Abstract. Artificial intelligence (AI) has been developed through repeated new discoveries since around 1960. The use of AI is now becoming widespread within society and our daily lives. AI is also being introduced into healthcare, such as medicine and drug development; however, it is currently biased towards specific domains. The present review traces the history of the development of various AI-based applications in healthcare and compares AI-based healthcare with conventional healthcare to show the future prospects for this type of care. Knowledge of the past and present development of AI-based applications would be useful for the future utilization of novel AI approaches in healthcare.

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1. Introduction

‘Big data’, large datasets that are difficult to record, store and analyze with conventional data management systems, has been accumulating in various fields in recent years with regard to the development of communication and sensor technology. The advances in technology regarding big data have emerged that the use of big data is expected to create new avenues of research. However, the overall trend of big data is difficult to understand based on general information processing by humans; thus, information processing by artificial intelligence (AI) has also attracted attention (1). In general, industries have succeeded in improving sales and work efficiency and decreasing costs using big data and AI (2).

In healthcare, the creation of new knowledge and the improvement in diagnostic and therapeutic outcomes are expected through the utilization of big data pertaining to life science information and medical data (3). In fact, the implementation of AI in healthcare has been actively investigated; however, it has not been used in a widespread manner due to a number of problems (4).

The present review looks back at the history of AI and AI-based applications, compares the advantages and the issues of conventional healthcare and AI-based healthcare, and considers the future development of AI-based applications.

2. Historical view of the clinical application of computational support

In the 1950s, McCarthy et al (5) proposed AI as a prediction machine (hardware or software that exhibits behavior which appears intelligence by predicting associations between variables). Samuel (6) developed machine learning in 1959, which triggered the first AI boom (Fig. 1). In this period, the discrimination of cells in microscopic images started to be investigated using machine learning (7,8). In the 1970s, progress with AI was temporarily halted, as the AI was only able to solve simple problems. By contrast, in the same period, expert systems consisting of knowledge bases and inference engines were invented, and tools for diagnosis in specific fields such as MYCIN and INTERNIST-1 were developed (9,10). Subsequently, deep learning was proposed by Dechter (11)
in 1986 and a convolutional neural network was proposed by LeCun et al (12) in 1988, leading to the second AI boom. In this boom, to allow adaptation to real-world problems, experts in various fields educated AI using parameters, including marketing, healthcare and life science data. In addition, surgical robots began to flourish during this period. Among them, PUMA 200 was developed to automatically identify the appropriate location of lesions in computed tomography-guided brain tumor biopsies and was the first robot used for assisting human neurosurgery (13). AESOP was a breakthrough in robotic surgery when introduced in 1994, as it was the first laparoscopic camera holder to be approved by the FDA (14). Moreover, in 2000, the da Vinci Surgical System obtained FDA approval for use in general laparoscopic procedures and became the first operative surgical robot in the US (15). In 2005, a surgical technique for the da Vinci Surgical System was documented in canine and cadaveric models called transoral robotic surgery; this was the only FDA-approved robot to perform head and neck surgery at the time (16).

In addition, medications based on a computational analysis of the crystal structure of molecules were developed (17,18). The RÖBODOC Surgical System was introduced and revolutionized orthopedic surgery by being able to assist with hip replacement surgeries. This was the first surgical robot to be approved for use in humans by the FDA in 2008 (19).

Thus, during the second AI boom, several tools were successfully developed. However, it was difficult for humans to provide the information that an AI needs to solve complex problems, and it was difficult for the machines of that time to learn the vast level of information available.

With the advent of deep learning in 2006 and the development of computers and communication equipment, the interest in AI was renewed (20,21). In particular, the historical victory of a deep learning program by utilizing a convolutional neural network, a deep learning method in image recognition, in an image recognition contest called the ImageNet Large Scale Visual Recognition Challenge (ILSVRC) triggered the third AI boom (22). As a result, image recognition has become the most applied AI-based technology in the clinical setting. When considering clinical applications based on image recognition using AI, IB Neuro is a diagnostic software used to detect brain tumors by MRI, and this was approved by the FDA in 2008 (19).

3. Current AI applied in medicine

Diagnosis. Diagnosis requires the ability to process different types of information about patients and detect abnormalities with high accuracy and reproducibility. In conventional diagnosis, physicians process various pieces of patient information using their own knowledge and/or experience, and detect abnormalities in patients using their own senses or through diagnostic equipment. This method sometimes fails to detect abnormalities in patients or results in the wrong decisions being made. In addition, the diagnostic ability is dependent on the experience of the physician. Therefore, AI is expected to have diagnostic performance with reproducibility and accuracy equal to or better than that of skilled physicians, and to compensate for differences in physician experience. Current AI for diagnosis is actively being developed to perform diagnostic imaging with computed tomography and tissue sections. In particular, convolutional neural networks perform well in the ILSVRC every year; therefore, convolutional neural networks are the most used for diagnostic imaging and perform as well as or better than skilled physicians (31). Moreover, systems have been developed to predict radiation or anticancer drug sensitivity using convolutional neural networks (32,33). In addition to diagnostic imaging, AI is also being developed to diagnose diseases such as cancer via machine learning of blood components (34). However, limitations in measurement sensitivity and technical artifacts such as noise are barriers to diagnosis using blood components. The development of improved measurement technology and/or more advanced machine learning models would be required for a diagnosis that applies machine learning of blood components (35).

As aforementioned, the current application of AI for diagnosis mainly improves the accuracy of each test. By contrast, for the identification of a disease from various symptoms in a patient and the results of tests, a wide range of knowledge, not specific knowledge, and advanced information processing is necessary. To meet this demand, AI assistants such as Watson are also being developed that can learn the literature on a subject by enabling the processing of natural language, and can make complex decisions using expert systems (28,36).

Thus, for diagnosis, AI is mainly developed to improve the accuracy of each test and make appropriate decisions using the large quantity of related literature available, and different algorithms suitable for each process are applied.
**Treatment.** For treatment, surgical robots are mainly being developed. Surgical robots are suitable for detailed work with precise movements that is beyond the reach of human hands. In conventional surgical robot algorithms, classification and detection of objects required during surgery are performed by the developer manually creating features of the region of interest; however, with the advent of deep learning, convolutional neural networks are being applied for the classification and detection of objects (37,38). In addition, real-time predictions are also being made with recurrent neural networks (39). Conventional surgical robots are operated by a physician; however, surgical robots that work automatically without operation by a physician are also being developed (40). Thus, the development of AI has also led to the development of robots that support physicians during surgery.

In addition, in drug therapy, AI-based applications are being introduced in diagnosis and follow-up rather than in the treatment process. Various AI applications have been introduced in the drug development process to develop therapeutic drugs. In the drug development process, developers need to process an enormous amount of information to discover just a few promising compounds from millions to tens of millions of candidate compounds (41). Various types of AI play active roles in processing this information, as described in detail later in this review.

Thus, in the treatment process, surgical robots are mainly being developed to make the operation more accurate and reduce the burden on the physician, while in the drug development process, AI is being used to process large quantities of information.

**Follow-up.** In medicine, no matter what type of disease or what type of treatment is given, follow-up is more or less always necessary. In addition, life expectancy in the world has increased by 20 years in the last 50 years, and as the population ages, the risk of having chronic diseases increases. Against this background, wearable devices equipped with AI that can constantly monitor health conditions and immediately detect any abnormality in wearers are actively being developed. In particular, wearable devices are expected to be used in cardiology, where the condition of the patient may change rapidly and there is a direct link with mortality status. In fact, more than half of the applications for follow-up approved by the FDA in 2017-2020, including the ECG app on the Apple™ Watch, are wearable cardiology devices (23,26). A number of the algorithms in wearable devices are applied artificial neural networks or adaptive algorithms (42).

In addition to the wearable devices, automated communication systems have also been introduced for follow-up. For example, Pharmabot was a chatbot developed in 2015...
Table I. FDA approved AI-based applications.

| Applications                          | Company                        | Purpose       | Medical specialty | FDA Cleared |
|---------------------------------------|--------------------------------|---------------|-------------------|-------------|
| IB Neuro                              | Imaging Biometrics, LLC        | Diagnosis     | Neuroradiology    | 2008        |
| Pathwork Tissue of Origin Test Kit-FFPE | Pathwork Diagnostics, Inc.    | Diagnosis     | Pathology         | 2010        |
| DeltaView Model 2.1                   | Riverain Technologies         | Diagnosis     | Radiology         | 2011        |
| AlphaPoint Imaging Software           | RadLogics, Inc.               | Diagnosis     | Radiology         | 2012        |
| BodyGuardian Remote Monitoring System | Preventice                    | Follow-up     | Cardiology        | 2012        |
| ClearRead +Confirm                    | Riverain Technologies         | Diagnosis     | Radiology         | 2012        |
| Temporal Comparison                   | Circle Cardiovascular Imaging, Inc. | Diagnosis | Radiology         | 2014        |
| AHead 100                             | BrainScope                    | Diagnosis     | Neurology         | 2014        |
| AliveCor                              | AliveCor                      | Diagnosis     | Cardiology        | 2014        |
| Lung Density Analysis                 | Imbio LLC                     | Diagnosis     | Radiology         | 2014        |
| Vitrea CT Lung Density Analysis Software | Vital Images, Inc.            | Diagnosis     | Radiology         | 2015        |
| Stroke VCAR                           | GE Medical Systems            | Diagnosis     | Neuroradiology    | 2016        |
| QbCheck                               | QbTech AB                     | Diagnosis     | Psychiatry        | 2016        |
| PixelShine                            | AlgoMedica                    | Diagnosis     | Radiology         | 2016        |
| Sth IO                                | Stratoscientific, Inc.        | Diagnosis     | General medicine  | 2016        |
| ClearRead CT                          | Riverain Technologies         | Diagnosis     | Radiology         | 2016        |
| Arterys Cardio DL                     | Arterys Inc                   | Diagnosis     | Radiology         | 2016        |
| CT CoPilot                            | ZepMed, LLC.                  | Diagnosis     | Neuroradiology    | 2016        |
| ClearView cCAD                        | ClearView Diagnostics Inc.    | Diagnosis     | Oncology          | 2016        |
| Arterys Cardio DL                     | Arterys Inc                   | Diagnosis     | Radiology         | 2017        |
| Cantab Mobile                         | Cambridge Cognition, Ltd.     | Diagnosis     | Neurology         | 2017        |
| Lung Nodule Assessment and Comparison Option | Philips Medical Systems      | Diagnosis     | Radiology         | 2017        |
| EnsoSleep                              | EnsoData, Inc.                | Diagnosis     | Neurology         | 2017        |
| AmCAD-US                               | AmCad BioMed Corporation      | Diagnosis     | Radiology         | 2017        |
| QuantX                                | Quantitative Insights, Inc.   | Diagnosis     | Radiology         | 2017        |
| NeuroQuant                            | Cortechs.ai                   | Diagnosis     | Neuroradiology    | 2017        |
| LesionQuant                           | Cortechs.ai                   | Diagnosis     | Neuroradiology    | 2017        |
| Arterys Oncology DL                   | Arterys Inc                   | Diagnosis     | Radiology         | 2017        |
| Rooti Rx System ECG Event Recorder, Rooti Link APP Software | Rooti Labs, Ltd.             | Diagnosis     | Cardiology        | 2017        |
| BioFlux                                | Biotricity, Inc.              | Diagnosis     | Cardiology        | 2017        |
| CNeuro cMRI                            | Combinotics Oy                | Diagnosis     | Neuroradiology    | 2018        |
| Idx                                    | IDx LLC                       | Diagnosis     | Ophthalmology     | 2018        |
| WAVE Clinical Platform                 | Excel Medical Electronics, LLC | Follow-up     | Hospital monitoring | 2018        |
| Insight BD                            | Siemens Healthineers          | Diagnosis     | Radiology         | 2018        |
| Viz LVO (ConataCT)                    | Viz. AI, Inc.                 | Diagnosis     | Neuroradiology    | 2018        |
| DM-Density                            | Densitas, Inc.                | Diagnosis     | Oncology          | 2018        |
| OsteoDetect                            | Imagen Technologies, Inc.      | Diagnosis     | Radiology         | 2018        |
| Quantib Brain                          | Quantib BV                    | Diagnosis     | Neuroradiology    | 2018        |
| Guardian Connect System                | Medtronic                     | Diagnosis     | Endocrinology     | 2018        |
| PowerLook Density Assessment Software | ICAD Inc.                     | Diagnosis     | Radiology         | 2018        |
| Viz CTP                                | Viz. ai, inc.                 | Diagnosis     | Neuroradiology    | 2018        |
| NeuralBot                              | Neural Analytics, Inc.        | Diagnosis     | Radiology         | 2018        |
| OsteoDetect                            | Imagen Technologies            | Diagnosis     | Radiology         | 2018        |
| EchoMD Automated Ejection Fraction Software | Bay Labs, Inc.             | Diagnosis     | Radiology         | 2018        |
| MindMotion GO                          | MindMaze SA                   | Follow-up     | Orthopedics       | 2018        |
| LungQ                                  | Thirona Corporation           | Diagnosis     | Radiology         | 2018        |
### Table I. Continued.

| Applications                                | Company                                      | Purpose  | Medical specialty | FDA Cleared |
|---------------------------------------------|----------------------------------------------|----------|-------------------|-------------|
| HealthCCS                                   | Zebra Medical Vision Ltd.                    | Diagnosis| Radiology         | 2018        |
| EchoMD Automated Ejection Fraction Software | Bay Labs, Inc.                               | Diagnosis| Cardiology        | 2018        |
| DenSeeMammo                                 | Statlife                                     | Diagnosis| Oncology          | 2018        |
| DreaMed                                     | DreaMed Diabetes, Ltd                        | Follow-up| Endocrinology     | 2018        |
| ProFound™ AI Software V2.1                 | iCAD, Inc                                    | Diagnosis| Radiology         | 2018        |
| BriefCase- ICH                              | Aidoc Medical, Ltd.                          | Diagnosis| Neuroradiology    | 2018        |
| AmCAD-UT Detection 2.2                     | AmCAD BioMed Corporation                     | Diagnosis| Endocrinology     | 2018        |
| Artery MICA                                 | Artery's, Inc.                               | Diagnosis| Radiology         | 2018        |
| ECG App                                     | Apple, Inc.                                  | Follow-up| Cardiology        | 2018        |
| Volpara Imaging Software                    | Volpara Health Technologies Limited          | Diagnosis| Oncology          | 2018        |
| AI-ECG Platform                             | Shenzhen Carewell Electronics, Ltd.          | Diagnosis| Cardiology        | 2018        |
| FibriCheck                                  | Qompium NV                                   | Follow-up| Cardiology        | 2018        |
| Irregular Rhythm Notification Feature       | Apple, Inc.                                  | Diagnosis| Cardiology        | 2018        |
| RightEye Vision System                      | RightEye, LLC                                | Diagnosis| Ophthalmology     | 2018        |
| Accipiolx                                   | MaxQ-AI, Ltd.                                | Diagnosis| Radiology         | 2018        |
| icobrain                                    | Icometrix NV                                 | Diagnosis| Radiology         | 2018        |
| FluoroShield™                               | Omega Medical Imaging, LLC                   | Treatment| Radiology         | 2018        |
| Vittrea CT Brain Perfusion                  | Vital Images, Inc.                           | Diagnosis| Neuroradiology    | 2018        |
| SubtlePET                                   | Subtle Medical, Inc.                         | Diagnosis| Neuroradiology    | 2018        |
| FerriSmart Analysis System                  | Resonance Health Analysis Service Pty, Ltd.  | Diagnosis| Radiology         | 2018        |
| Embrace                                     | Empatica Srl                                 | Follow-up| Neurology         | 2018        |
| Quantib ND                                  | Quantib BV                                   | Diagnosis| Neuroradiology     | 2018        |
| iSchemaView RAPID                           | iSchemaView, Inc.                            | Diagnosis| Radiology         | 2018        |
| Study Watch                                 | Verily Life Sciences LLC                     | Follow-up| Cardiology        | 2019        |
| cmTriage                                    | CureMetrix, Inc.                             | Diagnosis| Oncology          | 2019        |
| Thoracic VCAR with GSI Pulmonary Perfusion  | GE Medical Systems                           | Diagnosis| Radiology         | 2019        |
| KardiaAI                                    | AliveCor, Inc                                | Follow-up| Cardiology        | 2019        |
| Loop System                                 | Spry Health, Inc.                            | Follow-up| Hospital monitoring| 2019       |
| RhythmAnalytics                             | Biofourmis Singapore Pte, Ltd.               | Follow-up| Cardiology        | 2019        |
| Bone Vcar                                   | GE Medical Systems                           | Diagnosis| Radiology         | 2019        |
| Aidoc Briefcase- ICH and PE triage          | Aidoc Medical, Ltd.                          | Diagnosis| Radiology         | 2019        |
| Deep Learning Image Reconstruction          | GE Medical Systems, LLC.                     | Diagnosis| Radiology         | 2019        |
| eMurmer ID                                  | CSD Labs GmbH                                | Diagnosis| Cardiology        | 2019        |
| HealthPNX                                   | Zebra Medical Vision Ltd.                    | Diagnosis| Radiology         | 2019        |
| Aidoc BriefCase- CSF triage                 | Aidoc Medical, Ltd.                          | Diagnosis| Radiology         | 2019        |
| ReSET-O                                     | Pear Therapeutics, Inc.                      | Treatment| Psychiatry        | 2019        |
| HealthICH                                   | Zebra Medical Vision Ltd.                    | Diagnosis| Neuroradiology    | 2019        |
| Advanced Intelligent Clear-IQ Engine (AiCE) | Canon Medical Systems                        | Diagnosis| Radiology         | 2019        |
| Koiios DS                                   | Koiios Medical, Inc                          | Diagnosis| Oncology          | 2019        |
| DeepCT                                      | Deep01 Limited                               | Diagnosis| Neuroradiology     | 2019        |
| iNtuition-Structural Heart Module           | TeraRecon, Inc.                              | Diagnosis| Radiology         | 2019        |
| AI-Rad Companion (Pulmonary)                | Siemens Healthineers                         | Diagnosis| Radiology         | 2019        |
| ACR I LAB Urine Analysis Test System        | Healthy.io, Ltd.                             | Diagnosis| Urology           | 2019        |
| Current Wearable Health Monitoring System   | Current Health, Ltd.                         | Follow-up| Hospital monitoring| 2019       |
Table I. Continued.

| Applications | Company | Purpose | Medical specialty | FDA Cleared |
|--------------|---------|---------|-------------------|-------------|
| physIQ Heart Rhythm and Respiratory Module | physIQ, Inc | Diagnosis | Cardiology | 2019 |
| RayCare 2.3 | RaySearch Laboratories AB | Treatment | Radiology | 2019 |
| Critical Care Suite | GE Medical Systems | Diagnosis | Radiology | 2019 |
| Biovitals Analytics Engine | Biofourmis Singapore Pte. Ltd | Follow-up | Cardiology | 2019 |
| Caption Guidance | Caption Health, Inc. | Diagnosis | Radiology | 2019 |
| AI-Rad Companion (cardiovascular) | Siemens Healthineers | Diagnosis | Radiology | 2019 |
| SubtleMR | Subtle Medical, Inc. | Diagnosis | Radiology | 2019 |
| StoneChecker | Imaging Biometrics, LLC | Diagnosis | Radiology | 2019 |
| BrainScope TBI | BrainScope Company, Inc | Diagnosis | Neurology | 2019 |
| ProFound AI Software V2.1 | ICAD Inc. | Diagnosis | Oncology | 2019 |
| KOALA | IB Lab GmbH | Diagnosis | Radiology | 2019 |
| EechoGo Core | Ultronics, Ltd. | Diagnosis | Cardiology | 2019 |
| RSI-MRI+ | HealthLytx | Diagnosis | Radiology | 2019 |
| HealthCXR | Zebra Medical Vision, Ltd. | Diagnosis | Radiology | 2019 |
| icobrain | Icometrix NV | Diagnosis | Neuroradiology | 2019 |
| QyScore Software | Qynapse | Diagnosis | Neuroradiology | 2019 |
| Aidoc BriefCase- LVO | Aidoc Medical, Ltd. | Diagnosis | Neuroradiology | 2019 |
| AutoMISTar | Apollo Medical Imaging Technology Pty, Ltd. | Diagnosis | Neuroradiology | 2019 |
| TransparanTM | Screenpoint Medical B.V. | Diagnosis | Radiology | 2019 |
| ADAS 3D | Galgo Medical S.L. | Diagnosis | Radiology | 2020 |
| QuantX | Quantitative Insights, Inc. | Diagnosis | Radiology | 2020 |
| Eko Analysis Software | Eko Devices, Inc. | Follow-up | Cardiology | 2020 |
| densitas densityai | Densitas, Inc. | Diagnosis | Radiology | 2020 |
| red dot | Behold.AI Technologies, Ltd. | Diagnosis | Radiology | 2020 |
| icobrain-ctp | Icometrix NV | Diagnosis | Neuroradiology | 2020 |
| Broncholab | Fluida, Inc. | Diagnosis | Radiology | 2020 |
| Transpara | ScreenPoint Medical B.V. | Diagnosis | Oncology | 2020 |
| Al-Rad Companion (Musculoskeletal) | Siemens Healthineers | Diagnosis | Radiology | 2020 |
| Hepatic VCAR | GE Medical Systems | Diagnosis | Radiology | 2020 |
| MammoScreen | Therapixel | Diagnosis | Oncology | 2020 |
| RAPID ICH | iSchemaView, Inc. | Diagnosis | Neuroradiology | 2020 |
| AIMI-Triage CXR PTX | RadLogics, Inc. | Diagnosis | Radiology | 2020 |
| CuraRad-ICH | Keya Medical | Diagnosis | Neuroradiology | 2020 |
| NinesAI | Nines, Inc. | Diagnosis | Neuroradiology | 2020 |
| HealthVCF | Zebra Medical Vision, Ltd. | Diagnosis | Radiology | 2020 |
| Syngo.CT CaScoring | Siemens Healthineers | Diagnosis | Radiology | 2020 |
| MEDO ARIA | Medo.AI | Diagnosis | Orthopedics | 2020 |
| Auto 3D Bladder Volume Tool | Butterfly Network, Inc. | Diagnosis | Urology | 2020 |
| Al-Rad Companion Brain MR | Siemens Healthineers | Diagnosis | Neuroradiology | 2020 |
| qER | Qure.ai Technologies | Diagnosis | Neuroradiology | 2020 |
| BriefCase-IFG | Aidoc Medical, Ltd. | Diagnosis | Radiology | 2020 |
| CINA | AVICENNA.AI | Diagnosis | Neuroradiology | 2020 |
| Rapid ASPECTS | iSchemaView Inc. | Diagnosis | Neuroradiology | 2020 |
| EyeArt | Eyenuk, Inc. | Diagnosis | Ophthalmology | 2020 |
| InferRead Lung CT.AI | Beijing Infervision Technology Co., Ltd. | Diagnosis | Radiology | 2020 |
| Rapid LVO 1.0 | iSchemaView, Inc. | Diagnosis | Neuroradiology | 2020 |
| HealthMammo | Zebra Medical Vision, Ltd. | Diagnosis | Oncology | 2020 |
| Caption Interpretation Automated Ejection Fraction Software | Caption Health | Diagnosis | Cardiology | 2020 |
Table I. Continued.

| Applications                        | Company                        | Purpose     | Medical specialty | FDA Cleared |
|-------------------------------------|--------------------------------|-------------|-------------------|-------------|
| AI-Rad Companion Prostate MR        | Siemens Healthineers           | Diagnosis   | Radiology         | 2020        |
| FractureDetect (FX)                 | Imagen Technologies            | Diagnosis   | Radiology         | 2020        |
| VIDAvision                          | VIDA Diagnostics, Inc.         | Diagnosis   | Radiology         | 2020        |
| Accipiolox                          | MaxQ AI, Ltd.                  | Diagnosis   | Neuroradiology    | 2020        |
| Aidoc BriefCase for iPE Triage      | Aidoc Medical, Ltd.            | Diagnosis   | Radiology         | 2020        |
| Aview 2.0                           | Coreline Soft Co., Ltd.        | Diagnosis   | Radiology         | 2020        |
| AVA (Augmented Vascular Analysis)   | See-Mode Technologies Pte, Ltd.| Diagnosis   | Cardiology        | 2020        |
| THINQ                               | CorticoMetrics LLC             | Diagnosis   | Neuroradiology    | 2020        |
| Cleerly Labs V2.0                   | Cleerly, Inc.                  | Diagnosis   | Radiology         | 2020        |
| Syngo.CT Neuro Perfusion            | Siemens Healthineers           | Diagnosis   | Neuroradiology    | 2020        |
| Quantib Prostate                    | Quantib BV                     | Diagnosis   | Radiology         | 2020        |
| AVIEW LCS                           | Coreline Soft Co., Ltd.        | Diagnosis   | Radiology         | 2020        |
| Liver Surface Nodularity (LSN)      | Imaging Biometrics, LLC        | Diagnosis   | Radiology         | 2020        |
| WRDensity                           | Whiterabbit.ai Inc.            | Diagnosis   | Oncology          | 2020        |
| Neuro.AI Algorithm                  | TeraRecon, Inc.                | Diagnosis   | Neuroradiology    | 2020        |
| FastStroke, CT Perfusion 4D         | GE Medical Systems             | Diagnosis   | Neuroradiology    | 2020        |
| PROView                             | GE Medical Systems             | Diagnosis   | Radiology         | 2020        |
| Genius AI Detection                 | Hologic, Inc.                  | Diagnosis   | Radiology         | 2020        |
| HALO                                | NiCo-Lab B.V.                  | Diagnosis   | Neuroradiology    | 2020        |
| HealthJOINT                         | Zebra Medical Vision, Ltd.     | Diagnosis   | Radiology         | 2020        |
| HepaFat-AI                          | Resonance Health Analysis      | Diagnosis   | Radiology         | 2020        |
| SQuEEZ Software                     | Cardiowise, Inc.               | Diagnosis   | Radiology         | 2020        |
| EchoGo Pro                          | Ultromics, Ltd.                | Diagnosis   | Cardiology        | 2020        |
| AI Metrics                          | AI Metrics, LLC                | Diagnosis   | Radiology         | 2020        |
| BrainInsight                        | Hyperfine Research, Inc.       | Diagnosis   | Neuroradiology    | 2021        |
| HeartFlow Analysis                  | HeartFlow, Inc.                | Diagnosis   | Radiology         | 2021        |
| uAI EasyTriage-Rib                  | Shanghai United Imaging        | Diagnosis   | Radiology         | 2021        |
| Visage Breast Density               | Visage Imaging GmbH            | Diagnosis   | Oncology          | 2021        |
| CLEWICU System                      | CLEW Medical, Ltd.             | Diagnosis   | Hematology        | 2021        |
| qp-Prostate                         | Quibim                         | Diagnosis   | Radiology         | 2021        |
| Lvivo Software Application          | DiA Imaging Analysis, Ltd.     | Diagnosis   | Cardiology        | 2021        |
| Veolity                             | MeVis Medical Solutions AG     | Diagnosis   | Radiology         | 2021        |
| NinesMeasure                        | Nines, Inc.                    | Diagnosis   | Radiology         | 2021        |
| Optellum Virtual Nodule Clinic, Optellum Software, Optellum Platform | Optellum, Ltd. | Diagnosis | Radiology | 2021 |
| Imbio RV/LV Software                | Imbio LLC                      | Diagnosis   | Radiology         | 2021        |
| Vbrain                              | Vysioneer, Inc.                | Diagnosis   | Neuroradiology    | 2021        |
| Viz ICH                             | Viz. AI, Inc.                  | Diagnosis   | Neuroradiology    | 2021        |
| syngo.CT Lung CAD (VD20)            | Subtle Medical, Inc.           | Diagnosis   | Radiology         | 2021        |
| Saige-Q                             | DeepHealth                     | Diagnosis   | Oncology          | 2021        |
| MEDO- Thyroid                       | Medo.AI                        | Diagnosis   | Endocrinology     | 2021        |
| CINA CHEST                          | AVICENNA.AI                    | Diagnosis   | Radiology         | 2021        |
| Overjet Dental Assist               | Overjet, Inc.                  | Diagnosis   | Radiology         | 2021        |

AI, artificial intelligence.

to assist in medication education for pediatric patients and their parents using a Left-Right parsing algorithm and Care Angel, which applied an automated voice dialogue system to check on the condition of the person requiring care, to
might miss crucial therapeutic targets and drugs for various diseases. In AI-based drug development, AI can propose, and lead to the development of, important targets and candidate drugs for disease therapy (Table III). In particular, Watson is able to identify connections and relationships among diseases, drugs, genes and other factors, and can generate novel hypotheses by mining the scientific literature (28). This tool is useful not only for drug development, but also for drug repurposing. In addition, Watson is constantly and automatically updated. Automatic learning in AI is important, not only to decrease the effort involved, but also to create better methods to meet unmet needs in life sciences and medicine.

AI-based drug development can save time and money. In conventional drug development, screening is performed using millions to tens of millions of compound libraries, followed by synthetic development based on the candidate compounds obtained from the screening and the re-evaluation of their activities to identify those with promise. However, numerous identified compounds do not exhibit physical properties and safety profiles that are suitable for pharmaceutical applications; therefore, other compounds are often re-synthesized. To avoid such time and money loss, AI-based drug development can predict the activity, physical properties and safety of each compound using computers. Various AI-based applications have been developed to predict these parameters (Figs. 2 and 3) (28,46-62). Furthermore, applications have been developed that predict not only the properties of individual compounds, but also suitable routes of synthesizing pharmacological reagents or therapeutic compounds (61,62). The cost of drug development has been decreased by these applications; however, the accuracy of the AI prediction of the compound properties is not sufficient and further improvement of this factor is necessary. In particular, AI-based applications have been actively developed as screening steps, which require time and money. However, it is difficult to predict the affinities

| Medicine | Conventional | Computational |
|----------|--------------|---------------|
| Diagnosis | Doctors meet patients; patients are diagnosed using diagnostic equipment at the hospital; diagnostic accuracy depends on the experience of a doctor | AI can detect lesions with the same or better accuracy than a skilled doctor; AI support is used to avoid misdiagnoses; AI supports the decision of the doctor by processing of the medical literature |
| Treatment | Doctors perform surgery directly; doctors or nurses administer medications | Robotics support doctors in surgery; devices automatically administer medications based on time and symptoms |
| Follow-up | Doctors or nurses meet patients; patients are diagnosed using diagnostic equipment at a hospital | Devices, such as those that are wearable, can detect abnormalities at a very early stage; the AI can consult with patients about their medical conditions and medications |
| Advantages | Patients can meet their doctors and nurses; abstract expression is possible | AI decreases the burden on doctors and nurses; AI responds quickly in an emergency |
| Problems | The burden on doctors and nurses is heavy; sometimes it is not possible to respond immediately in an emergency | The process of outputting the data is incomprehensible to humans. Application cost is high. AI cannot take responsibility for mistakes. |

Table II. Comparison between conventional and computational medicine.
between a target protein and compounds, for the following reasons: i) Difficulties in predicting protein flexibility; ii) ambiguity regarding the complexity of a protein in an actual environment, and iii) difficulties in assessing the solvent effects of an actual environment (63,64). To solve these problems, a number of experiments and new algorithms would be necessary.

One of the most difficult steps in the process of drug development is the prediction of adverse effects. It has been reported that computational modeling using machine learning is useful for predicting adverse effects (65). Moreover, it is possible to manufacture synthetic patients and data artificially by analyzing existing data using machine learning techniques (66,67). As there are no ethical concerns regarding the privacy and costs of using synthetic data, this would be a powerful tool for clinical studies that require a large number of patients and may be an effective alternative for preparing training data for machine learning algorithms. These fields of research could be further enriched by AI in the near future and would also contribute to the realization of personalized precision medicine.

5. Perspectives for AI-based medicine and drug development

AI has been used for clinical purposes and drug development. However, the current AI-based applications are only being developed for specific applications at each stage of pharmacological or medical applications. In particular, AI-based applications with a high accuracy for diagnosis have actively been developed. However, a diagnosis is not determined based only on the result of one diagnostic method, and should be performed by comprehensively combining various types of information, such as chief complaints and physical findings; a system that integrates the various specific diagnostic data would be necessary in the future (Fig. 3A). If the disease remained unclear based only on the acquired information, the system would be a present a diagnostic method to determine the condition. The system would avoid missing information and improve the accuracy of the diagnosis. In addition, the system would not only be used for diagnosis, but also for monitoring the progress of treatment after surgery and drug therapy. At present, almost no AI-based application has been developed that predicts the therapeutic effect or proposes a therapeutic method. However, a system has been reported in basic research that predicts the sensitivity of anticancer agents and radiation therapy based on phase contrast image information (32,33). In the near future, AI may be able to predict the therapeutic effects of various therapeutic methods in advance and suggest an appropriate therapeutic method. Thus, clinical AI in the future should be a system that interprets and integrates various types of clinical information and considers the changes caused by each treatment, to promote the best flow toward the complete cure of the disease. In addition, by constantly collecting information on complaints and physical status, both inside and outside the hospital, AI systems should always support the ability of a patient to live without aggravating their condition.

In drug development, numerous specific AI-based applications are already in use. In particular, a number of applications for the simulation of the docking of compounds to target proteins have been developed (47-53). Moreover, in addition to having an excellent specific score (such as affinity for a target protein), a candidate compound needs to have comprehensive excellent safety and pharmacokinetics. Therefore, a system for identifying promising compounds by considering various characteristics, as well as learning specific scores, will be required in the future (Fig. 3B). Furthermore, in drug development, clinical trials impose a heavy financial and time burden. It is necessary to improve the efficiency of clinical trials by using portal devices, which configure and manage devices remotely over the network or via USB connection, and collecting and selecting applicable patients.

The most important key to solving the problems facing AI-based applications is making it possible for people to understand the judgment process of AI. AI-based clinical applications would be utilized in important aspects of future treatment decisions, such as the diagnosis and evaluation of treatment effectiveness. If the AI determination process is
unclear, the medical staff could not evaluate the validity of the AI determination, which would lead to the distrust of AI. To solve the uncertainty of AI, ‘Explainable AI’ has been actively researched (68). The development of Explainable AI would be essential for the widespread use of AI-based applications in healthcare.
In addition, as AI-based healthcare would accumulate a greater amount of medical information than the current healthcare system, it would be necessary to prepare an infrastructure and security systems to handle large amounts of information. Futuristic clinical AI might monitor not only medical information, but also the tasks of patients and medical staff, and might forecast workflow bottlenecks.

As aforementioned, the implementation of AI could facilitate more accuracy and greater efficiency in various fields of healthcare; however, it has some issues and limitations. Both
medical staff and developers would need to understand the issues and limitations, and then the coexistence of humans and AI could lead to better healthcare.

6. Conclusion

AI has evolved with the times and has been utilized in applications in drug development and healthcare. These applications are steadily producing results, and the use of AI is becoming established. The implementation of AI in society will need to overcome issues such as how to develop leading companies and train data scientists. However, company development may still face some obstacles, such as implementing AI, employment and cost. In the future, to improve human health, we should not only develop AI, but also think about the coexistence of humans with AI.

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Authors’ contributions

HI, MT and AV conceptualized the study. AA, MK and HI wrote the manuscript. All authors have read and approved the final version of the manuscript. Data authentication is not applicable.

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Not applicable.

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Not applicable.

Competing interests

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