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Research Article

The impact of AI applications in prostate segmentation on improving clinical diagnosis, and treatment: A review of the literature

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Abstract

Prostate cancer is regarded as the second most common cancer in the world. Review of the studies that had been done on this topic for the years 2018-2020 by searching in Scopus, Science Direct, PubMed, and Google Scholar databases. Keywords used in this searching were medical image processing, prostate ultrasound image segmentation, fuzzy segmentation, CNN segmentation, and deep learning segmentation. The overall obtained articles were 4731, after the limitations of the search strategy, there were only 8 articles involved in this study. Findings showed the necessity of prostate segmentation and its role in the diagnosis and treatment improvement; furthermore, there are various approaches to segment prostate gland, but not all of them are suitable to use, due to the accuracy and time limitation. In conclusion, according to the findings of 4 articles, which mean 50% of the included studies, the results stated that using the CNN algorithm and its different approaches is the highest accuracy method that can be used for prostate segmentation.

Keywords: medical image processing, prostate ultrasound image segmentation, fuzzy segmentation, CNN segmentation, and deep learning segmentation.

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Introduction

Prostate cancer (PC) can be regarded as the second recurrent public cancer that had been diagnosed around the world. Its proportion around shows a wide gap, Australia or New Zealand age standardized rate (ASR 86.4/100,000) presented the top, while the in the bottom South-Central Asia were seen (ASR 5.0/100,000) [1-3]. In Malaysia prostate cancer can be graded as the third commonest cancer in men [3]. According to the various races, the Malay males showed the lowest ratio (ASR 5.3/100,000), while the top-ranked rate was found in Chinese men (ASR 9.0/100,000), followed by Indians (ASR 6.1/100,000) [3]. Researchers came out with various studies they noticed that the number of prostate cancers that had been detected were 12-29% for 4.0 - 10.0 ng/ml, 17-37% and for 10.0-20.0 ng/ml, while 40-69% for ≥ 20.0 ng/ml total PSA level. The prostate biopsy of 12 cores unnoticed nearly 37% of PCA in males having a PSA level ranged between 4.0 and 10.0 ng/ml. Furthermore detection of prostate cancer ratio of men with PSA 4-10 ng/ml was 22%-43.5% [4-5], in the Western population, which shows higher grade compared to the Asian population (9.3-26%) [6-7]. However, factors such as aging, race, PSA level, and digital rectal examination findings, with prostate volume may improve the predictive positive value of prostate cancer diagnosing in males having PSA between 4.0 and 10.0 ng/ml [8]. Recent visions from Western and other Asian populations have driven the carious to study and improve the insights of prostate cancer detection ratio amongst Malaysian males with PSA 4.0-10.0 ng/ml. Malaysia is a high middle-income country in Southeast Asia having a multi-ethnic population. It mainly consists of Malays, Chinese, and Indians. To assess the PCA detection ratio by using a transrectal guided biopsy and its correlation with age, race, PSA level, and digital rectal examination with prostate volume, a cross-sectional study was conducted (A.H. Abdal Razack et al 2019)[1].

What is artificial intelligence AI

(Chen et al 2019) introduced Artificial Intelligence is the science that deals with creation a machine that can produce the human intellectual tasks by employing a modeling system that have a building blocks like human neurons such as complex non-linear mathematical model, it is started with human searching ways for thinking, reason, or carry out cognitive functions, then creating these intelligence functions to be performed by a machine. However the human intelligence is complicated such as thinking, imagination, patterns detection, language performance, and memory, but the aim of AI is to help in decision making by achieving some of these intelligence capabilities, such as detecting the differences between two difference patterns, or classifying various types of tissues according to their texture. AI had been used in different fields in the life, medical imaging is one of the important fields that used AI for diagnosis and prediction, it depends on teaching the machine how to detect and differentiate between the normal and abnormal tissues such as PCA [9].

Medical image processing

Absolutely, biomedical images play a crucial role in various aspects of healthcare, from diagnosis to treatment and ongoing patient management. They provide a non-invasive way to

visualize and assess internal structures of the body, eliminating the need for invasive procedures in many cases [10-11]. There are several modalities of medical imaging, each with its own unique strengths and limitations. There are several imaging modalities used for clinical diagnosis such as X-ray which provides a quick and relatively low-cost way to visualize bones and certain tissues. It's commonly used for detecting fractures, lung conditions, and dental issues. While Ultrasound Utilizes sound waves to produce real-time images, making it valuable for monitoring pregnancies, examining soft tissues, and guiding certain medical procedures. However Computed Tomography (CT) contains radiation but still it creates detailed cross-sectional images, allowing for precise visualization of internal structures. It's useful for diagnosing conditions like tumors, injuries, and vascular issues. Finally Magnetic Resonance Imaging (MRI) is one of the most important approaches that Uses powerful magnets and radio waves to create detailed images of soft tissues, making it particularly effective for studying the brain, joints, and abdominal organs [12].

Segmentation

Image segmentation is an essential step in the medical images analysis field. The purpose of such approach is to extract and to figure out the image content into a number of regions such as background and front ground, region of interest ROI based on specific criteria such as selecting all the pixels in a specific region which have significant difference from other pixels in neighboring regions that share the similar features and characteristics. There are some crucial parameters in segmentation used for diagnosis and monitoring such as time, accuracy and sensitivity [13]. The passage discusses the use of multi-modality segmentation techniques in medical image analysis, focusing on clustering algorithms, particularly the fuzzy c-means (FCM) algorithm and its variations. These algorithms are employed for automatic segmentation of medical images, aiming to improve the accuracy and efficiency of the segmentation process. Multi-Modality Segmentation and Pattern Recognition, Multi-modality segmentation involves analyzing medical images acquired from different imaging modalities to enhance segmentation accuracy. Pattern recognition methods are commonly used for this purpose, as they can automatically segment images based on patterns and features present in the data. Clustering algorithms are used in image segmentation to group pixels or voxels with similar characteristics together. The passage highlights two main clustering algorithms. Hard c-means Proposed by MacQueen and James in 1967, this algorithm is used for hard data classification and has been applied to image segmentation. Fuzzy c-means (FCM) algorithm An enhanced version of hard c-means proposed by Bezdek et al in 1984. FCM considers the uncertainty of pixel membership in clusters, leading to improved segmentation results. Spatial information incorporation Chuang et al., (2006) introduced spatial data to cluster centers and membership matrices to improve noise correction and MRI image segmentation. Bias field correction: Algorithms like BCFCM (Ahmed et al, 2002) and robust FCM (Pham et al, 2001) address intensity inhomogeneity artifacts, improving image quality. Fuzzy type 2 theory Hwang (2007) introduced type 2 fuzzy c-means, considering uncertain

membership status and noise signals. However, this approach may still suffer from time-consuming execution. Optimization and Computational Efficiency: Eschrich et al., (2003) optimized the br FCM algorithm to reduce computational time, making it more efficient for large datasets. This version clusters similar examples and utilizes weighted exemplars to expedite the clustering process. In summary, the passage discusses the evolution of clustering algorithms, particularly focusing on the fuzzy c-means (FCM) algorithm and its variations, for multi-modality segmentation of medical images. These algorithms aim to automatically segment images based on patterns and features, addressing challenges like noise, intensity inhomogeneity, and computational efficiency. The research highlights the continuous efforts to enhance the accuracy and practicality of medical image segmentation techniques[21]. There different approaches for image fusion, such as the fuzzy concept [22-23], probability theory [24-25], believe functions [26-27], and machine learning[28-29]have been proposed with success. It is difficult to model the methods based on the probability theory and machine learning using shallow models because they are using different data modalities with different statistical properties. While for the methods based on the fuzzy concept, the fuzzy measure quantifies the grade of membership relative to a decision for each source. Fuzzy operators are applied to fuzzy sets to combine information from multiple sources. This approach allows for the fusion of data from different sources, and it leverages the concept of fuzzy logic to handle uncertainty and imprecision in the data. The passage suggests that deep learning-based methods may have a greater potential to produce superior fusion results compared to conventional techniques. Deep learning networks can automatically learn complex patterns and relationships from large datasets, which may lead to more accurate and robust fusion outcomes. In summary, the passage discusses different approaches to information fusion from multiple sources, including fuzzy set theory, belief function theory, and deep learning-based networks. While traditional methods have limitations related to their underlying concepts, deep learning-based methods are highlighted as having the potential to offer improved fusion results by directly learning the mapping between different sources of information. There are several approaches of deep convolutional neural network had been proposed since 2012, such as Alex Net [30], ZF Net [31], VGG [32], Google Net [33], Residual Net [34], Dense Net [35], FCN [36] and U-Net [37], T. Zhou et al., (2019) stated that there are several success points related to these models in which they do not only provide state-of-the-art performance for image classification, segmentation, object detection, and tracking tasks but moreover, they provide a novel point of view for image fusion. These points can be stated mainly in four reasons: First, deep

learning can learn high-level features on data from the gradual manner which clear the need for domain expertise and hard feature extraction which cannot be seen in the traditional machine learning models. Furthermore, it finds solutions to issues in an end to end manner. Second, the open-source software packages can provide efficient GPU implementations by training the GPU-computing libraries to produce a model that is faster 10-30 times than the CPU. Thirdly, commonly the available datasets such as Image from internet sources can be used for training by the researchers to train and test it with various deep learning models. Finally, the updating of the weights and optimal performance can be obtained by using several available efficient optimization techniques and contribute the final success of deep learning, such as dropout, batch normalization, Adam optimizer, and others, Re LU activation function and its variants [38].

Prostate segmentation

There are various approaches to detecting prostate cancer, including conventional non-imaging screening tests like prostate-specific antigen (PSA) and digital rectal examination (DRE). However, these methods generally lack specificity, meaning they may not accurately distinguish between cancerous and non-cancerous conditions. Ultrasound is highlighted as a valuable screening imaging modality for prostate cancer diagnosis. It is widely available, cost-effective, non-invasive, and safe. Unlike the non-imaging tests, ultrasound provides visual information about the prostate gland and can contribute to more accurate diagnostics. Precise segmentation helps ensure the accurate placement of biopsy needles for obtaining tissue samples from the prostate gland. Accurate segmentation enables the calculation of the prostate gland's volume, which can be important for diagnostic and treatment planning purposes, the significance of accurate prostate segmentation in the context of low-dose-rate (LDR) brachytherapy treatment. This treatment involves implanting radioactive seeds in the prostate gland to target cancerous regions. Precise segmentation of the prostate gland is critical for effectively placing the radioactive seeds in the cancerous area, maximizing treatment success while minimizing damage to healthy tissues. The overarching importance of accurate prostate segmentation plays a vital role in both the diagnostic and treatment phases of prostate cancer management, contributing to better outcomes for patients. In summary, the passage underscores the value of ultrasound as a screening tool for prostate cancer detection and stresses the crucial role of accurate prostate segmentation in ultrasound images. This precision is essential for biopsy guidance, volume calculation, cancer localization, and successful implementation of treatment strategies, particularly in the context of brachytherapy [39].

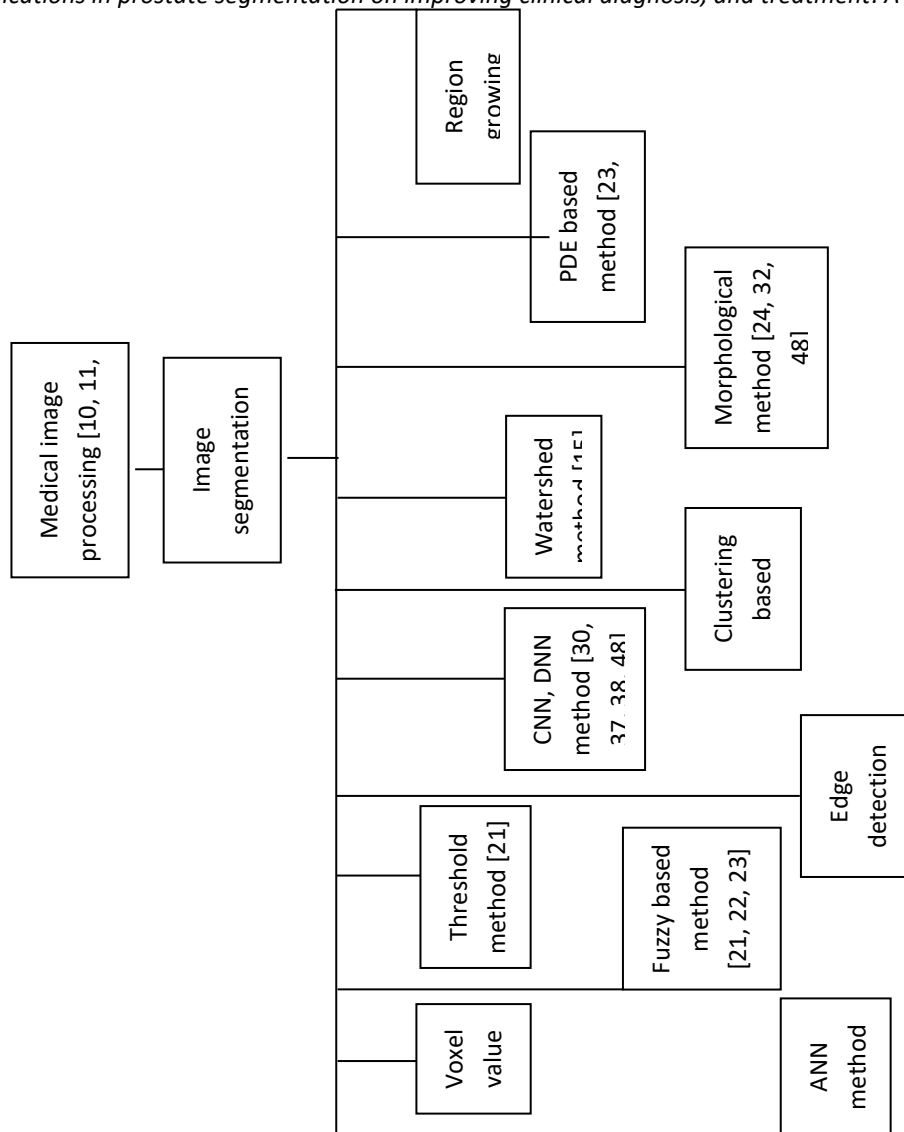


Figure 1: demonstrates the different image segmentation approaches

Literature searching strategy and article selection

This study used searching for articles in science direct, Scopus, PubMed, and Google scholar databases, the searching started by an independent author from (15th November – 20th December). Keywords and terms that had been used in this searching were “prostate ultrasound, prostate cancer, medical image processing, prostate ultrasound image segmentation, fuzzy segmentation, CNN segmentation, and deep learning segmentation.” They were connected to the relevant articles by using “and”, or “or” to find the studies that deals with human clinically and specifically on the prostate gland. The total number of the studies were (4731) articles, this number

had been limited according to the inclusion and exclusion criteria after selecting the articles by the publication year from (2018 – 2020), original articles that had been published as journal articles had been limited to (412) articles, then after removing the duplicated studies and the non-relevant articles with selecting the study language it had become (145) articles, furthermore, we have read the abstract and then some of these articles again removed, the remained studies underwent full-text reading to be limited to only (n=8) articles, all the included articles had been explained briefly according to the author’s name, publication year and place, the method that they used in their studies, and finally their results.

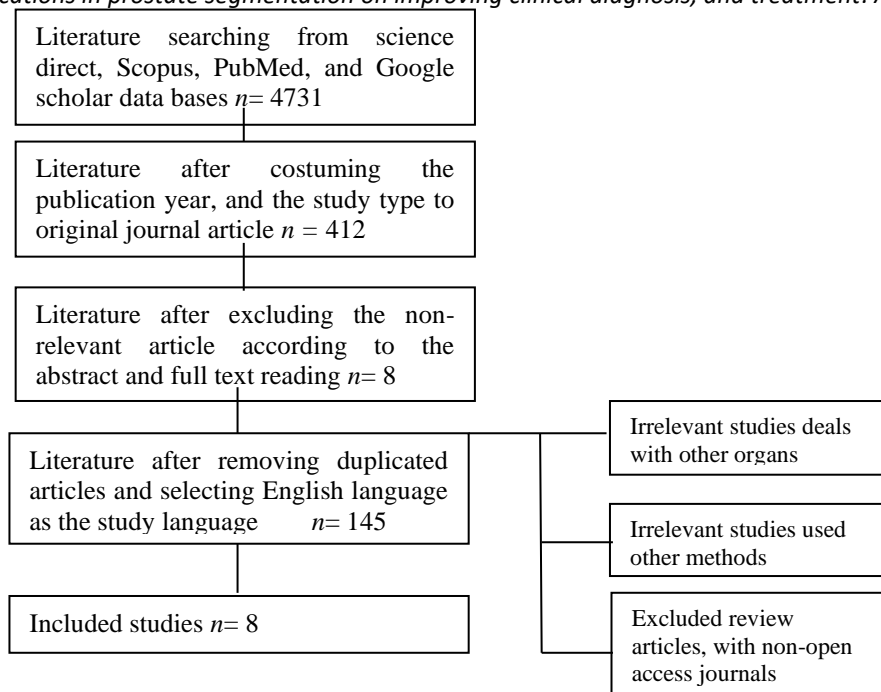


Figure 2: demonstrates the search strategy of the literature

n	Author	Year	Country	Method	Result
1	H. Bi et al [40]	2020	China	Active shape model (ASM) with Rayleigh mixture model Clustering (ASM-RMMC).	The findings stating that using this segmentation method shows less computational complexity with high accuracy achievements that meet the clinical requirements.
2	D. Karimi et al [41]	2019	Canada	CNN	CNN-based medical image segmentation methods performance can be improved significantly by the estimation of model uncertainty and use of prior shape information, especially on difficult images.
3	X. Yang et al [42]	2019	China	The shape constraint is incorporated into the different level set framework. A convex model that can be efficiently solved by a primal-dual hybrid gradient algorithm can be obtained by applying the convex relaxation.	The point distance shape constraint segmentation model shows significant high accuracy to segment organs and lesions with a number of shapes in medical images.
4	N. Ghavami et al [43]	2019	UK	Six different CNNs approaches had been used to segment the prostate patient.	To report the segmentation accuracy the findings recommended that the variance in the accuracy of downstream image analysis tasks that use a data output by automated segmentation approaches, such as CNN's, within a clinical pipeline must have a kind of specificity in selecting among different network architectures.
5	Singh. Shyam .S et al [44]	2019	India	Neural based fuzzy enhancement technique is used in this research. performing the wiener filter in the pre-processing of the images and the contrast enhancement had been obtained by the local transform histogram (LTH). Followed by neural	Findings showed that the highest PSNR value can be achieved by using this method.

				-based fuzzy enhancement and by three steps procedure which are fuzzification, membership function and defuzzification. finally evaluation and comparison of the PSNR and CNR with other studies.	
6	E.M.A. Anas et al [45]	2018	USA	A deep neural network-based real-time prostate segmentation DNN, nad CNN.	The proposed approach shows statistically significant improvement after comparing it with the reported results of the state of the art technique, depending on the mean Dice similarity coefficient of 93%, the mean surface distance error of 1.10 mm and the mean Hausdorff distance error of 3.0 mm.
7	Y. Hu et al [46]	2018	UK	This work describes a method to infer voxel-level transformation from higher-level correspondence information contained in anatomical labels. We argue that such labels are more reliable and practical to obtain reference sets of image pairs than voxel-level correspondence, and CNN.	A median target registration error of 3.6 mm on landmark centroids and a median Dice of 0.87 on prostate glands are achieved from cross-validation experiments, in which 108 pairs of multimodal images from 76 patients were tested with high-quality anatomical labels.
8	Reda. I et al [47]	2018	Egypt	The system is consists of three steps First, using a hybrid approach that combines a level-set model with nonnegative matrix factorization to select the boundaries of the prostate gland. Second, the estimation and normalization of the diffusion parameters then followed by refinement of those apparent diffusion coefficients using a generalized Gaussian Markov random field model.	After conducting 18 diffusion-weighted magnetic resonance imaging data sets to the Experiments for diagnosis as a result 94.4% diagnosis accuracy (sensitivity ¼ 88.9% and specificity ¼ 100%) had been achieved, the result of this study finds promising results of the presented computer-aided diagnostic system.

Table 1: explains the involved studies with the related details of the author, country of publication, publication year, the used method in the study, and their results.

Results and discussion

The necessity of prostate segmentation increased significantly and showed high interesting from the researchers in the present, there are different methods to segment prostate gland some of them are manual, others semi-automated, and the last type is full automated segmentation, but each approach have its limitations in time computing, PSNR value, the segmentation accuracy, and so many other parameters that can be compared to the other approaches to find the best method among them [13]. In this review study, there are only (8) articles remained after limitations of the search strategy according to the year of publication, the imaging modality, keywords, journal type, and the non-relevant articles. A study recently published in (2020) used Active shape model (ASM) with Rayleigh mixture model Clustering (ASM-RMMC) to segment the gland accurately, it starts their method in tow steps. Firstly, depending on Rayleigh mixture model (RMM) for clustering the image regions that shows similar speckle distributions. Then depending on the content-based clustered images initializing and deforming the ASM model can be guided and performed. Findings showed that using of this segmentation method shows less computational complexity with high accuracy achievements that meets the clinical

requirements, which means that the procedure is simple and not complex or not need for many algorithms to be involved which reduces time, and also its accuracy is at high level depending on the parameters that they found in the study such as PSNR and area of the extracted region [40]. The second article had been published in Canada (2019) their methodology started from the uncertainty of the segmentation procedure which had been improved by utilizing the prior shape information in the form of a statistical shape model by adopting two strategies for achieving the improved segmentation accuracy on difficult images. Firstly, for CNN training by depending on an adaptive sampling strategy, this training process leads to paying more attention to the images that are difficult to segment. Secondly, the CNN ensemble had been trained and used the disagreement among this ensemble to recognize the uncertain segmentations and to estimate a segmentation uncertainty map. They found that estimating the model uncertainty and using prior shape information, especially on difficult images can improve the CNN-based medical image segmentation methods performance significantly [41]. X. Yang (2019) introduced a method depends on different numbers of point selection that can generate different shape constraints so that it is more flexible

in dealing with different shapes. Then this shape constraint is incorporated into the different level set framework. A convex model that can be efficiently solved by a primal-dual hybrid gradient algorithm can be obtained by applying the convex relaxation. Their result shows that segmentation's accuracy of organs and lesions with a number of shapes in medical images can be significantly maximized by using the point distance shape constraint segmentation model [42]. A study recently published in the UK (2019), they used Six different CNNs approaches to segment the prostate in a 3D patient, then a quantification had been done for these methods, using T2-weighted MRI scans for the organ volume estimation compared with MRI-US images to find the most accurate approach. Then a set of 232 patients MRIs with an expert radiologist who provides labeling the networks had been tested and trained. Their findings stated that in order to report the segmentation accuracy the findings recommended that the difference in the accuracy of downstream image analysis tasks that use a data output by automated segmentation approaches, such as CNN's, within a clinical pipeline must have a kind of specificity in selecting among different network architectures [43]. Furthermore, there was another study that had been published in India in the same year, they used another method rather than CNN, they have used Neural based fuzzy enhancement technique. They started their procedure by performing the wiener filter in the pre-processing of the images and the contrast enhancement had been obtained by the local transform histogram (LTH). The enhanced image obtained is given to neural-based fuzzy enhancement and by three steps procedure which is fuzzification, membership function and defuzzification. The evaluation of the parameters such as PSNR (peak signal to noise ratio) and CNR (Contrast to noise ratio) for the used technique are compared with various types of result images of different methods. According to their results, this method can provide the highest PSNR value [44]. A study conducted in 2018 that introduces a deep neural network (DNN)-based approach for real-time prostate segmentation during prostate biopsy procedures. The aim of this approach is to enable dynamic registration of multiparametric MRI (mpMRI) and ultrasound data, which could potentially enhance the accuracy and effectiveness of prostate interventions. The study employs a DNN-based approach for real-time prostate segmentation. DNNs are a type of artificial neural network that can automatically learn and extract features from data, making them suitable for complex tasks like image segmentation. Convolutional neural networks (CNNs) are utilized for extracting spatial features from ultrasound images. CNNs are well-suited for image analysis tasks due to their ability to capture hierarchical patterns and features. Recurrent networks are introduced to incorporate temporal information among a series of ultrasound images. This helps the network understand the temporal changes and dynamics within the image sequence. Utilization of Residual Convolution and Recurrent Connections Residual convolution, a technique that involves the use of skip connections to mitigate vanishing gradient problems, is employed within the convolutional networks to enhance optimization and training efficiency. Recurrent connections are utilized both within and across different layers of the deep networks to maximize the utilization of temporal information. Handling Ultrasound

Artifacts to make the network more robust to ultrasound artifacts, dense and sparse sampling of the input ultrasound sequence is performed. This helps the network learn to handle variations and challenges present in ultrasound images. The proposed approach is validated using 637 images for validation and 1,017 images for testing. These images are unseen and distinct from the 2,238 labeled transrectal ultrasound (TRUS) images used in the study. Performance evaluation is conducted using metrics such as Dice similarity coefficient (DSC), surface distance error, and Hausdorff distance error. The proposed approach demonstrates statistically significant improvements compared to state-of-the-art techniques, with a mean DSC of 93%, mean surface distance error of 1.10 mm, and mean Hausdorff distance error of 3.0 mm. In summary, the study introduces a deep neural network-based approach for real-time prostate segmentation during biopsy procedures. By combining spatial and temporal information, utilizing residual convolution, and incorporating recurrent connections, the approach aims to enhance the accuracy of prostate segmentation. The proposed method's performance is evaluated using various metrics, showing promising results when compared to existing techniques. The goal of this technique is to accurately segment the prostate gland in real time during a prostate biopsy procedure [45]. Some different methods and algorithms are used in segmentation so that the researchers pay deep attention to this field to improve the accuracy, in a study published in the UK also in the same time (2018) their work describes a method to infer voxel-level transformation from higher-level correspondence information contained in anatomical labels a proposed approach that utilizes convolutional neural networks (CNNs) for 3D deformable image registration in medical imaging. This approach aims to align corresponding anatomical structures in multimodal images. The approach emphasizes the use of anatomical labels that are more reliable and practical to obtain than voxel-level correspondence. These labels are obtained for reference sets of image pairs and may include typical anatomical structures such as solid organs, vessels, ducts, structure boundaries, and landmarks. The proposed approach utilizes an end-to-end convolutional neural network (CNN) to predict displacement fields. These displacement fields are used to align labeled corresponding structures in individual image pairs during the training phase. During inference (testing), only unlabeled image pairs are used as input, and the network performs fully automated 3D deformable image registration. The strategy is versatile in that it can use diverse types of anatomical labels for training. The labels do not need to be identifiable across all training image pairs. This flexibility allows the method to accommodate a wide range of anatomical structures and variations. At inference, the proposed 3D deformable image registration algorithm operates in real-time and is fully automated. No anatomical labels or initialization are required during the inference phase. Different network architecture variants are compared using T2-weighted magnetic resonance images and 3D transrectal ultrasound images from prostate cancer patients. The approach is evaluated through cross-validation experiments involving 108 pairs of multimodal images from 76 patients. Results show that the proposed method achieves a median target registration error of 3.6 mm on landmark centroids and a median Dice coefficient of 0.87

The impact of AI applications in prostate segmentation on improving clinical diagnosis, and treatment: A review of the literature on prostate glands. Eventually, the proposed approach employs CNNs for 3D deformable image registration in medical imaging. It leverages anatomical labels to train the network and achieve accurate alignment of corresponding structures. The method's versatility, real-time inference, and performance results in cross-validation experiments make it a promising tool for multimodal image registration in clinical settings [46]. The final article discussed in the study, conducted by Reda. I et al in 2018, presents a computer-aided diagnostic system designed for the early diagnosis of prostate cancer. The study integrates clinical biomarkers (specifically prostate-specific antigen) with features extracted from diffusion-weighted MRI data collected at multiple b values. A hybrid approach combining a level-set model with nonnegative matrix factorization is employed to accurately select the boundaries of the prostate gland in the MRI images. The diffusion parameters, specifically the apparent diffusion coefficients (ADC), are estimated and normalized for the delineated prostate volumes at different b values. The diffusion parameters, specifically the apparent diffusion coefficients (ADC), are estimated and normalized for the delineated prostate volumes at different b values. The refined apparent diffusion coefficients are obtained using a generalized Gaussian Markov random field model. Cumulative distribution functions (CDFs) of the processed apparent diffusion coefficients at multiple b values are constructed. A K-nearest neighbor classifier is employed to convert the results of the prostate-specific antigen (PSA) test into diagnostic likelihoods. The PSA-based probabilities are then integrated with the initial diagnostic probabilities obtained from stacked non-negativity constraint sparse auto encoders that employ ADC-CDFs. The system is evaluated using 18 diffusion-weighted MRI datasets for diagnosis. The study reports a diagnosis accuracy of 94.4%, with a sensitivity of 88.9% and specificity of 100%. The results demonstrate the promising potential of the presented computer-aided diagnostic system for prostate cancer detection [47].

Conclusion

This study focused only on the studies that used different methods and approaches for prostate segmentation from ultrasound images, all the involved studies were (8) articles. Four of them used CNN algorithms to segment the gland completely and all of them stated that this method shows high segmentation accuracy comparing to the other methods depending on specific parameters such as PSNR, which means that (50%) of the included studies used the method and all shows the same results, however the other studies used different approaches for segmentation and their findings also showed promising improving in segmentation accuracy, but since most of the studies used CNN and increased the accuracy so that we recommend to use CNN for segmenting prostate gland using ultrasound images. According to the study that conducted to (A. H. Abdulrazack 2019) the findings stated that Prostate cancer detection in Malaysia is lower than the other counties comparatively. They suggested that in case of repeating TRUS-GB to detect PCA the ethnicity and PSA density should be considered in a multi-ethnic Malaysian population [1], so that, prostate segmentation with high

accuracy and non-missing borders is very important to detect the prostate abnormalities especially PCA.

Conflicts: The authors declared that is no conflict of interest.

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