductive_Technology_-_A_Review.
23. Saeedi, P., Yee, D., Au, J., Havelock, J.: *Automatic identification of human blastocyst components via texture.* IEEE transactions on biomedical engineering, 64(12), 2017. 2968-2978 pp. doi: 10.1109/TBME.2017.2759665.
24. Sahoo, A. J., Kumar, Y. *Seminal quality prediction using data mining methods.* Technology and health care, 22(4), 2014. 531-545 pp. doi: 10.3233/THC-140816.
25. Steptoe, P. C., Edwards, R. G.: *Birth after the reimplantation of a human embryo.* The Lancet, 312(8085), 1978. P. 366. doi: 10.1016/s0140-6736(78)92957-4.
26. Sun, H., Gong, T. T., Jiang, Y. T., Zhang, S., Zhao, Y. H., Wu, Q. J.: *Global, regional, and national prevalence and disability-adjusted life-years for infertility in 195 countries and territories, 1990-2017: results from a global burden of disease study, 2017.* Aging, 11(23), 2019. 10952-10991 pp. doi: 10.18632/aging.102497.
27. Tu, J. V.: *Advantages and disadvantages of using artificial neural networks versus logistic regression for predicting medical outcome.* Journal of clinical epidemiology, 49(11), 1996. 1225-1231 pp. doi: 10.1016/s0895-4356(96)00002-9.
28. Uyar, A., Bener, A., Ciray, H. N.: *Predictive modeling of implantation outcome in an in vitro fertilization setting.* Medical decision making: an international journal of the society for medical decision making, 35(6), 2015. 714-725 pp. doi: 10.1177/0272989X14535984.
29. VerMilyea, M., Hall, J. M. M., Diakiw, S. M., Johnston, A., Nguyen, T., Perugini, D., Miller, A., Picou, A., Murphy, A. P., Perugini, M. *Development of an artificial intelligence-based assessment model for prediction of embryo viability using static images captured by optical light microscopy during IVF.* Human reproduction, 35(4), 2020. 770-784 pp. doi: 10.1093/humrep/deaa013.
30. Wang, J., Sauer, M. V.: *In vitro fertilization (IVF): a review of 3 decades of clinical innovation and echnological advancement.* Therapeutics and clinical risk management, 2(4), 2006. 355-364 pp. doi: 10.2147/tcrm.2006.2.4.355.
31. Wang, R., Pan, W., Jin, L., Li, Y., Geng, Y., Gao, C., Chen, G., Wang, H., Ma, D., Liao, S.: *Artificial intelligence in reproductive medicine.* Reproduction, 158(4), 2019. 139-154 pp. doi: 10.1530/REP-18-0523.

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