

Deep learning in radiology: an overview of the concepts and a survey of the state of the art

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Abstract

Deep learning is a branch of artificial intelligence where networks of simple interconnected units are used to extract patterns from data in order to solve complex problems. Deep learning algorithms have shown groundbreaking performance in a variety of sophisticated tasks, especially those related to images. They have often matched or exceeded human performance. Since the medical field of radiology mostly relies on extracting useful information from images, it is a very natural application area for deep learning, and research in this area has rapidly grown in recent years. In this article, we review the clinical reality of radiology and discuss the opportunities for application of deep learning algorithms. We also introduce basic concepts of deep learning including convolutional neural networks. Then, we present a survey of the research in deep learning applied to radiology. We organize the studies by the types of specific tasks that they attempt to solve and review the broad range of utilized deep learning algorithms. Finally, we briefly discuss opportunities and challenges for incorporating deep learning in the radiology practice of the future.

1 Introduction

The field of deep learning encompasses a group of artificial intelligence methods which employ a large number of simple interconnected units to perform complicated tasks. Deep learning algorithms, rather than using a set of pre-programmed instructions, are capable of learning from large amounts of data. The tasks solved by these algorithms include localizing and classifying objects in images, understanding language, playing games, and many others. While the flagship of deep learning, convolutional neural networks, were first introduced decades ago, it is only the last 5 years that showed an astonishing success of these algorithms elevating their status from an interesting but mostly impractical idea to the go-to algorithm in artificial intelligence. In recent years, not only have deep learning algorithms been able to surpass performance of other methods in artificial intelligence [1] but in some tasks, they have shown performance superior to humans [2, 3, 4].

Arguably, the most well-known achievement of deep learning to date is its performance in the ImageNet competition. ImageNet is a database of more than 14,000,000 annotated natural images containing real world objects such as cars, animals, and buildings (image-net.org). One of the goals of the competition, started in 2009, is to assign each image to one of 1 000 predefined categories. When a deep learning-based algorithm first appeared in the competition in 2012, it dramatically improved the error rate from 0.258 in the previous year (image-net.org/challenges/LSVRC/2011/results) to 0.153 (image-net.org/challenges/LSVRC/2012/results). The performance of deep learning algorithms for image classification has been improving since then and is now considered to be comparable to or better than human performance. Other areas relevant to the topic of this article, where

deep learning algorithms have seen impressive results, is in the automatic generation of sophisticated captions for images that consist of full sentences [5] as well as localization and outlining of objects in images [6, 7]. To illustrate the capacity of current detection network, Figure 1 shows the result of a deep neural network approach applied to detect objects in an image.

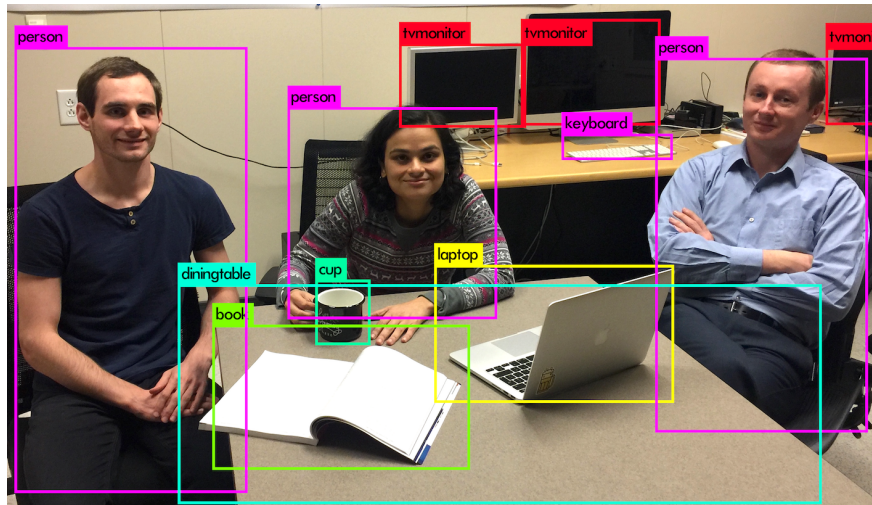


Figure 1: A picture of three of the authors of this article (Buda, Saha, Mazurowski) with detection labels generated by the YOLO detection network.

There are likely three reasons for the recent success of deep learning algorithms: availability of data, increased processing power, and rapid development of algorithms. These are highly connected: availability of large datasets of images and computing power made it possible to demonstrate the strength of the basic concepts of deep learning and, motivated the development of further datasets and algorithms. Increasing ease in applying algorithms and affordable graphical processing units have allowed for larger scientific and technical communities to get involved, and develop even more powerful algorithms which further advanced the field.

As the primary strength of deep learning has been in image analysis, the potential applications in radiology have become very quickly apparent. The development of algorithms for radiology has shown some inertia due to the time needed for acquisition of the appropriate expertise in the medical imaging community as well as limited availability of large medical imaging datasets. However, the last 2-3 years have seen remarkable productivity in the field. It is now well recognized by both researchers and clinicians that deep learning will play a significant role in radiology.

In this paper, we begin with a general overview of radiology as the application domain and consider where deep learning could have the most significant impact. Then, we introduce the general concepts of deep learning. This is followed by an overview of the recent work in the field. The article closes with remarks regarding the future of deep learning in radiology.

2 The practice of radiology

Radiology is a branch of medicine that focuses on using medical images for detection, diagnosis, and characterization of disease (diagnostic radiology) as well as guiding procedural interventions (interventional radiology). In the United States, a typical radiologist undergoes 14-15 years of education after high school including 4 years of college, 4 years of medical school, 1 year of internship, 4 years of radiology residency, and generally 1-2 years of fellowship training. While medical image

interpretation work is centered in radiology practices and academic departments, some of it is also performed within other branches of medicine including cardiology, orthopedics, and surgery.

In diagnostic radiology, personal interaction between a radiologist with patients and other physicians is often limited. The primary duty of a radiologist (particularly outside of an academic institution) is to view an image delivered to his/her reading station and generate a written report of findings. This well-structured and isolated nature of the radiologist's work makes it a particularly attractive application of artificial intelligence algorithms.

Deep learning techniques (and artificial intelligence algorithms in general) have a tremendous potential to influence the practice of radiology. Unlike most other facets of medicine, all or nearly all of the primary data utilized in imaging is digital, lending itself to analysis by artificial intelligence algorithms.

In this section, we describe some of the primary challenges that a radiologist faces in his/her daily diagnostic radiology practice and briefly point to opportunities for deep learning to address them. While this is not intended to be an exhaustive description of every task that radiologists perform in their practice, it reflects majority of diagnostic radiology practice. We conclude this section with a description of some medical image interpretation tasks that are currently not performed by radiologists, but could be incorporated in radiology practice using deep learning.

2.1 Disease Detection

One of the most challenging tasks in the interpretation of imaging is the rapid differentiation of abnormalities from normal background anatomy. For example, in the interpretation of mammography, each radiograph contains thousands of individual focal densities, regional densities, and geometric points and lines that must be interpreted to detect a small number of suspicious or abnormal findings. In most cases, the entire mammogram should be interpreted as normal or negative, adding further complexity to the interpretive task.

In order to be useful, a computer algorithm does not have to detect all objects of interest (e.g., abnormalities) and be perfectly specific (i.e., not mark any normal locations). For example, in screening mammography, approximately 80% of screening mammograms should be read as negative according to the ACR BI-RADS guideline, and of the 20% of examinations that trigger additional evaluation, many will ultimately be categorized as negative or benign [8]. An algorithm that could successfully categorize even half of screening mammograms as definitely negative would dramatically reduce the effort required to interpret a large batch of examinations.

2.2 Disease Diagnosis and Management

Once an abnormality has been detected, the often-complex task of determining a diagnosis and the disease management implications is undertaken. For focal masses generically, a large number of features must be integrated in order to decide how to appropriately manage the finding. These features can include size, location, attenuation or signal intensity, borders, heterogeneity, change over time, and others. In some cases, simple criteria have been established and validated for the management of focal findings. For example, most focal lesions in the kidney can be characterized as either simple or minimally complex cysts, which are almost uniformly benign. On the other hand, most lesions in the kidney that are solid are considered to have high malignant potential. Finally, a minority of focal kidney lesions is considered indeterminate and can be managed accordingly.

While for some types of abnormalities making the diagnostic and disease management decision follows straightforward guidelines, for other types of abnormalities, management algorithms are much more complex. In the BI-RADS guideline for assessing focal lesions in the breast, a mass

is categorized according to its shape (oval, round, or irregular), margin (circumscribed, obscured, microlobulated, indistinct, or spiculated), and its density (higher, equal to, or lower density than the glandular tissue, or fat-containing) [8]. Based on the constellation of features, the radiologist must then decide whether a mass is likely benign or requires follow-up or biopsy. In the LI-RADS criteria for assessing focal liver lesions in patients at risk for developing hepatocellular carcinoma, five major features, and up to 21 ancillary features, are assessed to risk-stratify lesions and determine their management [9].

Deep learning algorithms have the potential to assess a large number of features, even those previously not considered by radiologists, and arrive at a repeatable conclusion in a fraction of the time required for a human interpreter. Perhaps most promisingly, these algorithms could be used to categorize large amounts of existing imaging data and correlate features with downstream health outcomes, a process that is currently extremely laborious and time-consuming when human interpretation is required.

2.3 Workflow

While detection, diagnosis, and characterization of disease receive the primary attention among algorithm developers, another important area where artificial intelligence could contribute is in facilitating the workflow of the radiologists while interpreting images. With the widespread conversion from printed films to centralized Picture Archiving and Viewing Systems (PACS) as well as the availability of multi-planar, multi-contrast, and multi-phase imaging, radiologists have seen exponential growth in the size and complexity of image data to be analyzed. Additionally, interpretations must often be rendered in the context of a multitude of prior examinations. The simple task of finding and presenting these data is complex, and artificial intelligence systems may be well-suited for this role.

An example of a highly complex workflow is that for many cancer patients. Such patients are not uncommonly afflicted with more than one primary tumor, metastatic disease to numerous sites, and may have undergone a variety of biopsies, locoregional therapies, and systemic therapies with varying results. In the simplest scenario, interpretation of a follow-up imaging examination requires colocalization of all relevant sites of disease between the current and prior examinations. Measurements of size are performed, and in some cases functional features, such as tumor perfusion or diffusion restriction, are assessed either subjectively or objectively. Most radiology practices utilize imaging equipment of different types, generations, and often different vendors, thus simply identifying the appropriate image sets in prior examinations can be very challenging. After the appropriate images have been identified, the radiologist must colocalize disease sites and attempt to obtain precise repeated measurements in order to ensure that the values obtained from the current and prior examinations can be compared.

Each of the above tasks is time-consuming and does not necessarily require the full skill of a radiologist. However, standard PACS systems are not able to reliably present all of the above data for a variety of reasons, including the variability in labeling the types and components of imaging examinations, the variability in patient positioning and anatomy between examinations, the variability in modalities used to image the same portion of the anatomy, as well as other factors. In principle, an artificial intelligence algorithm could assess a patient's prior imaging, bring forward examinations that include the relevant body part(s), detect the image modality and contrast type, and determine the location of the area of interest within the relevant anatomy to reduce the radiologist's effort in performing these relatively mundane tasks.

2.4 Image interpretation tasks that radiologists do not perform but deep learning could

In addition to performing tasks that are a part of the current radiological practice, computer algorithms could perform medical image interpretation tasks that radiologists do not perform on a regular basis. The research toward this goal has been underway for some time, mostly using traditional machine learning and image processing algorithms. One example is radiogenomics [10], which aims to find relationships between imaging features of tumors and their genomic characteristics. Examples can be found in breast cancer [11], glioblastoma [12], low grade glioma [13], and kidney cancer [14]. Radiogenomics is not a part of the typical clinical practice of a radiologist. Another example is prediction of outcomes of cancer patients with applications in glioblastoma [12, 15], lower grade glioma, [13], and breast cancer [16]. While imaging features have a potential to be informative of patient outcomes, very few are currently used to guide oncological treatment. Deep learning could facilitate the process of incorporating more of the information available from imaging into the oncology practice.

3 An introduction to deep learning

3.1 Terminology

To understand deep learning, it is helpful to first understand the related concepts of artificial intelligence and machine learning. Artificial intelligence is a set of computer algorithms that are able to perform complicated tasks or tasks that require intelligence when conducted by humans. Machine learning is a subset of artificial intelligence algorithms which, to perform these complicated tasks, are able to learn from provided data and do not require pre-defined rules of reasoning. The field of machine learning is very diverse and has already had notable applications in medical imaging [17]. Deep learning is a sub-discipline of machine learning that relies on networks of simple interconnected units. In deep learning models, these units are connected to form multiple layers that are capable of generating increasingly high level representations of the provided input (e.g., images). Below, in order to explain the architecture of deep learning models, we introduce the artificial neural network in general and one specific type: the convolutional neural network. Then, we detail the "learning" process of these networks, which is the process of incorporating the patterns extracted from data into deep neural networks.

3.2 Artificial Neural Networks

Artificial neural networks (ANNs) are machine learning models based on basic concepts dating as far as 1940s, significant development in 1970s and 1980s and a period notable popularity in 1990s and 2000s followed by a period of being overshadowed by other machine learning algorithms. ANNs consist of a multitude of interconnected processing units, called neurons, usually organized in layers. A traditional ANN typically used in the practice of machine learning contains 2 to 3 layers of neurons. Each neuron performs a very simple operation. While many neuron models were proposed, a typical neuron simply multiplies each input by a certain weight, then adds all the products for all the inputs and applies a simple nondecreasing function at the end. Even though each neuron performs a very rudimentary calculation, the interconnected nature of the network allows for the performance of very sophisticated calculations and implementation of very complicated functions.

3.3 Convolutional Neural Networks

Deep neural networks are a special type of an ANN. The most common type of a deep neural network is a deep convolutional neural network (CNN). A deep convolutional neural network, while inheriting the properties of a generic ANN, has also its own specific features. First, it is deep. A typical number of layers is 10-30 but in extreme cases it could exceed 1000. Second, the neurons are connected such that multiple neurons share weights. This effectively allows the network to perform convolutions (or template matching) of the input image with the filters (defined by the weights) within the CNN. Other special feature of CNNs is that between some layers, they perform pooling which makes the network invariant to small shifts of the images. Finally, CNNs typically use a different activation function of the neurons as compared to traditional ANNs.

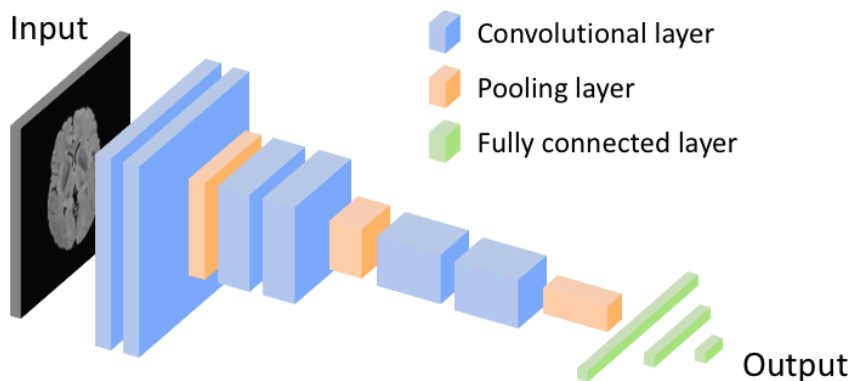


Figure 2: A diagram illustrating a typical architecture of a convolutional neural network.

Figure 2 shows an example of a small architecture for a typical CNN. One can see that the first layers are the convolutional ones which serve the role of generating useful features for classification. Those layers can be thought of as implementing image filters, ranging from simple filters that match edges to those that eventually match much more complicated shapes such as eyes, or tumors. Further from the network input are so called fully connected layers (similar to traditional ANNs) which utilize the features extracted by the convolutional layers to generate a decision (e.g., assign a label). A variety of deep learning architectures have been proposed, often driven by characteristics of the task at hand (e.g., fully convolutional neural networks for image segmentation). Some of these are described in more detail in the section of this paper that reviews the current state of the art.

3.4 The learning process in convolutional neural networks

Above, we described general characteristics of traditional neural networks and deep learning's flagship: the convolutional neural network. Next, we will explore how to make those networks perform useful tasks. This is accomplished in the process referred to as learning or training. The learning process of a convolutional neural network simply consists of changing the weights of the individual neurons in response to the provided data. In the most popular type of learning process, called supervised learning, a training example contains an object of interest (e.g., an image of a tumor) and a label (e.g., the tumor's pathology: benign or malignant). In our example, the image is presented to the network's input, and the calculation is carried out within the network to produce a prediction based on the current weights of the network. Then, the network's prediction is compared to the actual label of the object and an error is calculated. This error is then propagated

through the network to change the values of the network’s weights such that the next time the network analyzes this example, the error decreases. In practice, the adaptation of the weights is performed after a group of examples (a batch) are presented to the network. This process is called error backpropagation or stochastic gradient descent. Various modifications of stochastic gradient descent algorithm have been developed [18]. In principle, this iterative process consists of calculations of error between the output of the model and the desired output and adjusting the weights in the direction where the error decreases.

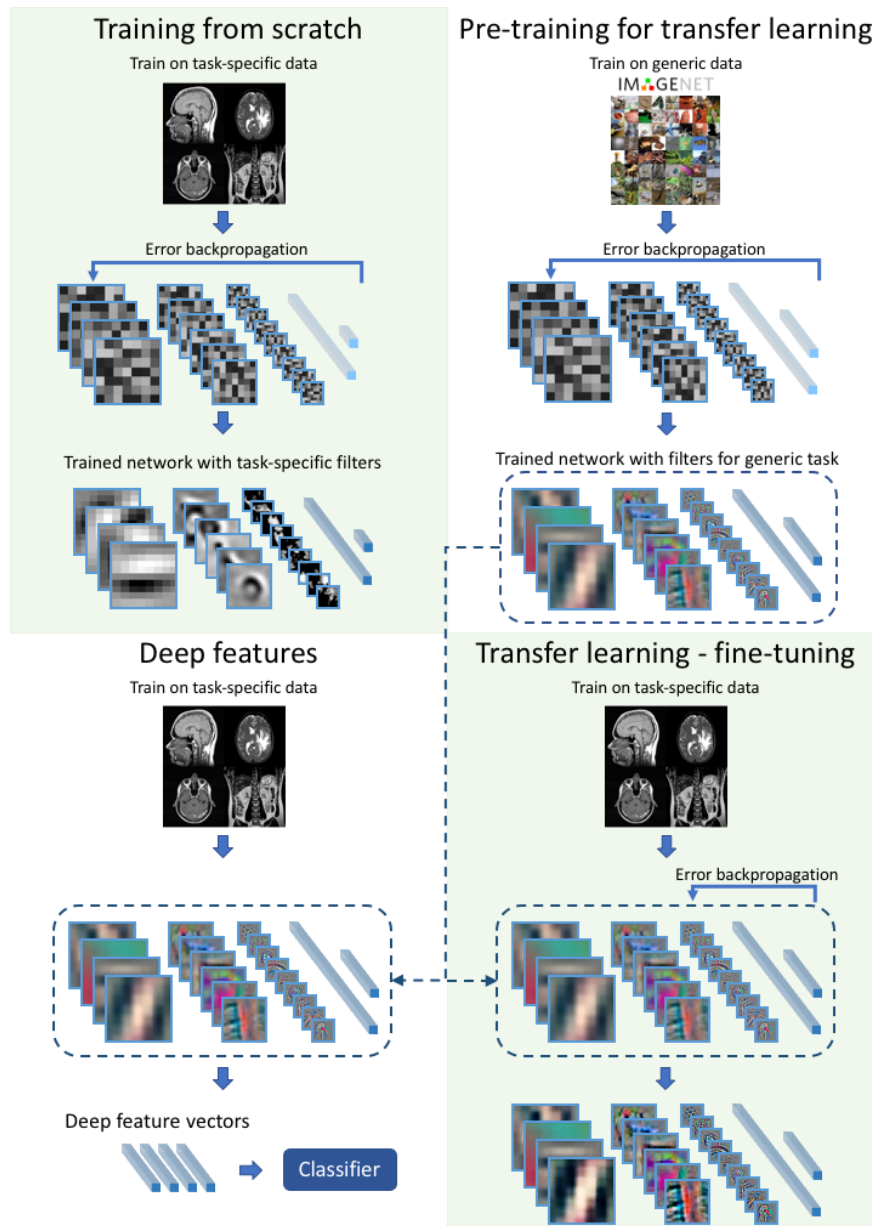


Figure 3: An illustration of different ways of training in deep neural networks.

The most straightforward way of training is to start with a random set of weights and train using available data specific to the problem being solved (training from scratch). However, given the large number of parameters (weights) in a network, often above 10 million, and a limited amount of training data (common in medical imaging), a network may overfit to the available data, resulting

in poor performance on test data. Two training methods have been developed to address this issue: transfer learning [19] and off-the-shelf features (a.k.a. deep features) [20]. A diagram comparing training from scratch with transfer learning and off-the-shelf deep features is shown in Figure 3.

In the transfer learning approach, the network is first trained using a different dataset, for example an ImageNet collection. Then, the network is "fine-tuned" through additional training with data specific to the problem to be addressed. The idea behind this approach is that solving different visual tasks shares a certain level of processing such as recognition of edges or simple shapes. This approach has been shown successful in, for example, prediction of survival time from brain MRI in patients with glioblastoma tumor [21] or in skin lesion classification [22]. Another approach that addresses the issue of limited training data is the deep "off-the-shelf" features approach which uses convolutional neural networks which have been trained on a different dataset to extract features from the images. This is done by extracting outputs of layers prior to the network's final layer. Those layers typically have hundreds or thousands of outputs. Then, these outputs are used as inputs to "traditional" classifiers such as linear discriminant analysis, support vector machines, or decision trees. This is similar to transfer learning (and is sometimes considered a part of transfer learning) with the difference being that the last layers of a CNN are replaced by a traditional classifier and the early layers are not additionally trained.

3.5 Deep learning vs "traditional" machine learning

Increasingly often we hear a distinction between deep learning and "traditional" machine learning (see Figure 4). The difference is very important, particularly in the context of medical imaging. In traditional machine learning, the typical first step is feature extraction. This means that to classify an object, one must decide which characteristics of an object will be important and implement algorithms that are able to capture these characteristics. A number of sophisticated algorithms in the field of computer vision have been proposed for this purpose and a variety of size, shape, texture, and other features were extracted. This process is to a large extent arbitrary since the machine learning researcher or practitioner often must guess which features will be of use for a particular task and runs the risk of including useless and redundant features and, more importantly, not including truly useful features. In deep learning, the process of feature extraction and decision making are merged and trainable, and therefore no choices need to be made regarding which features should be extracted; this is decided by the network in the training process. However, the cost of allowing the neural network to select its own features is a requirement for much larger training data sets.

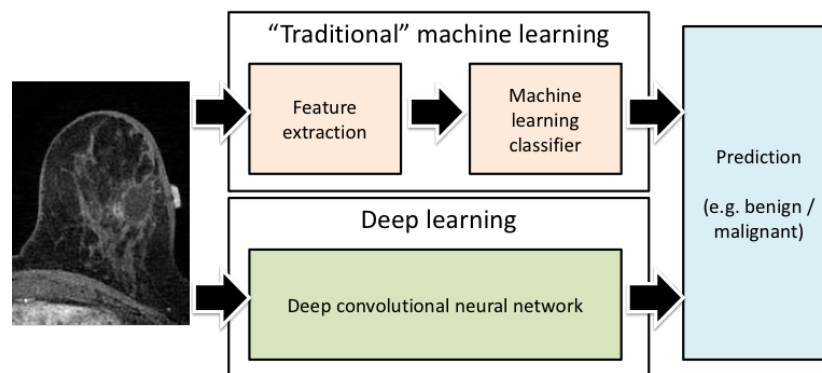


Figure 4: An illustration of difference between "traditional" machine learning and deep learning.

4 Deep learning in radiology: state of the art

In this section, we give an overview of applications of deep learning in radiology. We organized this section by the tasks that the deep learning algorithms perform. Within each subsection, we describe different methods applied, and when possible, we systematically discuss the evolution of these methods in the recent years.

4.1 Classification

In a classification task, an object is assigned to one of the predefined classes. A number of different classification tasks can be found in the domain of radiology such as: classification of an image or an examination to determine the presence or an absence of an abnormality; classification of abnormalities as benign or malignant; classification of cancerous lesions according to their histopathological and genomic features; prognostication; and classification for the purpose of organization radiological data.

Deep learning is becoming the methodology of choice for classifying radiological data. The majority of the available deep learning classifiers use convolutional neural networks with a varying number of convolutional layers followed by fully connected layers. The availability of radiological data is limited as compared to the natural image datasets which drove the development of deep learning techniques in the last 5 years. Therefore, many applications of deep learning in medical image classification have resorted to techniques meant to alleviate this issue: off-the-shelf features and transfer learning [23] discussed in the previous section of this article. Off-the-shelf features have performed well in a variety of domains [20], and this technique has been successfully applied to medical imaging [24, 25]. In [24], the authors combined the deep off-the shelf features extracted from a pre-trained VGG19 network with hand-crafted features for determining malignancy of breast lesions in mammography, ultrasound, and MRI. In [25], long-term and short term survival was predicted for patients with lung carcinoma. The transfer learning strategy, which involves fine tuning of a network pre-trained on a different dataset, has been applied to a variety of tasks such as classification of prostate MR images to distinguish patients with prostate cancer from patients with benign prostate conditions [26], identification of CT images with pulmonary tuberculosis [27], and classification of radiographs to identify hip osteoarthritis [28]. Most of the studies which apply the transfer learning strategy replace and retrain the deepest layer of a network, whereas shallow layers are fixed after the initial training. A variation of the transfer learning strategy combines fine-tuning and deep features approach. It fine-tunes a pre-trained network on a new dataset to obtain more task-specific deep feature representations. An example of this is the study [29], which performed ultrasound imaging-based thyroid nodule classification using features extracted from a fine-tuned pre-trained GoogLeNet. An ensemble of fine-tuned CNN classifiers was shown to predict radiological image modality in the study [30]. A comparison of approaches using deep features and transfer learning with fine tuning was shown in the study [31] identifying radiogenomic relationships in breast cancer MR images and in [32] for predicting the upstaging of ductal carcinoma in situ to invasive breast cancer from breast cancer MR images. In both of these problems, deep features performed better than transfer learning with the fine tuning approach. However, both of these studies faced the issue of a small size of the training set.

When sufficient data are available, an entire deep neural network can be trained from a random initialization (training from scratch). The size of the network to be trained depends on task and dataset characteristics. However, the commonly used architecture in medical imaging is based on AlexNet [1] and VGG [33] with modifications that have fewer layers and weights. Examples of training from scratch can also be found in various studies such as: assessing for the presence of

Alzheimer’s disease based on brain MRI using deep learning [34, 35], glioma grading in MRI [36], and disease staging and prognosis in chest CT of smokers [37]. Recent advances in the design of CNN architectures has made networks easier to train and more efficient. They have more layers and perform better while having fewer trainable parameters [38] which reduces the likelihood of overtraining. The most notable examples include Residual Networks (ResNets) [39] and the Inception architecture [40, 41]. A shift to these more powerful networks has also taken place in applications of deep learning to radiology both for transfer learning and training from scratch. Three different ResNets were used to predict methylation of the O6-methylguanine methyltransferase gene status from pre-surgical brain tumor MRI [42]. In [43], the InceptionV3 network was fine-tuned and served as a feature extractor instead of previously used GoogLeNet. In another work using chest X-ray images [4], the authors fine-tuned a DenseNet with 121 layers for the classification of miscellaneous pathologies, achieving radiologist-level classification performance for identifying pneumonia.

In another approach, auto-encoder (AE) [44] or stacked auto-encoder (SAE) [45, 46] networks have been trained from scratch, layer by layer in unsupervised way. A stacked denoising auto-encoder with backpropagation was used in [47] to determine the presence of Alzheimer’s disease. AEs and SAEs can also be used to extract feature representations (similarly to the deep features approach) from hidden layers for further classification. Such feature representation has been used in the classification of lung nodules into benign and malignant classes in CT [48], and in the identification of multiple sclerosis lesions in MRI [49].

Apart from the classification of radiological images, analysis of radiological text reports plays a significant role [50]. The most prominent approach in this type of classification is deep learning-based natural language processing (NLP) [51], which is based on the seminal work for obtaining vector representation of phrases using an unsupervised neural model [52]. An example of application of this architecture can be found in [53] where the authors classified CT radiology reports as representing presence or absence of pulmonary embolism (PE), as well as type (chronic or acute) and location (central or subsegmental) of PE when present. They showed an improvement as compared to a non-deep learning algorithm. The same architecture was used in [54] for classifying head CT reports of ICU patients with altered mental status as having different degrees of severity according to each of five criteria: severity of study, acute intracranial bleed, acute mass effect, acute stroke, acute hydrocephalus. Radiology reports using the International Coding of Diseases (ICD) were auto-encoded in [55] using a publicly available dataset. A third application of the same architecture can be found in [55] where radiology reports were classified according to the International Coding of Diseases9 (ICD9) using a publicly available dataset.

4.2 Segmentation

In an image segmentation task, an image is divided into different regions in order to separate distinct parts or objects. In radiology, the common applications are segmentation of organs, substructures, or lesions, often as a preprocessing step for feature extraction and classification [34, 56]. Below, we discuss different types of deep learning approaches used in segmentation tasks in a variety of radiological images.

The most straightforward and still widely used method for image segmentation is classification of individual pixels based on small image patches (both 2-dimensional and 3-dimensional) extracted around the classified pixel. This approach has found usage in different types of segmentation tasks in MRI, for example brain tumor segmentation in [57, 58, 59], white matter segmentation in multiple sclerosis patients [60], segmentation of 25 different structures in brain [61], and for rectal cancer segmentation in pelvis MRI [62]. It allows for using the same network architectures and solutions

that are known to work well for classification, however, there are some shortcomings of this method. The primary issue is that it is computationally inefficient, since it processes overlapping parts of images multiple times. Another drawback is that each pixel is segmented based on a limited-size context window and ignores the wider context. In some cases, a piece of global information, e.g. pixel location or relative position to other image parts, may be needed to correctly assign its label.

One approach that addresses the shortcomings of the pixel-based segmentation is a fully convolutional neural network (fCNN) [63]. Networks of this type process the entire image (or large portions of it) at the same time and output a 2-dimensional map of labels (i.e., a segmentation map) instead of a label for a single pixel. Example architectures that were successfully used in both natural images and radiology applications are encoder-decoder architectures such as U-Net [64, 65, 66] or Fully Convolutional DenseNet [67, 68, 69]. Various adjustments to these types of architectures have been developed that mainly focus on connections between the encoder and decoder parts of the networks, called skip connections. Applications of fCNNs in radiology include prostate gland segmentation in MRI [70], segmentation of multiple sclerosis lesions and gliomas in MRI [71], and ultrasound-based nerve segmentation [72]. Moreover, loss functions have been explored that account for class imbalance (differences in the number of examples in each class), which is typical in medical datasets, e.g. weighted cross entropy was used in [73] for brain structure segmentation in MRI or Dice coefficient-based loss for brain tumor segmentation in MRI [74].

In order to segment 3-dimensional data, it is common to process data as 2-dimensional slices and then combine the 2-dimensional segmentation maps into a 3-dimensional map since 3D fCNNs are significantly larger in terms of trainable parameters and as a result require significantly larger amounts of data. Nevertheless, these obstacles can be overcome, and there are successful applications of 3D fCNNs in radiology, e.g. V-Net for prostate segmentation from MRI [75] and 3D U-Net [76] for segmentation of the proximal femur in MRI [77] and tumor segmentation in multimodal brain MRI [78].

Finally, a deep learning approach that has found some application in medical imaging segmentation is recurrent neural networks (RNNs). In [79], the authors used a Boundary Completion RNN for prostate segmentation in ultrasound images. Another notable application is in [80], where the authors applied a recurrent fully convolutional neural network for left-ventricle segmentation in multi-slice cardiac MRI to leverage inter-slice spatial dependencies. Similarly, [81] used Long Short-Term Memory (LSTM) [82] type of RNN trained end-to-end together with fCNN to take advantage of 3D contextual information for pancreas segmentation in CT and MR images. In addition, they proposed a novel loss function that directly optimizes a widely used segmentation metric, the Jaccard Index [83].

4.3 Detection

Detection is a task of localizing and pointing out (e.g., using a rectangular box) an object in an image. In radiology, detection is often an important step in the diagnostic process which identifies an abnormality (such as a mass or a nodule), an organ, an anatomical structure, or a region of interest for further classification or segmentation [84, 85, 86]. Here, we discuss the common architectures used for various detection tasks in radiology along with example specific applications.

The most common approach to detection for 2-dimensional data is a 2-phase process that requires training of 2 models. The first phase identifies all suspicious regions that may contain the object of interest. The requirement for this phase is high sensitivity [87] and therefore it usually produces many false positives. A typical deep learning approach for this phase is a regression network for bounding box coordinates based on architectures used for classification [88, 89]. The second phase is simply classification of sub-images extracted in the previous step. In some ap-

plications, only one of the two steps uses deep learning. The classification step, when utilizing deep learning, is usually performed using transfer learning. The models are often pre-trained using natural images, for example for thoraco-abdominal lymph node detection in [90] and pulmonary embolism detection in CT pulmonary angiogram images [23]. In other applications, the models are pre-trained using other medical imaging dataset to detect masses in digital breast tomosynthesis images [91]. The same network architectures can be used for the second phase as in a regular classification task (e.g., VGG [33], GoogLeNet [92], Inception [40], ResNet [39]) depending on the needs of a particular application.

While in the 2-phase detection process the models are trained separately for each phase, in the end-to-end approach one model encompassing both phases is trained. An end-to-end architecture that has proved to be successful in object detection in natural images, and was recently applied to medical imaging, is the Faster Region-based Convolutional Neural Network (R-CNN) [7]. It uses a CNN to obtain a feature map which is shared between region proposal network that outputs bounding box candidates, and a classification network which predicts the category of each candidate. It was recently applied for intervertebral disc detection in X-ray images [93] and detection of colitis on CT images [94]. A domain specific modification that uses additional preprocessing before the region proposal step was used by [95] for detection of architectural distortions in mammograms.

Another approach to detection is a single-phase detector that eliminates the first phase of region proposals. Examples of popular methods that were first developed for detection in natural images and rely on this approach are You Only Look Once (YOLO) [96], Single Shot MultiBox Detector (SSD) [97] and RetinaNet [6]. In the context of radiology, a YOLO-based network called BC-DROID has been developed by [98] for region of interest detection in breast mammograms. SSD has been employed, for example in [99], for breast tumor detection in ultrasound images, outperforming other evaluated deep learning methods that were available at the time. The authors of [100] applied the same network for detection of pulmonary lung nodules in CT images.

In the examples above, 2-dimensional data was used. For 3-dimensional imaging volumes, common in medical imaging, results obtained from 2-dimensional processing are combined to produce the ultimate 3-dimensional bounding box. As an example, in [101] the authors performed detection of 3D anatomy in chest CT images by processing data slice by slice in one direction. Combining output from different planes was performed in several studies. Most of the them [102, 103, 104] used orthogonal planes of MRI and CT images performing detection in each direction separately. The results can then be combined in different ways, e.g. by an algorithm based on output probabilities [101] or using another machine learning method like random forest [100]. An alternative method for 3D detection has been proposed for automatic detection of lymph nodes using CT images by concatenating coronal, sagittal and axial views as a single 3-channel image in [87].

4.4 Other Tasks in Radiology

While the majority of the applications of deep learning in radiology have been in classification, segmentation, and detection, other medical imaging-related problems have found some solutions in deep learning. Due the variety of those problems, there is no unifying methodological framework for these solutions. Therefore below, we organize the examples according to the problem that they attempt to address.

Image Registration: In this task two or more images (often 3D volumes), typically of different types (e.g., T1-weighted and T2-weighted MRIs) must be spatially aligned such that the same location in each image represents the same physical location in the depicted organ. Several approaches can be taken to address the problem. In one approach, it is necessary to calculate similarity mea-

asures between image patches taken from the images of interest to register them. The authors of [105] used deep learning to learn a similarity measure from T1-T2 MRI image pairs of adult brain and tested it to register T1-T2 MRI interpatient images of the neonatal brain. This similarity measure performed better than the standard measure, called mutual information, which is widely used in registration [106]. In another deep learning-based approach to image registration, the deformation parameters between image pairs are directly learned using misaligned image pairs. In [107], the authors trained a CNN-based model to learn the sequence of movements that resulted in the misalignment of the image pairs of CT and cone-beam CT examinations of the abdominal spine and heart. In another study [108], chest CT follow-up examinations were registered by training a CNN to predict three-dimensional displacement vector fields between the fixed and moving image pairs. A CNN-based network was trained to correct respiratory motion in 3D abdominal MR images by predicting spatial transforms [109]. All of these techniques are supervised regression techniques as they were trained using ground truth deformation information. In another approach [110], which was unsupervised, a CNN was trained end-to-end to generate a spatial transformation which minimized dissimilarity between misaligned image pairs.

Image generation: Acquisition parameters of a radiological image strongly affect the visual quality and detail of the images obtained using the same modality. First, we discuss the applications that synthesize images generated using different acquisition parameters within the same modality. In [111], 7T like images were generated from 3T MR images by training a CNN with patches centered around voxels in the 3T MR images. Undersampled (in k-space) cardiac MRIs were reconstructed using a deep cascade of CNNs in [112]. A real-time method to reconstruct compressed sensed MRI using GAN was proposed by [113]. In another approach [114] in order to synthesize brain MRI images based on other MRI sequences in the same patient, convolutional encoders were built to generate a latent representation of images. Then, based on that representation a sequence of interest was generated. Reconstruction of "normal-dose" CT images from low-dose CT images (which are degraded in comparison to normal-dose images) has been performed using patch-by-patch mapping of low-dose images to high-dose images using a shallow CNN [115]. In contrast, a deep CNN has been trained with low-dose abdominal CT images for reconstruction of normal-dose CT [116]. In another study, CT images were reconstructed from a lower number of views using an U-Net inspired architecture [117].

Deep learning has also been applied to synthesizing images of different modalities. For example, CT images have been generated using MRIs by adopting an FCN to learn an end-to-end non-linear mapping between pelvic CTs and MRIs [118]. Synthetic CT images of brain were generated from one T1-weighted MRI sequence in [119]. In another application to aid a classification framework for Alzheimer’s disease diagnosis with missing PET scans, PET patterns were predicted from MRI using CNN [120].

Image enhancement: Image enhancement aims to improve different characteristics of the image such as resolution, signal-to-noise-ratio, and necessary anatomical structures (by suppressing unnecessary information) through various approaches such as super-resolution and denoising.

Super-resolution of images is important specifically in cardiac and lung imaging. Three dimensional near-isotropic cardiac and lung images often require long scan times in comparison to the time the subject can hold his or her breath. Thus, multiple 2D slices are acquired instead and the super-resolution methodology is applied to improve the resolution of the images. An example of using deep learning in super-resolution in cardiac MRI can be found in [121], where the authors developed different models for single image super-resolution and for generating high resolution

three-dimensional image volumes from two-dimensional image stacks. In another study using CT, a single image super-resolution approach based on CNN was applied in a publicly available chest CT image dataset to generate high-resolution CT images, which are preferred for interstitial lung disease detection [122]. In this study, upscaled bicubic-interpolated images were first passed through one convolutional layer to generate low-resolution features. Then, a non-linear transformation of those features was mapped to generate high resolution image features for the reconstruction.

An example of an application of deep learning in denoising can be found in [123] where the authors performed denoising of DCE-MRI images of a brain (for stroke and brain tumors) by training an ensemble of deep auto-encoders using synthesized data. Removal of Rician noise in MR images using a deep convolutional neural network aided with residual learning was performed in [124].

In an attempt to enhance the visual details of lung structure in chest radiographs, the effect of bone structures (ribs and clavicles) were suppressed. Bone structure has been estimated by conditional random field based fusion of the outputs of a cascaded architecture of CNNs at multiple scales [125]. Metal artifacts (caused by prosthetics, dental procedures etc.) have also been suppressed by using a trained CNN model to generate metal-free images using CT [126].

Content-based image retrieval: In the most typical version of this task, the algorithm, given a query image, finds the most similar images in a given database. To accomplish this task, in [127], a deep CNN was first trained to distinguish between different organs. Then, features from the three fully connected layers in the network were extracted for the images in the set from which the images were retrieved (evaluation dataset). The same features were then extracted from the query image and compared with those of the evaluation dataset to retrieve the image. In another study, a method was developed to retrieve, arrange, and learn the relationships between lesions in CT images [128].

Objective image quality assessment: Objective quality assessment measures of medical images aim to classify an image to be of satisfactory or unsatisfactory quality for the subsequent tasks. Objective quality measures of medical images are important to improve diagnosis and aid in better treatment [129]. Image quality of fetal ultrasound was predicted using CNN in a recent study [130]. Another study [131], attempted to reduce the data acquisition variability in echocardiograms using a CNN trained on the quality scores assigned by an expert radiologist. Using a simple CNN architecture, T2-weighted liver MR images were classified as diagnostic or non-diagnostic quality by CNN in [132].

5 Future of deep learning in radiology

There is a general agreement that deep learning will play a role in the future practice of radiology. Some predict that it will conduct mundane tasks leaving radiologists with more time to focus on intellectually demanding challenges. Some believe that radiologists and deep learning algorithms will work hand-in-hand to deliver performance superior to either of them alone. Finally, some predict that deep learning algorithms will replace radiologists (at least in their image interpretation capacity) altogether.

Incorporation of deep learning in radiology will be associated with multiple challenges. First, and currently foremost, is the technological challenge. While deep learning has shown extraordinary promise in other image-related tasks, the results in radiology are far from showing that deep learning algorithms will replace a radiologist in the entire scope of their diagnostic work. Some recent

studies [133, 134, 135, 136, 137, 138, 139, 4] indicate performance of these algorithms comparable to expert humans, but these results are only applicable to a very small minority of the tasks that radiologists perform. This is likely to change in upcoming years given the rapid progress in implementing the deep learning algorithms in the realm of radiology.

Implementation of deep learning in radiology practice also poses legal and ethical challenges. Primarily: who will be responsible for the mistakes that a computer will make? While this is a difficult question, similar questions have been posed and resolved when other technologies were introduced including elevators and cars. Since artificial intelligence penetrates various areas of human activity, questions of this type will likely be studied and answers proposed in the coming years.

Other challenges will include patient acceptance or non-acceptance of a radiologist's not being involved in the process of interpreting their images (regardless of the performance) as well as regulatory issues. Finally, an important practical issue is how to incorporate deep learning algorithms into the radiology workflow in order to improve, rather than disrupt the radiology practice.

6 Conclusion

In summary, in this paper we have discussed the principles of deep learning as well as the current practice of radiology to elucidate how these new algorithms can be incorporated into radiology workflow. We have discussed the progress and state of art in the field. Finally, we have discussed some challenges and questions related to implementation of deep learning in the current practice of medicine. All signs show that deep learning will play a significant role in radiology. The next 5 years will be a very exciting time in the field that may see many questions stated in this article answered through a collaboration of machine learning scientists and radiologists.

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