

OPEN ACCESS INTERNATIONAL JOURNAL OF SCIENCE & ENGINEERING SEMANTIC SEGMENTATION USING DEEP NEURAL NETWORKS IN MEDICINE – A SURVEY

Chandrakiran Dubey¹, Stephen Raj², Suresh Munuswamy^{*3}, Ajitha Katta⁴, Girija Chetty⁵

Research Scholar, Health Informatics, PHFI-Indian Institute of Public Health, Hyderabad, India¹² Assistant Professor, Health Informatics, PHFI-Indian Institute of Public Health, Hyderabad, India³ Associate Professor, School of Medical Sciences, University of Hyderabad, Hyderabad, India⁴ Associate Professor, Multimodal Systems & Information Fusion Group, University of Canberra, Canberra, Australia⁵ *chandrakiran.dubey@iiphh.org*¹, *raj.s@iiphh.org*², *s.munuswamy@iiphh.org*³, *kasmd@uohyd.ernet.in*⁴, *girija.chetty@canberra.edu.au*⁵

Abstract: It has always been the ardent pursuit of man to extend his capabilities through tools and technology, and one of the most promising technologies developed in the recent years is Computer Vision (CV). Though we have come a long way in this technology, image segmentation or scene understanding still remains one of the pivotal, yet a very difficult task in the field of CV. Lately, the availability of powerful graphics processing units coupled with complex image processing algorithms made CV a viable and promising tool. With the advent of deep neural networks, pixel-level segmentation and object recognition are reaching human-level speeds and accuracies, if not better. The benefits thereof, especially in the medical field, are only limited by our imagination. Its prospects are being explored in every phase of the medical field, like in early identification of diseases, faster and better diagnostics, impeccable micro-surgical abilities, better prediction of disease recurrence or patient recovery time, and reliable management suggestions in almost every specialty. In this paper, we attempt to review the recent work on semantic segmentation using deep neural networks in the field of medicine. Semantic segmentation has been studied on a wide range of anatomical systems, especially since well-trained models like ImageNet have been available since 2012. In just the last 5 to 10 years, there have been at least 30 well researched articles published in this field, some of which are very promising with highest accuracies achieved in their respective fields. As expected, the most explored field seems to be cancer, in various medical systems like neurology, respiratory, reproductive, etc., while other systems generally have also been studied like cardiovascular, endocrine, urinary, etc. Other interesting applications were in pretreatment risk analysis and forensic medicine.

Keywords: Medical Imaging, Computer Vision, Deep Learning, Machine Learning, Convolutional Neural Networks, Semantic Segmentation

I INTRODUCTION

------ ·

As humans continue to try to understand and maneuver the world around them, their dependence on machines continues to increase, and hence the need for machines with more human-like, but better, capabilities. Vision being one of the most important channels of observation of the situation at hand, researchers has employed machines to help them see better, faster, deeper, closer, farther, etc. In the field of medicine, healthcare providers rely on scopes, microscopes, x-rays, CTs, MRIs, PET scans, nuclear medicine, etc., to diagnose and treat patients; and in all of these methods, the results have to be scanned by human vision carefully, through every millimeter for abnormalities.

•

It is estimated that one in five patients may be diagnosed wrongly [1] and that the diagnostic error is the most common cause of malpractice suits filed on radiologists [2]. Among radiologists, the inter-observer variation is a real concern. For example, even in plain radiograph interpretation there was a 5-9% rate of disagreement in emergency department [3]. A 61% of cancer misdiagnosis (false positives) was observed in screening mammography [4]. A study on re-interpreting 60 abdominal and pelvic CTs found a staggering 32% discrepancy in intra-observer variation, along with a 26% in inter-observer variation. In the case of CTs and MRIs, there is a significant discrepancy rate (13% major and 26% minor) between specialist neuroradiology second opinion and general radiologists [5]. Analyzing screening mammograms performed in the US in 2013, the discrepancy rate had a significant effect on patient morbidity and anxiety. Misinterpretations of cancer related CT scans have been reported in 31-37% of cases [6]. If we look into it a bit deeper, perceptive errors, as opposed to cognitive errors, account to about 60% to 80% [7].

To tackle this pivotal issue, the prospects of machines diagnosing or aiding in diagnosing diseases more accurately has been studied widely. Technology has come a long way since the time of Larry Roberts (1960) and David Marr (1978) at MIT, who pioneered the study of computer vision and scene understanding. Computers started looking at human body fluids, radiological reports, sonograms, electrograms, and scope videos to help humans in reducing human error or detecting a disease faster. When a computer program tries to decipher an image, there are many different stages or approaches, like turning the image to grayscale, then trying to find lines/edges, segmentation, object localization, detection and labelling. Some applications try to reduce the dimensionality to simplify the process. Some applications find objects in an image based on some statistical algorithms, and then identify those objects based on feature extraction and matching with a database of object However, due to the sheer variety and features. unconventionality in the shapes or presentations of human anatomy, the task of separating objects in a medical image and identifying them and their abnormalities has been nothing less than a herculean task.

The answer to this seems to be lying in a process called image segmentation which though can be perceived as a fundamental part of image analysis, seems to have a significant effect on the rest of the processes that leads to object recognition and labelling. To segment medical images, even though there have been some working medical applications developed which are based on techniques such as thresholding, supervised and unsupervised clustering, and geometric deformable models, they seem to be limited in Ma et al. reviewed segmentation their capabilities. algorithms used for medical images and found that thresholdbased algorithms, though efficient, suffer from sensitivity to noise and difficulty in application to multi-channel images. Segmentation accuracy can be improved if supervised classification algorithms are properly modeled, even when structures are blurred or are influenced by noise. When there is a lack in number of samples or there is a large variation in shape, unsupervised classification algorithms can prove to be

very efficient. Albeit, the above techniques depend largely on the size and accurate demarking of the training sets along with proper definition of parameters, position of initial points and the number of clusters [8]. The fact remains that these techniques face a huge challenge because of the large variations in organ shape and structures in medical images.

Semantic segmentation (SS), is a different approach that seems to be giving encouraging results lately. SS attempts to classify each pixel in the image based on its discriminative characteristics like intensity, relativity, neighborhood, color, etc. Prior object knowledge is not necessary for semantic segmentation, which is a major advantage with this tool, making it a very useful step while dealing with human anatomy in medical images.





A segmented image, as shown in Figure 1, can then be used as a basis to analyze the image further for deeper insights, like counting cells or microorganisms, organ size or volume calculation, detecting abnormal shapes or appearances, etc. The increase in demand for better segmentation models, coupled with the ascent of complex deep learning models, has paved the way to even more enthusiastic research and resource allocation. Here, we attempt to review recently published work on the application of deep learning models to semantic segmentation in the field of medicine.

II MATERIALS AND METHOD

A comprehensive search was carried out in PubMed for papers with keywords deep learning, neural networks, image segmentation and medicine. Elimination criteria was where either deep neural network was not employed or semantic segmentation technique was not used. In order to limit the review to the specific task at hand, this paper tries to avoid articles dealing with 3D images/volumetric analysis as much as possible, though there could be an overlap in some places.

III TECHNOLOGIES

A. Deep Convolutional Neural Networks

Deep convolutional neural networks (DNN) are a type of artificial neural networks which are inspired by the

way neurons are connected and organized in a human visual cortex. Cortical neurons respond to stimuli in a region called the receptive field, which partially overlap and tile the visual field. This model of stimulus reception and delegation to a specific neuron within its specific field is mathematically cloned by a convolution module. As depicted in Figure 2, there are mainly four main operations at work in convolutional neural networks (CNN): convolution, pooling or subsampling, classification and sometimes non-linearity based on the requirement.

A.1) Convolution: Basically, the purpose of convolution is to extract features from the input image using small squares of data. Computers interpret images as a matrix of pixel values. The small square matrices (filters/kernels) of a particular size are slid through the image to understand what is in the image. Filters extract what are called as feature maps. The higher the number of filters, the better the image features extracted, but at the same time there is always a tradeoff between the processing resources/speed versus the number of filters, filter size, stride, depth of the architecture, etc.

A.2) **Non-Linearity:** Most of the real-world data is non-linear, especially the medical/anatomical data, and this complexity is addressed by the non-linear operators like ReLU, tanh, or sigmoid in combination with the regular convolutional layers.

A.3) *Pooling*: This operation helps reduce the dimensionality of feature maps, gradually decreasing the size of the input at each layer. Pooling works by representing the given matrix in a smaller size. Max pooling works by taking the maximum or largest element from the feature map. There are other methods like average pooling (average of the matrix), sum (sum of the matrix), etc.

A.4) Classification: Based on the training dataset, this fully connected layer classifies the input image, using the high-level features extracted from prior layers using various classifiers like SVM, Softmax, etc.



NEURAL NETWORKS

Guo et al. did a comprehensive review of the best approaches in semantic segmentation (in general) using deep neural networks, summarizing the strengths, weaknesses, and major challenges [9]. Shi et al. tried to review the major applications of neural networks in medical image processing and the major strengths and weakness thereof [10]. Jiang et al provide a focused literature survey on recent neural network developments in computer-aided diagnosis, medical image segmentation and edge detection towards visual content analysis, and medical image registration for its preprocessing and post-processing, with the aims of increasing awareness of how neural networks can be applied to these areas and to provide a foundation for further research and practical development [11].

The articles have been divided into two main categories, applications in oncology versus non-oncological applications, and then subdivided into organ systems of the human body. A couple of general applications in medicine are also talked about at the end.

A. Oncology Related Applications

One of the most studied fields in medicine today would be that of cancers with a significant effort in early detection along with treatment optimization and better outcome prediction. Application of semantic segmentation using DNN to this field of study is presented below:

A.1) Nervous System

A modified fully convolutional network was used by Ronnenberger et al., using a contracting path (a typical CNN model) and an expansive path (upsampling and upconvolution) with a total of 23 convolutional layers. The U-Net architecture achieved a very good performance on a cell segmentation task in light microscopic images that contained Glioblastoma-astrocytoma U373 cells on a polyacrylimide substrate recorded by phase contrast microscopy. Their model presents a network and training strategy that relies on the strong use of data augmentation to use the available annotated samples more efficiently [12]. Pereira et al. proposed an automatic segmentation method based on CNN, with small 3×3 kernels which permits the designing of a deeper architecture for brain tumor segmentation in MRI images. They used intensity normalization as a preprocessing step, which together with data augmentation proved to be very effective [13]. Kamnitsas et al. have proposed a dual pathway, 11-layers deep, three-dimensional CNN for the task of brain lesion segmentation. They have devised an efficient and effective dense training scheme which joins the processing of adjacent image patches into one pass through the network while automatically adapting to the inherent class imbalance present in the data [14]. Choi and Jin worked on automated segmentation of brain structures and developed a fast and accurate method for the striatum segmentation using deep convolutional neural networks [15]. Xu et al. postulated that an automatic analysis of these images could reduce the load on the pathologists while at the same time eliminating

the human error. They successfully transferred ImageNet knowledge as deep convolutional activation features to the classification and segmentation of histopathology images with little training data. Their approach showed state-of-theart performance on a brain tumor (won the MICCAI brain tumor challenge contest for segmentation) and also colon cancer datasets. They successfully distinguished necrosis versus non-necrosis regions from glioblastoma multiforme histopathology images [16].

Convolutional neural networks, though successful in computer vision, lack the natural ability to incorporate the anatomical location in their decision-making process, thereby hindering success in some medical image analysis tasks. To tackle this issue, Ghafoorian et al. propose several deep CNN architectures that consider multi-scale patches or take explicit location features while training. Applying this technique to white matter hyperintensities, also known as leukoaraiosis or white matter lesions (a common finding on brain MR images of patients diagnosed with brain related diseases), they achieved close to human level performance [17]. AlBadawy et al. assessed the effect of cross-institutional (data from two different institutions) training on the performance of CNNs on automatic glioblastoma segmentation and found that there was a very strong effect of selecting data from multiinstitutional setting, although they did not investigate the reasons behind this [18]. Milletari et al. proposed a novel approach to perform segmentation by leveraging the abstraction capabilities of CNN. The method is based on Hough voting, a strategy that allows for fully automatic localization and segmentation of the anatomies of interest, especially the deep brain regions [19]. Wang et al. have tried to solve the problem of randomness of brain tumors' spatial location by using the model of CNN in the deep learning approach to cope with classification and labeling tasks of brain tumor images [20]. Wang et al. have developed a novel deep learning-based interactive segmentation framework by incorporating CNNs into a bounding box and scribble-based segmentation pipeline. They propose image-specific finetuning to make a CNN model adaptive to a specific test image, which can be either unsupervised (without additional user interactions) or supervised (with additional scribbles); and also, they propose a weighted loss function considering network and interaction-based uncertainty for the fine-tuning. They applied this framework to two applications: 2D segmentation of multiple organs from fetal Magnetic Resonance (MR) slices, where only two types of these organs were annotated for training; and 3D segmentation of brain tumor core (excluding edema) and whole brain tumor (including edema) from different MR sequences, where only the tumor core in one MR sequence was annotated for training [21].

Zhao et al. proposed a novel brain tumor segmentation method developed by integrating fully convolutional neural networks (FCNNs) and Conditional Random Fields (CRFs) in a unified framework to obtain segmentation results with appearance and spatial consistency. The approach trains three segmentation models using 2D image patches and slices obtained in axial, coronal and sagittal views respectively, and combine them to segment brain tumors using a voting based fusion strategy [22].

Valverde et al. have presented a novel automated method for White Matter lesion segmentation of Multiple Sclerosis patient images. Their approach is based on a cascade of two 3D patch-wise CNN [23]. A method for automatic segmentation of MR brain images into a number of tissue classes using CNN was presented by Moeskops et al. [24]. Their method uses multiple patch sizes and multiple convolution kernel sizes to obtain precise segmentation details. Chen et al. proposed a novel framework to automatically segment stroke lesions in diffusion-weighted MR imaging. The framework consists of two CNNs: one an ensemble of two DeconvNets (Noh et al. [26]), which is the EDD Net; the second CNN is the multi-scale convolutional label evaluation net (MUSCLE Net), which aims to evaluate the lesions detected by the EDD Net in order to remove potential false positives [25]. Thus, a considerable amount of work seems to have been done on detecting abnormalities in brain images and now we move on to the other anatomical systems.

A.2) Reproductive System

Ciresan et al. in 2013 used deep max pooling CNN to detect mitosis in breast histology images. Using as context a patch centered on the pixel, the networks were trained to classify each pixel in the images. However, this approach suffered from slow speeds and redundancy along with a tradeoff between localization accuracy and use of context [27].

A.3) Respiratory System

The importance of lung nodule segmentation from computed tomography images in lung cancer diagnosis cannot be over stated, but heterogeneity and similarity in visual characteristics between nodules and their surroundings make nodule segmentation a complex task. Wang et al. propose a data-driven model, Central Focused Convolutional Neural Network (CF-CNN), to segment lung nodules from heterogeneous CT images [28]. They tackle the image voxel (3D version of pixel) classification issue with a novel central pooling layer retaining much information on voxel patch center, followed by a multi-scale patch learning strategy. In addition, they designed a weighted sampling to facilitate the model training, where training samples are selected according to their degree of segmentation difficulty.

A.4) Integumentary System

Jafari et al. proposed a deep neural network-based skin image segmentation and accurate extraction of a lesion region that performed better than the state-of-the art algorithms currently available. The use of standard cameras for image capture, which translates to cheaper costs and ubiquitous availability of the equipment, is worth mentioning [29]. Bi et al. proposed a working method to segment dermoscopic images via multistage fully convolutional networks [30]. This approach claims to overcome the current hurdles in this technique where the existing segmentation methods tend to over- or under-segment the lesions when they have fuzzy boundaries, low contrast, inhomogeneous textures, or artifacts. Furthermore, fine tuning of a huge number of parameters affects the performance of the current methods along with their dependence on preprocessing techniques, like hair removal and illumination correction.

A.5) Digestive System

Kainz et al. achieved good accuracy with deep neural network-based approach for segmentation and classification of glands in tissue of benign and malignant colorectal cancer [31]. Their model used two distinct CNNs, one to separate glands from background and the other to identify gland-separating structures, achieving a tissue classification accuracy of 98% and 95%.

A.6) Skeletal System

Xu et al. employed two CNNs (V-Net and W-Net) to segment and detect bone lesions in multiple myeloma on Ga-Pentixafor PET/CT scans, and showed that deep learning method can leverage multimodal information for spatial feature representation [32]. They also showed that W-Net obtained the best result for segmentation and lesion detection, outperforming traditional machine learning methods such as random forest classifier (RF), k-Nearest Neighbors (k-NN), and support vector machine (SVM).

B. Non-Oncology Applications

B.1) Cardiovascular System

Avendi et al. showed that deep learning algorithms can be effectively used for automatic segmentation of the right ventricle from cardiac MRI using a fully automatic learning-based method [33]. Tan et al. tried the same with left ventricle but with a different approach [34]. Although the aim was to segment the ventricle using CNN, they did not go with the pixel-based segmentation, but rather used parameter regression, which allows the network to inherently reflect domain-specific physical constraints. They have used CNN regression to infer LV segmentation task in terms of the radial distances between the LV center point and the endoand epicardial contours in polar space.

B.2) Endocrine System

Ma et al. used cascade DNN to develop a very effective fully automatic detection of thyroid nodules from

2D ultrasound images [35]. Specifically, they employed a deep CNN to learn the segmentation probability maps from the ground truth data. Then, all the segmentation probability maps are split into different connected regions by the splitting method. Finally, another deep CNN is used to automatically detect the thyroid nodules from ultrasound thyroid images.

Cai et al. used a new deep neural network architecture for pancreas segmentation, via tailor-made CNN followed by convolutional long short-term memory network to regularize the segmentation results on individual image slices [36]. The contextual regularization permits to enforce the pancreas segmentation spatial smoothness explicitly. Combined with the proposed Jaccard loss function for CNN training to generate threshold-free segmentation results, their quantitative pancreas segmentation results improve the previous state-of-the-art approaches on both CT and MRI datasets.

B.3) Nervous System

Xu et al. worked on segmenting the pigment epithelium detachment (PED), from optical coherence tomography images to reduce the time consuming manual interpretation which is also prone to error [37]. They proposed a novel DNN-based framework to automatically segment PEDs in polypoidal choroidal vasculopathy (PCV) patients. This approach employs a dual-stage DNN learning, first learns the BM layers on images via DNN and then employs the obtained BM layers as constraints to assist another DNN to segment PED regions. Xiao et al. have created an open-source, fully automated pipeline for the quantification of key values of oxygen-induced retinopathy (OIR) images using deep learning neural networks [38]. OIR is a widely used model to study ischemia-driven neovascularization (NV) in the retina and to serve in proofof-concept studies in evaluating antiangiogenic drugs for ocular as well as non-ocular diseases. Ji et al. propose a model to automatically and accurately segment geographic atrophy (GA) (in age-related macular degeneration) by using spectral-domain optical coherence tomography (SD-OCT) images by constructing a voting system with deep neural networks without the use of retinal layer segmentation [39].

B.4) Urinary System

Measuring total kidney volume (TKV) is a prerequisite to diagnose polycystic kidney disease (PKD). Automating this task would alleviate the inherent variance in human-derived measurements while increasing measurement throughput at the same time. Kline et al. showed that their complete framework performed fully automated segmentation at a level comparable with inter observer variability and that it could be considered as a replacement for the task of segmentation of PKD kidneys by a human [40].

C. Other Applications

C.1) Microscopy

Van Valen et al. used DNN and a supervised machine learning method to robustly segment fluorescent images of cell nuclei as well as phase images of the cytoplasm's of individual bacterial and mammalian cells from phase contrast images without the need for a fluorescent cytoplasmic marker [41].

C.2) Pretreatment Risk Analysis

Many physicians depend on eyeballing for pretreatment risk stratification to assess patients' capability to tolerate major surgery or chemotherapy, which is inherently subjective and prone to quantification errors. The concept of morphometric age derived from cross-sectional imaging has been found to correlate well with outcomes such as length of stay, morbidity, and mortality. Lee et al. propose a fully automated deep learning system for the segmentation of skeletal muscle cross-sectional area on an axial computed tomography image taken at the third lumbar vertebra [42]. They utilized a fully automated deep segmentation model derived from an extended implementation of a fully convolutional network with weight initialization of an ImageNet pre-trained model, followed by post processing to eliminate intramuscular fat for a more accurate analysis. Accurate segmentation of organs-at-risks (OARs) is the key step for efficient planning of radiation therapy for head and neck cancer treatment. Ibragimov et al. demonstrated accurate segmentation of most OARs using CNN in head and neck CT images, although inclusion of additional information like MR images could enhance the outcome [43]. Ibragimov et al. in consecutive work showed that CNNs and anatomical analysis can be used for accurate segmentation of portal vein for liver radiotherapy planning, a task with many challenges like low vasculature contrast, complex anatomy and image artifacts, fiducial markers and vasculature stents [44].

C.3) Forensic Medicine

Ebert et al. ventured to assess the potential for automated image analysis of radiological images in forensic medicine [45]. They used two separate networks, one to classify images into hemopericardium/not hemopericardium and the other to segment the blood content, to automate the detection of hemopericardium on post mortem CT images, which can be used as a triage tool to better identify cases with a possibly non-natural cause of death, especially when high caseloads make it impossible to perform autopsies on all cases.

V DISCUSSION

It would not come as a surprise that a significant effort in this field seems to be directed towards the most pressing issues in the medical field, such as cancer (Figure 3), especially of the brain, has been studied widely. Various approaches have been tried, like dual paths (contracting path and expansive path) with up-sampling and up-convolution methods, fine tuning of a huge number of parameters, etc., yielding better performance. The dependence of these methods on pre- and post-processing techniques cannot be completely ruled out, at least for now. For example, Hough voting, a strategy that allows for fully automatic localization and segmentation of the anatomies of interest, especially the deep brain regions, was used by Milletari et al. Smaller kernels allowed deeper architecture, which when used again with preprocessing steps and data augmentation were found to be more efficacious. Some models simply used pretrained ImageNet models and some trained their models completely on their data, while others used multi-scale patches or took explicit location features to incorporate anatomical location details, etc. AlBadawy et al. observed that data from multiinstitutional setting had a very strong effect on better outcomes by integrating FCNNs and Conditional Random Fields (CRFs).



Figure 3 Semantic Segmentation using DNN in Medicine.

Moeskops et al. used multiple patch sizes and multiple convolution kernel sizes to obtain precise segmentation details while others used methods like Central Focused CNN. Jafari et al. used standard cameras for image capture in skin image segmentation, an approach that could see a good demand in the future, when and where it is possible. Xu et al. employed two CNNs (V-Net and W-Net) to segment and detect bone lesions in multiple myeloma on Ga-Pentixafor PET/CT scans. Applications in cardiology were promising with right and left ventricle segmentation which was an interesting application where fully automated training was employed in one case, and in the other, a CNN regression was only used to infer the segmentation task. Ma et al. used probability maps split into different connected regions in training, and later used another deep CNN to detect nodules. Dual stage DNN Learning and other voting systems were employed in ophthalmology related applications to detect retinopathies and degenerations. Table 1 lists the significant technologies used against the objects of interest worked on.

Author	Technology/Combina tion	Organ/Object of Interest
Ronnenberger et al. (2015)	FCNN	Glioblastoma-astrocytoma U373 cells
Kamnitsas et al(2017)	FCNN	Brain Lesion Segmentation
Choi and Jin(2016)	FCNN	Striatum Segmentation
Xu et al.(2017)	FCNN	Glioblastoma Multiforme
Ghafoorian et al.(2017)	FCNN	White Matter Hyperintensities
AlBadawy et al. (2018)	FCNN	Glioblastoma Segmentation
	CNN with Image Specific	2D Segmentation of Multiple Organs of Fetal and 3D
Wang et al. (2018)	Fine Tunning	Segmentation of Core Brain Tumor
Zhao et al.(2018)	FCNNS ,CRFs	Brain Tumor Segmentation
Kamnitas et al. (2017)	3DCNN, CRF	Brain Lesion Segmentation
Milletari et al. (2017)	Hough CNN	Brain Region Segmentation
Moeskops et al. (2016)	CNN	Brain Tissue Classification
Wang et al. (2017)	Multi-Pooling CNN	Classification and Labelling of Brain Tumor Tissue
Pereira et al. (2016)	CNN	Brain Tumor Segmentation
Avendi et al. (2017)	CNN	Right Ventricle Segmentation
Chen et al.(2017)	CNN	Ischemic Lesion Segmentation
Ibragimov and Xing(2017)	CNN	Segmentation of Organs-at-Risks in Head and Neck
Jafari et al. (2017)	CNN	Accurate Extraction of a Lesion Region
Ji et al.(2018)	CNN	Automated Geographic Atrophy Segmentation
		Segmentation and Classification of Tissues in
Kainz et al.(2017)	CNN	Corectal Cancer
	Artificial Multi-observer	
Kline et al. (2017)	CNN	Segmentation of Polycystic Kidneys
Lee et al.(2017)	CNN	Muscle Quantification
Tan et al.(2017)	CNN Regression	Left Ventricle Segmentation
		Automated Lesion Segmentation in Multiple Sclerosis
Valverde et al. (2015)	CNN	and Filling
Van Valen et al. (2016)	CNN	Quantitative Analysis of Individual Cells in Live-Cell

Table 1 Technologies used – object of interest.

Microscopic applications to segment cell nuclei was another important research that could take a significant amount of load off the pathologists. The use of CNNs in pretreatment risk analysis was an interesting application where one could quantify patient's tolerance capabilities and readiness to undergo surgeries or chemo/radio therapies. Finally, detecting the hemopericardium in postmortem images to automate segregation of non-natural deaths is also a good application where automation could be resource economic.

VI CONCLUSION

A majority of the research in semantic segmentation using deep neural networks seems to be dedicated to cancer related applications, especially tumor segmentation in the brain. Other systems also included in the cancer related segmentation studies were lung nodules, skin images, breast, and bone lesions. Non-cancer related applications were in identifying cardiac structures like ventricles, thyroid nodules, pancreas, abnormalities in the eye, kidney volume measurement, cell nuclei segmentation, etc. Other interesting applications were also in pretreatment risk analysis, before surgical procedures or chemo or radiotherapies, and in forensic medicine where the detection of hemopericardium was studied. The results have been very promising and stateof-the-art, winning global challenges in the respective fields. The ubiquitous motivating factors in these efforts seem to be to reduce human error and improve diagnostic speeds. The need in this research is quality data that is labelled/curated/annotated.

The sheer variety in approaches and models along with their combinations call for a systemic study of the models with their advantages and disadvantages along with the combinations thereof. The dependence on pre- and postprocessing techniques and their efficacy needs to be rated on a scale along with their specialties and specific point of applications. Thus, better combinations and approaches of models with algorithms will continue to be experimented for a better throughput with faster and accurate results.

REFERENCES

- Berner, Eta S., and Mark L. Graber. "Overconfidence as a Cause of Diagnostic Error in Medicine." *The American Journal of Medicine* 121, no. 5 Suppl (May 2008): S2-23. https://doi.org/10.1016/j.amjmed.2008.01.001.
- [2] Whang, Jeremy S., Stephen R. Baker, Ronak Patel, Lyndon Luk, and Alejandro Castro. "The Causes of Medical Malpractice Suits against Radiologists in the United States." Radiology 266, no. 2 (February 2013): 548–54. https://doi.org/10.1148/radiol.12111119.
- [3] Robinson, P. J., D. Wilson, A. Coral, A. Murphy, and P. Verow. "Variation between Experienced Observers in the Interpretation of Accident and Emergency Radiographs." *The British Journal of Radiology* 72, no. 856 (April 1999): 323–30. https://doi.org/10.1259/bjr.72.856.10474490.
- [4] Hubbard, Rebecca A., Karla Kerlikowske, Chris I. Flowers, Bonnie C. Yankaskas, Weiwei Zhu, and Diana L. Miglioretti. "Cumulative Probability of False-Positive Recall or Biopsy Recommendation after 10 Years of Screening Mammography: A Cohort Study." *Annals of Internal Medicine* 155, no. 8 (October 18, 2011): 481–92. https://doi.org/10.7326/0003-4819-155-8-201110180-00004.
- [5] Briggs, G. M., P. A. Flynn, M. Worthington, I. Rennie, and C. S. McKinstry. "The Role of Specialist Neuroradiology Second Opinion Reporting: Is There Added Value?" *Clinical Radiology* 63, no. 7 (July 2008): 791–95. https://doi.org/10.1016/j.crad.2007.12.002.
- [6] Siewert, Bettina, Jacob Sosna, Ann McNamara, Vassilios Raptopoulos, and Jonathan B. Kruskal. "Missed Lesions at Abdominal Oncologic CT: Lessons Learned from Quality Assurance." *Radiographics: A Review Publication of the Radiological Society of North America, Inc* 28, no. 3 (June 2008): 623–38. https://doi.org/10.1148/rg.283075188.
- [7] Bruno, Michael A., Eric A. Walker, and Hani H. Abujudeh. "Understanding and Confronting Our Mistakes: The Epidemiology of Error in Radiology and Strategies for Error Reduction." *Radiographics: A Review*

WWW.OAIJSE.COM

Publication of the Radiological Society of North America,Inc35,no.6(October2015):1668–76.https://doi.org/10.1148/rg.2015150023.

- [8] Ma, Zhen, João Manuel R. S. Tavares, Renato Natal Jorge, and T. Mascarenhas. "A Review of Algorithms for Medical Image Segmentation and Their Applications to the Female Pelvic Cavity." *Computer Methods in Biomechanics and Biomedical Engineering* 13, no. 2 (April 1, 2010): 235–46. https://doi.org/10.1080/10255840903131878.
- [9] Guo, Yanming, Yu Liu, Theodoros Georgiou, and Michael S. Lew. "A Review of Semantic Segmentation Using Deep Neural Networks." *International Journal of Multimedia Information Retrieval*, November 24, 2017, 1–7. https://doi.org/10.1007/s13735-017-0141-z.
- [10] Shi, Zhenghao, Lifeng He, Kenji Suzuki, Tsuyoshi Nakamura, and Hidenori Itoh. "Survey on Neural Networks Used for Medical Image Processing." *International Journal of Computational Science* 3, no. 1 (February 2009): 86–100.
- [11] Jiang, J., P. Trundle, and J. Ren. "Medical Image Analysis with Artificial Neural Networks." *Computerized Medical Imaging and Graphics* 34, no. 8 (2010): 617–31. https://doi.org/10.1016/j.compmedimag.2010.07.003.
- [12] Ronneberger, Olaf, Philipp Fischer, and Thomas Brox.
 "U-Net: Convolutional Networks for Biomedical Image Segmentation." In *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015*, 234–41.
 Lecture Notes in Computer Science. Springer, Cham, 2015. https://doi.org/10.1007/978-3-319-24574-4_28.
- [13] Pereira, S., A. Pinto, V. Alves, and C. A. Silva. "Brain Tumor Segmentation Using Convolutional Neural Networks in MRI Images." *IEEE Transactions on Medical Imaging* 35, no. 5 (May 2016): 1240–51. https://doi.org/10.1109/TMI.2016.2538465.
- [14] Kamnitsas, Konstantinos, Christian Ledig, Virginia F. J. Newcombe, Joanna P. Simpson, Andrew D. Kane, David K. Menon, Daniel Rueckert, and Ben Glocker. "Efficient Multi-Scale 3D CNN with Fully Connected CRF for Accurate Brain Lesion Segmentation." *Medical Image Analysis* 36 (2017): 61–78. https://doi.org/10.1016/j.media.2016.10.004.
- [15] Choi, Hongyoon, and Kyong Hwan Jin. "Fast and Robust Segmentation of the Striatum Using Deep Convolutional Neural Networks." *Journal of Neuroscience Methods* 274 (December 1, 2016): 146–53. https://doi.org/10.1016/j.jneumeth.2016.10.007.
- [16] Xu, Yan, Zhipeng Jia, Liang-Bo Wang, Yuqing Ai, Fang Zhang, Maode Lai, and Eric I.-Chao Chang. "Large Scale Tissue Histopathology Image Classification, Segmentation, and Visualization via Deep Convolutional

Activation Features." *BMC Bioinformatics* 18, no. 1 (May 26, 2017): 281. https://doi.org/10.1186/s12859-017-1685-x.

- [17] Ghafoorian, Mohsen, Nico Karssemeijer, Tom Heskes, Inge W. M. van Uden, Clara I. Sanchez, Geert Litjens, Frank-Erik de Leeuw, Bram van Ginneken, Elena Marchiori, and Bram Platel. "Location Sensitive Deep Convolutional Neural Networks for Segmentation of White Matter Hyperintensities." *Scientific Reports* 7, no. 1 (July 11, 2017): 5110. https://doi.org/10.1038/s41598-017-05300-5.
- [18] AlBadawy, Ehab A., Ashirbani Saha, and Maciej A. Mazurowski. "Deep Learning for Segmentation of Brain Tumors: Impact of Cross-Institutional Training and Testing." *Medical Physics* 45, no. 3 (March 2018): 1150– 58. https://doi.org/10.1002/mp.12752.
- [19] Milletari, Fausto, Seyed Ahmad Ahmadi, Christine Kroll, Annika Plate, Verena Rozanski, Juliana Maiostre, Johannes Levin, et al. "Hough-CNN: Deep Learning for Segmentation of Deep Brain Regions in MRI and Ultrasound." *Computer Vision and Image Understanding* 164 (2017). https://doi.org/10.1016/j.cviu.2017.04.002.
- [20] Wang, Feng, Siwei Huang, Lei Shi, and Weiguo Fan. "The Application of Series Multi-Pooling Convolutional Neural Networks for Medical Image Segmentation." *International Journal of Distributed Sensor Networks* 13, no. 12 (December 1, 2017): 1550147717748899. https://doi.org/10.1177/1550147717748899.
- [21] Wang, G., W. Li, M. A. Zuluaga, R. Pratt, P. A. Patel, M. Aertsen, T. Doel, et al. "Interactive Medical Image Segmentation Using Deep Learning with Image-Specific Fine-Tuning." *IEEE Transactions on Medical Imaging* PP, no. 99 (2018): 1–1. https://doi.org/10.1109/TMI.2018.2791721.
- [22] Zhao, Xiaomei, Yihong Wu, Guidong Song, Zhenye Li, Yazhuo Zhang, and Yong Fan. "A Deep Learning Model Integrating FCNNs and CRFs for Brain Tumor Segmentation." *Medical Image Analysis* 43 (January 2018): 98–111.

https://doi.org/10.1016/j.media.2017.10.002.

- [23] Valverde, Sergi, Arnau Oliver, Eloy Roura, Deborah Pareto, Joan C. Vilanova, Lluís Ramió-Torrentà, Jaume Sastre-Garriga, Xavier Montalban, Àlex Rovira, and Xavier Lladó. "Quantifying Brain Tissue Volume in Multiple Sclerosis with Automated Lesion Segmentation and Filling." *NeuroImage : Clinical* 9 (October 28, 2015): 640–47. https://doi.org/10.1016/j.nicl.2015.10.012.
- [24] Moeskops, Pim, Max A. Viergever, Adrienne M. Mendrik, Linda S. De Vries, Manon J. N. L. Benders, and Ivana Isgum. "Automatic Segmentation of MR Brain Images with a Convolutional Neural Network." *IEEE*

Transactions on Medical Imaging 35, no. 5 (2016): 1252–61. https://doi.org/10.1109/TMI.2016.2548501.

- [25] Chen, Liang, Paul Bentley, and Daniel Rueckert. "Fully Automatic Acute Ischemic Lesion Segmentation in DWI Using Convolutional Neural Networks." *NeuroImage*. *Clinical* 15 (2017): 633–43. https://doi.org/10.1016/j.nicl.2017.06.016.
- [26] Noh, Hyeonwoo, Seunghoon Hong, and Bohyung Han.
 "Learning Deconvolution Network for Semantic Segmentation." In *Proceedings of the 2015 IEEE International Conference on Computer Vision (ICCV)*, 1520–1528. ICCV '15. Washington, DC, USA: IEEE Computer Society, 2015. https://doi.org/10.1109/ICCV.2015.178.
- [27] Cireşan, Dan C., Alessandro Giusti, Luca M. Gambardella, and Jürgen Schmidhuber. "Mitosis Detection in Breast Cancer Histology Images with Deep Neural Networks." In *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2013*, 411–18. Lecture Notes in Computer Science. Springer, Berlin, Heidelberg, 2013. https://doi.org/10.1007/978-3-642-40763-5_51.
- [28] Wang, Shuo, Mu Zhou, Zaiyi Liu, Zhenyu Liu, Dongsheng Gu, Yali Zang, Di Dong, Olivier Gevaert, and Jie Tian. "Central Focused Convolutional Neural Networks: Developing a Data-Driven Model for Lung Nodule Segmentation." *Medical Image Analysis* 40 (August 2017): 172–83. https://doi.org/10.1016/j.media.2017.06.014.
- [29] Jafari, M. Hossein, Ebrahim Nasr-Esfahani, Nader Karimi, S. M. Reza Soroushmehr, Shadrokh Samavi, and Kayvan Najarian. "Extraction of Skin Lesions from Non-Dermoscopic Images for Surgical Excision of Melanoma." *International Journal of Computer Assisted Radiology and Surgery* 12, no. 6 (June 2017): 1021–30. https://doi.org/10.1007/s11548-017-1567-8.
- [30] Bi, Lei, Jinman Kim, Euijoon Ahn, Ashnil Kumar, Michael Fulham, and Dagan Feng. "Dermoscopic Image via Multistage Fully Convolutional Segmentation Networks." **Transactions** IEEE on **Bio-Medical** Engineering 64, 9 (2017): 2065-74. no. https://doi.org/10.1109/TBME.2017.2712771.
- [31] Kainz, Philipp, Michael Pfeiffer, and Martin Urschler.
 "Segmentation and Classification of Colon Glands with Deep Convolutional Neural Networks and Total Variation Regularization." *PeerJ* 5 (2017): e3874. https://doi.org/10.7717/peerj.3874.
- [32] Xu, Lina, Giles Tetteh, Jana Lipkova, Yu Zhao, Hongwei Li, Patrick Christ, Marie Piraud, Andreas Buck, Kuangyu Shi, and Bjoern H. Menze. "Automated Whole-Body Bone Lesion Detection for Multiple Myeloma on 68Ga-Pentixafor PET/CT Imaging Using Deep Learning

Methods." Research article. Contrast Media & Molecular Imaging, 2018. https://doi.org/10.1155/2018/2391925.

- [33] Avendi, Michael R., Arash Kheradvar, and Hamid Jafarkhani. "Automatic Segmentation of the Right Ventricle from Cardiac MRI Using a Learning-Based Approach." *Magnetic Resonance in Medicine* 78, no. 6 (December 2017): 2439–48. https://doi.org/10.1002/mrm.26631.
- [34] Tan, Li Kuo, Yih Miin Liew, Einly Lim, and Robert A. McLaughlin. "Convolutional Neural Network Regression for Short-Axis Left Ventricle Segmentation in Cardiac Cine MR Sequences." *Medical Image Analysis* 39 (2017): 78–86. https://doi.org/10.1016/j.media.2017.04.002.
- [35] Ma, Jinlian, Fa Wu, Tian'an Jiang, Jiang Zhu, and Dexing Kong. "Cascade Convolutional Neural Networks for Automatic Detection of Thyroid Nodules in Ultrasound Images." *Medical Physics* 44, no. 5 (May 2017): 1678–91. https://doi.org/10.1002/mp.12134.
- [36] Cai, Jinzheng, Le Lu, Zizhao Zhang, Fuyong Xing, Lin Yang, and Qian Yin. "Pancreas Segmentation in MRI Using Graph-Based Decision Fusion on Convolutional Neural Networks." *Medical Image Computing and Computer-Assisted Intervention: MICCAI ... International Conference on Medical Image Computing and Computer-Assisted Intervention* 9901 (October 2016): 442–50. https://doi.org/10.1007/978-3-319-46723-8_51.
- [37] Xu, Yupeng, Ke Yan, Jinman Kim, Xiuying Wang, Changyang Li, Li Su, Suqin Yu, Xun Xu, and Dagan David Feng. "Dual-Stage Deep Learning Framework for Pigment Epithelium Detachment Segmentation in Polypoidal Choroidal Vasculopathy." *Biomedical Optics Express* 8, no. 9 (September 1, 2017): 4061–76. https://doi.org/10.1364/BOE.8.004061.
- [38] Xiao, Sa, Felicitas Bucher, Yue Wu, Ariel Rokem, Cecilia
 S. Lee, Kyle V. Marra, Regis Fallon, et al. "Fully Automated, Deep Learning Segmentation of Oxygen-Induced Retinopathy Images." *JCI Insight* 2, no. 24 (December 21, 2017). https://doi.org/10.1172/jci.insight.97585.
- [39] Ji, Zexuan, Qiang Chen, Sijie Niu, Theodore Leng, and Daniel L. Rubin. "Beyond Retinal Layers: A Deep Voting Model for Automated Geographic Atrophy Segmentation in SD-OCT Images." *Translational Vision Science & Technology* 7, no. 1 (January 2018): 1. https://doi.org/10.1167/tvst.7.1.1.
- [40] Kline, Timothy L., Panagiotis Korfiatis, Marie E. Edwards, Jaime D. Blais, Frank S. Czerwiec, Peter C. Harris, Bernard F. King, Vicente E. Torres, and Bradley J. Erickson. "Performance of an Artificial Multi-Observer Deep Neural Network for Fully Automated Segmentation of Polycystic Kidneys." *Journal of Digital Imaging* 30, no.

4 (August 2017): 442–48. https://doi.org/10.1007/s10278-017-9978-1.

- [41] Van Valen, David A., Takamasa Kudo, Keara M. Lane, Derek N. Macklin, Nicolas T. Quach, Mialy M. DeFelice, Inbal Maayan, Yu Tanouchi, Euan A. Ashley, and Markus W. Covert. "Deep Learning Automates the Quantitative Analysis of Individual Cells in Live-Cell Imaging Experiments." *PLoS Computational Biology* 12, no. 11 (November 2016): e1005177. https://doi.org/10.1371/journal.pcbi.1005177.
- [42] Lee, Hyunkwang, Fabian M. Troschel, Shahein Tajmir, Georg Fuchs, Julia Mario, Florian J. Fintelmann, and Synho Do. "Pixel-Level Deep Segmentation: Artificial Intelligence Quantifies Muscle on Computed Tomography for Body Morphometric Analysis." *Journal of Digital Imaging* 30, no. 4 (August 2017): 487–98. https://doi.org/10.1007/s10278-017-9988-z.
- [43] Ibragimov, Bulat, and Lei Xing. "Segmentation of Organsat-Risks in Head and Neck CT Images Using Convolutional Neural Networks." *Medical Physics* 44, no. 2 (February 2017): 547–57. https://doi.org/10.1002/mp.12045.
- [44] Ibragimov, Bulat, Diego Toesca, Daniel Chang, Albert Koong, and Lei Xing. "Combining Deep Learning with Anatomical Analysis for Segmentation of the Portal Vein for Liver SBRT Planning." *Physics in Medicine and Biology* 62, no. 23 (November 10, 2017): 8943–58. https://doi.org/10.1088/1361-6560/aa9262.
- [45] Ebert, Lars C., Jakob Heimer, Wolf Schweitzer, Till Sieberth, Anja Leipner, Michael Thali, and Garyfalia Ampanozi. "Automatic Detection of Hemorrhagic Pericardial Effusion on PMCT Using Deep Learning - a Feasibility Study." *Forensic Science, Medicine, and Pathology* 13, no. 4 (December 2017): 426–31. https://doi.org/10.1007/s12024-017-9906-1.