Segmentation in Medical Image Analysis: A Review

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Abstract—**Segmentation is involved throughout the clinical process, making it a topic of great interest in medical image analysis. Automatic segmentation supports medical professionals in performing several tasks which is where deep learning may be of great use. There exists a solid and rich literature in the field of blood vessel segmentation due its difficulty and how different methods vary in performance with differing types of blood vessels. This review aims at analysing the most innovative segmentation techniques with a particular focus on vessel segmentation based on machine learning. The goal is to provide comprehensive information and gain a thorough understanding of existing techniques and their advantages and limitations. There exists no single segmentation approach which is suitable for all the different anatomical regions or imaging modalities. Thus, there exists potential for research into techniques which can be broadly used across vessels in different regions and furthermore extended to other tubular structures.**

Index Terms—**Vessel segmentation, deep learning, computer vision, medical image analysis**

I. Introduction

IN the medical industry nowadays, imaging is a crucial component in a many applications. These applications continue throughout the clinical process; not only in a diagnostic settings, but an addition in preparation before surgical operations. The developments of imaging techniques such as Magnetic Resonance Imaging (MRI), Computer Tomography (CT), Fundus Photography and Nuclear Medicine offer doctors with high resolution images. Segmentation is usually a necessary step for the task of processing a excessive number of medical images with great detail.

Generally, image segmentation is the procedure of separating an image into several parts. Instead of considering the whole data presented in an image all at once, it is better to focus on a certain region-based semantic object in image segmentation [1]. The goal of image segmentation is therefor to find the meaningful regions that represent parts of objects for easier analysis [2]. Manual segmentation can be an expensive procedure with respect to time producing results which lack reproducibility or suffer from inter-observer and/or intra-observer variability. On the other hand, automatic methods require at least one expert clinician to evaluate the segmentation results. Algorithms used on medical images may require more concrete application background than those used for common image processing. Furthermore, medical images are usually influenced by high levels of noise and partial volume effect [3], thus algorithms should be complex and robust enough to handle the task. This partial volume effect may be particularly present in problems of blood vessel segmentation.

Blood vessel analysis plays a fundamental role in different clinical fields, such as neurosurgery [4], [5], oncology [6], [7], and ophthalmology [8], right through the clinical process. Automatic blood vessel segmentation could assist clinicians and, therefore, are topics of major interest in healthcare research, as demonstrated by the large number of papers published in this field. In the past few years, with the rise of deep learning, numerous algorithms have been proposed to perform the computer-aided segmentation.

This review aims at analysing some of the most recent and innovative segmentation techniques and literature in medical image analysis with a particular focus on vessel segmentation based on machine learning. Furthermore, it reports the most commonly adopted evaluation of the segmentation results. The goal is to provide comprehensive information and gain a thorough understanding of existing segmentation algorithms and their advantages and limitations. This paper concludes with a discussion of interesting dissertation topics as well as future directions for research of segmentation in medical image analysis.

II. Literature Review

A. General medical image segmentation

General medical image segmentation refers to the automatic segmentation of organs, tumours, or any other structure present in medical images. The most common of these are tumour and brain lesion segmentation.

Region growing segmentation is an iterative process which looks at neighbouring pixels of initial seed points and determines whether or not the pixel neighbours should be added to the region. Melouah and Layachi [9] proposed an algorithm for automatic selection of seed point for seed region growing in mammograms. They applied a mean maximum raw threshold of the image for black and white intensity, and divided the image into black and white regions. Black regions were ignored, while the white were declared as a suspected region. The original image was then reverted where k-nearest neighbours was applied to determine statistical features of base entries and find the seed point. Afifi et al. [10] proposed a region growing segmentation method for MRIs which combines the local search process with the traditional seed region growing to gain an increase in performance. The method automatically finds the seed point for region growing and finds a threshold using an average of the maximum and the minimum grey value of the image. These algorithms were tested on real and simulated databases.

Segmentation is the most common subject of papers applying deep learning to medical imaging (Figure 1), and therefore has also seen the widest variety in methodology, including the development of unique convolutional neural network (CNN)-based segmentation architectures and the application of recurrent neural networks (RNN) [11]. The most well-known of these novel CNN architectures used in medical image analysis is *UNet*. Ronneberger et al. [12] proposed a network (dubbed *UNet*) as well as a training strategy that relies on the use of data augmentation in order to use available annotated samples more effectively and efficiently. The architecture is made up of a contracting path to capture context and a symmetric expanding path that allows accurate localisation. They were able to show that this network can be trained end-to-end from few images and outperforms the previous best method (a sliding-window convolutional network) on the ISBI challenge for segmentation of neuronal structures in electron microscopic stacks. Moreover, *UNet* was fast which is essential for practical applications in industry. It is claimed that the state-of-the-art models for image segmentation consist of variants of the encoder-decoder architecture used in *UNet* [13].

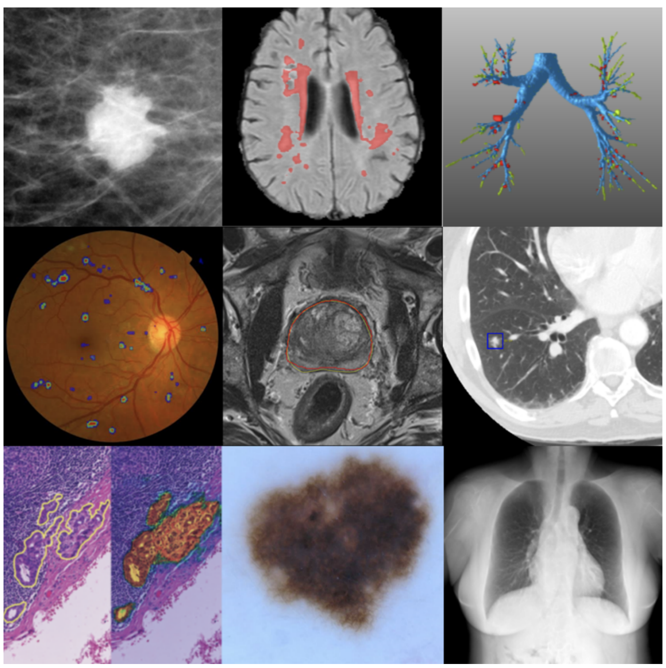

Fig. 1. Collage of some medical imaging applications in which deep learning has achieved state-of-the-art results. From top-left to bottom-right: mammographic mass classification [14], segmentation of lesions in the brain image from [15], leak detection in airway tree segmentation [16], diabetic retinopathy classification [17], prostate segmentation (top rank in PROMISE12 challenge), nodule classification, breast cancer metastases detection in lymph nodes, human expert performance in skin lesion classification [18], and state-of-the-art bone suppression in x-rays, image from [19]

Çiçek et al. [20] used a similar approach for 3D data. They introduced a network for volumetric segmentation that learns from sparsely annotated volumetric images and provides a dense 3D segmentation. The proposed architecture extends the previous *UNet* architecture from [12] by replacing the 2D operations with their 3D counterparts. The implementation performs online elastic deformations for data augmentation during training.

Milletari et al. [21] proposed an extension to [12] that incorporates ResNet-like residual blocks for 3D image segmentation based on a volumetric. Their CNN was trained end-to-end on MRI volumes depicting prostate, which learned to predict a segmentation for the whole volume in one go. A novel objective function was introduced, based on Dice coefficient [22], which was optimised during training. They were able to deal with situations which presented a strong imbalance between the number of foreground and background voxels. They augmented the data applying random non-linear transformations and histogram matching to cope with the limited number of annotated volumes available for training. Their approach achieved good performance on challenging data while requiring much less processing time needed by other previous methods.

Zhou et al. [13] presented *UNet++*, a newer, more powerful network for segmentation of medical images than *UNet*. Their architecture is a "deeply-supervised encoder-decoder network where the encoder and decoder sub-networks are connected through a series of nested, dense skip pathways" [13]. The skip pathways aimed at reducing the gap between the feature maps of the encoder and decoder networks. They show that the optimiser would have an easier learning task when the feature maps from the encoder and decoder are semantically similar.

RNNs have become more popular for segmentation tasks over recent years. For example, Xie et al. [23] used a spatial clockwork RNN to segment H&E-histopathology images. This network takes into account prior spatial information of the current patch.

Stollenga et al. [24] was the first to use a 3D Long Short Term Memory (LSTM) network with convolutional layers in six directions. They re-arranged the traditional cuboid order of computations in multidimensional-LSTM in pyramidal schemes. The resulting *PyraMiD-LSTM* is easy to parallelise, which is beneficial for 3D data such as stacks of brain slice images. Their PyraMiD-LSTM achieved state-of-the-art results of pixel-wise brain image segmentation on MRBrainS13 [25].

Andermatt et al. [26] presented an RNN to segment 3D volumes of biomedical images. Their segmentation method makes use of a neural network with the main layers consisting of multi-dimensional gated recurrent units. They applied an online data augmentation technique which allowed for accurate estimations without the need for either a large training set. Their method performed amongst the state-of-the-art in terms of speed, accuracy and memory efficiency on a popular brain segmentation challenge dataset.

Incorporating both UNet architectures with RNN would then prove beneficial. Chen et al. [27] combined bi-directional LSTMs with 2D UNet-like-architectures to segment regions in anisotropic 3D electron microscopy images. This was the first deep learning framework for 3D image segmentation that explicitly leverages 3D image anisotropism.

Poudel et al. [28] proposed a recurrent fully-convolutional network (RFCN) which learnt image representations from a full group of 2D slices with the ability to leverage inter-slice spatial dependencies through memory units. Their RFCN combines anatomical detection and segmentation into a single network which is trained end-to-end allowing a significant decrease in computational time, simplifying the analysis pipeline, and enabling several real-time applications.

Summarising, segmentation in medical imaging has seen a huge interest of deep learning related methods. Custom architectures have been designed to directly solve the segmentation problem. These have obtained promising results, rivalling and often improving results obtained with fully-CNNs [11].

B. Vessel segmentation

From the early attempts of using machine learning for vessel segmentation (including [29], [30], [31]), multiple algorithms have been proposed. So far, supervised learning has been mostly applied to retinal images, since there exists many different publicly available labelled databases [32].

Rodrigues et al. [33] segmented retinal vasculature using Optical Coherence Tomography (OCT) images. A group of 2D fundus reference images is computed from the 3D OCT volume and used as input data to a Support Vector Machine (SVM) classifier which uses a Gaussian kernel. The tuning parameters and the kernel of the SVM played a large role in the effectiveness of the method. The method was able to effectively segment healthy and pathological retinal vessels. As such, this method can be used in the study of disease progression.

Jiang et al. [34] presented a method for retinal vessel tree segmentation based on a pre-trained fully convolutional network through transfer learning. This method simplified the common retinal vessel segmentation issue from whole slide image segmentation to regional vessel element recognition and result merging. The accuracy of the cross-database test was among the top performing, and also presented great robustness.

Zhu et al. [35] proposed a supervised method which used an Extreme Learning Machine (ELM) for retinal vessel segmentation. It begun by extracting a set of discriminative feature vectors, consisting of local features, morphological features, phase congruency, Hessian and divergence of vector fields, for each pixel of the fundus image. Then a matrix is constructed for each individual pixel of a training set based on these feature vectors and the manual labels, which acts as the input of the ELM. The output of the ELM classifier is binary retinal vascular segmentation. They then implement an optimisation process in order to remove regions less than 30 pixels which are isolated from the retinal vascular.

Liu et al. [36] utilised a 17-layer CNN to segment the vessel in fundus images. Furthermore, a dense connection method, in series was also used. Here, the back layer of the network may be used as the features of the front layer, and the gradient is prevented from disappearing. The results of experimentation showed that the proposed framework was a state-of-the-art vessel segmentation method.

The segmentation procedure of these applications can be extended to other imaging modalities as well as different anatomical areas. Charbonnier et al. [37] proposed a method to improve airway segmentation in thoracic CT by detecting and then removing leaks. This leak detection can be formulated as a classification problem, in which a CNN is trained in a supervised fashion to perform the classification task. They made use of the fact that several segmentations can be extracted from a given algorithm by changing the parameters that influence the amount of leaks and the tree length. This allowed the segmented airway tree length to be increased.

Smistad and Lovstakken [38] presented an algorithm using a CNN for detecting blood vessels from B-mode ultrasound images. The proposed method is able to determine the position and size of the vessels in images in real-time.

Tetteh et al. [39] presented a feature extraction method based on inception networks for segmentation tasks through pixel classification. They extracted features under multi-layer and multi-scale schemes through convolutions. Layers of fully convolutional networks are then stacked up on these feature extraction layers and trained end-to-end for the purpose of classification. The method was tested for the purpose of segmentation and it outperformed most existing hand crafted or deterministic feature schemes found in literature. Furthermore, ways of extending this feature extraction scheme to handle 3D datasets were proposed.

Tetteh et al. [40] presented *DeepVesselNet*, a network which uses deep learning and is tailored to the challenges faced when extracting vessel networks or trees and corresponding features in 3D angiographic volumes.

Existing CNN methods have relied on local appearances learned on the regular image grid, without consideration of the graphical structure of vessel shape. Efficient use of the relationship that exists between vessel neighbourhoods may improve the vessel segmentation accuracy. Shin et al. [41] incorporated a graph neural network into a CNN architecture in order to jointly exploit both local appearances and global vessel structures. Ablation studies support the choices of algorithmic detail and hyperparameter values of their proposed method. The architecture is widely applicable since it can be applied to expand any type of CNN-based vessel segmentation method to significantly enhance the performance.

Like any deep learning problem, there needs to be common procedures of reporting the performance of segmentation methods.

III. Evaluation Metrics

Manual segmentation performed eg. by a radiologist is considered the gold standard. However, this is not extremely precise, it is prone to inter-observer and intra-observer variability and it might include non-enhancing tissue [42]. Segmentation performance is commonly evaluated with respect to this gold standard. To alleviate intra-subject variability when performing the manual segmentation, and obtain a more truthful standard, a combination of segmentations by multiple experts is adopted. Different strategies have been proposed to combine the segmentations: for example, a voting rule, often used in practice, selecting as a standard all voxels where the majority of experts agree the structure to be segmented, is present [43]. However, “such approach does not allow for incorporating a priori information of the structure being segmented or estimating the presence of an imperfect or limited reference standard” [32].

In the evaluation of segmentation techniques and methods with respect to the gold standard, a contingency table is used, where positives and negative refer to pixels belonging to vessels and background as in accord with the expert segmentation, respectively. Using True Positive, True Negative, False Negative, and False Positive, performance measures such as sensitivity, accuracy, and specificity may also be adopted. A common evaluation metric is also the area under the curve of the receiver operating characteristic curve. Another metric that is often used is the Matthews Correlation Coefficient [44].

Spatial overlapping indexes have been used. The most common of these is the Dice Similarity Coefficient [22], which is "computed as the ratio of the number of elements (card) in the intersection of two clusters A and B by the mean label image, where A and B indicate the segmented vessels and its corresponding gold standard, respectively". The metrics described above are mostly based on pixel-to-pixel comparison between the vessels segmented by the algorithms and those by gold standard, without considering the fact that vessel pixels are part of a connected vascular structure with specific features, including connectivity, area and length [32]. The work in [45] describes the suggested calculation.

IV. Conclusion

In the above sections, I have presented a set of state-of-the-art medical image segmentation methods primarily based on deep learning. It is evident that the UNet and its variations including recurrent variations are among the most prominent techniques. Vessel segmentation dates almost 70 year and there exists a solid and rich literature. However, despite the efforts and the already achieved results, there are still several opportunities for improvements and further research is still highly necessary.

As presented, a large range of methods has been presented and enhanced for segmenting blood vessels in medical images. However, none of them are appropriate for all applications and anatomical regions. Image quality also highly affects the performances of segmentation methods and a well performing method in one context may not be appropriate in another. This shows a further limitation in the ability to compare different algorithms. An important issue still remaining exists in the segmentation of pathological vessels. Unfortunately not much research effort has been dedicated to this issue yet. Research is needed since "some of the main assumptions made for healthy vessels (such as linearity and circular cross-section) do not hold in pathological tissues, requiring new vessel model formulations" [32].

To conclude, undertaking research in this domain has the potential to effectively and immediately contribute to the scientific community while also impacting the the medical industry transferring into the overall well-being of many people's lives.

References

[1] H. A. Sulaiman, M. A. Othman, M. F. I. Othman, Y. A. Rahim, and N. C. Pee, *Advanced Computer and Communication Engineering Technology: Proceedings of the 1st International Conference on Communication and Computer Engineering*, 1st ed. Springer Publishing Company, Incorporated, 2016.

[2] G. Stockman and L. G. Shapiro, *Computer Vision*, 1st ed. USA: Prentice Hall PTR, 2001.

[3] H. Zaidi and W. Erwin, "Quantitative analysis in nuclear medicine imaging," *Journal of Nuclear Medicine*, vol. 48, pp. 1401–1401, 08 2007.

[4] H. Ramakonar, B. C. Quirk, R. W. Kirk, J. Li, A. Jacques, C. R. P. Lind, and R. A. McLaughlin, "Intraoperative detection of blood vessels with an imaging needle during neurosurgery in humans," *Science advances*, vol. 4, no. 12, pp. eaav4992–eaav4992, 12 2018. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/30585293

[5] E. De Momi, C. Caborni, F. Cardinale, G. Casaceli, L. Castana, M. Cossu, R. Mai, F. Gozzo, S. Francione, L. Tassi, G. Russo, L. Antiga, and G. Ferrigno, "Multi-trajectories automatic planner for stereoelectroencephalography (seeg)," *International journal of computer assisted radiology and surgery*, vol. 9, 04 2014.

[6] J. Folkman, "Angiogenesis in cancer, vascular, rheumatoid and other disease," *Nature Medicine*, vol. 1, no. 1, pp. 27–30, 1995. [Online]. Available: https://doi.org/10.1038/nm0195-27

[7] D. M. McDonald and P. Baluk, "Significance of blood vessel leakiness in cancer," *Cancer Research*, vol. 62, no. 18, pp. 5381–5385, 2002. [Online]. Available: https://cancerres.aacrjournals.org/content/62/18/5381

[8] M. Miri, Z. Amini, H. Rabbani, and R. Kafieh, "A comprehensive study of retinal vessel classification methods in fundus images," *Journal of medical signals and sensors*, vol. 7, no. 2, pp. 59–70, Apr-Jun 2017. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/28553578

[9] M. Ahlem and S. Layachi, "A novel automatic seed placement approach for region growing segmentation in mammograms," 11 2015, pp. 1–5.

[10] A. Afifi, G. Said, E. Zanaty, and S. El-Zoghdy, "New region growing based on thresholding technique applied to mri data," *International Journal of Computer Network and Information Security*, vol. 7, pp. 61–67, 06 2015.

[11] G. Litjens, T. Kooi, B. E. Bejnordi, A. A. A. Setio, F. Ciompi, M. Ghafoorian, J. A. van der Laak, B. van Ginneken, and C. I. Sánchez, "A survey on deep learning in medical image analysis," *Medical Image Analysis*, vol. 42, pp. 60 – 88, 2017. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1361841517301135

[12] O. Ronneberger, P. Fischer, and T. Brox, "U-net: Convolutional networks for biomedical image segmentation," 2015.

[13] Z. Zhou, M. M. Rahman Siddiquee, N. Tajbakhsh, and J. Liang, "Unet++: A nested u-net architecture for medical image segmentation," in *Deep Learning in Medical Image Analysis and Multimodal Learning for Clinical Decision Support*, D. Stoyanov, Z. Taylor, G. Carneiro, T. Syeda-Mahmood, A. Martel, L. Maier-Hein, J. M. R. Tavares, A. Bradley, J. P. Papa, V. Belagiannis, J. C. Nascimento, Z. Lu, S. Conjeti, M. Moradi, H. Greenspan, and A. Madabhushi, Eds. Cham: Springer International Publishing, 2018, pp. 3–11.

[14] T. Kooi, G. Litjens, B. Ginneken, A. Gubern-Mérida, C. Sánchez, R. Mann, G. Heeten, and N. Karssemeijer, "Large scale deep learning for computer aided detection of mammographic lesions," *Medical Image Analysis*, vol. 35, 08 2016.

[15] M. Ghafoorian, N. Karssemeijer, T. Heskes, I. Uder, F. Leeuw, E. Marchiori, B. Ginneken, and B. Platel, "Non-uniform patch sampling with deep convolutional neural networks for white matter hyperintensity segmentation," 04 2016, pp. 1414–1417.

[16] J.-P. Charbonnier, E. M. v. Rikxoort, A. A. A. Setio, C. M. Schaefer-Prokop, B. v. Ginneken, and F. Ciompi, "Improving airway segmentation in computed tomography using leak detection with convolutional networks," *Medical image analysis*, vol. 36, p. 52—60, February 2017. [Online]. Available: https://doi.org/10.1016/j.media.2016.11.001

[17] M. J. J. P. van Grinsven, B. van Ginneken, C. B. Hoyng, T. Theelen, and C. I. Sánchez, "Fast convolutional neural network training using selective data sampling: Application to hemorrhage detection in color fundus images." *IEEE Trans. Med. Imaging*, vol. 35, no. 5, pp. 1273–1284, 2016. [Online]. Available: http://dblp.uni-trier.de/db/journals/tmi/tmi35.htmlGrinsvenGHTS16

[18] A. Esteva, B. Kuprel, R. Novoa, J. Ko, S. Swetter, H. Blau, and S. Thrun, "Dermatologist-level classification of skin cancer with deep neural networks," *Nature*, vol. 542, 01 2017.

[19] W. Yang, Y. Chen, Y. Liu, L. Zhong, G. Qin, Z. Lu, Q. Feng, and W. Chen, "Cascade of multi-scale convolutional neural networks for bone suppression of chest radiographs in gradient domain," *Medical Image Analysis*, vol. 35, pp. 421–433, 01 2017.

[20] Özgün Çiçek, A. Abdulkadir, S. S. Lienkamp, T. Brox, and O. Ronneberger, "3d u-net: Learning dense volumetric segmentation from sparse annotation," 2016.

[21] F. Milletari, N. Navab, and S. Ahmadi, "V-net: Fully convolutional neural networks for volumetric medical image segmentation," in *2016 Fourth International Conference on 3D Vision (3DV)*, Oct 2016, pp. 565–571.

[22] L. R. Dice, "Measures of the amount of ecologic association between species," *Ecology*, vol. 26, no. 3, pp. 297–302, 1945. [Online]. Available: https://esajournals.onlinelibrary.wiley.com/doi/abs/10.2307/1932409

[23] Y. Xie, Z. Zhang, M. Sapkota, and L. Yang, "Spatial clockwork recurrent neural network for muscle perimysium segmentation," *Medical image computing and computer-assisted intervention : MICCAI ... International Conference on Medical Image Computing and Computer-*

Assisted Intervention, vol. 9901, pp. 185–193, 10 2016. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/28090603

[24] M. Stollenga, W. Byeon, M. Liwicki, and J. Schmidhuber, "Parallel multi-dimensional lstm, with application to fast biomedical volumetric image segmentation," 06 2015.

[25] A. van Opbroek, F. van der Lijn, and M. de Bruijne, "Automated brain-tissue segmentation by multi-feature svm classification," in *The MICCAI Grand Challenge on MR Brain Image Segmentation (MRBrainS13)*, ser. The MIDAS Journal, 2013, oA; The MICCAI Grand Challenge on MR Brain Image Segmentation, MRBrainS13 ; Conference date: 26-09-2013 Through 26-09-2013.

[26] S. Andermatt, S. Pezold, and P. Cattin, "Multi-dimensional gated recurrent units for the segmentation of biomedical 3d-data," 10 2016, pp. 142–151.

[27] J. Chen, L. Yang, Y. Zhang, M. Alber, and D. Z. Chen, "Combining fully convolutional and recurrent neural networks for 3d biomedical image segmentation," 2016.

[28] R. P. K. Poudel, P. Lamata, and G. Montana, "Recurrent fully convolutional neural networks for multi-slice mri cardiac segmentation," 2016.

[29] R. Nekovei and Ying Sun, "Back-propagation network and its configuration for blood vessel detection in angiograms," *IEEE Transactions on Neural Networks*, vol. 6, no. 1, pp. 64–72, Jan 1995.

[30] J. V. B. Soares, J. J. G. Leandro, R. M. Cesar, H. F. Jelinek, and M. J. Cree, "Retinal vessel segmentation using the 2-d gabor wavelet and supervised classification," *IEEE Transactions on Medical Imaging*, vol. 25, no. 9, pp. 1214–1222, Sep. 2006.

[31] J. Staal, M. D. Abramoff, M. Niemeijer, M. A. Viergever, and B. van Ginneken, "Ridge-based vessel segmentation in color images of the retina," *IEEE Transactions on Medical Imaging*, vol. 23, no. 4, pp. 501–509, April 2004.

[32] S. Moccia, E. D. Momi, S. E. Hadji, and L. S. Mattos, "Blood vessel segmentation algorithms — review of methods, datasets and evaluation metrics," *Computer Methods and Programs in Biomedicine*, vol. 158, pp. 71 – 91, 2018. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0169260717313421

[33] P. Rodrigues, P. Guimarães, T. Santos, S. Simão, T. Miranda, P. Serranho, and R. Bernardes, "Two-dimensional segmentation of the retinal vascular network from optical coherence tomography," *Journal of biomedical optics*, vol. 18, p. 126011, 12 2013.

[34] Z. Jiang, H. Zhang, Y. Wang, and S.-B. Ko, "Retinal blood vessel segmentation using fully convolutional network with transfer learning," *Computerized Medical Imaging and Graphics*, vol. 68, pp. 1 – 15, 2018. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0895611118302313

[35] C. Zhu, B. Zou, R. Zhao, J. Cui, X. Duan, Z. Chen, and Y. Liang, "Retinal vessel segmentation in colour fundus images using extreme learning machine," *Computerized Medical Imaging and Graphics*, vol. 55, pp. 68 – 77, 2017, special Issue on Ophthalmic Medical Image Analysis. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0895611116300416

[36] Z.-F. Liu, Y.-Z. Zhang, P.-Z. Liu, Y. Zhang, Y.-M. Luo, Y.-Z. Du, Y. Peng, and P. Li, "Retinal vessel segmentation using densely connected convolution neural network with colorful fundus images," *Journal of Medical Imaging and Health Informatics*, vol. 8, no. 6, pp. 1300–1307, 2018. [Online]. Available: https://www.ingentaconnect.com/content/asp/jmihi/2018/00000008/00000006/art00028

[37] J.-P. Charbonnier, E. van Rikxoort, A. Setio, C. Schaefer-Prokop, B. Ginneken, and F. Ciompi, "Improving airway segmentation in computed tomography using leak detection with convolutional networks," *Medical Image Analysis*, vol. 36, 11 2016.

[38] E. Smistad and L. Lovstakken, "Vessel detection in ultrasound images using deep convolutional neural networks," 10 2016.

[39] G. Tetteh, M. Rempfler, C. Zimmer, and B. H. Menze, "Deep-fext: Deep feature extraction for vessel segmentation and centerline prediction," in *Machine Learning in Medical Imaging*, Q. Wang, Y. Shi, H.-I. Suk, and K. Suzuki, Eds. Cham: Springer International Publishing, 2017, pp. 344–352.

[40] G. Tetteh, V. Efremov, N. D. Forkert, M. Schneider, J. Kirschke, B. Weber, C. Zimmer, M. Piraud, and B. H. Menze, "Deepvesselnet: Vessel segmentation, centerline prediction, and bifurcation detection in 3-d angiographic volumes," 2018.

[41] S. Y. Shin, S. Lee, I. D. Yun, and K. M. Lee, "Deep vessel segmentation by learning graphical connectivity," *Medical Image Analysis*, vol. 58, p. 101556, 2019. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1361841519300982

[42] A. Meyer-Baese and V. Schmid, "Chapter 13 - computer-aided diagnosis for diagnostically challenging breast lesions in dce-mri," in *Pattern Recognition and Signal Analysis in Medical Imaging (Second Edition)*, second edition ed., A. Meyer-Baese and V. Schmid, Eds. Oxford: Academic Press, 2014, pp. 391 – 420. [Online]. Available: http://www.sciencedirect.com/science/article/pii/B9780124095458000133

[43] L. P. Cordella, P. Foggia, C. Sansone, F. Tortorella, and M. Vento, "Reliability parameters to improve combination strategies in multi-expert systems," *Pattern Analysis & Applications*, vol. 2, no. 3, pp. 205–214, 1999. [Online]. Available: https://doi.org/10.1007/s100440050029

[44] D. Powers, "Evaluation: From precision, recall and f-factor to roc, informedness, markedness correlation," *Mach. Learn. Technol.*, vol. 2, 01 2008.

[45] M. E. Gegundez-Arias, A. Aquino, J. M. Bravo, and D. Marin, "A function for quality evaluation of retinal vessel segmentations," *IEEE Transactions on Medical Imaging*, vol. 31, no. 2, pp. 231–239, Feb 2012.

[46] M. H. Hesamian, W. Jia, X. He, and P. Kennedy, "Deep learning techniques for medical image segmentation: Achievements and challenges," *Journal of Digital Imaging*, vol. 32, no. 4, pp. 582–596, 2019. [Online]. Available: https://doi.org/10.1007/s10278-019-00227-x

[47] N. Sharma and L. M. Aggarwal, "Automated medical image segmentation techniques," *Journal of medical physics*, vol. 35, no. 1, pp. 3–14, 01 2010. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/20177565

[48] J. Tavares and R. Natal Jorge, "A review on the current segmentation algorithms for medical images." 01 2009, pp. 135–140.

[49] L. Lee, S.-C. Liew, and W. J. Thong, "A review of image segmentation methodologies in medical image," *Lecture Notes in Electrical Engineering*, vol. 315, pp. 1069–1080, 11 2015.

[50] K. Kamnitsas, C. Ledig, V. F. Newcombe, J. P. Simpson, A. D. Kane, D. K. Menon, D. Rueckert, and B. Glocker, "Efficient multi-scale 3d cnn with fully connected crf for accurate brain lesion segmentation," *Medical Image Analysis*, vol. 36, pp. 61 – 78, 2017. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1361841516301839

[51] B. H. Menze, A. Jakab, S. Bauer, J. Kalpathy-Cramer, K. Farahani, J. Kirby, Y. Burren, N. Porz, J. Slotboom, R. Wiest, L. Lanczi, E. Gerstner, M. Weber, T. Arbel, B. B. Avants, N. Ayache, P. Buendia, D. L. Collins, N. Cordier, J. J. Corso, A. Criminisi, T. Das, H. Delingette, Demiralp, C. R. Durst, M. Dojat, S. Doyle, J. Festa, F. Forbes, E. Geremia, B. Glocker, P. Golland, X. Guo, A. Hamamci, K. M. Iftekharuddin, R. Jena, N. M. John, E. Konukoglu, D. Lashkari, J. A. Mariz, R. Meier, S. Pereira, D. Precup, S. J. Price, T. R. Raviv, S. M. S. Reza, M. Ryan, D. Sarikaya, L. Schwartz, H. Shin, J. Shotton, C. A. Silva, N. Sousa, N. K. Subbanna, G. Szekely, T. J. Taylor, O. M. Thomas, N. J. Tustison, G. Unal, F. Vasseur, M. Wintermark, D. H. Ye, L. Zhao, B. Zhao, D. Zikic, M. Prastawa, M. Reyes, and K. Van Leemput, "The multimodal brain tumor image segmentation benchmark (brats)," *IEEE Transactions on Medical Imaging*, vol. 34, no. 10, pp. 1993–2024, Oct 2015.

[52] O. Oktay, E. Ferrante, K. Kamnitsas, M. Heinrich, W. Bai, J. Caballero, S. A. Cook, A. de Marvao, T. Dawes, D. P. O'Regan, B. Kainz, B. Glocker, and D. Rueckert, "Anatomically constrained neural networks (acnns): Application to cardiac image enhancement and segmentation," *IEEE Transactions on Medical Imaging*, vol. 37, no. 2, pp. 384–395, Feb 2018.

[53] W. Bai, C. Chen, G. Tarroni, J. Duan, F. Guitton, S. E. Petersen, Y. Guo, P. M. Matthews, and D. Rueckert, "Self-supervised learning for cardiac mr image segmentation by anatomical position prediction," in *Medical Image Computing and Computer Assisted Intervention – MICCAI 2019*, D. Shen, T. Liu, T. M. Peters, L. H. Staib, C. Essert, S. Zhou, P.-T. Yap, and A. Khan, Eds. Cham: Springer International Publishing, 2019, pp. 541–549.

[54] C. Dai, Y. Mo, E. Angelini, Y. Guo, and W. Bai, "Transfer learning from partial annotations for whole brain segmentation," in *Domain Adaptation and Representation Transfer and Medical Image Learning with Less Labels and Imperfect Data*, Q. Wang, F. Milletari, H. V. Nguyen, S. Albarqouni, M. J. Cardoso, N. Rieke, Z. Xu, K. Kamnitsas, V. Patel, B. Roysam, S. Jiang, K. Zhou, K. Luu, and N. Le, Eds. Cham: Springer International Publishing, 2019, pp. 199–206.

[55] W. Bai, W. Shi, D. P. O'Regan, T. Tong, H. Wang, S. Jamil-Copley, N. S. Peters, and D. Rueckert, "A probabilistic patch-based label fusion model for multi-atlas segmentation with registration refinement: Application to cardiac mr images," *IEEE Transactions on Medical Imaging*, vol. 32, no. 7, pp. 1302–1315, July 2013.

[56] M. Ebner, G. Wang, W. Li, M. Aertsen, P. A. Patel, R. Aughwane, A. Melbourne, T. Doel, S. Dymarkowski, P. D. Coppi, A. L. David, J. Deprest, S. Ourselin, and T. Vercauteren, "An automated framework for localization,

segmentation and super-resolution reconstruction of fetal brain mri," *NeuroImage*, vol. 206, p. 116324, 2020. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1053811919309152

[57] J. Shapey, G. Wang, R. Dorent, A. Dimitriadis, W. Li, I. Paddick, N. Kitchen, S. Bisdas, S. R. Saeed, S. Ourselin, R. Bradford, and T. Vercauteren, "An artificial intelligence framework for automatic segmentation and volumetry of vestibular schwannomas from contrast-enhanced t1-weighted and high-resolution t2-weighted mri," *Journal of Neurosurgery JNS*, pp. 1 – 9, 2019. [Online]. Available: https://thejns.org/view/journals/j-neurosurg/aop/article-10.3171-2019.9.JNS191949/article-10.3171-2019.9.JNS191949.xml

[58] H. Williams, L. Cattani, W. Li, M. Tabassian, T. Vercauteren, J. Deprest, and J. D'hooge, "3d convolutional neural network for segmentation of the urethra in volumetric ultrasound of the pelvic floor," in *2019 IEEE International Ultrasonics Symposium (IUS)*, Oct 2019, pp. 1473–1476.

[59] S. P. Rajan and V. Kavitha, "Diagnosis of cardiovascular diseases using retinal images through vessel segmentation graph," *Current Medical Imaging Reviews*, vol. 13, no. 4, pp. 454–459, 2017. [Online]. Available: https://www.ingentaconnect.com/content/ben/cmir/2017/00000013/00000004/art00013

[60] C. Zhu, B. Zou, R. Zhao, J. Cui, X. Duan, Z. Chen, and Y. Liang, "Retinal vessel segmentation in colour fundus images using extreme learning machine," *Computerized Medical Imaging and Graphics*, vol. 55, pp. 68 – 77, 2017, special Issue on Ophthalmic Medical Image Analysis. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0895611116300416

[61] S. Moccia, E. D. Momi, S. E. Hadji, and L. S. Mattos, "Blood vessel segmentation algorithms — review of methods, datasets and evaluation metrics," *Computer Methods and Programs in Biomedicine*, vol. 158, pp. 71 – 91, 2018. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0169260717313421

[62] L. Lenchik, L. Heacock, A. A. Weaver, R. D. Boutin, T. S. Cook, J. Itri, C. G. Filippi, R. P. Gullapalli, J. Lee, M. Zagurovskaya, T. Retson, K. Godwin, J. Nicholson, and P. A. Narayana, "Automated segmentation of tissues using ct and mri: A systematic review," *Academic Radiology*, vol. 26, no. 12, pp. 1695 – 1706, 2019. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1076633219303538

[63] N. Tajbakhsh, L. Jeyaseelan, Q. Li, J. Chiang, Z. Wu, and X. Ding, "Embracing imperfect datasets: A review of deep learning solutions for medical image segmentation," 2019.

[64] N. Shrivastava and J. Bharti, "A comparative analysis of medical image segmentation," in *International Conference on Advanced Computing Networking and Informatics*, R. Kamal, M. Henshaw, and P. S. Nair, Eds. Singapore: Springer Singapore, 2019, pp. 459–467.