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Going Deep: The Role of Neural Networks for Renal Survival and Beyond

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Neural networks are an advanced set of algorithms designed to determine patterns from data. Since 1959, researchers have speculated that neural networks could support clinical decision making.[1] Despite the conceivable value of neural networks, many are still unclear how these methods work and what function they may serve.

Although they may be varied in their details, all neural networks share a foundational architecture. A neural net is composed of *layers of nodes* (sometimes called *neurons*). The node is the basic unit of computation in neural nets. All nodes, in any single layer, are connected to all nodes in the adjacent layers. With any net, data are fed into the network through the *input layer*. Each node that results from the input layer has an associated weight and is connected to an unobservable layer of nodes, called the *hidden layer*. In the hidden layer, each node calculates the *weighted sum* of its input nodes and passes the sum, adjusted for a *bias,* through an *activation function* that allows the net to solve nontrivial (nonlinear) problems. The calculations from the hidden layer then connect to the *output layer*, which finalizes computations and returns the result.[2]

Historically, the use of neural networks in health care and other domains was discouraged due to weak processing power, but advances in computational ability in the past 20 years have thrust these methods back into the spotlight as a relevant viable tool for a number of tasks. This new computational power not only encouraged the use of artificial neural networks for a wider variety of tasks, but additionally encouraged the development of increasingly complex neural network architectures. One class of complex architectures, known as *deep learning* models*,* is a subgroup of artificial neural networks that is characterized by an increasing number of hidden layers to improve abstraction and prediction from data.[2,3] Deep learning models, or *deep neural nets*, are able to efficiently represent complex data through a larger set of activation functions than is typical in a neural net with a single hidden layer. This makes deep neural nets particularly well suited for multifarious tasks, such as natural language processing and image analysis.[2]

The recent article by Kolachalama *et al.*[4] leveraged deep learning to classify phenotypes of chronic kidney disease from patient-specific histological images. This research used one of the most popular deep learning architectures, the convolutional neural network (CNN). CNNs, like the traditional neural net, are composed of layers of nodes; however, unlike the traditional net, CNNs assume that the input is a multichanneled image. The image is composed of *patches* of neurons that overlay each other to represent the input image. This architecture exploits spatial invariance of parts of the image; that is, an object in the image that is transformed or otherwise distorted, would still be recognized by the CNN.[2]

The authors wanted to explore the utility of CNNs for classifying chronic kidney disease severity from kidney biopsy images. They used a training set of 171 renal biopsies with varying degrees of interstitial fibrosis. This research used Google's *Inception-v3,* a CNN architecture pretrained on millions of images from the ImageNet dataset. With this architecture as a starting point, the top layers were trained to predict 1 of 6 outcomes: (i) chronic kidney disease stage (1–5) based on estimated glomerular filtration rate, (ii) high gender-specific serum creatinine levels, (iii) nephrotic range proteinuria at the time of biopsy, (iv) 1-year renal survival, (v) 3-year renal survival, and (vi) 5-year renal survival. For each of the 6 classification outcomes, the authors developed separate models, including linear discriminant analysis, Naïve Bayes, and support vector machine classifiers, to relate pathologist-estimated

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fibrosis scores to the outcome, as a basis for comparison. The CNN models outperformed the pathologist-estimated fibrosis scores for all classification tasks, with CNN-reported areas under the curve ranging from 8% to 24% higher than their pathologist-estimated fibrosis score counterparts.

The most interesting of the outcomes are those that pertain to renal survival. Renal biopsies contain histological clues of renal function, as there are observable differences in the tissue between stable patients and those patients with impaired or declining kidney function. In the past, assessments of kidney health from biopsies were done by clinical experts (pathologists), which is likely a lengthy process that is prone to subjectivity and human error. A failure to recognize a histological abnormality could result in a missed opportunity to seek targeted, potentially life-saving or kidney-saving treatments for patients. So, the prognostic value of neural nets for kidney survival that is presented represents real promise of these techniques for clinical decision support.

The use of machine learning and artificial intelligence methods, such as neural networks, to support medical image analysis is not a novel concept. Similar models to that presented by Kolachalama *et al*.[4] have been used to support oncology, radiology, ophthalmology, and cardiovascular medicine, with moderate success.[5] However, the adoption of these methods lags far behind their utility. Despite the demonstration of their predictive power and reliability in many domains, artificial intelligence tools are relegated to the sidelines, often cited as disruptive to workflow.[6] This is at odds with the fact that artificial intelligence tools will be beneficial only when integrated into standard clinical protocol.[5–7] When considering the attributes of artificial intelligence tools, the disruption to clinical practice has historically outweighed their advantages. Nevertheless, these methods persist. Researchers, like Kolachalama *et al*.,[4] continue to develop models to support clinical decision making despite the lackluster adoption of similar methods in the past. This is likely driven by the impressive performance of these methods. However, to bring these models into practice, researchers and clinicians should not be solely preoccupied with speed and accuracy, but should assess how these methods integrate into the medical setting.

DISCLOSURE

AJA has a financial interest in Vitalis Pharmaceuticals. The other author declared no competing interests.

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