# Deep Learning for Medical Image Recognition: Open Issues and A Way to Forward

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Abstract. In the recent decade, deep learning has taken lead over available analysis techniques. Today's deep learning is used in diversified sectors like healthcare, traffic management, agriculture, etc. The expectations of researchers or people concerned with deep learning are very high. On another side, healthcare sector is totally different from other industry. It required serious attention, care of people and services (regardless of cost) towards patients, here issue is a matter of patient's life. Also, this sector requires a high budget and many people to work in parallel, to provide efficient services to each patient. The interpretations of data in the medical field are vested in the hands of medical experts and this proves to be quite restrained because of the intervening sophistication, wide ranging varieties spread across a number of compilers, etc. The great victory of deep learning in real time applications has led to the creation of striking results with extreme accuracy and precision, hence, paving way to the spotlight in futuristic health sector applications. In this paper, we discussed state of the art deep learning architecture and its optimization used for medical image segmentation and classification. Also, this sector discusses several useful components like open issues, challenges deep learning based methods for medical imaging, and future research directions.

# Keywords- Bioinformatics, Medical Image Processing, Data Analytics, Machine Learning, Deep Learning.

# 1. Introduction

Deep learning is a developing pattern of information investigation and has been named as one of the 10 innovation technologies of 2013[1]. The enhanced version of artificial neural network is deep learning which consists of more layers that allow precise predictions on data and higher abstraction levels [2]. In the current year, only one tool in machine learning is a current trending tool that is deep learning in imaging and computer vision domains.

#### 1.1 Feed-Forward Neural Networks

The foundation of most deep learning models is deep feedforward networks and also known as multi-layer network of neurons (MLN) [3]. These model networks are known as feed forward, as the information only travels on input nodes, through the hidden layers (individual or multiple layers) and then through the output nodes. Feedback connections are not usable in MLN, so that the network output will be returned. Such networks are described by a combination of several basic models (sigmoid neurons). Some special cases of Feed forward networks are Convolution Neural Network (CNNs) and Recurrent Neural Network (RNNs) networks. The multi-layered neuron network contains a multitude of sigmoid neurons. MLNs are able to manage data that are not linearly separable. The layers between the input and output layers are referred to as invisible. The hidden layers are used to deal with the dynamic non-linear relationships between input and output. These networks are mainly used to monitor supervised machine learning activities, for which we already know the objective, that is to say to the outcome that we want our network to achieve and are extremely important to machine learning and form the foundation to a wide range of commercial applications. The role of these networks has been greatly affected by areas such as Computer vision and Natural Language Processing (NLP).

# 1.2 Convolution Neural Networks

The development in deep-learning computer vision has been developed and improved over time, mainly through a specific algorithm, i.e., a Convolution neural network. Another type of neural network is Convolution Neural

Network (CNN) [4] which is used by machines to picturize things and perform image classification, image recognition, object detection and instance segmentation tasks are some of the most common areas of CNN use. We have a set of inputs for our convolution operations, and based on all previous outputs and weight, we determine the value of the present input. The CNN (ConvNet / CNN) is a Deep Learning algorithm that allows an image to be entered, assigns the importance to various aspects / objects in the image (learnable weights and biases) and can distinguish between one aspect and the other. The required pre-processing in a ConvNet is considerably lower in other classification algorithms. While hand-made filters with sufficient training are manufactured in primitive methods, ConvNets are able to learn these filters. ConvNet's structure is identical to the communication pattern of neurons in the Human brain, influenced by Visual Cortex organization. In a restricted area of the visual field only, individual neurons respond to stimuli, known as the receptive field. The entire visual area is covered by a collection of such fields. With the application of the appropriate filters, a ConvNet can successfully capture the spatial and temporal dependence of an object. The network can be equipped to better comprehend object complexity. The ConvNet's role is to reduce images in a more easily processable form without losing features critical to good prediction. This is critical when designing an architecture that is not just good in learning but can also be scaled to large datasets.

### 1.3 Deep Models [5]

Deep learning has shown its power and has stood up to be one of the nascent fields of growth across a number of fields. It's is of utmost important for every person who is new to this field to grab and conceptualize the true essence of Deep Learning and its other models. Itmainly include controlled and uncontrolled models. The supervised models are moulded by the examples of some data sets while the un-supervised models are bestowed with input data alone and don't posses any particular results from which they can learn. Supervised models possess regression and classification task and develop a formula for the same while unsupervised models are often exposed to gathering and association rules. Classic neural networks (multi-layer perceptions), Convolutional Neural Networks (CNN), Recurrent Neural Networks (RNNs) come under supervised models and un-supervised models include Self-Organizing Maps (SOMS), Boltzmann machines, auto encoders, etc.

Hence, the remaining part of this work is organized as follows:

- Section 2 discusses work related to medical image recognition, detection, etc., in the previous decade etc.
- Section 3 discusses our motivation behind writing this work (i.e., on medical related sectors/ applications).
- Section 4 discusses Medical Image Detection and Recognition
- Section 5 explains about Medical Image Segmentation in detail.
- Section 6 discusses a Medical Image Registration
- Section 6 discusses about computer Aided Diagnosis and Disease Quantification in detail.
- Section 8 discusses various tools and methods existing/ available for Deep Learning for medical applications.
- Section 9 discusses various open research issues, challenges faced in Medical care/ medical imaging and opportunities for future as including research directions.
- Finally, section 10 concludes this work with various research gaps and future enhancements.

Hence in this work, our main goal is to fill many identified research gaps in current era through providing an effective literature on medical image recognition research and its related areas.

#### 2. Related Work

This work joins the information on big data and machine learning, and applies the simple algorithms of machine learning to take care of the issues of medicinal big data, for example, huge amount of information, wide multifaceted nature and difficulty in maintenance. It allows doctors to improve patient treatment by accurate assessment and forecasting accurately [6]. When we take an insight into the supervision of medical images, CAD (Computer-aided detection) takes the prime spot and it is highly beneficial to Deep Learning. Candidate lesions are found in the standard approach to CAD [7] either through supervised methods or by traditional image processing methods such as filtering and computational morphology. Candidate Lesions are generally fragmented and feature large handcrafted techniques. Classifiers are essential to spot the vectors and to check the authenticity of the lesion. Deep Learning can be directly implemented by deploying it to train CNN functioning on certain image patches dotted on the candidate lesion. This method is used by many publications and prominent one is Setio et al., [8]. They haveinvolved the combination of pulmonary nodules which were created earlier on 3D chest CT scans and then separating the 2D patches into nine different routes, Each of these candidates acquire a unique combination of CNNs. There is a slight improvement in contrast to the classic CAD system previously published for the same job. Rothetal. [9], CNNs were used to improve the three existing CAD

detection systems for sclerotic spine metastases on body CT, colonic polyps on CT colonography, and CT body lymph nodes. They also used previously developed candidate detectors and 2D patches in three directional orthogonal, and up to 100 random rotated viewing systems. CNNs were used for enhanced CT detection. CNN projections on these 2.5D visions are then aggregated in order to achieve more accuracy benefit. The randomly rotated 2.5D views are a way of representing a de-compositional image from the original 3D data. On these 2.5D views, the CNN forecasts are then aggregated for further precision gains. In all three CAD systems using CNNs, the tolerance for lesion detection increased by 13 - 34 percent, indicating that the solution was general and observable. It was almost impossible to improve this size by using non-deep classifiers such as support vector machines committee.

Further, Dou et al. [9] detected susceptibility weighted cerebral microbleed scans by MRI. They use 3D CNNs, replacing a two-stage approach to detect candidates with a CNN. In comparison to several classical and 2D literature strategies that have been re-implemented and trained and evaluated by the researchers on the same dataset, they show improved results for their 3D CNN. Sirinukunwattana et al. [11], in his path of logical images identified and listed nuclei. Instead of determining if the core pixel of the patch was a cell nucleus, they model the production as the high peak close to the centre of each nucleus and elsewhere. They implement the usage of a CNN which acquires minute patches as the input. Along with this, they incorporate a merger of super facing these patches in the test phase, thus resulting in spatially constrained CNN which creates enhances results in comparison to the previous approaches. Furthermore, this constrained CNN leads to improved solutions which often underlies the CNNs and the traditional technique-based approach. In [12], Anthimopoulos et al. emphasis on identifying interstitial lung disease patterns from 2D chest CT scanning patches. They are one of three gatherings in this issue [13] and [14] by using public dataset from [15]. We train a CNN to identify 32-32-pixel patches into one of seven categories and report higher accuracy than three previously published methods using hand-crafted features. The subject of concern is also lesion detection in several other articles of this issue, but the focus of those papers is wider or zooms on particular methodological issues.

#### 3. Motivation

In current era, many learning algorithms or discovery tools are available to refine data. These tools extract useful value or info ration form a large number of data/ billions of maples. Numerous data mining techniques or statistical testing approaches can be taken into account and implemented for the monitoring and supervision of reproducibility issues. In the previous decade, it was relay a difficult task to extract this large amount of data. But, today due to technological advancements and shifting of people towards smart era/use of smart devices, more and more data is generating every-day. To extract useful data, for curing diseases and saving lives of maximum people, we start to work on efficient learning techniques, which are used by many research groups and communities worldwide.

Deep learning is one of popular learning techniques and being used in many applications, especially in healthcare or bio-medical imagingFor example, we have MRI, CT-Scan, etc., here deep learning can be useful to predict diseases previously, i.e., chance of occurring/ possibility based on probability (in near future) or can provide prefect (optimal) solution based on its refining process (i.e., by hidden layers). Hence, keeping such things in our mind and saving as many lives is our primary aim, so we choose this area and topic to write our thoughts. In this paper we will discuss topics like medical image detection and recognition, medical image segmentation, medical image registration, computer aided diagnosis and disease quantification, open-source tools, models/ algorithms available for deep learning for medical applications/ bio-medical applications today with including several opportunities for future researchers, etc.

# 4. Medical Image Detection and Recognition

The process of identifying the elements in medical image are image detection and recognition. The pictures are volumetric in many situations and effective parsing is therefore a must. A common strategy used in this case involves marginal space learning [16], the main reason being its efficiency and quick detection and spotting of organs. It's very close to Deep Learning [17] and is highly robust and efficient as it has its probable boosting trees replaced with network neural boost cascade. Nevertheless, it is important to process the entire volume in order to detect anatomical structures with reliability. [17] Drives even more productivity by replacing the search process with an artificial agent that uses deep reinforcement learning to identify anatomical points of interest. The approach can detect hundreds of landmarks in just a few seconds in a full CT range.

Further, Bier et al. [18] proposed an interesting method by which anatomical landmarks were detected in 2-D X-ray screenings. They use a deep network to train 3D-annotated landmarks in projection-invariant feature descriptors. The so-called region-proposal neural networks are another popular detection method. Tumours in mammographic images are identified accurately by the method in [19]. The identification and recognition are also used in many other ways and a wide range of literature is available. We are reporting only two additional applications here. In histology, cell detection and classification are important tasks that are explained by Aubreville et al. [20] are tackling through directed networks of spatial transformers that allow the detection to be refined prior to actual classification. This technique benefits from the role of mitosis classification, for other image classification tasks, convolutional neural networks are very efficient. In [21] their job is to identify images automatically in confocal laser-endoscopy which contains motion artifacts.

### 5. Medical Image Segmentation

Image segmentation is incredibly profited by the ongoing improvements in deep learning. Image segmentation involves the determination of contoured organs or other structures with at most precision and finesse. Here, we put forth the reports of Holger Roth's Deeporgan [22], the brain MR segmentation CNN by Moeskops et al. [23], a complete convolutional multi-vitality 3-D U-net introduced by Chen et al. [24], and Breininger et al. [25] stated U-net based stent segmentation in X-ray projection domain as envoy example. In [26] shown segmentation using deep convolutional networks works in 2-D for histopathologic images. Fu et al. [27] are followed a concept by mapping a neural network from Frangi vesselness. This shows that they can change kernels for the specific vessel segmentation function of ophthalmic fundus imaging in the first step of the algorithm. Segmentation algorithms used by RNN for image segmentation in medical field demand attention. In [28] poudel et al. proved this for recurrent fully CNN on multi-slice MRI cardiac data, the another author andermatt et al. proved the efficiency of GRUs for brain segmentation [29].



Figure 1. Detection and Segmentation [17, 18 and 25].

In figure 1, the left side demonstrates the identification of artificial agent monuments after Ghesu et al. [17], Bier et al. [18] shows X-ray transform-invariant landmark detection. Breininger et al. [25] on the right side is the U-net-based segmentation of the stent. Note that the authors [17, 18 and 25] are permitted to reproduce the images.

# 6. Medical Image Registration

While most of the perceptive tasks of image detection and classification have gained great attention in terms of deep learning applications, the registration of images has not yet seen this large increase. There are many interesting works in the literature that show clearly that many opportunities exist as well. One common issue with point-based registration is to identify good feature descriptors that can correctly identify the points. Wu et al. are proposing to use auto encoders to mine in unsupervised way have good features [30]. Schaffert et al. [31] push this further and use the registration metric as a loss function to learn good functionality. The 3D-pose estimate directly from 2-D point features [32] is another method for addressing 2-D/3-D registration problems. Definitions of deep learning methods can also be found for full volumetric registration. The quicksilver algorithm can model a deformatable registration and directly from the image appearance uses a patch-specific prediction [33]. Another approach in modelling is the registration issue as an agent- and enhancer learning control problem. For comprehensive registration, Liao et al. proposes to do this in aligning all quantities, predicting the next optimum movement [34]. So method also can be extended with a numerical deformation model for non-rigid registration [35]. In this scenario, movements are in the deformation model vector space. For instance, also point-based registration issues are applicable to agent-based approaches. Zhong et al. prove this with imitation learning for intraoperative brain shifts [36].

# 7. Computer Aided Diagnosis and Disease Quantification

One of the biggest issues in medical image processing is diagnoses in computer-aided diagnosis. Here, we not just act to quantify evidence for diagnosis in a supportive role. Rather, it is necessary to predict the diagnosis itself. Decisions must therefore be made very carefully and decisions must be reliable. The analysis of chest radio-graphs includes a large amount of radiological work which is routinely performed. Reliable support is therefore highly desirable to prevent human error. Diamant et al. use transfer learning techniques in [37] to provide an example of this. In the reading of volumetric optical coherence tomography data, ophthalmologists are charged with a similar workload. Google's Deep Mind recently suggested to help the referral decision process [38]. Many other studies have been found here, including automated cancer assessment in confocal laser endoscopy of the head and neck tissue [39], deep learning for mammograms [40], and skin cancer identification [41].

### 8. Open-Source Tools, Models/ Algorithms Available for Deep Learning for Medical Applications

These artificial intelligence technologies push your deep learning to next level. Here is a list of 8 best open source AI technologies that you can use to take your deep learning projects to the next level [42]. These tools are included here as:

- a) TensorFlow: TensorFlow is an open source training application that was initially released in 2015 and can now be widely used and implemented across a number of platforms. It is one of the most popular and commonly used deep learning framework. Google has developed Tensor-flow to support research and production goals, and several companies, including Dropbox, eBay, Intel, Twitter, and Uber, are now widely using it. In Python, C++, Haskell, Java, Go, Rust and JavaScript, TensorFlow is available. Packages for third-party programming languages are also available. The system allows you to use flowgraphs to build neural networks (and even other software templates).
- b) Caffe/Caffe2: Feedforward network open source and suitable for image processing.
- c) Theano: Open Source is made up of most sophisticated neural networks that came into existence in 2007 at the Numerical University of Montreal.
- d) Pytorch: Open source deep learning framework, which was originally developed at the New York University in 2002. Facebook and Twitter are commonly used. Ideal for convnets and a rich RNN package.
- e) CNTK: it is an open source tool. Cognitive toolkit from Microsoft, and recognized in the speech culture.
- f) Google Cloud machine learning platform: Allow the use of TensorFlow in Google Cloud Platform to build and train machine learning models.it is a commercial tool.
- g) Amazon machine learning: It is a commercial tool. Cloud-based use of machine learning technology services for users.
- h) Microsoft Azure: Machine learning library.it is a commercial tool.
- i) IBM Watson analytics: It is a commercial tool. Cloud-based data exploration, visualization and predictive analysis of machine learning tool.

The most popular deep learning models are explained below [5]:

**Classic Neural Networks:** It is also known as multi-layer perceptions. American psychologist Frank Rosenblatt designed the model of perceptron in 1958. Its singular nature enables it to adapt through a series of inputs to basic binary patterns, simulating the learning patterns of a human-brain. The classical neural network design consists of more than two layers (refer figure 2).



Figure 2: Classic neural network

**Convolutional Neural Networks (CNNs):**In order to deal with a greater degree of complicity around preprocessing and information computation, a more sophisticated version of classic artificial neural networks is built up using convolutional neural network. CNNs have been developed for image data and could be the most powerful and scalable image classification problem template. CNNs have not been especially developed to use non-image data, but with non-image data they can also produce astonishing results. There are four components to create the CNN after you have imported your data into the model:

- a) Convolution: a process by which maps from our input data are formed. The filter maps are then used with a function.
- b) Max-Pooling: helps our CNN to detect a picture when updated.
- c) Flattening: CNN can read the data flattening in an array.
- d) Full connection: the secret layer that measures our design loss function.

**Recurrent Neural Networks (RNNs):** Recurrent Neural Networks (RNNs) for predicting sequences have been developed. LSTM (Long short-term memory) is a common RNN algorithm, with many possible applications:

- a) One by one: one entry mapped to one exit. For example-Classification of Image
- b) One to many: one input mapped to an output set. For example-Image subtitling,
- c) Many in one: The input sequence generates a single image. For example-Sentiment Analysis (multiple words binary output)
- d) Many to many: a sequence of inputs generates an output sequence. For example: Video classification (division of the video into frames and labeling of each frame separately).

**Self-organizing Maps:** The self-organizing maps or SOMs function with unsupervised data and typically help to reduce dimensionality (reduces the model's number of random variables).For a map of its own structure, the output dimension is always 2-dimensional. Therefore, the output is reduced to two dimensions if we have more than 2 input features. They are assigned weight for each synapse that connects the input and output nodes. Therefore, the representation in the model competes for each data point. The closest node is the BMU, and the SOM changes its weight to get closer to the BMU.As the model progresses the BMU neighbours continue to decline. The nearer a node to BMU, the greater its weight.

**Boltzmann machines:** One aspect is similar in the four models discussed above. Such models work to some degree. Even if SOMs are unsupervised, they continue to work as directed models in a specific direction. By address, I mean: Input- Hidden Layer -Output. By way of direction. The Boltzmann machines do not follow a specific direction. In a circular hyperspace, all nodes are connected to each other, as in the image. In addition to working with defined input parameters, a Boltzmann machine can generate all models' parameters. This model is called stochastic and varies from all the above-mentioned deterministic models. The Boltzmann Restricted Machines are more convenient.

**AutoEncoders:** Autoencoders work with automatic encoding of input-based information based onactivation function and then with output decoding. The input features are condensed in smaller categories by a kind of bottleneck. So the autoencoder model defines and leverages the data to achieve the output, if some inherent structure exists within the data.

#### **Types of AutoEncoders:**

Few types of AutoEncoders discussed here in brief as:

- **Sparse AutoEncoders:** Sparse autoencoders have nodes that are hidden larger than input nodes. They are still able to discover important data features. A generic sparse autoencoder is displayed where a node's obscurity matches the activation level.
- **Denoising AutoEncoders:** By adding some noise, Denoising autoencoders create a corrupted copy of the data. It helps to avoid copying the input to the output by the autoencoders without knowing about the information. Autoencoders of this type was take up a slightly tarnished input during training sessions to retrieve the authentic input. Thus, the model grasps a vector field which is suitable for mapping the received data into a reduced dimensional manifold, thus describing the natural data to eradicate external noises.
- **Contractive AutoEncoders:** The main aim of a contractive autoencoder is to possess a stable, well trained representation which is very insensitive towards small data variations. The robust nature of data representation is achieved by imposing a penalty sanction to the loss function. Contractive autoencoder is a better choice to practice useful feature extraction than denoising autoencoder. This model learns an encoding that has identical encoding inputs. We are therefore pushing the design to learn how to compact an input quarter into a smaller output portion.

• **Stacked AutoEncoders:** A neural network consisting of many layers of sparse autoencoders where each hidden layer's output is connected to the next hidden layer's input.

# **Deep Belief Network**

Deep Belief Network (DBN) is a Probabilistic Deep learning algorithm that is un-supervised. DBN is a profound neural network category consisting of a multiple layer of both directed and non-directed edges of a graphic model. It is made up of various layers of secret units where each layer is connected to each other but units are not connected. It is a stack of Autoencoders or Restricted Boltzmann Machine (RBM).

# 9. Issues, Challenges and Opportunities Towards Deep Learning in Medical Applications

Despite successful results achieved through deep learning architectures, the clinical application of deep learning in health care remains a number of unresolved challenges. They stress the following key issues in particular [43]:

S.No	Challenges	Description
1	Data Volume	Deep learning refers to a group of computational models which are highly intensive. A very popular example is the completely interlinked neural multilayer networks which embodies numerous parameters for precise calculations. A great deal of data is available to achieve this goal. In addition, while the minimum of training materials are not tough to direct, here is a general rule that at least ten times the number of samples as network parameter. This is also one cause for the success of deep learning in the fields that collect large volumes of data (e.g. computer vision, speech, natural language) easily. Healthcare is however a different area; we currently have around 7.5 billion people worldwide, with most of them having access to primary health care (as of September 2016). Therefore, we probably still won't have as many patients as we want to develop an integrated deep learning model. Therefore, it is much more complex to understand disease and its complexity than other activities, like the identification of objects or speech recognition. In consequence, the amount of medical data necessary to train an efficient and robust deep learning model would be considerably more than in other media from the perspective of big data.
2	Data Quality	Generally, in all domains the data will be clean and well-structured. But, in healthcare domain the data is extremely miscellaneous, not-cleared, noisy and in complete. An efficient and superior Deep Learning model with huge and varied data sheets are to be trained and moulded while considering the plausible threats like data sparsity, redundancy and the lack of values In the course of time, the diseases continue to evolve and improve. However, numerous present-day deep
	Tomportany	learning models which are even present in the medical arena, do possess static vector-based inputs which generally do not control the time parameter. Creation o Deep Learning perspectives which can tolerate temporal health care data is a necessity which calls for the creation of new solutions.
4	Domain complexity	In contrast, the issues in biomedicine and health care are more complex than in other fields of practice (e.g. image and speech analysis). The diseases are extremely heterogeneous, and for most diseases, their origins and development are still not fully known. In fact, in a realistic medical setting, the number of patients is generally limited and we can not request as many patients as we want.
5	Interoprebility	Although in a number of application domains deep learning models have been successful, they are sometimes considered as black boxes. In other deterministic areas (for the end user can objectively validate the tags assigned to the images), it may not be an problem, however, but it is important not only in health care for quantitative algorithms performance, but also the reason the algorithms work. In fact, such model interpretability (i.e., which phenotypes drive the prediction) is critical to convince physicians of the actions the prediction system recommends.

Table 1: Open Challenges Towards Deep Learning in Medical Applications

These issues put forward a number of chances for betterment and upcoming research ideas and methodologies. Keeping these in mind, we pin point the following paths which are likely to guarantee the future of deep learning in the medical sector.

Table 2. Future	Research Onn	ortunities Tow	ards Deen Lea	arning in Media	al Annlications
Table 2. Future	Kusuarun Opp	fitumites 10m	arus Deep Dea	ai ming in Micul	a Applications

5.IN0	Opportunities	Description
1	Feature enrichment	We will accumulate all possible features so as to spot and discover novel techniques processing, given the limited number of patients worldwide. Data sources to generate these features must contain, and must not be restricted to, wearable devices, environments, online surveys, online community, genome profiles, omic data such as proteoms (such as social media information reported on patients for pharmacovigilance [44-45]). Successful incorporation of highly dispersed data and getting a knack of using it the right way in Deep Learning is an extremely important focus point from the research aspect.
2	Federated inference	Each hospital has a patient population of its own. Developing deep learning models with the help of patients from a number of spots while assuring safety and security of their identity and information is a critical issue. As a consequence, training deep models securely in this federated environment will be another important research subject interfacing with other mathematical domains, such as cryptography (e.g. homomorphic encryption [46] and secure multiparty computing [47]).
3	Model privacy	It is even more challenging to preserve the privacy of deep learning models, as there are more parameters to be protected and several recent works have pushed the fronts in this area [48–49]. Nevertheless, taking into account all personal information likely to be handled by deep models in clinical applications, the implementation of smart technologies for next-generation health care needs to consider these risks and try to implement a differential privacy norm.
4	Incorporating expert knowledge	Taking into account a majority of the personal details and data which are likely to be configured by deep models in clinical approaches, the implementation of smart tools for futuristic health care requirements to account for these risks and try out a varied standard for privacy. Semi-supervised learning, a perfect method for learning from huge quantities of unlabelled samples with only a few labelled ones is likely to possess greater strength due to its capacity to handle both labelled and unlabelled samples [45].
5	Temporal modelling	Knowing that the parameter of time is an important factor in majority of the health-care issues, especially in those which involve EHRs and supervision of devices, training time-linked deep learning model which is highly important for the better outlook of the patients conditions. Temporary deep learning is therefore key to solving problems of health care. To this end, we expect RNNs as well as memory-coupled architectures (for example [50]) and attention mechanisms (for example [10]) to play the most major role in improving deep clinical architecture.

Thus, this elucidation opens up numerous challenging tasks and an ocean of opportunities with Deep Learning in the medical sector (table 1 and table 2). Now, next section will conclude this work in brief with including some interesting research gaps for future researchers.

# 10. Conclusion

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Today's due to recent development of technology, many changes have been seen in current era. Big data is popular one in among all game – changing technologies/ concepts. As narrated in this paper, Big Data is the new oil for many sectors. Especially for e-healthcare, big data is helping a lot, i.e., in determining useful and productive decision for curing disease in early stages. Moreover of this sensitive applications, today's big data has more potential/ power to impact many other sectors from social science to political science, from financial industry to business, from medical science to public health, from health care to genetics, and from personalized medicine to patient/custom-centered outcomes. As future, deep learning can be use in previously mentioned listed applications. The emerging field of Big Data science provides new opportunities to us like biomedical data science, etc., but these enhancements come with many challenges in all fields. For example, in biomedical and health science fields, which make improved understanding of human life, health, diseases, and behaviour possible, are facing issues like not having efficient tools/ methods to analysis this big data, also security of user's personal information and leaking of user's privacy are few names listed here. But, it is sure that big data has involved various levels of human life: individuals to community, and industrial to university to government. Hence, as summary of this paper/ article, we used many useful articles that are representative of a line of work; this helps us provide a critical analysis of challenges, i.e., preparing table 1 and 2.

In this work, we have discussed several challenges which have not been identified in the past by previous researchers (all issues together) towards bio-medical imaging, including the lack of long-term confidentiality protection, the over-reliance on non-collusion assumptions, the challenges presented by making strong data representations assumptions, as well as the lack of solutions applicable to current medical image detection, recognition, and segmentation. Also, we discussed several open-source tools, models/ algorithms which are available for deep learning for medical applications/ bio-medical applications today with including several opportunities for future researchers. This work will be more useful to our future readers (with a straightforward

manner) in the future, for example, to assess progress in the field, also for many research communities as a guideline for future work.

#### References

- [1] MIT Technol. Rev., 2013, https://www.technologyreview.com/s/513696/deep-learning
- [2] Y. LeCun, Y. Bengio, and G. Hinton, "Deep learning," Nature, vol. 521, no. 7553, pp. 436-444, 2015.
- [3] Wang, Xizhao, and Weipeng Cao, "Non-iterative approaches in training feed-forward neural networks and their applications", 2018, 3473-3476.
- [4] Rakhlin, Alexander, Alexey Shvets, Vladimir Iglovikov, and Alexandr A. Kalinin, "Deep convolutional neural networks for breast cancer histology image analysis." International Conference Image Analysis and Recognition. Springer, Cham, 2018.
- [5] Zhou, S. Kevin, Hayit Greenspan, and Dinggang Shen, "Deep learning for medical image analysis", Academic Press, 2017.
- [6] H. Wang, Y. Chunfeng, H. Weiming, and S. Changyin, "Supervised classspecific dictionary learning for sparse modeling in action recognition," Pattern Recognit., vol. 45, no. 11, pp. 3902–3911, 2012.
- [7] B.vanGinneken, C.M.Schaefer-Prokop, and M.Prokop, "Computeraided diagnosis: How to move from the laboratory to the clinic," Radiol., vol. 261, no. 3, pp. 719–732, 2011.
- [8] H. Roth et al., "Improving computer-aided detection using convolutional neural networks and random view aggregation," IEEE Trans. Med. Imag., vol.35, no.5, pp.1170–1181, May2016.
- [9] Q.Douetal., "Automatic detection of cerebral micro bleeds from MR images via 3D convolutional neural networks," IEEE Trans. Med. Imag., vol.35, no.5, pp.1182–1195, May2016.
- [10] Hermann KM, Kocisky T, Grefenstette E., et al. Teaching machines to read and comprehend. Adv Neural Inf Process Syst 2015;201:1693–701.
- [11] K. Sirinukunwattana et al., "Locality sensitive deep learning for detection and classification of nuclei in routine colon cancer histology images,"IEEETrans.Med.Imag., vol.35, no.5, pp.1196–1206,May 2016.
- [12] M. Anthimopoulos, S. Christodoulidis, A. Christe, and S. Mougiakakou, "Lung pattern classification for interstitial lung diseases using a deep convolutional neural network," IEEE Trans. Med.Imag., vol.35,no.5, pp.1207–1216, May2016.
- [13] H.-C. Shin et al., "Deep convolutional neural networks for computer aided detection: CNN architectures, data set characteristics and transfer learning,"IEEETrans.Med.Imag.,vol.35,no.5,pp.1285–1298,May 2016.
- [14] G.vanTulderandM.deBruijne,"Combining generative and discriminative representation learning in convolutional restricted Boltzmann machines," IEEE Trans. Med. Imag., vol. 35, no. 5, pp. 1262–1272, May 2016.
- [15] A.Depeursingeetal., Comput.Med.Imag.Graph., vol.36, no.3, pp. 227–238, 2012.
- [16] Zheng Y, Comaniciu D. Marginal space learning. In: Marginal space learning for medical image analysis. Springer; 2014. p. 25–65.
- [17] Ghesu, Florin C., Edward Krubasik, Bogdan Georgescu, Vivek Singh, Yefeng Zheng, Joachim Hornegger, and Dorin Comaniciu," Marginal space deep learning: efficient architecture for volumetric image parsing", IEEE Trans Med Imaging 2016,35:1217–28
- [18] Bier B, Unberath M, Zaech J-N, Fotouhi J, Armand M, Osgood G, et al. X-ray-transform invariant anatomical landmark detection for pelvic trauma surgery. In: Frangi AF, Schnabel JA, Davatzikos C, Alberola-López C, Fichtinger G, editors. Medical Image Computing and Computer Assisted Intervention – MICCAI 2018. Cham: Springer International Publishing; 2018. p. 55–63.
- [19] Akselrod-Ballin A, Karlinsky L, Alpert S, Hasoul S, Ben-Ari R, Barkan E. A region based convolutional network for tumor detection and classification in breast mammography. In: Deep learning and data labeling for medical applications. Springer; 2016. p. 197–205.
- [20] Aubreville M, Krappmann M, Bertram C, Klopfleisch R, Maier A. A guided spatial transformer network for histology cell differenti- ation. In: Association TE, editor. Eurographics workshop on visual computing for biology and medicine. 2017. p. 21–5.
- [21] Aubreville M, Stöve M, Oetter N, de Jesus Goncalves M, Knipfer C, Neumann H, et al. Deep learningbased detection of motion artifacts in probe-based confocal laser endomicroscopy images. Int J Comput Assist Radiol Surg 2018, http://dx.doi.org/10.1007/s11548-018-1836-1.
- [22] Roth HR, Lu L, Farag A, Shin H-C, Liu J, Turkbey EB, et al. DeepOr- gan: multi-level deep convolutional networks for automated pancreas segmentation. In: International conference on medical image computing, computer-assisted intervention. Springer; 2015. p. 556–64.
- [23] Moeskops P, Viergever MA, Mendrik AM, de Vries LS, Benders MJ, Is<sup>\*</sup>gum I. Automatic segmentation of MR brain images with a convolutional neural network. IEEE Trans Med Imaging 2016;35: 1252–61.
- [24] Chen S, Zhong X, Hu S, Dorn S, Kachelriess M, Lell M, et al. Automatic multi-organ segmentation in dual energy CT using 3D fully convolutional network. In: van Ginneken B, Welling M, editors. MIDL.

2018.

- [25] Breininger K, Albarqouni S, Kurzendorfer T, Pfister M, Kowarschik M, Maier A. Intraoperative stent segmentation in X-ray fluoroscopy for endovascular aortic repair. Int J Comput Assist Radiol Surg 2018;13.
- [26] Nirschl JJ, Janowczyk A, Peyster EG, Frank R, Margulies KB, Feldman MD, et al. Deep learning tissue segmentation in cardiac histopathology images. In: Deep learning for medical image analysis. Elsevier; 2017. p. 179–95.
- [27] Middleton I, Damper RI. Segmentation of magnetic resonance images using a combination of neural networks and active contour models. Med Eng Phys 2004;26:71–86.
- [28] Poudel RP, Lamata P, Montana G. Recurrent fully convolutional neural networks for multi-slice MRI cardiac segmentation. In: Reconstruction, segmentation, and analysis of medical images. Springer; 2016. p. 83–94.
- [29] Andermatt S, Pezold S, Cattin P. Multi-dimensional gated recurrent units for the segmentation of biomedical 3D-data. In: Deep learning and data labeling for medical applications. Springer; 2016. p. 142–51.
- [30] Wu G, Kim M, Wang Q, Munsell BC, Shen D. Scalable high-performance image registration framework by unsupervised deep feature representations learning. IEEE Trans Biomed Eng 2016;63:1505–16.
- [31] Schaffert R, Wang J, Fischer P, Borsdorf A, Maier A. Metric-driven learning of correspondence weighting for 2-D/3-D image registration. In: German Conference on Pattern Recognition (GCPR). 2018.
- [32] Miao S, Wang JZ, Liao R. Convolutional neural networks for robust and real-time 2-D/3-D registration. In: Deep learning for medical image analysis. Elsevier; 2017. p. 271–96.
- [33] Yang X, Kwitt R, Styner M, Niethammer M. Quicksilver: fast predictive image registration a deep learning approach. NeuroImage 2017;158:378–96.
- [34] Liao R, Miao S, de Tournemire P, Grbic S, Kamen A, Mansi T, et al. An artificial agent for robust image registration. In: AAAI. 2017. p. 4168–75.
- [35] Krebs J, Mansi T, Delingette H, Zhang L, Ghesu FC, Miao S, et al. Robust non-rigid registration through agent-based action learning. In: Medical Image Computing and Computer-Assisted Intervention– MICCAI. Springer; 2017. p. 344–52.
- [36] Zhong X, Bayer S, Ravikumar N, Strobel N, Birkhold A, Kowarschik M, et al. Resolve intraoperative brain shift as imitation game. In: MIC- CAI Challenge 2018 for Correction of Brainshift with Intra-Operative Ultrasound (CuRIOUS 2018). 2018.
- [37] Diamant I, Bar Y, Geva O, Wolf L, Zimmerman G, Lieberman S, et al. Chest radiograph pathology categorization via transfer learning. In: Deep learning for medical image analysis. Elsevier; 2017. p. 299–320.
- [38] De Fauw JR, Ledsam B, Romera-Paredes S, Nikolov N, Tomasev S, Blackwell H, et al. Clinically applicable deep learning for diagnosis and referral in retinal disease. Nat Med 2018;24:1342.
- [39] Aubreville M, Knipfer C, Oetter N, Jaremenko C, Rodner E, Denzler J, et al. Automatic classification of cancerous tissue in laserendomi- croscopy images of the oral cavity using deep learning. Sci Rep 2017;7:41598-017.
- [40] Carneiro G, Nascimento J, Bradley AP. Deep learning models for classifying mammogram exams containing unregistered multi-view images and segmentation maps of lesions. In: Deep learning for med- ical image analysis. Elsevier; 2017. p. 321–39.
- [41] Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, et al. Dermatologist-level classification of skin cancer with deep neural net- works. Nature 2017;542:115.
- [42] Shi, S., Wang, Q., Xu, P., and Chu, X. "Benchmarking state-of-the-art deep learning software tools." 2016 7th International Conference on Cloud Computing and Big Data (CCBD). IEEE, 2016.
- [43] Miotto, Riccardo, F Wang, S Wang, X Jiang, and J.T. Dudley,"Deep learning for healthcare: review, opportunities and challenges." Briefings in bioinformatics 19.6,2017, 1236-1246.
- [44] Correia RB, Li L, Rocha LM. Monitoring potential drug interactions and reactions via network analysis of instagram user timelines. Pac Symp Biocomput 2016;21:492–503.
- [45] Nikfarjam A, Sarker A, O'Connor K., et al. Pharmacovigilance from social media: mining adverse drug reaction mentions using sequence labeling with word embedding cluster features. J Am Med Inform Assoc 2015;22:671–81
- [46] Gilad-Bachrach R, Dowlin N, Laine K., *et al.* CryptoNets: applying neural networks to encrypted data with high throughput and accuracy. In: International Conference on Machine Learning, New York, NY, USA, 2016, 201–10.
- [47] Yao AC. Protocols for secure computations. In: 23rd Annual Symposium on Foundations of Computer Science (SFCS 1982), Los Angeles, CA, USA, 1982, 160–4.
- [48] Abadi M, Chu A, Goodfellow I., et al. Deep learning with differential privacy. In Proceedings of the 2016 ACM SIGSAC Conference on Computer and Communications Security, 2016, 308–18
- [49] Shokri R, Shmatikov V. Privacy-preserving deep learning. In: *Proceedings of the 22<sup>nd</sup> ACM SIGSAC Conference on Computer and Communications Security*, Denver, CO, USA, 2015, 1310–21.
- [50] Hochreiter S, Schmidhuber J. Long short-term memory. Neural Comput 1997;9:1735–80.