Review Article

Cervical cancer segmentation based on medical images: a literature review

Xiu Wang[1]^, Chaolu Feng[2,3], Mingxu Huang[3], Shiqi Liu[1], He Ma[1,2], Kun Yu[1,2]^

[1]College of Medicine and Biological Information Engineering, Northeastern University, Shenyang, China; [2]Key Laboratory of Intelligent Computing in Medical Image, Ministry of Education, Shenyang, China; [3]School of Computer Science and Engineering, Northeastern University, Shenyang, China

Contributions: (I) Conception and design: K Yu, C Feng, H Ma; (II) Administrative support: K Yu; (III) Provision of study materials or patients: K Yu; (IV) Collection and assembly of data: X Wang, M Huang, S Liu; (V) Data analysis and interpretation: X Wang, M Huang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Kun Yu, PhD. College of Medicine and Biological Information Engineering, Northeastern University, Chuangxin Street 195, Shenyang 110016, China; Key Laboratory of Intelligent Computing in Medical Image, Ministry of Education, No. 3-11, Wenhua Road, Heping District, Shenyang 110819, China. Email: yukun@bmie.neu.edu.cn.

Background and Objective: Cervical cancer clinical target volume (CTV) outlining and organs at risk segmentation are crucial steps in the diagnosis and treatment of cervical cancer. Manual segmentation is inefficient and subjective, leading to the development of automated or semi-automated methods. However, limitation of image quality, organ motion, and individual differences still pose significant challenges. Apart from numbers of studies on the medical images' segmentation, a comprehensive review within the field is lacking. The purpose of this paper is to comprehensively review the literatures on different types of medical image segmentation regarding cervical cancer and discuss the current level and challenges in segmentation process.

Methods: As of May 31, 2023, we conducted a comprehensive literature search on Google Scholar, PubMed, and Web of Science using the following term combinations: "cervical cancer images", "segmentation", and "outline". The included studies focused on the segmentation of cervical cancer utilizing computed tomography (CT), magnetic resonance (MR), and positron emission tomography (PET) images, with screening for eligibility by two independent investigators.

Key Content and Findings: This paper reviews representative papers on CTV and organs at risk segmentation in cervical cancer and classifies the methods into three categories based on image modalities. The traditional or deep learning methods are comprehensively described. The similarities and differences of related methods are analyzed, and their advantages and limitations are discussed in-depth. We have also included experimental results by using our private datasets to verify the performance of selected methods. The results indicate that the residual module and squeeze-and-excitation blocks module can significantly improve the performance of the model. Additionally, the segmentation method based on improved level set demonstrates better segmentation accuracy than other methods.

Conclusions: The paper provides valuable insights into the current state-of-the-art in cervical cancer CTV outlining and organs at risk segmentation, highlighting areas for future research.

Keywords: Cervical cancer; medical image segmentation; deep learning; review

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^ ORCID: Xiu Wang, 0009-0006-8158-4280; Kun Yu, 0000-0002-9973-3321.

Introduction

Cervical cancer is a highly malignant tumor that originates in the cervix and is among the most lethal cancer globally. Epidemiologic studies have shown that almost all cervical cancers are caused by persistent infection with one of approximately 15 high-risk human papillomavirus (HPV) types (1). According to 2020 World Health Organization statistics on 36 malignant tumors in 185 countries, cervical cancer ranks as the fourth most common malignant tumor in women. Each year, there are approximately 600,000 new cases of cervical cancer worldwide, resulting in around 340,000 deaths (2).

The treatment method of cervical cancer varies according to the stage of cervical cancer. Cervical cancer is categorized into four stages based on the location of the tumor. For patients with stage I B3 and II A2 cervical cancer, which is also locally advanced cervical cancer, the most common treatment is a combination of radiotherapy and chemotherapy (3). Radiotherapy includes conformal radiotherapy, intensity-modulated radiation therapy (IMRT) and precision radiotherapy. IMRT is the most widely used radiation technique for cervical cancer, as it provides high precision treatment dose to the tumor and reduces the dose to the organs at risk (4). For patients with severe parametrial and paravaginal involvement, their radiotherapy plans include external radiation therapy and brachytherapy (5). External radiation therapy involves irradiating the radiation source at a fixed distance from a lesion in the body. Brachytherapy, on the other hand, is a type of precision radiotherapy in which an interpolation needle is inserted inside the tumor for irradiation, based on the size, site of invasion, and depth of invasion of the cervical tumor. This provides additional local irradiation to the residual lesion and the cervix, completing the radiation therapy dose requirements.

The guideline for radiation therapy is to find a balance between delivering a sufficient dose to the tumor while minimizing radiation exposure to surrounding areas and healthy organs. The accurate outlining of the clinical target volume (CTV) and organs at risk is essential for developing, evaluating, and optimizing radiation treatment plans. Generally, the target volume includes gross target volume (GTV), CTV, and planning target volume (PTV). According to consensus guidelines for CTV delineation, the CTV should include cervical tumor, cervical, uterine, parametrial, ovarian, vaginal tissue, and lymph node CTVs (6), while organs at risk for cervical cancer radiation therapy generally include the bladder, vagina, rectum, sigmoid colon, small intestine, and bilateral femoral bones adjacent to the cervix. CTV, PTV and organs at risk outlines are shown in *Figure 1*. In order to maximize the treatment efficacy, the precise contouring of the CTV and adjacent normal organs is crucial in the radiation planning for cervical cancer. During radiation therapy, several imaging sessions are needed to verify the tumor's location and constantly adjust the radiation plan due to uncertain factors such as tumor regression and movement of organs in the body, including the effect of bladder filling level and rectal movement (7). The organ movement is shown in *Figure 2*.

Modern imaging techniques, such as magnetic resonance imaging (MRI), computed tomography (CT) and 18F-fluorodeoxyglucose positron emission tomography (FDG-PET), play a crucial role in adjusting the radiation dose to different target volumes and minimizing the impact of radiation on healthy organs. By providing accurate information on tumor location and surrounding structures, image-guided radiotherapy has significantly improved the accuracy of brachytherapy for cervical cancer and the treatment outcomes for patients.

Currently, the segmentation of cervical cancer's CTV and organs at risk is mainly performed manually by physicians, which is time-consuming and prone to subjective errors. Therefore, it is highly demanding for accurate, efficient, and objective segmentation methods in cervical cancer diagnosis. Ghose *et al.* (8) firstly reviewed the segmentation of CT and magnetic resonance (MR) images by using registration method for cervical cancer in 2015. Recently, Yang *et al.* (9) introduced the studies on the segmentation of CT images by using deep learning method, while Zaki *et al.* (10) reviewed the graph-based method of segmenting cervical cancer based on colposcopic images and Pap smears. Apart from numbers of studies on the automatic medical images' segmentation, a comprehensive review for cervical cancer is lacking.

Therefore, starting from three modalities of CT/MR/PET images, this paper reviews the segmentation methods in the field of cervical cancer. Both traditional and deep learning methods are comprehensively described. The similarities and differences of related methods are analyzed, and their advantages and limitations are discussed in-depth. By reviewing the relevant literature and methods of cervical cancer medical image segmentation, we can fully understand the current research status and latest progress in the field, including segmentation methods of different modes of images, technical characteristics, and applications. Through the comparison and analysis of various segmentation

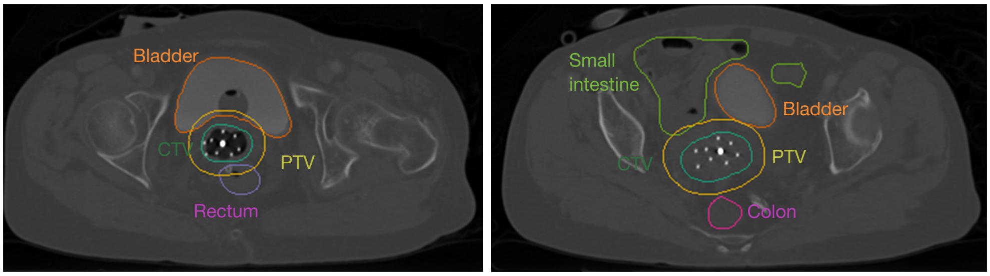

Figure 1 CTV and the location of organs at risk. CTV, clinical target volume; PTV, planning target volume.

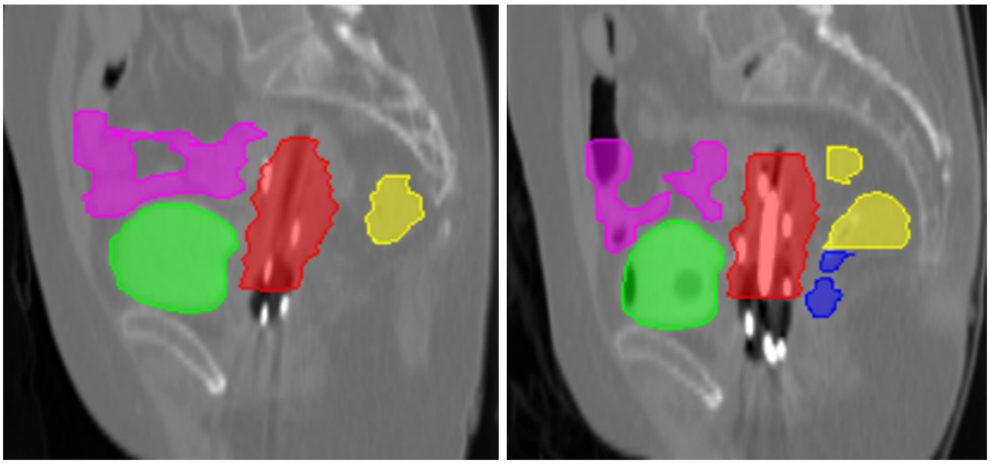

Figure 2 Changes of bladder, colon, intestine, rectum and CTV movement under different CT scans (bladder: green, rectum: blue, intestines: pink, colon: yellow, CTV: red). CTV, clinical target volume; CT, computed tomography.

methods, their advantages, limitations, and applicable scenarios can be evaluated. This helps researchers and clinicians to choose appropriate segmentation methods and improve the accuracy and stability of segmentation results. The results indicate that the residual module and squeeze-and-excitation blocks module can significantly improve the performance of the model. Additionally, the segmentation method based on improved level set demonstrates better segmentation accuracy than other methods. Our finding provides valuable insights into the current state-of-the-art in cervical cancer CTV outlining and organs at risk segmentation, highlighting areas for future research. We present this article in accordance with the Narrative Review reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-369/rc).

Methods

Literature search method

For this review, the detailed research strategies are shown in *Table 1* and 64 eligible papers have been included in our reference list.

Integration of information

At present, the segmentation methods of cervical cancer radiological CTV and organs at risk by CT, MRI and PET images are mainly divided into two categories, which are traditional segmentation methods and deep learning segmentation methods. Traditional segmentation methods, including registration, atlas segmentation, level set, region

Table 1 The search strategy summary

Items	Specification
Date of search	June 10, 2023
Databases and other sources searched	Google Scholar, PubMed, and Web of Science
Search terms used	Use a combination of the following terms: "cervical cancer images", "segmentation", and "outline"
Timeframe	January 1, 2000 to May 31, 2023
Inclusion and exclusion criteria	No language restrictions were set during the search, and cervical cancer segmentation literature using colposcopy images, Pap Smear, and cell images were excluded
Selection process	Two researchers independently conducted the literature screening, and in case of any disagreements, a third researcher made the final judgment

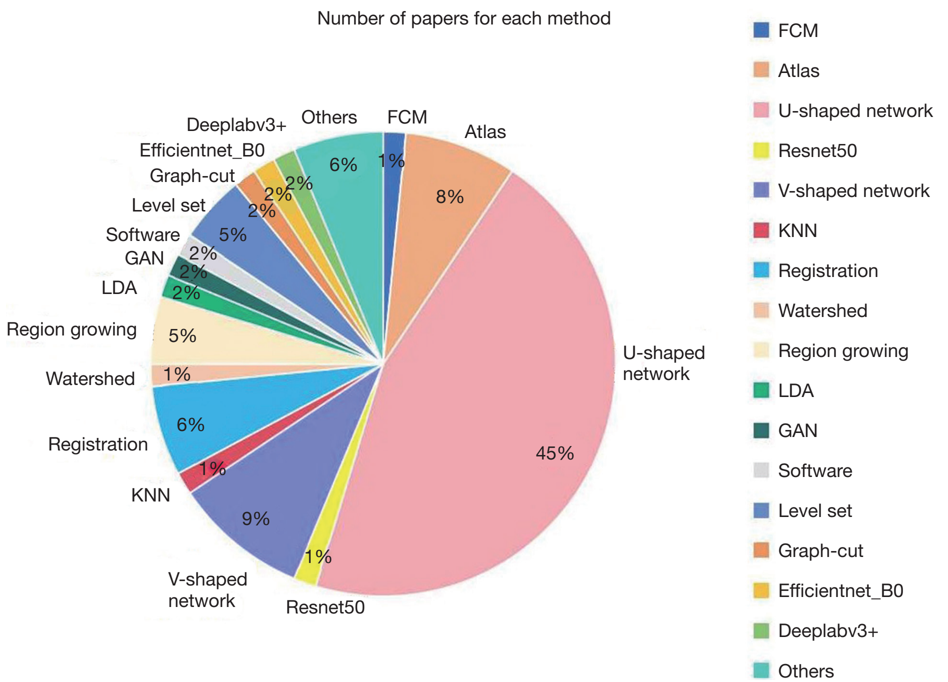

Figure 3 Summary of methods for searching papers. FCM, fuzzy c-means; KNN, K nearest neighbors; LDA, linear discriminant analysis; GAN, generative adversarial network.

growth, graph cut, and watershed segmentation, have been widely applied. In recent years, deep learning-based segmentation methods, such as UNet, V-Net, and their improved networks, have gained people's attention due to their superior performance. The percentage of these methods in the retrieved papers is shown in *Figure 3*.

Among the 64 papers retrieved, the earliest one was published in 2011 and the number of cervical cancer image segmentation papers has increased substantially since 2019. The statistics of paper publication year and image modality are shown in *Figure 4*. The images characteristics of these three modalities differ in their ability to present cervical cancer CTV and organs at risk. CT can obtain continuous thin layer images by multi-phase scanning and enable observation of tumors from different angles by reconstruction techniques. It can display the size, depth of infiltration, and invasion of the primary tumor, as well as identify whether the cancer has spread to bones and other

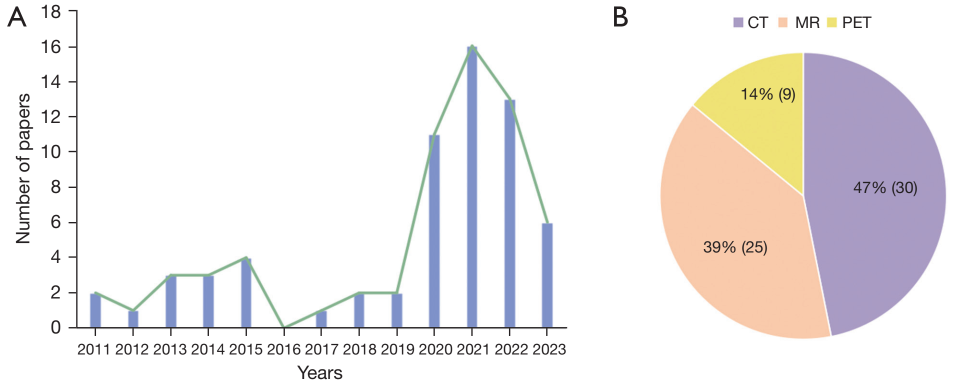

Figure 4 The statistics of paper publication year and image modality. (A) Summary of the year of publication of the retrieved papers, (B) modal summary of the retrieved papers. CT, computed tomography; MR, magnetic resonance; PET, positron emission tomography.

places. CT imaging is also not affected by metal. However, CT images have poor resolution and contrast, which can make it difficult to distinguish smaller tumors, and the upper edge of the cervix may not be clearly displayed. Compared with CT images, MRI images have higher tissue resolution and can achieve accurate diagnosis of cervical cancer. It can also perform multi-directional and multi-sequence scans to understand the cervical cancer site, parametrial invasion, lymph node metastasis. Internal pelvic organs and inter-tissue signals can be observed to identify the cervical cancer stage. MRI images with high contrast are important for cervical cancer patients, as the lesions' large geometry and the soft tissue borders are not obvious in the images. But MRI is susceptible to metal, prone to artifacts and relatively expensive. Compared to the first two imaging modalities, PET complements MRI in assessing the extent of localized disease and helps to depict the margins of invasive tumors. In cases where the tumor extends upward into the uterine cavity and caudally into the vaginal cuff, PET is particularly helpful (11). FDG-PET is more sensitive in detecting pelvic and para-aortic lymph node metastases. Detection of lymph nodes by PET allows physicians to modify treatment plans and enables radiation oncologists to expand the radiation treatment volume to include metastatic lymph nodes (12).

Current state of cervical cancer segmentation methods for different image techniques

Cervical cancer segmentation based on CT images

CT-based brachytherapy for cervical cancer is widely used in treatment centers for cervical cancer radiation therapy programs. Many automatic segmentation methods relying on CT images to segment target areas and organs at risk have been proposed. Because cervical cancer and normal cervical regions have similar attenuation in CT images and cannot be accurately distinguished, there is less literature on the segmentation of cervical cancer CT images using traditional methods. By searching Google Scholar, PubMed, and Web of Science websites, only four articles met the requirements. Putri *et al.* (13) used the fuzzy C-mean method to achieve segmentation of the cervical region and localization of cervical cancer in 2015. Other three studies utilized atlas for their segmentation. With the rapid development of deep learning, K nearest neighbors (KNN) (14) and convolutional neural networks (CNNs) have been used to segment cervical cancer CT images. In a recent study, Wang *et al.* (15) used ResUNet as a segmentation model to compare the variability of resident and model's learning ability. The model was first trained using a gold standard outlined by a particular senior physician. In the meanwhile, residents were mentored by the same senior physician for eight months. The segmentation results obtained by the model segmentation were compared with those obtained by the residents. There was little difference in segmentation accuracy between two. However, the model takes only 2 minutes to complete segmentation, while the residents required 90 minutes to complete the same task. This suggests that the model was much more efficient than manual segmentation by residents. The implementation of deep learning models holds tremendous promise for enhancing both the efficiency and accuracy of medical image segmentation. UNet, V-Net and their variants have shown state-of-the-art performance in various image

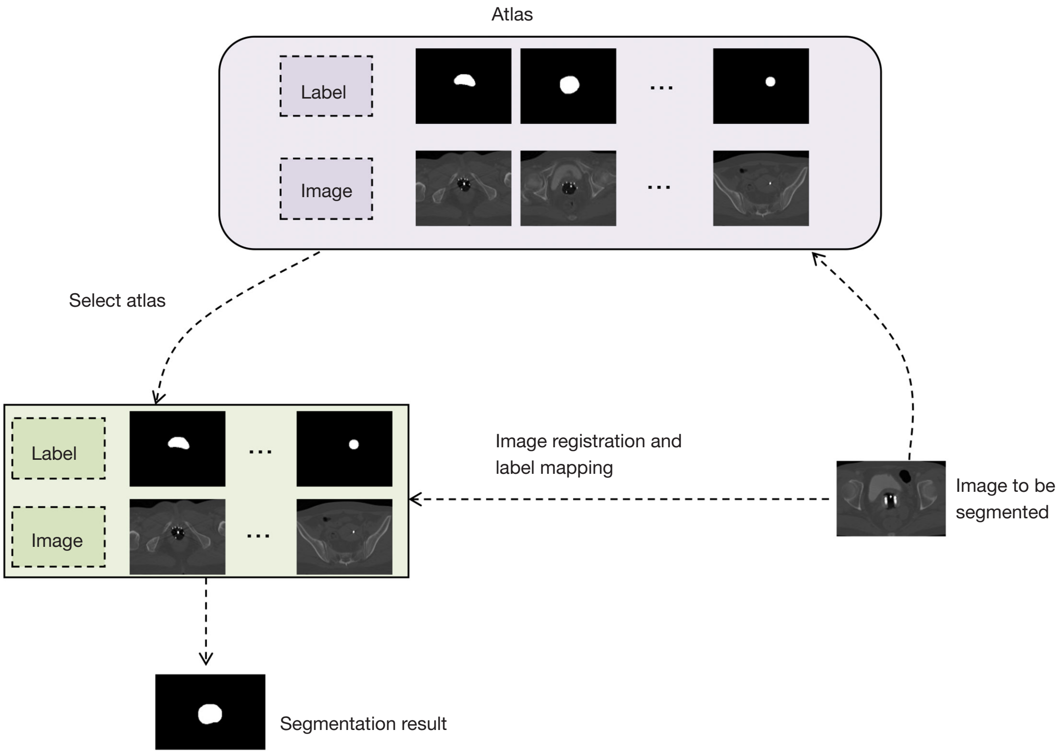

Figure 5 Atlas segmentation process.

segmentation tasks.

Atlas-based segmentation

One commonly used traditional method is atlas-based segmentation. It involves deformable image registration to obtain the contours of the target area and the organs at risk. To be more specific, an accurately labeled image is obtained as an atlas, and then the image to be segmented is mapped onto the atlas using the registration method. The resulting transformation is then used to propagate the atlas labels onto the new image, generating a segmentation result. The whole process is depicted in *Figure 5*. The segmentation accuracy of the atlas method is closely related to the quality of the atlas library. Typically, the accuracy is higher when the images in the atlas library are more similar to the image being segmented. Langerak *et al.* (16), Kim *et al.* (17) and Li *et al.* (18) have used the atlas method in their studies for the segmentation of cervical cancer. The effect of atlas library size on the accuracy and efficiency of the automatic atlas-based segmentation (ABAS) method has also been explored by Kim *et al.* (17) and Li *et al.* (18). However, they reached opposite conclusions regarding the optimal atlas library size. Kim *et al.* (17) showed experimentally that the worst outline results were obtained with a small number of patients in the atlas. They found that increasing the number of patients in the atlas improved the segmentation accuracy. On the other hand, Li *et al.* (18) concluded that no significant differences were found in the segmentation accuracy, measured using the dice similarity coefficient (DSC) and hausdorff distance (HD) metrics, between different atlas library sizes. These differing conclusions highlight the importance of carefully selecting the optimal atlas library size for the specific application at hand. While increasing the size of the atlas library can improve segmentation accuracy, it may not always be necessary, as a small atlas library combined with appropriate registration algorithms can also yield accurate results.

Two-dimensional UNet (2D UNet)

In recent years, the UNet network and its variants have emerged as some of the most popular architectures for this task (19-30). UNet was developed for biomedical image segmentation at the Computer Science Department of the University of Freiburg (31). The network is based on the fully convolutional network and its architecture has been modified and extended to work with fewer training images and to yield more precise segmentations. The structure of a typical UNet network consists of a contracting path, which captures context and reduces the spatial resolution of the input image, and an expanding path, which recovers the spatial information and generates the segmentation mask. Segmentation of a 512×512 image using either UNet or its variants can take less than a second on a modern GPU. UNet adopts an encoder-decoder structure, in which the encoder learns features of different scales through multiple convolutional and pooling operations, and the decoder maps global features to the pixel level. The inclusion of skip connections facilitates the transmission of information to capture features of objects at different scales and levels, enhancing the model's understanding of the target (32). Moreover, the encoder-decoder approach can be trained end-to-end, enabling the network to simultaneously learn feature extraction and pixel-level classification, simplifying model design and training processes. Additionally, the flexibility to modify the encoder, decoder, and skip connections further enhances the model's feature extraction and fusion capabilities (33,34). Mohammadi *et al.* (35) and Liu *et al.* (36,37) successively used the improved UNet to segment cervical cancer and achieved accurate segmentation of cervical cancer CTV and organs-at risk (OARs). To get the 3D information of CT scans, Liu *et al.* (6) and Huang *et al.* (28) designed the model as a 2.5D architecture by assigning different amount of adjacent slices into the three channels. The output was the delineation result of the middle slice. To gain a comprehensive overview of 2D UNet-based segmentation, summaries of representative methods and their performance on segmenting cervical cancer images are listed in *Table 2*. The datasets they used were unpublished private datasets, and the evaluation metrics were chosen as DSC and HD, which are commonly used in the segmentation field.

Three-dimensional UNet (3D UNet)

Medical images are volumetric data because their slices have continuity, the anatomical environment of 3D images is much more complex compared to 2D images. 3D CNN do not need to process the input volume in a 2D slice by slice manner. They can take the whole picture as input to the model. In cervical cancer image segmentation, networks with 3D UNet and V-Net as the basic architecture are commonly used (38-49). The structure of V-Net network is shown in *Figure 6*. Ding *et al.* (44) verified the feasibility of the V-Net network to outline CTV and organs at risk in cervical cancer. In comparison with the 2D network UNet, the study found that the V-Net performed significantly better in the colon segmentation. *Table 3* shows the summary of papers on segmentation of cervical cancer target areas and organs at risk using V-net-based architecture.

Jiang *et al.* (50) and Xiao *et al.* (51) validated the feasibility of RefineNet segmentation of cervical cancer and proved that RefineNetPlus3D achieves better performance than 2D-RefineNet in the organ segmentation task. The RefineNet structure is shown in *Figure 7*. In general, 3D neural networks can obtain contextual connections between images and obtain better segmentation results. *Table 4* lists the segmentation performance of the representative methods of cervical cancer image segmentation based on 3D U-shaped network.

One of the main drawbacks of the 3D networks is that their memory consumption is very large. A 3D UNet requires a specific amount of input data in the spatial dimension, and many patients' data may not meet the input requirements of the network. Therefore, Chang *et al.* (43) proposed a method for segmentation of high-risk clinical target volume (HRCTV) and GTV of cervical cancer that combines 3D UNet with long short-term memory (LSTM) network. This method was developed to address the challenges of segmenting cervical cancer images containing organs at risk such as bladder, bowel, and uterus. The use of LSTM networks with bidirectional convolution allows the network to achieve good performance with only seven consecutive CT images, reducing the limitations associated with spatial dimensionality and memory. The LSTM structure is shown in *Figure 8*.

While 3D networks have high advantages in processing medical images, they often face various optimization difficulties such as overfitting and gradient disappearance. These challenges arise due to the large size and complexity of 3D images. To address these challenges, researchers have developed various techniques. Ju *et al.* (45) combined two network models, Dense Net and V-Net, to improve the ability of the model to extract features and to solve the problems of gradient disappearance and insufficient training data. To minimize the training time, the two models were trained separately and then fused together when the best training results were achieved. The parameters of both Dense Net and V-Net models were optimized separately. The fusion layer is fine-tuned when the loss functions of both models reached their optimal values. This process allowed the Dense V-Net model to achieve the best network fusion in the shortest time and improving the

Table 2 Summary list of 2D UNet-based CT image segmentation technique for cervical cancer

Author, year	Method	Number of patients	Data volume	Evaluation metrics	Result	Highlights
Wang J 2022 (21)	U-shaped network	375 patients	NA	DSC	CTV: 77%	The network consists of three encoders and three decoders, with skip connections in the middle
					Organs at risk: 88–93%	
				95% HD	CTV: 5.81	
					Organs at risk: 1.03–2.96	
Wang J 2023 (26)	U-shaped network	60 patients	NA	DSC	HRCTV: 87%	The segmentation results were scored by two experienced radiation oncologists
					Bladder: 94%	
					Rectum: 86%	
					Sigmoid: 79%	
					Small intestine: 92%	
				HD	HRCTV: 1.45	
					Bladder: 4.52	
					Rectum: 2.52	
					Sigmoid: 10.92	
					Small intestine: 8.83	
Mohammadi R 2021 (35)	ResUNet	113 patients	NA	DSC	Bladder: 95.7%	ResUNet deep convolutional neural network architecture is used, which uses long and short jump connections to improve the accuracy of the feature extraction process and segmentation
					Rectum: 96.6%	
					Sigmoid colon: 92.2%	
				HD	Bladder: 4.05	
					Rectum: 1.96	
					Sigmoid colon: 3.15	
Liu Z 2020 (36)	Improved UNet	105 patients	NA	DSC	Bladder: 92.4%	(I) Formulated this OARs segmentation problem as a binary pixel-level classification problem (II) The convolutional layers in the UNet are replaced by Context Aggregation Blocks (III) Use the Squeeze-Extract block to assign different weights to each channel, thus, to reweight each organ mask importance
					Bone marrow: 85.4%	
					Rectum: 79.1%	
					Small intestine: 83.3%	
					Spinal cord: 82.7%	
				HD	Bladder: 5.098	
					Bone marrow: 1.993	
					Rectum: 5.949	
					Small intestine: 5.281	
					Spinal cord: 3.269	

Table 2 (*continued*)

Table 2 (*continued*)

Author, year	Method	Number of patients	Data volume	Evaluation metrics	Result	Highlights
Liu Z 2021 (37)	Improved DpnUNet	237 patients	NA	DSC 95% HD	CTV: 88% CTV: 3.46	(I) A novel adversarial deep-learning-based auto-segmentation model is hence proposed (II) All encoder and decoder components in UNet are replaced with DPN components (III) A three-stage multicenter randomized controlled evaluation was used, including performance metrics, oncologist evaluation and the Turing imitation test

2D UNet, two-dimensional UNet; CT, computed tomography; NA, not applicable; DSC, dice similarity coefficient; CTV, clinical target volume; HD, hausdorff distance; HRCTV, high-risk clinical target volume; DPN, Dual Path Networks.

model's accuracy and robustness. They experimentally demonstrated that the segmentation results of the fusion model were higher than either single model (46).

In addition to fusing the two network models to improve the model segmentation capability, the researchers have utilized the registration in combination with the network model. Ma *et al.* (47) proposed a novel VB-Net network for cervical cancer segmentation. This network reduced the model parameters by replacing the convolutional, normalization, and activation layers in V-Net with a bottleneck structure. This replacement made the model easier to be generalized. The model outlining results were compared with those of primary, secondary, and advanced doctors. The accuracy of the outlining obtained using the VB-Net model was comparable to that of advanced doctors. This suggests that the VB-Net method has great potential for assisting doctors in clinical practice. They further investigated the effect of combining VB-Net network with registration to improve segmentation accuracy (48). The performance of four cervical cancer target area segmentation methods were compared, namely, rigid registration method, deformable registration method, combination of rigid registration and VB-Net, and combination of deformable registration and VB-Net. The experimental results showed that the segmentation results after combining the deep learning network with the registration were higher than those of the registration method alone. This highlights the potential of combining deep learning methods with traditional image processing techniques to achieve more accurate medical image segmentation.

Cervical cancer segmentation based on MR images

MRI is the most advanced equipment in radiological examination. Compared with the single parameter index of CT, MRI is capable of performing multiple weighted imaging and responding to different characteristics of different tissues. It can also perform multi-directional imaging with high image contrast, resulting in clear soft tissue images that are crucial for cervical cancer images segmentation. The main methods for segmentation of cervical cancer target areas and organs at risk using MRI images include atlas registration methods, level sets, region growth, UNet networks, and their variants.

Traditional methods

Before deep learning became popular, atlas-based, and registration-based segmentation methods were the primary techniques used for segmentation of cervical cancer organs at risk in MR images. Registration is the process of aligning two images by estimating the coordinate geometric transformation. The two images used for registration are called the moving image and the target image, respectively. During the coordinate transformation, the appropriate similarity metric is optimized to align the two images. The key to the registration technique depends on the optimization method used to achieve the best transformation (52). As early as 2011, Berendsen *et al.* (53) used an atlas and registration method to segment the bladder in cervical cancer organs at risk. In their study, the registration was divided into two parts. Firstly, a global transformation involves the B spline method to obtain a

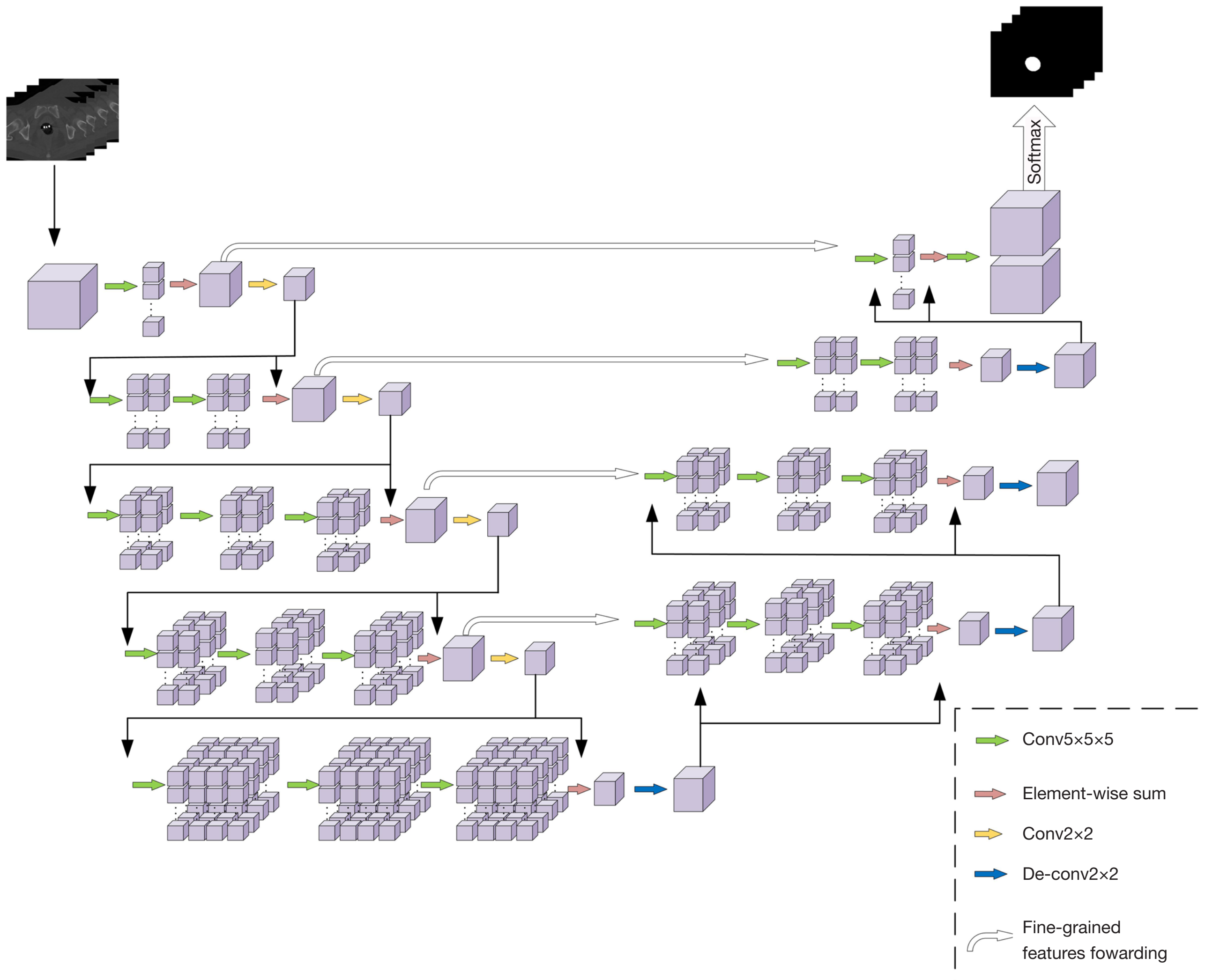

Figure 6 V-Net network structure. The figure was reproduced from Ding *et al.* (44) under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY -NC-ND 4.0).

roughly aligned image. And then, a local registration of the image used a statistical model combined with a prior knowledge to improve the accuracy of the registration. The accuracy of DSC was 0.5 when the global transformation was applied, and the accuracy was further improved to 0.67 after local registration. This value was higher than the accuracy of bladder segmentation reached by other traditional methods. However, when large and complex deformations are encountered, it is common for the registration to end up in a local minimum. To address this issue, Berendsen *et al.* (54) proposed incorporating prior knowledge-based regularization terms into the registration and using statistical models to improve the accuracy of the inter-patient registration. The considerable discrepancy between organ structure and size in the MR images of the two patients can cause great difficulties for registration. However, the proposed method successfully achieved segmentation of CTV with bladder for cervical cancer, and its effectiveness was validated using the leave-one-out method.

Since the tumor size changes during radiation treatment, tumor regression in the registration of MR Images after different doses of radiotherapy poses a challenge for registration. Lu *et al.* (55) defined the registration problem as a mixture of two different distributions, the tumor category, and the normal tissue category. They

Table 3 Summary of V-shaped network-based CT image segmentation technique for cervical cancer and its performance

Author, year	Method	Number of patients	Data volume	Highlights
Ding Y 2022 (44)	3D V-net	130	NA	The CT images of the upper and lower layers are integrated into a new input data to form a pseudo-3D image for learning. The data processing time of input terminal is reduced, so the learning effect and efficiency of CT image are improved
Ju Z 2020 (45)	Dense V-Network	190	NA	The isodose lines of 5, 10, 15 and 20 Gy in the radiotherapy scheme were transformed into structures for learning in the neural network to predict a suitable location for ovarian transposition
Ju Z 2021 (46)	Dense V-Net	133	NA	Dense V-Net is a deep learning network that integrates two deep learning models of Dense Net and V-Net
				The residual connections are used between convolution operations to break network symmetry and enhance the sensitivity of gradient calculations
Ma CY 2022 (47)	VB-Net	535	NA	The convolution, normalization, and activation layers in V-Net are replaced by a bottleneck structure, which is the B in VB-Net
				During the network training process, the multi-scale strategy with a 3D network was applied, by which we first trained a coarse-scale network for rapid positioning of target area and then a fine-scale segmentation model for precisely delineating targets' contours based on previous coarse-scale network output
Ma CY 2022 (48)	Registration and VB-Net	107	NA	The performance of four cervical cancer target volume segmentation methods were compared, which were rigid registration method, deformable registration method, rigid registration and VB-Net combination, and deformable registration and VB-Net combination
Rhee DJ 2020 (49)	3D V-net and 2D FCN-8s	NA	2,254	Registration between the planning CT and the during-treatment CT is applied to align the CT series and the corresponding contour. The aligned planning CT and the corresponding CTV contour are then used as another two channels of input to the network. The output of the network is the estimated CTV contour on the during-treatment CT
				In order to overcome the problem that the GPU memory was not sufficient to train the full-resolution CT images, the size of the input image is adjusted to segment the primary CTV, and the center of mass of the primary CTV is estimated. Then the box that surrounds the primary CTV is cropped and placed on the center of mass predicted in the original CT scan. Finally, the V-Net segmentation model is applied to the cropped 3D image

CT, computed tomography; NA, not applicable; 3D, three-dimensional; CTV, clinical target volume; GPU, graphics processing unit.

described the statistical image grayscale changes for both categories. These mixture distributions were weighted by the tumor detection map, which assigned its abnormality probability to each voxel. The Jacobi determinant of the transformation was also constrained, which ensures the smoothness of the transformation and simulates the tumor regression process. Their study demonstrated that the method was highly suitable for applications in image-guided radiotherapy and computer-aided diagnosis. To improve the model's performance, a Bayesian framework was utilized for registration, detection, and segmentation of cervical tumors in T2-weighted MR images (56). This method also generated tumor probability maps, which provided a better understanding of the tumor location and extent. The registration uses data to align the planned day images to the treatment day images. Then, the segmentation extends the level set model using shape prior information. One of their innovations is to perform non-rigid registration considering not only the organ surface but also the intensity. The intensity matching takes into account the distribution of both tumor and normal tissues. They used the tumor probability map to mix and weight the two distributions, thereby linking registration, detection, and segmentation together in an interdependent manner. This approach

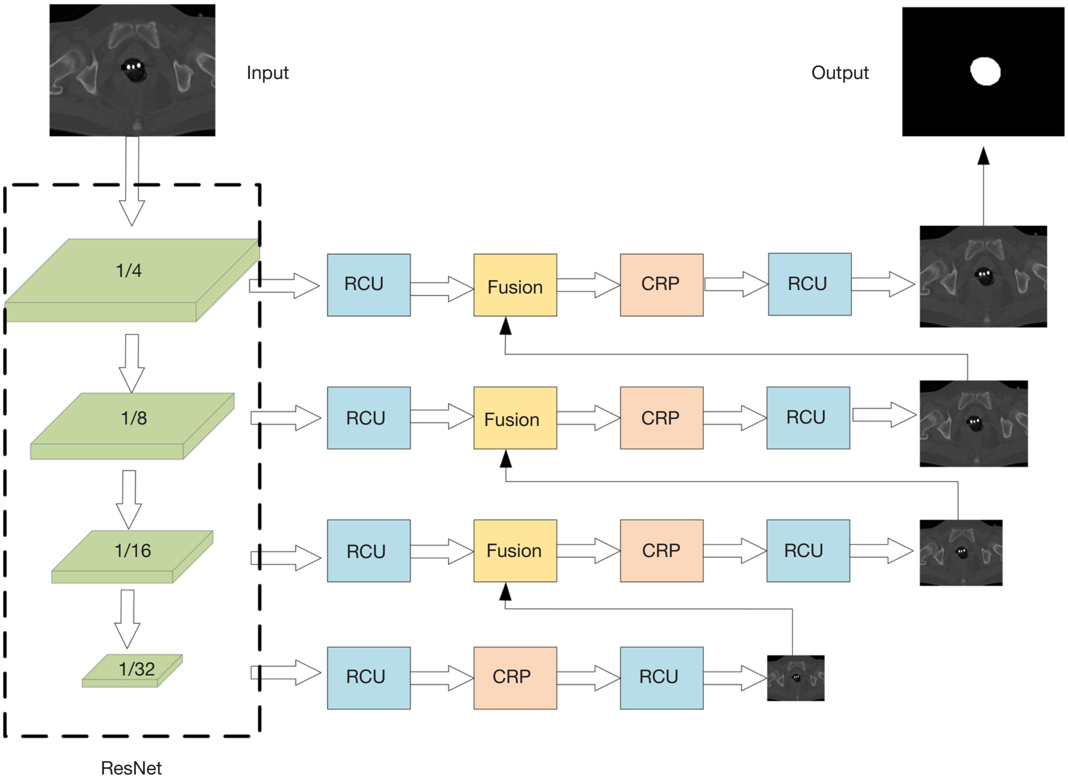

Figure 7 RefineNet structure. The figure was reproduced from Jiang *et al.* (51) under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY -NC-ND 4.0). RCU, residual convolution unit; CRP, chained residual pooling.

achieved higher accuracy across all tasks.

In atlas-based segmentation, the accuracy of multi-atlas segmentation is higher compared to single atlas. One potential challenge of using multi-atlas segmentation is that as the number of images in the atlas increases, the computational volume of segmentation can become significantly larger. Moreover, because there are many organs that can be endangered in cervical cancer, a multi-atlas registration approach is often required for each of these organs to select the appropriate atlas, leading to a substantial computational demand. To overcome these problems, Daly *et al.* (52) proposed a multi-atlas segmentation method, which can automatically select atlases based on the similarity metric. In order to reduce the computational effort during the registration process, a two-step registration was performed. First, a global radiometric registration is performed to obtain preliminary registration results. Then, a local non-rigid registration is applied for fine matching. This approach can significantly reduce the computational time required while still achieving accurate registration results.

Because of the intricated structure of the human abdomen, there is often intensity overlap in the images and noise can have a negative impact on the image quality, making it more difficult for distinguishing cervical tumors from other structures in a single image. Kao *et al.* (57) aligned T2-weighted images with diffusion-weighted MR images using a mutual information method and used the Confederative Maximum a Posterior (CMAP) algorithm to automatically segment cervical tumors. To mitigate the influence of surrounding structure such as the rectum and bladder walls, the authors segmented these structures first and then segmented the cervical tumor within the region of interest.

In addition to atlas and registration segmentation methods, traditional segmentation methods such as level set, region growing, and watershed are also widely used. Garg *et al.* (58) demonstrated an effective approach for segmenting cervical cancer tumor regions in MR images by combining thresholding and watershed techniques, which

Table 4 Summary of 3D U-shaped network-based CT image segmentation technique for cervical cancer and its performance

Author, year	Method	Number of patients	Data volume	Evaluation metrics	Result
Wang Z 2020 (15)	3D ResUNet	125	NA	DSC	CTV: 86%
					Bladder: 91%
					Femoral head right: 88%
					Femoral head left: 88%
					Small intestine: 86%
					Rectum: 81%
				HD	CTV: 14.84
					Bladder: 7.82
					Femoral head right: 6.18
					Femoral head left: 6.17
					Small intestine: 22.21
					Rectum: 7.04
Sartor H 2020 (19)	3D Full Convolutional Network	75 cases of cervical cancer and 191 cases of anorectal cancer	NA	DSC	Femoral head left: 92%
					Femoral head right: 91%
					Bladder: 83%
					Bowel: 86%
					CTVNs: 81%
Beekman C 2022 (20)	3D UNet	84	NA	DSC	CTV: 87%
Chung SY 2023 (27)	3D EfficientNet-B0	180	NA	DSC	CTV: 80%
					Bladder: 88%
				HD	CTV: 13
					Bladder: 6.93
Zhang D 2020 (38)	DSD-UNet	91	91	DSC	HRCTV: 82.9%
					Bladder: 86.9%
					Small intestine: 80.3%
					Sigmoid colon: 64.5%
					Rectum: 82.1%
				HD	HRCTV: 8.1
					Bladder: 12.1
					Small intestine: 27.8
					Sigmoid colon: 19.6
					Rectum: 9.2
Shi J 2021 (39)	RA-CTVNet	462	NA	DSC	CTV: 79.2%
Yi H 2021 (40)	GML	87	NA	DSC	CTV: 81.6%
				HD	CTV: 5.672

Table 4 (*continued*)

Table 4 (*continued*)

Author, year	Method	Number of patients	Data volume	Evaluation metrics	Result
Chang Y 2021 (41)	Improved 3D UNet	400	NA	DSC	CTV: 88.2%
				95% HD	CTV: 6.853
Chen A 2022 (42)	UNet	127	127	DSC	OAR: 82–96%
				95% HD	OAR: 2.30–17.31
Chang JH 2021 (43)	3D UNet and LSTM	51	136	DSC	HRCTV: 87%
					GTV: 72%
					Bowel: 72%
					Foley: 95%
					Bladder: 86%
					Rectum: 77%
					Sigmoid colon: 73%
					Uterus: 93%

3D UNet, three-dimensional UNet; CT, computed tomography; NA, not applicable; DSC, dice similarity coefficient; CTV, clinical target volume; HD, Hausdorff distance; CTVNs, clinical target volume of lymph nodes; HRCTV, high-risk clinical target volume; RA-CTVNet, area-aware reweight strategy and recursive refinement strategy; GML, global multi-level attention; LSTM, long short-term memory; OARs, organs-at risk; GTV, gross target volume.

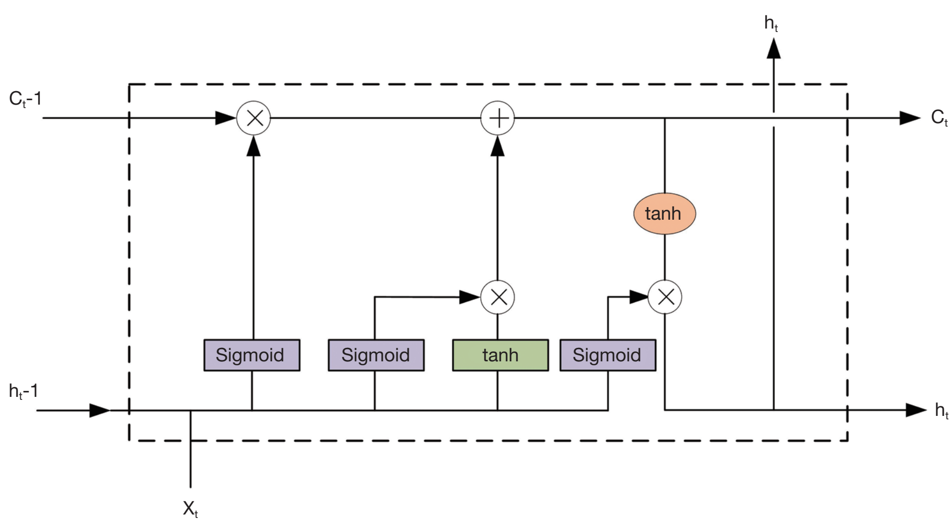

Figure 8 LSTM structure. Ct-1 represents the memory cell internal state, ht represents the hidden state. LSTM, long short-term memory.

allowed for improved accuracy of the segmentation and successful identification of the tumor regions. Su *et al.* (59) presented a global adaptive region growing algorithm that combines image global information with region growing to achieve automatic threshold initialization segmentation. The proposed method sets reasonable thresholds based on different grayscale features of different images, which reduces human involvement and minimizes subjectivity and uncertainty. The algorithm was compared with the traditional methods, such as Region Growing, CV Level Set, and Threshold square, and outperformed these methods. Khoulqi *et al.* (60) introduced a region growth to achieve segmentation of cervical tumor regions. To obtain more information about the tumor, they used axial and vectorial

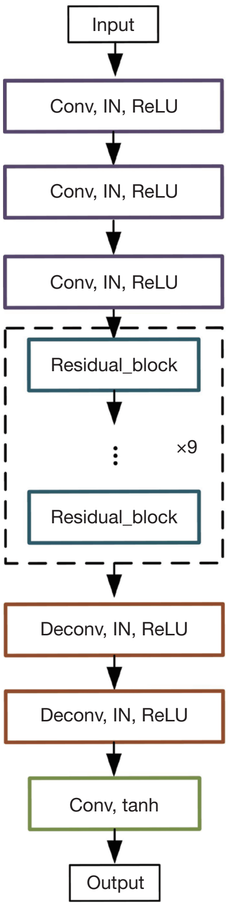

Figure 9 Generator structure. ReLU, rectified linear unit.

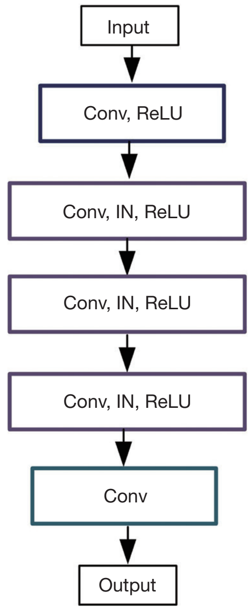

Figure 10 Discriminator structure. ReLU, rectified linear unit.

views of MR images. They preprocessed the images by K-means clustering to enhance the image quality before applying the region growth algorithm for segmentation. The authors also classified the segmented images using the cervical cancer classification criteria described in FIGO (International Federation of Gynecology and Obstetrics). However, this method was overly dependent on the quality of the images after preprocessing. Torheim *et al.* (61) used linear discriminant analysis (LDA) for voxel classification to achieve segmentation of cervical cancer tumor regions on multimodal MR images.

Deep learning methods

In the same way as segmenting cervical cancer in CT images, deep learning segmentation methods have been widely applied for segmentation of cervical cancer CTV with organs at risk on MR images. Bnouni *et al.* (62) first proposed a dynamic multiscale CNN forest to achieve segmentation of cervical tumors on T2-weighted MR images, involving aggregating different CNNs and obtaining bidirectional information flow between two consecutive CNNs. Since the low contrast between organs endangered and the real tumor in MRI images, cervical cancer is difficult for segmentation. Bnouni *et al.* (63) then proposed a new synergetic multiplex network (SMN) for the segmentation of pelvic multi-organs using multi-view (MV) MRI. This method is based on the multi-stage deep learning architecture of cyclic GAN. The generator and discriminator structures in cyclic GAN are shown in *Figures 9,10*. The SMN enhances the spatial coherence between adjacent pixels within the same tissue, making it easy to distinguish various organs at risk with only small contrast differences. Zabihollahy *et al.* (64,65) evaluated 2D Attention UNet, 3D UNet and 3D Dense UNet in the segamentaiton of CTVs and ORAs by using MRI images. Rodríguez Outeiral *et al.* (29) used nnUNet to segment cervical cancer and evaluated model performance based on FIGO stage and GTV volume. Lin *et al.* (66) used DeepLab V3+ as the pre-trained model and then adjusted the training data size and fine-tuning layers through transfer learning. Although the selection and union of models are important for image segmentation, the models become less effective for image segmentation due to image noise, intensity inhomogeneity, and other factors. To overcome this, Bnouni *et al.* (67) proposed a framework for automatic image preprocessing using histogram, smoothing, sharpening, and morphological processing methods. The preprocessed image is segmented using three identical CNN models. A voting mechanism is used to obtain the final segmented image. The approach was found to improve the segmentation accuracy compared to a baseline CNN model, and the effect of image preprocessing on segmentation was demonstrated.

Apart from image preprocessing, the use of prior knowledge can also improve the accuracy of cervical cancer segmentation (20). In practical, the definition of the cervical CTV is partially driven by clinical experience, which leads to different degrees of the inclusions of parametrial and vaginal regions. The boundaries of CTVs do not strictly correspond to the visible boundaries on medical images, which creates great difficulties in segmenting the CTV using CNNs. Incorporating prior knowledge about the expected shape and location of the cervical cancer can improve accuracy by guiding the segmentation process. Since the target area of cervical cancer is located behind the bladder, Zabihollahy *et al.* (65) used information about the location of the bladder and the target area to improve the segmentation accuracy of the target area.

In addition, researchers have developed a combination of 2D models with 3D models in MR images to improve model segmentation performance (23), overcoming the limitations of insufficient 3D data and lack of continuity in 2D data. Another approach is to use 2.5D models. Yoganathan *et al.* (68) used MV MR images combined with axial, coronal and sagittal images to construct a 2.5D model. The final experimental results of Yoganathan *et al.* (68) showed that the segmentation accuracy of the 2.5D network for the target area of cervical cancer with the organs at risk was higher than that of the 2D model. Gou *et al.* (69) proposed the MVFA-Net network to overcome specific challenges such as large MR slice thickness and image intensity inhomogeneity to achieve segmentation of cervical tumors. A multi-view attention (MVA) block was improved based on the residual network by replacing its convolutional layers with a MV block and a channel attention (C-Att) block. In the proposed MV block, multiple convolutional branches with different convolutional kernel sizes are used to target the problem of inconsistent spatial resolution in different views. Thus, they have leveraged information from the context of MR images to improve accuracy.

One of the most significant features of MRI is that it has multiple sequences that provide a rich source of information. However, using a single MRI sequence for segmentation tasks can limit the accuracy of the results. To address this, researchers have explored the use of multiple MRI sequences to improve segmentation accuracy. Huang *et al.* (70) proposed a modified FuseNet network to segment the organs at risk of cervical cancer and prostate cancer. The network used an attention mechanism to fuse multimodal images from T1-weighted, T2-weighted, and enhanced Dixon T1-weighted sequences. Similarly, Wang *et al.* (71) proposed a 3D CNN model to segment the full tumor region, core tumor region, and enhanced tumor region in multi-sequence MR cervical images. The model features a jump structure and residual connections to address gradient dispersion and a Group Normalization layer for faster convergence. Jin *et al.* (30) used EfficientNet as an encoder for UNet++ to achieve cervical cancer segmentation in multi-sequence MR Images. The use of multiple MRI sequences in segmentation tasks has shown promising results, highlighting the importance of leveraging the full potential of MRI data. *Table 5* summarizes the literatures on MR image segmentation of cervical cancer using U-shaped networks.

Cervical cancer segmentation based on PET images

18F-FDG is often used as a radiotracer during PET imaging to reveal metabolic activities *in vivo* (72). When patients are injected with 18F-FDG, PET scanners can construct images that reflect the distribution of 18F-FDG in the human body. Since tumor cells are more metabolically active than normal cells, tumor areas in the patient's body will be more easily observed in PET images, reflecting the shape and size of tumors. 18F-FDG has been widely used for the diagnosis and staging of tumors (73). Several studies have used 18F-FDG PET for radiation therapy planning for different types of tumors (74,75). While CT and MR images provide detailed anatomical information, they may not be sufficient for accurately distinguishing between tumors and normal tissues based on metabolic activity. Therefore, PET imaging, either alone or in combination with CT and MR imaging, has been widely used for the segmentation of cervical cancer.

Tumor volumes in PET images are influenced by threshold selection (76), which causes interference in the outlining of tumor. Erlich *et al.* (77) evaluated semi-automatic segmentation algorithms for GTV depiction in cervical cancer patients using PET images. They compared metabolic PET-derived volumes with MR-based anatomical volumes using three different threshold values, GTV2SD,

Table 5 Summary of U-shaped network-based MR image segmentation technique for cervical cancer and its performance

Author, year	Method	Number of patients	Data volume	Evaluation metrics	Result
Kano Y 2021 (23)	2DUNet and 3DUNet	98	NA	DSC	Tumor (median value): 83%
				HD	Tumor (median value): 4.7
Lu P 2022 (24)	AugMS-Net	NA	894	DSC	Tumor: 87.21%
				HD	Tumor: 0.7012
Lin YC 2020 (25)	UNet	169	NA	DSC	Tumor: 82%
Rodríguez Outeiral R 2023 (29)	3D nnUNet	195	524	DSC	GTV: 73%
				95% HD	GTV: 6.8
Jin S 2023 (30)	UNet++	228	NA	DSC	CTV: 78.6%
				95% HD	CTV: 3.779
Zabihollahy F 2021 (64)	3D UNet and 3D Dense UNet	181	283	DSC	Bladder: 93%
					Rectum: 87%
					Sigmoid colon: 80%
Zabihollahy F 2022 (65)	2D Attention UNet and 3D UNet	125	213	DSC	CTV: 85%
				95% HD	CTV: 3.7
Gou S 2022 (69)	MVFA-Net	160	160	DSC	Tumor: 74.4%
				95% HD	Tumor: 11.18
Huang S 2021 (70)	Improvement of UNet	87	84	DSC	Bladder: 89.8%
					Rectum: 78.1%
				95% HD	Bladder: 8.738
					Rectum: 11.775

MR, magnetic resonance; NA, not applicable; DSC, dice similarity coefficient; HD, Hausdorff distance; GTV, gross target volume; CTV, clinical target volume.

GTV40% and GTV50%. GTV2SD was defined as pixels with 2 standard deviations of the mean plus liver intensity, while GTV40% and GTV50% were defined as pixels with 40% and 50% of the maximum tumor intensity, respectively. The comparison validated the GTV2SD method is more accurate for PET tumor segmentation in cervical cancer patients. Monteiro *et al.* (78) verified the effectiveness of the region growth algorithm for segmentation of cervical tumor regions in PET images. They combined the information from PET, CT, and MR images. Firstly, the MR images were affine aligned with PET/CT images to ensure the correspondence between each patient image. Then, a region growth algorithm was used to segment the tumor regions. To improve the accuracy and reliability of the segmentation results, a multi-criteria decision process was implemented by applying four classifiers KNN, LDA, PROAFTN (79) and Naive Bayes to different image pattern combinations. Recently, Baydoun *et al.* (80) implemented automatic segmentation of cervical tumors on small datasets of PET/MR images using shallow UNet networks, by invoking the concepts of focus and sequential training to achieve accurate segmentation on small datasets.

PET images are highly sensitive to the metabolic activity of tissues and organs, including the bladder, which can interfere with accurate segmentation of cervical tumors. To overcome this issue, several studies have been focused on separating the bladder from the tumor before segmentation. One approach is to use morphological manipulation, regional growth, and other image processing methods to remove the influence of the bladder (81). Another approach is to construct a hyper-image by combining CT and PET images to depict rough tumor regions based on tissue specificity. Additionally, gradient information from the hyper-image can be introduced into the level set function to reduce the influence of the bladder on tumor segmentation (82). Mu *et al.* (83) segmented cervical tumors by adding intensity and gradient field information to the level set framework after Gaussian filtering of PET images. In addition to this, they also investigated the effect of image texture features on cervical cancer staging and verified that texture features are highly correlated with tumor staging and can provide valuable prognostic information. Overall, their methods offer a more precise and comprehensive approach to cervical tumor segmentation. Chen *et al.* (84) segmented cervical tumors in PET images by a two-stage segmentation. First, coarse segmentation was performed by measuring voxel local similarity using a graphical cut method. Then, the initial segmentation was fine-tuned using a similarity-based variational model. This was done by using the information that the tumor shape and location did not vary much between adjacent slices, which helped to improve the accuracy of the final segmentation results. The authors then (85) proposed a prior information constrained (PIC)-spatial information embedded CNN model (S-CNN) by combining prior knowledge into CNN model to separate bladder and cervical tumor before segmenting cervical tumor. Since roundness has been shown to be a feature of cervical tumors in previous studies (86-88) and the location of the bladder and cervical tumor is fixed, with the bladder always in front of the cervical tumor, adding this prior knowledge to the CNN model reduces the influence of the bladder on subsequent cervical tumor segmentation. Iantsen *et al.* (22), on the other hand, used manual separation of the bladder from the cervical tumor. They determined the volume of the cervical tumor using the FLAB algorithm, which was used as the gold standard. Then, they used a modified 3D UNet network to achieve automatic segmentation of the cervical tumor, where the maximum pooling operation in the network was replaced with downsampling and a concurrent spatial and channel squeeze and excitation (scSE) module was included in the residual block. The original UNet network was optimized, and the model applicability was assessed using five-fold cross-validation.

Current challenges and limitations

The main treatment modality for middle and advanced cervical cancer involves a combination of external pelvic irradiation therapy, intracavitary brachytherapy, and chemotherapy. In brachytherapy, precise positioning of the tumor area and organs at risk is critical for doctors to determine the appropriate radiation dose and develop accurate outlines for the CTV and organs at risk. This process enables reasonable dose planning that can deliver a high radiation dose to the tumor area while minimizing damage to healthy surrounding organs. Failure to achieve precise positioning can result in deviations in plan evaluation and dose projection, negatively impacting the effectiveness of tumor treatment.

The segmentation of cervical tumors and organs at risk is based on image data from three modalities: CT, MR, and PET, and the segmentation methods are broadly classified into two categories: deep learning segmentation methods based on UNet networks and their variants, and traditional methods that rely on registration and atlas for segmentation.

Comparison between the atlas-based and deep learning based automatic segmentation

Berendsen *et al.* (53) used a single-atlas approach to segment the bladder in cervical cancer patients by combining global rigid registration and local registration. However, the volume and location differences between the target image and the atlas image were too large, which significantly decreased the resulting segmentation accuracy. Multi-atlas registration can solve the problems that arise from single-atlas registration (52,54). It relies more on the topology established between the moving image and the target image (17). Since the soft tissue resolution of CT images is low, the segmentation method of atlas is more dependent on the image quality. Rhee *et al.* (49) compared the difference in the results of cervical cancer segmentation using the atlas method with the deep learning method. The accuracy of segmentation of CT images of cervical cancer using atlas is relatively low compared with that using deep learning methods, among which U- and V-shaped networks and their variants are the most frequently used networks for cervical cancer segmentation (35-41,43-47). Additionally, UNet can be trained from scratch to achieve accurate segmentation results with very little labeled training data, which is important for medical image segmentation. Because the process of acquiring medical image datasets may involve patient privacy and other issues, and medical image annotation is time-consuming and laborious, medical image datasets are generally small and difficult to obtain.

MR imaging can distinguish between normal soft tissue and tumor-infiltrated soft tissue and can characterize deformable structures with excellent visualization. MR images of cervical cancer can be segmented using an atlas-registration method. This process involves a transformation between the two images. In atlas-based automatic segmentation methods, the segmentation structure from the atlas library can be propagated to the target image using a deformable image registration algorithm. Deformable image registration methods can be divided into two categories, an intensity method based on image gray values and another one based on image features. Considering the effect of cervical tumor fading during the treatment process, in the registration of cervical cancer images, feature-based methods have better results than intensity-based registration methods (89). Lu *et al.* (56) proposed to use a maximum a posteriori (MAP) framework based on a non-rigid registration considering organ surface registration and intensity matching, and the final model segmentation achieved an accuracy comparable to manual segmentation.

Existing segmentation accuracy of CTV and OARs

The most commonly used assessment metric for cervical cancer image segmentation is the use of quantitative measures such as DSC and HD for comparison with gross target contours, and *Tables 6-8* show the papers using DSC/HD as an assessment metric and their segmentation results.

For cervical cancer with organs at risk segmentation the most used methods were based on the UNet architecture for improvement. For organs at risk segmentation, taking the bladder as an example, as shown in *Table 6*, the DSC of these methods basically reached more than 90%, with the lowest DSC for software-based, mapping, registration, and full convolution methods, which may be related to differences in the size and shape of the patient's bladder. The segmentation results of CTV are a bit worse than bladder, as shown in *Table 7*, and the DSC basically reached more than 80%, which is due to the complex composition and blurred boundary of CTV. The highest DSC of CTV among these methods was achieved by Mu *et al.* (83) using a level set approach to CTV segmentation combining intensity and gradient field information, with a DSC result of 91.78%. This is not much different from their accuracy in segmenting cervical tumors (82), which is due to the fact that CTV is obtained from GTV expansion, which is the cervical tumor region. The level set method showed high accuracy in segmenting cervical cancer. In addition, 3D models generally have higher accuracy in the segmentation of cervical cancer compared to 2D models (20,37,41).

Squeeze-and-excitation (SE), res, and dilated convolution

The UNet-based methods used by the researchers differ significantly from each other. One part fuses the UNet network with another network, and the fused network has the advantages of two single networks, which improves the segmentation of the fused network (45,46) and the fused model segmentation DSC accuracy is 0.07 higher than that of the single model (46), but its training time is higher than that of the single model. Another part of them embeds a part of other networks into the UNet network or replaces the convolutional layers in UNet and V-Net as a way to overcome the problem of unclear boundaries of the CTV of cervical cancer, which endangers organs with different sizes, shapes and locations (6,35,37,39,41,43,44,47).

The full use of SE blocks and residual blocks in a UNet network can improve the ability of the model to acquire certain features (15,35,38-41). SE blocks automatically acquire the importance of each feature channel by a squeeze operation and an excitation operation. This allows the network to promote useful features and suppress less informative features for the current task according to this importance. The residual block can be used to avoid gradient disappearance. This is because the residual connection allows the gradients to flow directly through the block, avoiding the vanishing gradient problem that can occur in deep neural networks. Residual blocks also help to preserve the details of the image, especially at the boundaries of abnormal cells, by allowing the model to learn residual mapping functions that capture the fine-grained details of the image. In addition to SE blocks and residual blocks, dilation convolution is also widely used in cervical cancer segmentation to improve the model's ability to extract features. During the model segmentation, the feature maps are gradually down sampled to capture semantic contextual information at different image scales. Additionally, through the down sampling process, a larger receptive field is achieved, which can help improve the model's ability to localize object boundaries and other fine details in the image. However, this down sampling process will reduce image resolution and lose information. Dilated convolution is proposed in response to this effect. It can obtain features in a larger receptive field without increasing the number of parameters. When being used in bottleneck structures, dilated convolution allows the model to better handle multi-scale information, preserve the image resolution, and improve the model's ability to identify cervical cancer boundaries (36,38,40). Experiments by Mohammadi (35), Shi (39), etc. proved that the addition of residual structure and SE block can significantly improve the ability of the model to segment cervical cancer organs at risk.

Since there is no public data set in the field of cervical

Table 6 Summary of performance of papers using DSC/HD as an evaluation metric for segmentation of the bladder

Author, year	Method	Number of patients	Data volume	Mode of image	Evaluation metrics	Result
Liu Z 2020 (6)	DpnUNet	237	22,356	CT	DSC	91%
					HD	4.05
Wang Z 2020 (15)	3D ResUNet	125	NA	CT	DSC	91%
					HD	7.82
Kim N 2020 (17)	Atlas	75	NA	CT	DSC	54%
					HD	60.2
Li Y 2022 (18)	Atlas	140	140	CT	DSC	86.6%
					HD	1.591
Sartor H 2020 (19)	3D Full Convolutional Network	75 cases of cervical cancer and 191 cases of anorectal	NA	CT	DSC	83%
Wang J 2023 (26)	U-shaped network	60	NA	CT	DSC	94%
					HD	4.52
Chung SY 2023 (27)	3D EfficientNet-B0	182	NA	CT	DSC	88%
					HD	6.93
Mohammadi R 2021 (35)	ResUNet	113	NA	CT	DSC	95.7%
					HD	4.05
Liu Z 2020 (36)	Improvement of UNet	105	NA	CT	DSC	92.4%
					HD	5.098
Zhang D 2020 (38)	DSD-UNet	91	91	CT	DSC	86.9%
					HD	12.1
Chang JH 2021 (43)	3D UNet and LSTM	51	136	CT	DSC	86%
Ding Y 2022 (44)	3DV-net	130	NA	CT	DSC	94%
					HD	4.52
Ju Z 2020 (45)	Dense V-Network	190	NA	CT	DSC	95%
					HD	0.65
Rhee DJ 2020 (49)	3DV-net and 2D FCN-8s	NA	2254	CT	DSC	89%
					HD	1.07
Jiang X 2021 (50)	RefineNet	200	NA	CT	DSC	86.0%
					HD	19.981
Xiao C 2022 (51)	RefineNetPlus3D	313	44,222	CT	DSC	97%
Berendsen FF 2011 (53)	Atlas	17	NA	MR	DSC	67%
Berendsen FF 2013 (54)	Alignment	17	84	MR	DSC	73%
					HD	20
Bnouni N 2020 (63)	Synergetic Multiplex Network (SMN)	15	NA	MR	DSC	95.75%
Zabihollahy F 2021 (64)	3-D UNet and 3-D Dense UNet	181	283	MR	DSC	93%
Huang S 2021 (70)	Improvement of UNet	87	84	MR	DSC	89.8%
					95% HD	8.738

DSC, dice similarity coefficient; HD, Hausdorff distance; CT, computed tomography; NA, not applicable; MR, magnetic resonance.

Table 7 Summary of performance of papers using DSC/HD as an evaluation index for segmentation of CTV in cervical cancer

Author, year	Method	Number of patients	Data volume	Mode of image	Evaluation metrics	Result
Liu Z 2020 (6)	DpnUNet	237	22,356	CT	DSC	CTV: 86%
					HD	CTV: 5.34
Wang Z 2020 (15)	3D ResUNet	125	NA	CT	DSC	CTV: 86%
					HD	CTV: 14.84
Kim N 2020 (17)	Atlas	75	NA	CT	DSC	CTV: 79%
					HD	CTV: 19.7
Li Y 2022 (18)	Atlas	140	140	CT	DSC	CTV: 81.6%
					HD	CTV: 2.195
Beekman C 2022 (20)	3D UNet	84	NA	CT	DSC	CTV: 87%
Wang J 2022 (21)	U-shaped network	375	NA	CT	DSC	CTV: 77%
					95% HD	CTV: 5.81
Wang J 2023 (26)	U-shaped network	60	NA	CT	DSC	HRCTV: 87%
					HD	HRCTV: 1.45
Chung SY 2023 (27)	3D EfficientNet-B0	180	NA	CT	DSC	CTV: 80%
					HD	CTV: 13
Huang M 2023 (28)	Improved MNet	53	5,438	CT	DSC	CTV: 88.28%
					95% HD	CTV: 3.2013
Jin S 2023 (30)	UNet++	228	NA	MR	DSC	CTV: 78.6%
					95% HD	CTV: 3.779
Liu Z 2021 (37)	Improvement of DpnUNet	237	NA	CT	DSC	CTV: 88%
					HD	CTV: 3.46
Zhang D 2020 (38)	DSD-UNet	91	91	CT	DSC	HR-CTV: 82.9%
					HD	HR-CTV: 8.1
Shi J 2021 (39)	RA-CTVNet	462	NA	CT	DSC	CTV: 79.2%
Yi H 2021 (40)	GML	87	NA	CT	DSC	CTV: 81.6%
					HD	CTV: 5.672
Chang Y 2021 (41)	Improved 3D UNet	400	NA	CT	DSC	CTV: 88.2%
					95% HD	CTV: 6.853
Chang JH 2021 (43)	3D UNet and LSTM	51	136	CT	DSC	HRCTV: 87%
Ding Y 2022 (44)	3DV-net	130	NA	CT	DSC	CTV: 85%
					HD	CTV: 11.2
Ju Z 2021 (46)	Dense V-Net	133	NA	CT	DSC	CTV: 82%
					HD	CTV: 1.86
Ma CY 2022 (47)	VB-Net	535	NA	CT	DSC	CTV: 70%
					HD	CTV: 22.44

Table 7 (*continued*)

Table 7 (*continued*)

Author, year	Method	Number of patients	Data volume	Mode of image	Evaluation metrics	Result
Ma CY 2022 (48)	Registration and VB-Net	107	NA	CT	DSC	CTV: 89%
					HD	CTV: 6.14
Rhee DJ 2020 (49)	3DV-net and 2D FCN-8s	NA	2254	CT	DSC	CTV: 86%
					HD	CTV: 2.02
Jiang X 2021 (50)	RefineNet	200	NA	CT	DSC	CTV: 86.1%
					HD	CTV: 6.005
Xiao C 2022 (51)	RefineNetPlus3D	313	44,222	CT	DSC	CTV: 82%
Berendsen FF 2013 (54)	Registration	17	84	MR	DSC	CTV: 57%
					HD	CTV: 36
Mu W 2015 (83)	FCM-LSGF	42	NA	PET	DSC	CTV: 91.78%
					HD	CTV: 7.94

DSC, dice similarity coefficient; HD, Hausdorff distance; CTV, clinical target volume; NA, not applicable; CT, computed tomography; MR, magnetic resonance; HRCTV, high-risk clinical target volume; PET, positron emission tomography.

cancer segmentation at present, in order to verify the generalization of res module and SE module, as well as explore the application of transformer-based U-Net networks, we used a private data set from our lab to verify the performance of selected methods. The data set included CT images of 53 cervical cancer patients, which were divided into training set, validation set, and test set according to the ratio of 8:1:1. The experimental results are shown in *Table 9*. We have obtained similar conclusions as pervious reports. By adding residual structure and SE module on the basis of UNet, the accuracy of cervical cancer CTV segmentation can be significantly improved. However, when residual structure and SE module are added into UNet, the network segmentation result is lower than that of ResUNet. Therefore, the effective combination of residual structure and SE module should be determined according to the nature of the data set.

High precision of segmentation and low clinical availability

Evaluation metrics such as mean DSC and HD are objective and represent the degree to which geometrically modeled segmentation results resemble the underlying facts, providing good reproducibility but not incorporating physician judgment (37). Since the CTV boundaries of cervical cancer depend on the definition of other tissues and organs in a given region, its boundaries are not clear, and the CTV may contain regions such as lymph nodes. These areas are small but clinically important, but performance indicators such as DSC and HD treat these important areas as the same as other normal tissues. Although high DSC/HD has been achieved in experiments, in clinical practice it may omit important regions and make the model much less valuable to effectively assess its accuracy and applicability in real clinical settings (19,37). Sartor *et al.* (19) achieved a quantitative assessment of 0.82 for CTV by DSC, but qualitative results suggest that CNN segmentation for CTV is mostly unacceptable in clinical settings. Therefore, physician assessment as well as Turing test are important for model evaluation.

Inaccurate dose calculation

The evaluation indexes of cervical cancer target area and organs at risk include dose indexes besides geometric indexes such as DSC and HD. Wang *et al.* (21) used dose metrics such as D_{mean} and V100 to measure the segmentation accuracy of the model, where D_{mean} was defined as the average dose received by the structure and V100 was defined as the volume of CTV receiving 100% of the prescribed dose. Their results showed that most of the segmentation contours were more accurate, and the radiotherapy dose met the clinical requirements, but for CTV the dose did not meet the clinical requirements and needed further correction by radiation oncologists. Chen

Table 8 Summary of performance of papers using DSC/HD as an evaluation index for segmentation of rectum in cervical cancer

Author, year	Method	Number of patients	Data volume	Mode of image	Evaluation metrics	Result
Wang Z 2020 (15)	3D ResUNet	125	NA	CT	DSC	81%
					HD	7.04
Li Y 2022 (18)	Atlas	140	140	CT	DSC	68.5%
					HD	2.508
Wang J 2023 (26)	U-shaped network	60	NA	CT	DSC	86%
					HD	2.52
Mohammadi R 2021 (35)	ResUNet	113	NA	CT	DSC	96.6%
					HD	1.96
Liu Z 2020 (36)	Improvement of UNet	105	NA	CT	DSC	79.1%
					HD	5.949
Zhang D 2020 (38)	DSD-UNet	91	91	CT	DSC	82.1%
					HD	9.2
Chang JH 2021 (43)	3D UNet and LSTM	51	136	CT	DSC	77%
Ding Y 2022 (44)	3DV-net	130	NA	CT	DSC	85%
					HD	4.35
Ju Z 2020 (45)	Dense V-Network	190	NA	CT	DSC	87%
					HD	0.79
Rhee DJ 2020 (49)	3DV-net and 2D FCN-8s	NA	2,254	CT	DSC	81%
					HD	1.66
Jiang X 2021 (50)	RefineNet	200	NA	CT	DSC	85.8%
					HD	12.273
Xiao C 2022 (51)	RefineNetPlus3D	313	44,222	CT	DSC	91%
Zabihollahy F 2021 (64)	3-D UNet and 3-D Dense UNet	181	283	MR	DSC	87 %
Huang S 2021 (70)	Improvement of UNet	87	84	MR	DSC	78.1%
					HD	11.775

DSC, dice similarity coefficient; HD, Hausdorff distance; NA, not applicable; CT, computed tomography; LSTM, long short-term memory; MR, magnetic resonance.

et al. (42) focused on the same point as Wang *et al.* (21), who used automatically segmented and manually segmented organ contours for treatment plan optimization to explore the dose differences between automatically segmented and manually segmented treatment plans for organs at risk and target areas. The results showed that the dose distribution in the target area was unaffected when automatically segmented organ contours were used to design the treatment plan, whereas the effect of automatic segmentation on OAR dose was complex and required physician modification if necessary. This suggests that DL-based methods do not produce accurate dosimetric endpoints in cohorts of cervical cancer patients compared to standard manual contour lines.

No public dataset

Since there are few studies on brachytherapy for cervical cancer, no published imaging datasets during brachytherapy

Table 9 Comparison of the CTV segmentation accuracy on our dataset by selected methods (mean)

Model	DSC	HD95
UNet	0.8670	3.9143
Res UNet	0.8759	3.1488
SE UNet	0.8727	3.4188
SE Res UNet	0.8750	3.3923
Swin UNet	0.8466	4.6447

CTV, clinical target volume; DSC, dice similarity coefficient; HD, Hausdorff distance; SE, squeeze-and-excitation.

for cervical cancer have been seen in published papers, and all experiments have been performed with private datasets. However, because there is no uniform clinical standard for CTV and organs at risk segmentation in cervical cancer, the personal experience of different oncologists in their segmentation varies, leading to different results in their manual segmentation (90,91). In addition, the use of imaging equipment parameters, different image acquisition protocols and the diversity of tumor staging in different centers make the data appear variable. Chang *et al.* (41) found that the variation of data from the same hospital was less than that from different hospitals, and too much variation in the dataset made it difficult to generalize the model, so consistent segmentation criteria with a common dataset is important for measuring the accuracy of the model.

Conclusions

This paper summarizes the segmentation methods of cervical cancer and organs at risk based on three modality images and introduces the applicable segmentation methods for different images and the improvements between different methods. Accurate segmentation of cervical cancer target areas and organs at risk requires extensive clinical experience for clinicians. In practical applications, computer-aided segmentation to help doctors obtain accurate segmentation results of CTV and organs at risk can reduce a lot of marking work and variability for doctors, making radiotherapy planning more effective and reliable and avoiding irreversible damage to patients caused by overtreatment.

Although many methods have been proposed to achieve segmentation of CTV for cervical cancer, the complexity of CTV composition and image quality have prevented its segmentation from achieving higher accuracy. Among them, the best segmentation results were achieved by methods based on improved level sets. In addition, because the datasets were not uniform, which prevented meaningful comparisons between the model proposed in the article and other models, it is important to establish a standard and uniform public dataset for cervical cancer and organs at risk segmentation in the future.

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Footnote

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