ORIGINAL ARTICLE

Role of Big Data and Machine Learning in Diagnostic Decision Support in Radiology

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Abstract

The field of diagnostic decision support in radiology is undergoing rapid transformation with the availability of large amounts of patient data and the development of new artificial intelligence methods of machine learning such as deep learning. They hold the promise of providing imaging specialists with tools for improving the accuracy and efficiency of diagnosis and treatment. In this article, we will describe the growth of this field for radiology and outline general trends highlighting progress in the field of diagnostic decision support from the early days of rule-based expert systems to cognitive assistants of the modern era.

Key Words: Diagnostic decision support, artificial intelligence, deep learning, machine learning, cognitive assistants, medical image analysis, knowledge and reasoning

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INTRODUCTION

The field of artificial intelligence (AI) is making a strong comeback literally in all its senses. From the sense of vision with self-driving cars [1] to the sense of taste through AI-generated recipes [2], many new applications are emerging that expand the role of AI. This revolution has largely been spurred by big data, that is, large amounts of data now easily available in many fields either on the web, collected by smart devices, or in the case of health care, through large-scale health records becoming electronically available. In health care, the role of AI is particularly felt in nearly all fields, from drug discovery where drug candidates are being found faster through the use of machine learning techniques on big data [3] to consumer health where wearable devices are collecting large amounts of data to enable better monitoring and prediction through use of machine learning techniques [4].

With medical imaging now being analyzed through AI and deep learning techniques, the role of big data and machine learning has taken on an added significance for radiologists [5-7]. The largest impact of machine learning on big data is being felt in the field of diagnostic decision support, which has been undergoing a dramatic transformation since the early days of AI and rule-based expert systems [42,43]. In this article, we will describe the growth of this field for radiology and outline general trends. Specifically, we describe the growth of the field from rule-based expert systems, through computer-aided diagnosis systems and big data-driven decision support systems, to data and knowledge-driven systems in their current form as cognitive assistants. We use specific examples from our own research in this field to illustrate the evolved thinking in clinical decision support.

RULE-BASED EXPERT SYSTEMS—EARLY APPLICATIONS

Early applications of AI in radiology were in rule-based expert systems for decision support [8,9]. The rules would form associations of specific conditions and symptoms with relevant tests to order [10], with differential diagnosis or recommended treatments including drugs [9]. The AI technology used in these cases was rule-based inference and reasoning using several knowledge representation methods including semantic networks [11,12], which have survived in the form of knowledge graphs in the unified medical language system currently [13]. For diagnosis in particular, these systems did not really scale because the rules were either incomplete for a specialty or did not completely apply to a patient to trigger in appropriate systems. The most common use of clinical decision

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support is in the form of alerts in the electronic medical record system such as for drug dosage [14], based on a priori defined rules and not necessarily customized for the current patient. Later rule-based systems point to guidelines based on matches to a patient's conditions [15,18]. The rules in these systems are derived from guidelines composed by experts such as American College of Cardiology guidelines [15] into conveniently organized pages such as those in UptoDate (Wolters Kluwer, Waltham, Massachusetts) [16], Medscape (WebMD, New York) [17], StatDx (Elsevier, Philadelphia) [63], DiagnosisPro [19], Dynamed (Ebsco Health Ipswich, Massachusetts) [20], Pepid (Chicago, Illinois) [21], among others. The knowledge offered through these browser-based technologies is primarily meant for visual examination by specialists. The mapping of a patient's condition to these guidelines is provided through simple search techniques. Thus, most of the rule-based expert systems for clinical decision support in use in clinical practice are based on fixed a priori developed rules and using simple search or rule-based inference techniques to pull up the relevant information for diagnosis, treatment, or outcome with input provided to such systems in structured textual or numeric data form.

COMPUTER-AIDED DIAGNOSIS SYSTEMS

The computer-aided diagnosis (CAD) systems were developed as a specific field of AI that used input from images to reach conclusions about potential anomalies or offer differential diagnosis [22-24]. They coupled data-driven feature extraction methods from image processing, computer vision, and medical image analysis with inferences rules to reason about regions in images containing potential anomalies. Most of these stopped short of giving a diagnosis (computer aided diagnosis [CADx]) [25,26] and instead simply point to potential anomalies and allow semi-automatic calculation of measurements (computer aided detection [CADe]) [22,27]. Due to the large number of false-positives generated and because they do not offer differential diagnosis, many of these systems are therefore used as second readers in radiology to ensure that an anomaly is not accidentally missed. Whether they are CADe or CADx systems, rule-based inference principles of AI are still employed, and the deduction is made on the basis of a priori rules built into the system and applied to a single patient's data. More recent CAD systems use machine learning to do a feature-based classification, and still newer methods have used deep learning as well [27]. Figure 1 illustrates the evolution of CADe systems that identified potential anomalies in a single patient's data based on image analysis, feature extraction, and classification. Thus, although initial CAD systems were rule-based, all the newer systems use some form of machine learning to classify candidate regions as normal or abnormal after sufficient training images are provided, so that they are also now beginning to exploit big data.

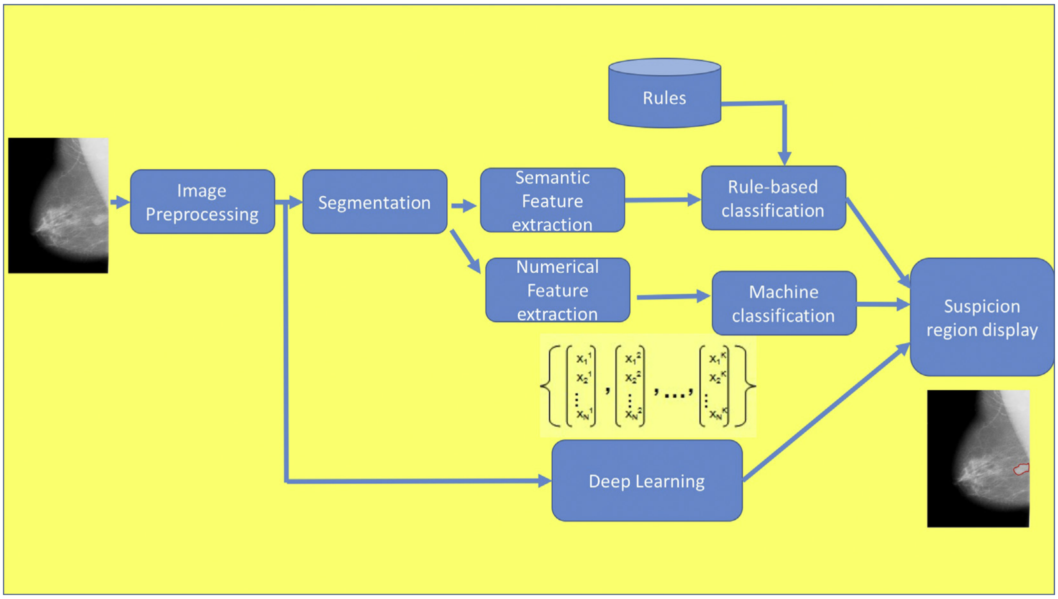

Fig 1. Illustration of computer-aided diagnosis (CAD) systems over three generations of classifiers. The first generation was based on rules and used semantic and qualitative features. The second generation used statistical machine learning with handcrafted features. The most recent CAD systems directly use deep learning to do simultaneous feature extraction and classification.

DATA-DRIVEN PATIENT SIMILARITY CLINICAL DECISION SUPPORT

With the advent of electronic health records, the field of clinical decision support took a turn for the better through the emergence of rule-free statistical machine learning-driven systems such as Advanced Analytics for Information Management (AALIM) [64,65], which pioneered the concept of patient similarity. In these systems, instead of a machine hypothesizing a diagnosis, a set of differentials could easily be obtained by leveraging big data in a large electronic health record system of prediagnosed patients using collaborative filtering. The key idea was to use statistical machine learning and content-based searching to find clinically similar patients in the database, using all available multimodal clinical data about the current patient. Once similar patients were identified, the prerecorded diagnosis, treatment, and outcome associated with these patients in electronic records could be statistically ranked to give recommendations. Figure 2 illustrates this approach. All patients were modeled as clinical feature vectors derived from their input multimodal clinical data but excluding the output prediction variables, which were usually diagnosis, treatments, and outcomes. By searching in the neighborhood of the given patient's feature vector, similar patients were found and ranked in a list [64,65]. By pooling the associated diagnosis, treatments, and outcomes from similar patients using collaborative filtering [69], clinical decision support could be achieved. Thus, there were no built-in rules; instead, the system dynamically discovered similar patients and pooled their diagnosis, treatments, and outcomes to form a scalable clinical decision support system leveraging the big data in electronic records.

The patient similarity function could be learned in either supervised or unsupervised fashion. *Supervised learning* refers to techniques in which the machine is provided an output label or labels to associate with a set of input variables. In *unsupervised learning*, the labels are not known for given sets of input variables and the machine is expected to rely on the correlations found in the input variables to infer a group or label. Several research articles explored supervised or unsupervised machine learning techniques for patient similarity, leading to many advancements in extracting diagnostically relevant features for finding similar patients [28,29]. In supervised patient similarity, patients were rated similar to each other by clinical experts, and their underlying clinical data were used to learn the similarity function using many techniques that generally fall under the class of metric learning [28-30,40,41]. Several measures were used ranging from information-theoretic measures [29]

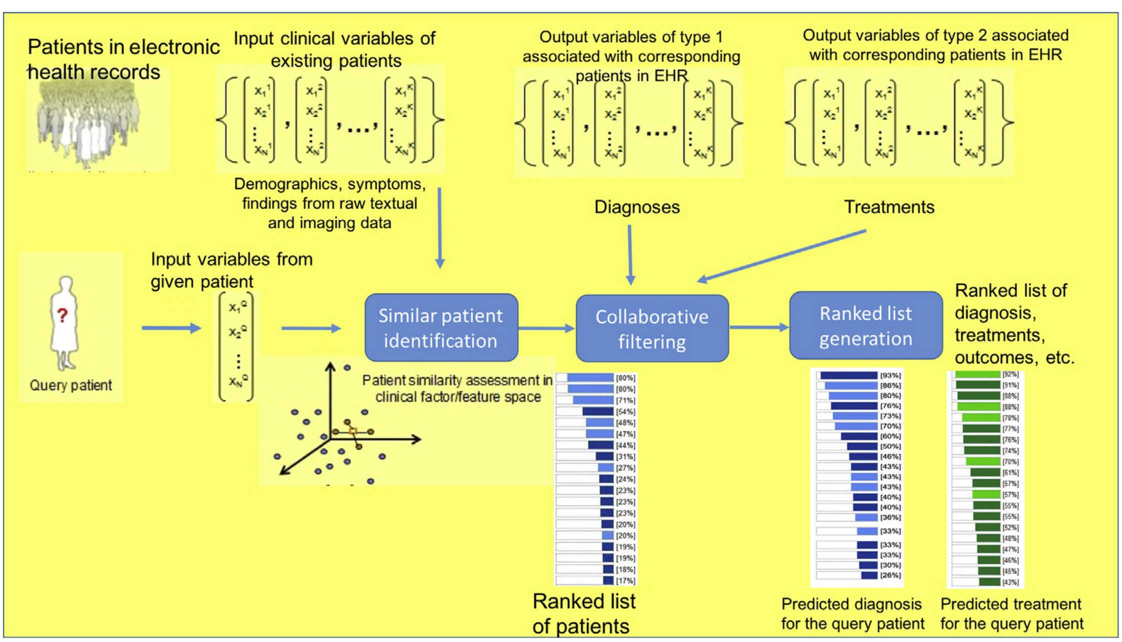

Fig 2. Patient similarity guided decision support using collaborative filtering. The electronic health record (EHR) is divided into input variables and prediction variables desired such as diagnosis, treatments, and outcomes. The feature vectors formed from input variables are used to obtain a ranked list of patients based on various similarity measures. Using collaborative filtering, a ranked list of the output variables can be made to result in a rule-free way of clinical decision support.

to kernel-based nonlinear metric learning methods [30]. Similarity between patients was also learned in an unsupervised fashion using content-based search and retrieval techniques in which each clinical data item from a given patient was used to search a database of prelabeled clinical data of the same type, and their corresponding patient information was used to obtain statistical distributions. Our research group pioneered the unsupervised patient similarity methods, with several methods ranging from techniques that find similar patients based on heart sounds [31] or electrocardiogram morphological shapes [32] to Doppler spectra in echocardiograms for diagnosis of valvular diseases [33].

MACHINE LEARNING FOR MEDICAL IMAGING

Many medical imaging decision support tasks can also be solved by classifying the data set into one or more label classes and use the confidence in the classified labels to infer a differential diagnosis. With the many machine learning techniques available, the medical imaging community has used a variety of methods ranging from support vector machines [34], random forests [35], and other ensemble learners [36,37]. In our own research, we have used statistical machine learning techniques to classify various fracture types in MSK imaging [38] and for separating normal from abnormal left ventricles in echocardiography [39], among other uses. Statistical machine learning can be done in both supervised and unsupervised fashion and has varying requirements for data labeling. However, in both forms of conventional machine learning, the medical imaging community is a user of these tools and has focused on crafting of clinically relevant features such as features highlighting the bones for viewpoint classification [66] or deviations from a prolate spheroidal shape to describe left ventricular dysfunction [39]. Most of the extensions to machine learning algorithms for dealing with medical imaging data sets also dealt with incomplete and inaccurate labeling issues as well [44].

Development of custom diagnostically relevant features, however, meant that a close relationship had to be established between data scientists and clinicians who guided the choice of features. Although this approach may work for a small number of diseases, developing thousands of such feature extractors and determining which are applicable for a given imaging study would not scale for a broad approach to clinical decision support. With the advent of deep learning techniques, a potential solution to this problem emerged. The basic deep learning network for medical imaging data typically has two parts: (1) a feature extractor that extracts possible features from the raw images and (2) an objective function that learns the correlation between the features and their labels [45-47,60]. Instead of choosing features a priori, a set of training images and their target labels are provided to a deep learning network. The feature extractor portion usually consists of several layers on nonlinear processing units and transformation functions besides using conventional image processing operators such as filters. For example, many popular networks such as convolutional neural networks [48] or their many adaptations such as U-net [49], V-net [50], and M-net [51] use a set of convolutional filters applied to an image at multiple possible positions with multiple window sizes to span object structures of different shapes and sizes. Thus rather than choosing a fixed set of feature detectors, these networks use a generate-and-test paradigm to use a variety of filters at all possible scale and resolution, and they let the learner (the objective function) judge how good any of these features are for label discrimination and learning. Many different objective functions are possible such as linear regression, logistic regression, KL-divergence, 0/1 loss function, ambiguous loss function, among others, although recent working in deep learning is also learning the objective function itself! The correlation between the labels and the input feature vectors is learned via the objective function using artificial neural networks with hidden layers. The labels themselves can be discrete as needed for classification or in the form of region annotations. If all regions of a medical imaging study are annotated, it can be used to learn an anatomical atlas for the area of the body depicted in study. If the regions marked are anomaly regions, they can be used for anomaly segmentation. Thus deep learning networks have become a popular approach to decision support by enabling *classification*, *segmentation*, and *anomaly detection* using a uniform paradigm of multilayer neural networks for feature extraction and correlation.

The ability of all such networks to learn patterns is a function of number of labeled data sets, the number of convolutional layers to build feature abstractions, and choice of optimization functions. Most deep learning researchers primarily tune these parameters to reach satisfactory convergence of networks. Thus big data is driving the training of such networks and is bringing about a fundamental change in clinical decision support.

In the field of radiology imaging, deep learning is rapidly becoming pervasive as a topic in most medical imaging conferences including RSNA, Medical Image

Computing and Computer-Assisted Interaction, and Society for Imaging Informatics (SIIM). Furthermore, more than 100 startups as well as big companies have embraced the field of deep learning for use for medical image interpretation [5-7]. Many of them attempt constrained problems such as classification of a lesion identified by a radiologist into BI-RADS category [52] or calculation of measurements by completing lesion boundaries by semiautomatic localization process. Recently, the FDA has approved for commercial use systems such as a heart failure estimator, which calculates key performance indicators for the disease through stable segmentation of the short-axis-view cardiac MRI for myocardium [6]. The predominant problems being solved using these techniques range from classification and segmentation to anomaly detection and characterization. Automatic disease detection in many anatomical structures is now possible, ranging from valvular disease detection in echocardiogram [53] to lung nodule classification in chest CTs [54].

COGNITIVE ASSISTANTS LEVERAGING BIG DATA AND KNOWLEDGE IN AI

With recent work reporting higher than clinician-grade accuracy in reading imaging in limited specialties (dermatology [55], ophthalmology [56]), radiologists are beginning to wonder whether machine learning, AI, and its use of big data will lead one day to machines replacing radiologists. Although the field will continue to advance, replacement of radiologists is a much farther proposition when considered generally across the field where a large number of variations of modalities, modes, viewpoints, anatomy variations, and disease manifestations need to be considered. Instead, a new generation of machines is attempting to assist radiologists rather than replace them by augmenting their decision making by pre-analyzing the data and offering recommendations. Such machines that work hand in hand with radiologists and cardiologists are called cognitive assistants. Recent results have shown that such machines have a greater chance of being adopted by clinicians in their clinical workflow than those that attempt to replace the specialists altogether.

Cognitive assistants are driven not only by machine learning of large amounts of patient data but also by clinical knowledge. This new type of clinical decision support machines is being pioneered in our research group. We approach the diagnostic decision support problem through a systematic modeling of the radiologist's diagnosis process. The aim is to solve the problem in an end-to-end fashion by answering a series of questions about an incoming imaging study. As shown in Figure 3, we first analyze the imaging study to infer the modality, mode, and viewpoint. Using knowledge of the anatomy through atlases, we next understand the position in the body and recognize known anatomical structures using a variety of approaches including the multi-atlas label fusion algorithms described elsewhere [57]. Finally, we look for

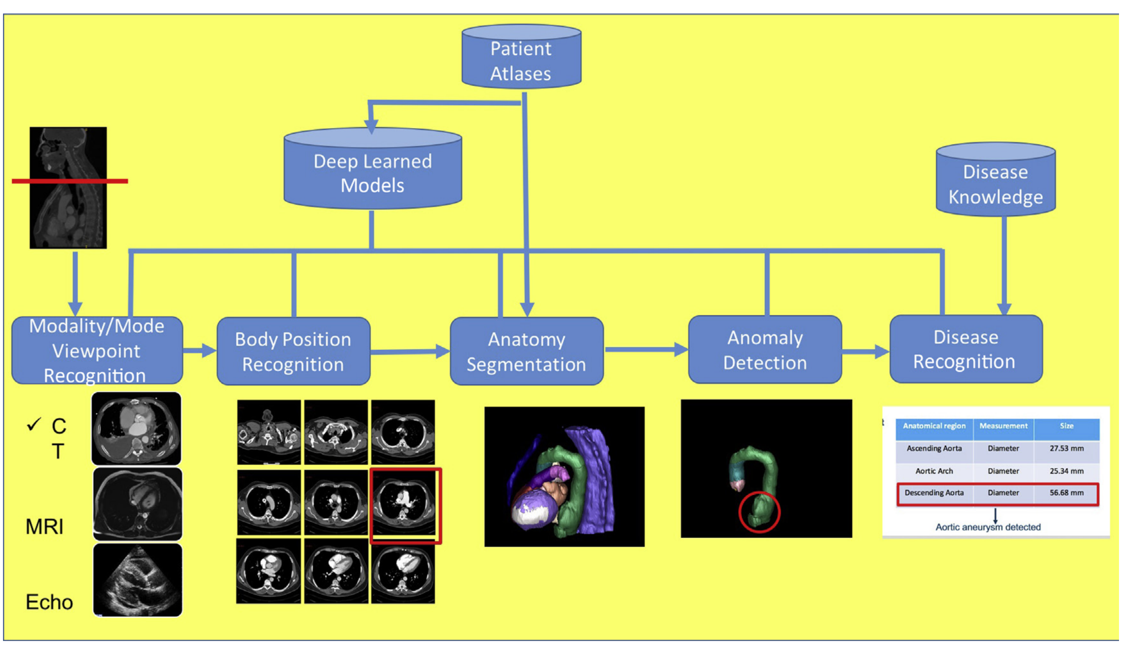

Fig 3. Illustration of a systematic modeling of the radiologist's diagnostic process in cognitive assistants.

anomalies in selected anatomical regions based on deviations from their normal appearance [58]. To enable each of these operations, machines are trained on large clinician-annotated data sets with machine learning techniques ranging from variants of support vector machines [34], random forests [35], to deep learning networks [59]. Once the anomalous regions are detected, cognitive assistants examine other sources of clinical data, particularly textual data to find additional information as clinical features [53]. All the assembled clinical facts from the patient are then used to reason against a large knowledge base of clinical facts and relationships that have already been weighted by patient data statistics from electronic health record analysis. Both declarative knowledge and procedural knowledge are used to arrive at new conclusions regarding recommendations for diagnosis, treatment including next best test, and prediction of outcomes associated with the findings. This multimodal reasoning with clinical knowledge that inherently incorporates learned distributions from big patient data records makes for a powerful inference engine for clinical decision support in a cognitive assistant machine. A system exhibiting such a cognitive assistant was recently demonstrated at the RSNA conference in 2016 under the exhibit “Eyes of Watson” [67].

WHAT ARE SOME CHALLENGING PROBLEMS IN THIS FIELD?

Despite the rapid advances in deep learning and reasoning techniques in cognitive assistants, the biggest challenge in this field remains in obtaining sufficiently large number of accurate labels for imaging studies and their anomalous regions by clinical experts. Web-based annotation tools deployed in the cloud using a crowd-sourcing model for clinician annotations are now beginning to emerge [68], but rolling such efforts out on a massive scale is still a challenge. The field needs rapid development of semi-automatic ground truth labeling methods in which the machine iteratively learns the patterns through increasingly smaller number of annotations supplied by clinicians using active learning paradigms.

Advances are also needed in deep learning network research. Although deep learning can potentially learn the features automatically through the corrective learning process, researchers are beginning to question the need for such networks with a large number of layers that take a long time to converge. If clinically meaningful features are known a priori for a particular domain, it seems reasonable to exploit such knowledge to bias the deep learners. Learning from partially, inaccurately, or ambiguously labeled data also remains an active research problem in the community.

As the cognitive aspects of learning come to the fore, deep learning techniques begin to incorporate a priori clinical knowledge into the learning process instead of applying it later through reasoning algorithms. These higher-layer semantic deep learning networks have also been pointed out by established researchers such as Yan Le Cun in his recent NIPS presentation in 2015 [71].

Finally, researchers are beginning to question the current approach of building deep learning networks task by task and are considering giant deep learning networks that simultaneously solve the problem of anomaly detection, anatomy segmentation, viewpoint recognition, and so on, all in one network.

As researchers continue to address the technical challenges in developing robust techniques of utilizing big data in medical imaging, commercial applications of these technologies are already beginning to emerge in a variety of use cases where machines can be in an assistive capacity. Examples include work list prioritization for brain bleed cases [61], comparison with prior examinations and recording deviations [62], discrepancy detection in patient records [62], and semi-automatic report generation [70]. Seamless integration of these technologies into clinical workflow, however, remains a challenging problem.

CONCLUSIONS

Diagnostic clinical decision support in radiology is undergoing rapid changes with big data and machine learning helping the transformation. In this article, we have emphasized three key ingredients for achieving meaningful clinical decision support, namely (1) modeling the radiologist’s diagnostic process and solving key imaging recognition problems systematically through deep learning, (2) incorporation of clinical knowledge, and (3) combination of imaging and clinical data with clinical knowledge to enable integrated clinical inference and reasoning.

Although there are still quite a few challenges to producing practical systems that cover a wide variety of diseases, the technologies are rapidly maturing. Cognitive assistant machines that are the latest in a series of clinical decision support systems offer a new role for machines in an assistive capacity to radiologists and cardiologists working hand in hand with them to expedite their work. With such advances, days are not far where we will see active use of cognitive clinical assistants in daily clinical workflows.

TAKE-HOME POINTS

- The field of diagnostic decision support in radiology is undergoing rapid transformation due to the development of new machine learning algorithms based on deep learning that provide cognitive assistance.
- Major developments in this field happened along five phases, namely (1) rule-based expert systems, (2) computer-aided diagnosis systems, (3) patient similarity systems, (4) deep learning-based systems, and (5) cognitive assistant systems.
- There are three key ingredients for achieving meaningful clinical decision support, namely (1) modeling the radiologists diagnostic process and solving key imaging recognition problems systematically through deep learning, (2) incorporation of clinical knowledge, and (3) combination of imaging and clinical data with clinical knowledge to enable integrated clinical inference and reasoning.
- Cognitive assistant machines offer a new role for machines in an assistive capacity to radiologists and cardiologists working hand in hand with them to expedite their work.
- Rolling out meaningful decision support systems that fit into clinical workflows is still a challenge both due to algorithmic enhancements needed and FDA regulatory considerations.

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