



Utilizing machine learning to discern hidden clinical values from big data in urology

Suppose you are asked to choose the single most important information technology that has given decision-making processes a massive upgrade. Many of us would choose machine learning (ML). The application of ML is defined as “giving computers the ability to learn without being explicitly programmed”. The main purpose of ML is to introduce algorithms that ingest input data, apply computer analysis to predicting output values within an acceptable range of accuracy, identify patterns and trends in data, and to learn from previous experience. ML is often applied to complicated and poorly understood natural phenomena, such as complex biological systems, climate change, astronomy, or particle physics.

The two major pathways in ML are supervised and unsupervised learning. In supervised learning, an algorithm is often provided with data, $X_{N \times P}$ (N samples with P number of features) and a desired target y . The goal is to train a model f (e.g., a decision function), that performs prediction on for X , i.e., $f(X)=y$. Supervised learning primarily deals with classification and regression problems. In unsupervised learning, an algorithm is provided with data, X , without any labels/annotations, to find latent patterns, sometimes producing both answers and questions that may not have been conceived by the investigators. Unsupervised learning typically deals with clustering and dimensionality reduction problems. The patterns identified in unsupervised learning often need to be evaluated for utility by human interrogation or via application within a supervised learning task.

While validation of unsupervised algorithm can only be performed with a hidden ground, the performance of a supervised learning algorithm can be evaluated by various metrics based on the objective of a task. A dataset is typically divided into two independent sets, i.e., training and testing sets; where training of an algorithm is performed using the training set and then the trained model is evaluated using the testing set. In order to remove bias introduced in a single division of training/testing sets, cross validation is often used to evaluate supervised learning algorithms.

HOW IS ML APPLIED TO DEVELOP PRECISION MEDICINE?

Many of us in the healthcare and science field would agree that big data will transform medicine. In recent years, large amounts of data have been accumulated through big omics studies of genome, epigenomes, transcriptomes, proteomes, metabolomes, and other sources. This immense data needs to be analyzed, interpreted, and manipulated to provide biological meaning. Where ML shines is in handling enormous numbers of predictors. ML has become ubiquitous and indispensable for solving complex problems in most sciences. ML will become an indispensable tool for clinicians seeking to truly understand their patients. However, there are several shortcomings when it comes to applying ML to big data [1]. First, algorithms might “overfit” predictions to spurious correlations in the data; multicollinear, correlated predictors could produce unstable estimates. Second, ML algorithms often require a large number of observations to reach acceptable performance levels.

Precision medicine is one of the important developments in modern medicine. It provides clinicians with early intervention by using advanced diagnostic procedures and customizes personalized treatments for patients. Many scientists and physicians are convinced of the importance of information technology and ML in precision medicine. This includes data storage and analysis for disease outcomes, and identification of patient characteristics and optimal treatment. Utilizing ML for pattern recognition, development of statistical models, creation of knowledge bases for existing phenotype categories and diseases, organization of clinical datasets of population size, and development of open software platforms for statistical analysis of high-dimensional healthcare and multi-omics data are crucial for practical realization of precision medicine.

As one can imagine, ML will have a huge impact on disease (especially cancer) diagnostics and prognostics; in par-

ticular, on the development of novel computational tools for stratification, grading, and prognostication of patients with the overall goal of improving care. There are various ML techniques, which have been widely used in disease diagnosis, and prognosis. A series of previous studies have shown how ML can improve diagnostic performance and prediction accuracy in clinically relevant patient cohorts [2]. One study demonstrated how ML can improve on already established standards, such as Gleason scoring; thus, providing more precise prognostication. Another study engineered a ML-based system to predict microsatellite instability in patients with gastrointestinal or endometrial cancers; both accuracies were higher than prediction with molecular markers. Some studies have also shown that ML can lead to higher accuracy in drug response prediction. ML is becoming a popular tool for medical researchers and has demonstrated promising ability to effectively predict future disease outcomes.

So how is ML currently being used in clinical research? For digitalized pathology, various applications incorporating ML are developed to assist in processing pathological diagnoses. Major applications include detection of specific objects, such as cancer cells, cell nuclei, cell division, and blood vessels, classification/grading of tumors, and evaluation of immunostaining. The major obstacle in using ML in pathological imaging is inadequate image annotations. At present, there exist many technologies to address this concern [3]. For example, generative adversarial networks are used for pathological data analysis to automatically prepare image datasets necessary for subsequent deep learning. Pathologists are looking forward to this potential new gold standard technology for processing images.

Applications of ML in radiology are designed to help computers analyze medical imaging data and support diagnoses by associating clinical outcomes. These radiomic techniques can predict diseases with higher accuracy than humans. Using ML to recognize and analyze image data will fundamentally change our understanding of disease risk and treatment. ML can often extract image information that humans cannot recognize, which can lead to the discovery of novel disease patterns and predictive markers.

At present, the use of omics research to drive cancer biomarker discovery is very popular. Because of large datasets, researchers need advanced information technology, such as ML, to analyze and understand data. ML has already been applied to mass spectrometry (MS) data across different biological disciplines, including various cancers. ML can be useful in determining which proteins from MS data can be used as biomarkers to differentiate between classes. ML is also useful for interpreting large genomic datasets and annotating a

wide variety of genomic sequence elements, which has led to the identification of potentially valuable disease biomarkers.

HOW ABOUT APPLYING ML INTO UROLOGICAL RESEARCH?

When it comes to prostate cancer (PC), many technology platforms for diagnosis, prognosis, and treatment have demonstrated potential benefits of ML. The ML methods can be extended into treatment planning and intervention by augmenting surgeries with information, such as tumor localization and other image-guided options. Computer-assisted diagnosis of PC in histopathological slides can be achieved by ML to enhance accuracy. ML can also help genomics research. By identifying specific genes, ML can be used to develop diagnostic and risk stratification tools, determine the best individualized treatments, and generate targeted drug treatment schemes.

ML can be used to read radiological or pathological images of bladder cancer (BC) to provide useful information. Previous studies have used ML models to analyze magnetic resonance imaging data of BC; they were able to identify low and high-grade BC before surgery with 83% accuracy. ML-based methods have been further applied to accurately quantify tumor buds from immunofluorescence-labeled slides of muscle-invasive BC patients. ML algorithms have also been employed to create recurrence and survival predictive models from imaging and operative data. These algorithms can be used to identify genes at initial presentation that are most predictive of recurrence and can be applied as molecular signatures to predict recurrence risk within 5 years after transurethral resection of the bladder tumor [4].

ML technology has been used to analyze the clinical and imaging data of renal cell carcinoma (RCC) to provide disease diagnoses, prognostic information, and assist in treatment plans. Previous studies have shown that the ML model can accurately distinguish high-grade and low-grade RCC by analyzing computed tomography (CT) image feature [4]. In recent years, ML has been developed to identify biomarkers and multiple gene expression-based signatures to predict survival and disease prognosis in clear cell RCC. Moreover, some studies have demonstrated how noninvasive deep learning models constructed from radiomic features have comparable performance to percutaneous renal biopsy in predicting International Society of Urological Pathology grading.

ML has also been applied to various modalities of urinary stone therapy. Computer-assisted detection using image features can support radiologists in identifying stones. With large datasets, artificial neural networks (ANN) can predict

outcomes after various forms of endourologic intervention. ANN has been used to differentiate ureteral stones from phleboliths in thin slice CT volumes due to their similarity in shape and intensity. ANN also can be used for the early detection of kidney stone types and most influential parameters to provide a decision-support system. The model resulted in 97.1% accuracy for predicting kidney stone type. Recently, ML algorithms have been used to predict treatment success after a single-session shock wave lithotripsy in ureteral stone patients.

Additionally, ML can be applied to benign bladder diseases, such as overactive bladder syndrome [5]. A ML model using a random forest-based algorithm was studied to identify patients for whom anticholinergic medications are likely to fail. A validated ML prediction model can predict treatment failure in a 3-month standard anticholinergic treatment experiment with accuracy rate higher than 80%.

HOW WILL ML BE EVOLVED INTO TOMORROW'S UROLOGY?

In today's fast-moving technologically enhanced world, ML is still in its evolution. The steps needed to integrate ML into the clinic are still unknown. How the new algorithms will influence diagnosis and management of patients remains within our realm of decision. Future research should focus on the construction of larger medical databases and further development of artificial intelligence techniques. The predictive precision of ML will continue to provide and enhance personalized medicine with the further inclusion of data and model retraining. There are limitless future applications for artificial intelligence in the field of urology.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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