

Hot Topic**Artificial Intelligence Meets Chinese Medicine***GUO Yan¹, REN Xue², CHEN Yu-xin³, and WANG Teng-jiao³

ABSTRACT As an interdisciplinary subject of medicine and artificial intelligence, intelligent diagnosis and treatment has received extensive attention. The standardization of Chinese medicine (CM) diagnosis has been always a bottleneck in the modernization and globalization of CM. Studying the application technology of artificial intelligence in CM and solving the problems is an urgent need for the development of modern CM in the era of artificial intelligence. Taking the pneumonia with dyspnea and cough in CM as an example, this article gives an overview of intelligent medical technology and application development, brings forward the present technical problems faced and the new advances in intelligent technology on CM diagnosis and treatment.

KEYWORDS artificial intelligence, Chinese medicine, diagnosis and treatment

In recent years, application of artificial intelligence (AI) technology in the medical field is in a rapid development stage, represented by deep learning. As an interdisciplinary subject of medicine and AI, intelligent diagnosis and treatment has received extensive attention in both academia and industry. Even some scholars believe that intelligent diagnosis and treatment is reshaping the diagnosis and treatment ways and industry schemas in the medical and health fields.

For thousands of years, Chinese medicine (CM) has gradually formed its own unique medical theoretical system during practical experience, and has made an indelible contribution to the health of the Chinese nation. It still plays a pivotal role today. However, the standardization of CM diagnosis has been always a bottleneck in the modernization and globalization of CM. From the perspective of modern information technology, the medical books and records passed down are mainly unstructured data samples. Also, CM is characterized by individual syndrome differentiation as well as personalized treatment, eg., the "same disease treated with different therapies" or "different diseases treated with same therapy" mode of CM is a typical example of individualized analysis, which might lead to distortion for the common law in mining technology of big data and AI appear in study on CM diagnosis and treatment.

Therefore, studying the application technology of AI in CM and solving the new problems during intelligent analysis of CM is not only the need of

interdisciplinary research, but also the urgent demand for the development of modern CM in the era of AI.

This paper analyzes the developing history of intelligent medical technology and its application, as well as the technical problems faced by intelligent CM and the current progress of intelligent CM technology. The authors are willing to provide a reference for both CM and AI scholars to engage in this new interdisciplinary research.

Overview of Intelligent Medical Technology and Application Development

The concept of AI was first clarified at the Dartmouth College Summer Symposium in 1956.^(1,2) With the continuous advancement of AI technology, human beings have been exploring the application of AI technology to the medical field.⁽³⁾ In the 1970s, the expert system was the mainstream technology of AI at that time. Stanford University developed the expert system-based diagnosis and treatment system MYCIN in 1972.⁽⁴⁾ The system uses medical records, illnesses,

©The Chinese Journal of Integrated Traditional and Western Medicine Press and Springer-Verlag GmbH Germany, part of Springer Nature 2019

Supported by the National Nature Science Foundation of China (No. 81774138)

1. Xiyuan Hospital, China Academy of Chinese Medicinal Sciences, Beijing (100091), China; 2. Department of Pediatrics, Jinan Municipal Hospital of Traditional Chinese Medicine, Jinan (250012), China; 3. School of Electrical Engineering and Computer Sciences, Peking University, Beijing, China

Correspondence to: Dr. REN Xue, E-mail: higher0314@163.com

DOI: <https://doi.org/10.1007/s11655-019-3169-5>

and laboratory results as raw data and the knowledge of medical experts to make inferences that can be diagnosed for infectious diseases. After experiencing the early medical expert system, researchers also tried to introduce AI technologies such as fuzzy set theory, Bayesian networks and artificial neural networks into the medical field. The typical works of early smart healthcare are summarized in Table 1.

The early AI application technology was not mature. The software and hardware conditions and data resources were also limited at that time. Therefore, such intelligent diagnosis and treatment technology did not form an influential medical practical system. With the development of computing environment, especially big data technology, AI technology represented by deep learning has developed rapidly, and intelligent healthcare has received unprecedented attention.

In the academic world, the achievements of intelligent medical research have emerged in recent years. In January 2019, *Nature Medicine* published 8 papers, giving great focus on the application of deep learning and AI in medicine. These include the latest scientific research achievements of famous AI scientists, such as Andrew Y. Ng⁽⁸⁾ and Jeff D,⁽¹¹⁾ and the top medical institution Mayo Clinic,⁽¹⁰⁾ covering areas including heart diseases,^(8,10) chronic kidney disease and genetic diseases⁽¹¹⁾ and so on,⁽¹²⁾ who seek to influence at three levels through the integration of human and machine intelligence: analyzing images more quickly and accurately for clinicians; improving

workflow and reducing medical errors for health systems; processing and analyzing their own data to promote individual health for patients. Researchers of FDNA have proposed a deep learning application, Face2Gene,⁽⁹⁾ which helps doctors identify rare genetic diseases by identifying facial features. They proposed a facial image analysis framework that quantified the similarities of hundreds of syndromes using computer vision and deep learning algorithms. The accuracy of the technique reached 91%, surpassing clinicians. The smart healthcare works that involve deep learning are summarized in Table 2.

In addition to academia, the industry is also actively involved in the field of medical AI. According to the market research report⁽¹³⁾ by Markets, the investment in medical AI technology is 2.1 billion US dollars in 2018, and the data is expected to exceed 36 billion US dollars by 2025.

In 2015, Watson Health was founded to focus on providing solutions for the healthcare industry with cognitive computing systems.⁽¹⁴⁾ Google's DeepMind Health has partnered with the UK's National Health Service (NHS).⁽¹⁵⁾ The US Food and Drug Administration (FDA) approved diagnostic auxiliary products like IDX, OsteoDetect and medication auxiliary products such as DreamMed Advisor Pro from April 2018.⁽¹⁶⁾ The domestic Big three (Baidu, Alibaba, Tencent) are also intensively involved in the medical + AI field. Tencent released the medical AI imaging product "Tencent Shadow" and announced that it has cooperated with more than 100 hospitals;

Table 1. Early Smart Healthcare Technology

AI technology	System name	Time	Affiliation	Function
Expert system	MYCIN ⁽⁴⁾	1972	Stanford University	Diagnose infectious diseases
Fuzzy set theory	Fuzzy Logical Model of Computer-Assisted Medical Diagnosis ⁽⁵⁾	1980	University of Vienna	Medical diagnosis
Bayesian network	Bayesian Network Model for Diagnosis of Psychiatric Diseases ⁽⁶⁾	2009	University of Timisoara	Diagnose psychiatric diseases
Artificial neural network	ED-ANN ⁽⁷⁾	2012	Masaryk University	Chemical kinetics

Table 2. Summary of Intelligent Medical Technology Represented by Deep Learning

Deep learning technology	System name	Time	Affiliation	Function
Convolutional neural networks (CNN)	Face2Gene ⁽⁹⁾	2019	FDNA	Diagnose rare genetic diseases
Deep neural network (DNN)	Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network ⁽⁸⁾	2019	Stanford University	Arrhythmia detection
Convolutional neural network (CNN) + Long short-term memory (LSTM)	Screening for cardiac contractile dysfunction using an AI ⁽¹⁰⁾	2019	Mayo Clinic	Identify asymptomatic left ventricular dysfunction

Baidu announced the medical AI program; Ali Health released the medical AI product "Doctor You". The recent summary of smart healthcare progress in the industry is shown in Table 3.

Table 3. Recent Summary of Smart Healthcare Progress in the Medical Industry

Product	Enterprise	Time	Function
Watson Health	IBM	2015	Tumor, gene, etc.
Deep Mind Health	Google	2016	Eye disease detection, breast cancer diagnosis, and kidney damage prediction
Doctor You, ET Brain	Alibaba	2017	Image detection, assisted diagnosis, chronic disease management, genetic testing, etc.
Tencent Miying	Tencent	2017	Medical imaging and AI-assisted diagnosis
Baidu CDSS	Baidu	2018	Medical imaging

Under the joint promotion of academia and industry, the successful application of AI technology is mostly concentrated in the field of Western medicine, including medical image analysis, medical wearable devices and intelligent medical auxiliary equipment.

Relatively speaking, the breakthrough research and application results of AI in the CM field are few.⁽¹⁷⁻¹⁹⁾ This is a new era in which AI changes the way of human life. Modern CM urgently needs rapid development with the help of AI technology.

Technical Problems Faced by Intelligent CM

The processing of the computer system is "input–calculation–output". Corresponding to the diagnosis and treatment process of CM, "inspection, listening and smelling, inquiry, pulse taking and palpation" can be regarded as an "input" process. Based on the input, the doctor can make a diagnosis and treatment plan based on the knowledge learned, which can be regarded as a "calculation" and "output" process.

There are many technologies that can be replaced or partially replaced in the "input" process of "inspection, listening and smelling, inquiry, pulse taking and palpation". "Inspection" can be realized by computer vision through image analysis. "Listening and smelling" can be supported by computer auditory through speech recognition system. "Inquiry" can be implemented by the intelligent question answering system. "Pulse taking and palpation" can be realized by a large number of wearable pulse-analysis medical devices.

After solving the input process, the core problem of intelligent CM is "computation". That is how to learn CM knowledge for a machine and form a machine reasoning and judgment mechanism. However, current machine learning techniques face two types of technical problems in the field of CM as follows.

Syndrome Differentiation in CM Might Lead to the Machine Learning Model Distortion

The "same disease treated with different therapies" is a treatment principle based on the CM theory of "syndrome differentiation", for which individualized analysis is suitable. However, current big data and AI technologies mainly focus on common patterns and laws in the training process. Direct application of the existing machine learning model in CM may lead to distortion, which we believe is also an important reason for the poor performance of present CM intelligent diagnosis systems.

CM Expert-Experience Knowledge System is Difficult to Incorporate into the Deep Learning Process

The expert system in early AI technology is essentially a rule-based reasoning system. Therefore, it is convenient to incorporate the medical knowledge of Western medicine into the expert system as a rule. However, in that case, the lack of analysis on large-scale data would result in insufficient necessary adaptive capabilities of the expert system. The system could only rely on rule-based reasoning and showed poor results. The current deep learning technology could identify the implied patterns and provide new technical ways for mining valuable knowledge in medical data. Therefore, deep learning has good adaptability, learning ability and fault tolerance.

Unfortunately, deep learning and rule-based reasoning are two completely different technical systems. If smart healthcare only relies on deep learning of medical records and other data without incorporating medical knowledge rules, it is difficult to play a substantial role.

The CM knowledge system is based on long-term medical practice experiences, and forms an unique wholism system including pathogenesis, treatment rules, prescriptions, and medicines. How to combine these principles extracted from the CM knowledge system with the deep learning algorithm to achieve joint learning is a challenging problem.

New Advances in Intelligent CM Technology

The unique CM principle and its knowledge system are difficult to be included in the deep learning process, which is the main problem faced by CM intelligent diagnosis and treatment. In this section we focus on the recent exploration of theories and methods for these two types of issues.

CM Symptom -Aware Knowledge Graph

The knowledge graph⁽²⁰⁾ is a model to describe the various entities or concepts that exist in the real world, as well as the relationships between them. The medical knowledge graph can reflect the connection between various medical entities or concepts. With the medical knowledge graph, medical knowledge reasoning and analysis can be carried out to realize disease diagnosis and treatment. An example of the CM knowledge graph on pneumonia with dyspnea and cough is shown in Figure 1.

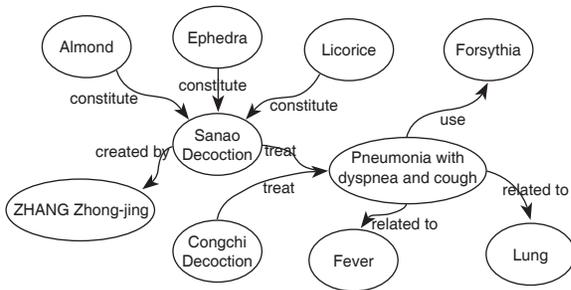


Figure 1. An Example of CM Knowledge Graph on Pneumonia with Dyspnea and Cough

However, the general knowledge graph technology is difficult to solve the complicated principle of CM, such as the "same disease treated with different therapies". From the perspective of knowledge graph, the principle for diagnosis and treatments is not only from the analysis of various "concepts" and "relationships" in the knowledge graph, but also the detailed analysis of the differences among the "syndromes" related to "concepts".

In order to realize the unique analytical method of CM, we improved our "opinion-aware knowledge graph",⁽²¹⁾ and replaced the "opinion" with "symptom status" to construct a "knowledge graph of symptom". The new knowledge graph has achieved good performance.

Taking the pneumonia with dyspnea and cough in CM as an example, we illustrate how the symptom-aware knowledge graph can describe two different syndromes in the knowledge graph and achieve two different treatments for the same disease, as shown in Table 4 and Figure 2.

Table 4. "Different Treatments for Same Disease of Different Syndromes" in Pneumonia with Dyspnea and Cough

Treatment	Pneumonia with dyspnea and cough	
	Wind-cold syndrome type	Wind-heat syndrome type
Symptom	Aversion to cold, fever, without sweating and thirst, cough, rapid breath, white watery sputum, light red tongue with thin and white fur, floating and tight pulse	Fever, aversion to wind, sweating, thirsty, cough, rapid breath, yellow thick sputum, throat congestion, red lip of tongue with thin and yellow fur, floating and rapid pulse
Therapy	Diffuse Fei (Lung) with pungency and warmth, resolve phlegm and relieve cough	Diffuse Fei (Lung) with pungency and cold, clear heat and resolve phlegm
Recipe	San-ao Decoction (三拗汤) and Congchi Decoction (葱豉汤)	Yinqiao Powder (银翘散) and Moxing Shigan Decoction (麻杏石甘汤)

We know that "fever, cough, phlegm, and asthma" are typical symptoms of pneumonia with dyspnea and cough. Even if the patients are all diagnosed as pneumonia with dyspnea and cough, the prescriptions might be different depending on the syndrome types. For example, wind-cold type and wind-heat type are two of the different syndrome-types of pneumonia with dyspnea and cough. They have a clear distinction in CM, as shown in Table 4. However, the existing machine learning process

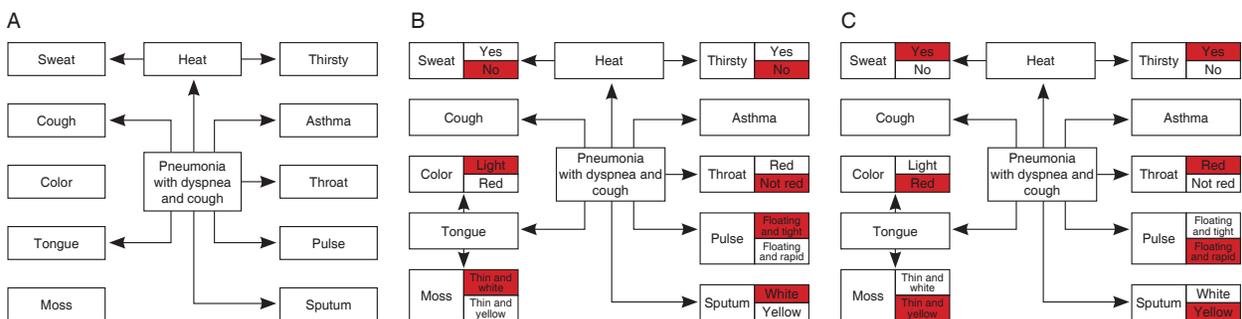


Figure 2. "Pneumonia with Dyspnea and Cough" Fragment in the Symptom-Aware Knowledge Graph

Notes: A: Indiscriminate knowledge graph; B: Knowledge graph of wind-cold syndrome type; C: Knowledge graph of wind-heat syndrome type

cannot read this difference, so that it could only get one disease diagnosis and give one treatment plan.

After the entity extraction and analysis, the indiscriminate pneumonia with dyspnea and cough knowledge graph is generated as shown in Figure 2A. According to this knowledge graph, it is impossible to give different treatments for the same disease of different syndrome types.

We put forward the symptom-aware knowledge graph construction method that can generate two different knowledge graphs of wind-cold type and wind-heat type (Figures 2B and 2C). In addition to concepts and relationships, we also recorded different symptom characteristics of the concept, such as "white" and "yellow" tongue coating, and "tight and floating" and "rapid and floating" pulse. We have designed a construction method to support this model, so that it can construct a symptom-aware knowledge graph through CM knowledge, and support symptom-based reasoning mechanism, which may effectively support the principles of CM treatment.

"CM Rule-Deep" Learning Model

As mentioned above, how to combine the rules extracted from the CM knowledge system with the deep learning algorithm to achieve joint learning is a very challenging problem.

The authors have proposed a method for incorporating entity extraction rules in natural language

processing into deep learning, and published the results in the Association for the Advance of Artificial Intelligence (AAAI) Workshop 2019.⁽²²⁾ In order to solve the problem of incorporating CM knowledge system in deep learning, we proposed and designed the "CM Rule-Deep" learning model. The core idea is to combine the CM disease diagnosis rules and the generalization ability of the deep learning model. Through the modeling of rules to optimize the training of deep machine learning, it is desired to simulate CM doctors under the guidance of diagnostic rules and take advantage of deep learning in large-scale data analysis to achieve accurate CM diagnosis and treatment.

We have established a joint team of CM and AI scholars. The team combed the knowledge system of common diseases in CM, and organized them into a set of rules that can quantify description and reasoning.

The above rules can be entered into the network structure of the "CM Rule-Deep" learning model shown in Figure 3 along with the CM case data. The "CM Rule-Deep" model effectively supports the inclusion of CM diagnostic rules into the deep learning process, which not only exerts the advantage of deep learning to automatically extract features, but also incorporates the CM knowledge system.

Prospects for Intelligent CM Technology and Application

Internet and AI technologies have deeply impacted and continue to profoundly change the way

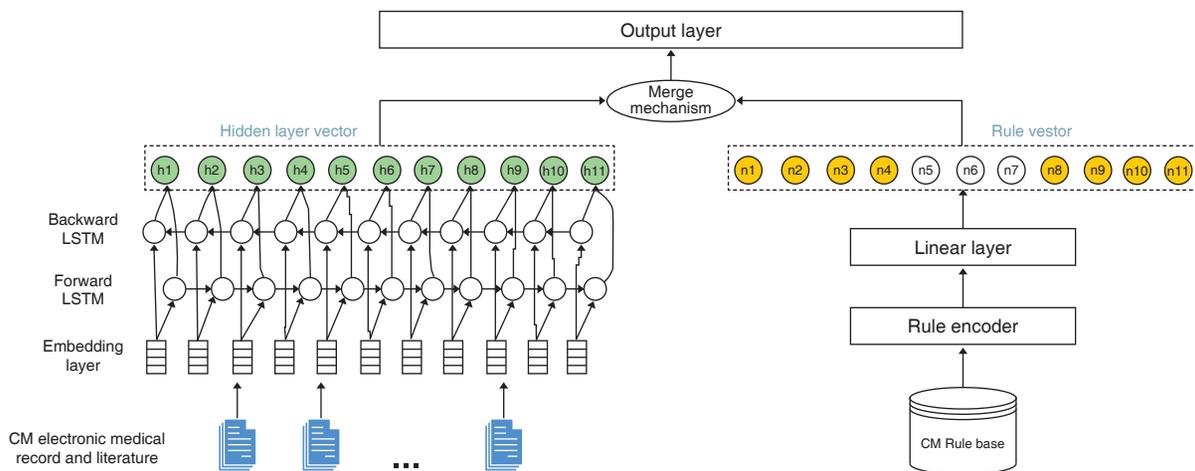


Figure 3. "CM Rule-Deep" Learning Model

Notes: The lower left side of the figure is a deep learning process (LSTM), which can automatically project CM case data into the feature representation space through deep learning methods. The lower right side of the figure is the CM rule learning process, and the diagnostic rules can be automatically learned by the rule encoder to generate the rule representation results. Two parts eventually complete the training and decision process through joint learning.

people live. In this era of AI, CM not only needs to be passed down, but also to actively adapt and develop.

Through the analysis of this article, we can see that although there are many special technical problems in intelligent CM compared with Western medicine, the existing technology has established a feasible technical route and important information infrastructure for its development and application.

In order to enable CM to continue to benefit the society in the future, CM scholars should take active actions, seize opportunities, conduct cross-disciplinary research with experts in the information field, and strive to achieve breakthrough development of CM in the era of AI.

REFERENCES

- Alpaydin E, ed. Introduction to machine learning. Cambridge: MIT Press; 2009:4.
- Bishop CM, ed. Pattern recognition and machine learning. Heidelberg: Springer; 2006.
- Deo RC. Machine learning in medicine. *Circulation* 2015;132:1920-1930.
- <https://en.wikipedia.org/wiki/Mycin>.
- Adlassnig KP. A fuzzy logical model of computer-assisted medical diagnosis. *Methods Informat Med* 1980;19:141-148.
- Curiac DI, Vasile G, Baniias O, Volosencu C, Albu A. Bayesian network model for diagnosis of psychiatric diseases. *Proceedings of the ITI 2009 31st International Conference on Information Technology Interfaces*; 2009 June 22-25; Cavtat/Dubrovnik, Croatia. 2009:61-66.
- Amato F, González-Hernández JL, Havel J. Artificial neural networks combined with experimental design: a "soft" approach for chemical kinetics. *Talanta* 2012;93:72-78.
- Hannun AY, Rajpurkar P, Haghpanahi M, Tison GH, Bourn C, Turakhia MP, et al. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. *Nature Med* 2019;25:65.
- Esteva A, Robicquet A, Ramsundar B, Kuleshov V, DePristo M, Chou K, et al. A guide to deep learning in healthcare. *Nature Med* 2019;25:24.
- Attia ZI, Kapa S, Lopez-Jimenez F, McKie PM, Ladewig DJ, Satam G, et al. Screening for cardiac contractile dysfunction using an artificial intelligence-enabled electrocardiogram. *Nature Med* 2019;25:70.
- Gurovich Y, Hanani Y, Bar O, Nadav G, Fleischer N, Gelbman D, et al. Identifying facial phenotypes of genetic disorders using deep learning. *Nature Med* 2019;25:60.
- Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. *Nature Med* 2019;25:44.
- <https://www.marketsandmarkets.com/Market-Reports/artificial-intelligence-healthcare-market-54679303.html>.
- <https://www.computerworld.com/article/2909534/ibm-launches-watson-health-global-analytics-cloud.html>.
- <https://deepmind.com/blog/scaling-streams-google/>.
- <https://www.scimmit.com/9-medical-artificial-intelligence-products-that-have-been-certified-by-the-us-fda/>.
- Leung EL, Wong VK, Jiang ZH, Li T, Liu L. Integrated network-based medicine: the role of traditional Chinese medicine in developing a new generation of medicine. *Science* 2014;346:S16-S18.
- Tu Y. The discovery of artemisinin (qinghaosu) and gifts from Chinese medicine. *Nature Med* 2011;17:1217.
- Chan M. Supporting the integration and modernization of traditional medicine. *Science* 2014;346:S2-S2.
- https://en.wikipedia.org/wiki/Knowledge_Graph
- Chen W, Zhang X, Wang T, Yang B, Li Y. Opinion-aware knowledge graph for political ideology detection. *Proceedings of the Twenty-Sixth International Joint Conference on Artificial Intelligence (IJCAI)*; 2017 Aug 19-25; Melbourne, Australia. 2017:3647-3653.
- Han Y, Chen W, Xiong XL, Li Q, Qiu Z, Wang TJ. Wide & deep learning for improving named entity recognition via text-aware named entity normalization. *Proceedings of The AAAI-19 Workshop on Recommender Systems and Natural Language Processing (REC/NLP), Thirty-Third AAAI Conference on Artificial Intelligence (AAAI 19)*; 2019 Jan 28; Honolulu, Hawaii, USA.

(Accepted June 19, 2019)
Edited by YUAN Lin