Can artificial intelligence drive optimal sperm selection for in vitro fertilization?

Since the late 1990s, the improved accessibility of biomedical data has hastened the application of artificial intelligence (AI) in reproductive medicine. AI can guide optimal clinical management for infertile couples, improving clinical and patient-reported outcomes as well as promoting cost-effectiveness. Previously, AI for artificial reproduction has been applied to gamete selection and for predicting the outcomes of in vitro fertilization (IVF) (1). Sperm selection techniques using AI that correlate with fertilization potential and successful IVF cycles are limited. For example, a computer-aided sperm analysis vector machine model has been used to classify human sperm into five kinetic classes (2). Prior techniques using AI that assess capacitation as an indication of fertilization potential, including Cap-Score (Androvia, Mountainside, NJ) and penetration assays, ultimately yield sperm that cannot be used for treatment, since they will be destroyed or wasted.

In the current study, Gunderson et al. (3) show that human sperm intracellular pH, measured using flow cytometry in normospermic men, is associated with conventional IVF success in a single institution series. A gradient boosted decision tree machine learning algorithm was able to predict success accurately with conventional IVF. This includes clinical and demographic variables for each partner, sperm intracellular pH and sperm membrane potential, sperm hyperactivated motility, sperm linearity coefficient, sperm lateral head displacement, and sperm curvilinear velocity. Additionally, these assays for sperm intracellular pH and sperm membrane potential offer reliable assessment of sperm capacitation when compared to penetration assays.

Several technologies have been previously described for sperm sorting. These include microfluidics, which uses small fluid streams to sort cells; magnetic-activated cell sorting, which uses a magnetically charged water column that can sort antibody-cell surface antigen tagged cells; and fluorescence-activated cell sorting, where fluorescent-labeled cells are sorted on the basis of scatter from a laser (4). Sperm sorting may help select for optimal sperm function from the ejaculate for artificial reproduction. However, AI has yet to be applied routinely to sperm sorting techniques.

There must be a greater emphasis on the few sperm that have the opportunity to fertilize and the one sperm that eventually will fertilize an egg. Compared to the relatively limited number of oocytes that are available for selection, most men have millions of sperm for selection. Although we currently use many adjunctive techniques to purify sperm for IVF, the identification of the optimal sperm for intracytoplasmic sperm injection or IVF most often relies on a skilled human selecting for the best-appearing sperm under a microscope, without any information regarding its fertility potential. Sperm selection is an area of artificial reproduction that is primed for transformation as novel technologies are developed to allow for interrogation of a few or a single sperm without inducing cell damage. AI can help accelerate this transformation.

However, there are several barriers to the incorporation of AI into sperm selection. Even a methodically sound AI model is limited by the data from which it is developed, as is the case in the current study, where the data are drawn from a relatively small, singe-center cohort. This creates inherent selection bias that limits direct real-world clinical applications of this algorithm. Additionally, similar to other machine learning algorithm studies, the results often are difficult to reproduce. Future studies aimed at reproducing the accuracy of this algorithm using a larger, heterogeneous, multicenter cohort are needed before this algorithm is used clinically, beyond research related purposes. Flow cytometry also is costly and less efficient compared to alternatives, which also may impact broader clinical applications.

Although this study relies on a decision tree machine learning algorithm that is relatively simple to interpret and apply, applications in artificial reproduction using neural networks and deep learning that can adjust in real-time on the basis of new circumstances and handle missing values are relatively limited. Ultimately, the success of AI for gamete selection and prediction of IVF success is dependent on high-quality training data. Increased collaboration between reproductive experts, bioinformaticists, computational scientists, and biostatisticians who can leverage the power of big data will enable broader applications for AI in artificial reproduction. Although sperm intracellular pH and the decision tree machine learning algorithm presented in the current study are not ready for direct clinical applications, this represents another significant development in the future of AI for sperm selection and prediction of IVF outcomes.

Darshan P. Patel, M.D.
Kelli X. Gross, M.D.
James M. Hotaling, M.D., M.S.
Division of Urology, Department of Surgery, University of Utah, Salt Lake City, Utah

https://doi.org/10.1016/j.fertnstert.2021.02.004

You can discuss this article with its authors and other readers at https://www.fertstertdialog.com/posts/32411

REFERENCES

1. Wang R, Pan W, Jin L, Li Y, Geng Y, Gao C, et al. Artificial intelligence in reproductive medicine. Reproduction 2019;158:R139–54.
2. Goodson SG, White S, Stevans AM, Bhat S, Kao CY, Jaworski S, et al. CASAnova: a multiclass support vector machine model for the classification of human sperm motility patterns. Biol Reprod 2017;97:698–708.
3. Gunderson SJ, Puga Molina LC, Spies N, Balestrini PA, Buffone MG, Jungheim ES, et al. Machine-learning algorithm incorporating capacitated sperm intracellular pH predicts conventional in vitro fertilization success in normospermic patients. Fertil Steril 2021;115:930–9.
4. Mangum CL, Patel DP, Jafek AR, Samuel R, Jenkins TG, Aston KI, et al. Towards a better testicular sperm extraction: novel sperm sorting technologies for non-motile sperm extracted by microdissection TESE. Transl Androl Urol 2020;9(Suppl 2):S206–14.