Image Guided Radiotherapy for Cervical Cancer: A Review

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Abstract

Cervical cancer (CC) is one of the most common cancers in female worldwide. Radiotherapy plays an important role in the treatment of cervical cancer, and about 80% of CC patients need radiotherapy. However, many factors, including body position, body mass index and bladder filling state and so on, can affect the set-up errors during the treatment of radiotherapy. Recently, image guided radiotherapy has been widely used in clinic to reduce set-up errors and improve the accuracy of radiotherapy. Besides, image guided radiotherapy is applied for the analysis of cervical cancer target expansion. There is no doubt that radiotherapy could improve the therapeutic effect of cervical cancer, but the complications caused by radiotherapy should also draw our attentions.

Keywords

Cervical cancer, set-up errors, BMI, bladder filling state, image guided radiotherapy

1. Introduction

Tumor is a common disease, which is caused by many factors. Recently, operation, radiotherapy and chemotherapy are the convention treatment methods of tumor in clinic.

Radiotherapy is very common among all the treatments, which can be used for the treatment of local tumor [1-3].

Ionizing radiation was discovered to be used to treat pituitary tumors as an adjunctive therapy [4]. Cell death is induced by radiotherapy through cellular level. Since the process takes a long time to normalize hormone levels, adjunctive medical therapies are required at the same time [5]. External beam radiation is most commonly applied for the treatments of pituitary adenomas with conventional radiotherapy (CRT) [6]. CT/MRI is involved in targeted treatment planning, besides, the customized mask is also used for stabilization of head and target of precise tumor. Stereotactic radiosurgery (SRS), including proton beam therapy and Gamma Knife, require neuroimaging techniques, for instance, CT/MRI or PET scan mapping [7].

The basic principle of precise radiotherapy for tumor is to ensure that the radiation can concentrate on the tumor area to the maximum extent, and the surrounding normal tissue can be well protected [8]. This requires accurate diagnosis, precise location, precise radiotherapy plan and precise treatment before radiotherapy treatment [9]. It is very important to improve the fitness of target area as well as the dose of target area. There are many uncertain factors that affect the accuracy of radiotherapy in the process of tumor radiotherapy, including the displacement of tumor and normal tissue, the positioning error in treatment, the reliability and stability of treatment equipment and other factors [10]. How to solve these problems and improve the accuracy of target irradiation is very essential in the field of radiotherapy [11].

Cervical cancer (CC) is one of the most common cancers in female worldwide. It's reported that there are

98,900 new cases and 30,500 thousand deaths every year in China [12]. For postoperative patients with cervical cancer, IMRT is associated with comparable survival and decreased toxicity. Radiotherapy plays an important role in the treatment of cervical cancer, and about 80% of CC patients need radiotherapy [13]. Radiotherapy planning refers to the calculation of dose deposition throughout the patient, based upon quantitative electron density images from computed tomography (CT) scans taken before treatment. Cone beam CT (CBCT), consisting of a point source and flat panel detector, is often built onto radiotherapy delivery machines and used during a treatment session to ensure alignment of the patient to the plan [14]. There are many factors that can affect the accuracy of radiotherapy target area in the process of CC radiotherapy. In addition to the inherent error of the system, the positioning error, the involuntary movement of human organs and the displacement caused by different filling states, and the change of tumor volume in the treatment are the common causes of radiotherapy error [15].

2. Application of image guided radiotherapy in the analysis of cervical cancer set-up error

The set-up error can be divided into system error and random error. The precision of machine is the mainly cause of system error, while random error is resulted from the movement of tissues and organs, positioning technology as well as the performance of radiotherapy doctors [16]. System error refers to the difference between the position of patients in the treatment of different times and the position in the simulation positioning. It's caused by the inconsistency of the machine system itself, such as the inconsistency between the accelerator and the simulator, the error between the accelerator and the simulation positioning, etc. It's possible to reduce the system error by regular quality assurance and quality control of the machine [17]. However, random error refers to the difference of position repeatability of patients during each treatment, which occurs during the actual treatments. Random error is related to the operation of technicians, the position maintenance of patients and the movement of organs [18]. Therefore, we pay attentions to random error in clinic because it significantly affects the treatment effect.

3. Set-up error in image guided radiotherapy of cervical cancer

Two kinds of set-up errors occur in treatment: random error and systematic error. Random error may lead to the change of dose distribution, which will cause the decrease of local control rate of tumor or the increase of complications of normal tissue. Therefore, we should take random error into consideration and try to minimise error and improve the accuracy during the treatment [19].

Image guided radiation therapy (IGRT) is a new radiotherapy technology following three-dimensional conformal radiotherapy and intensity-modulated radiotherapy. According to classification of image dimension, image guided radiotherapy technology can be divided into a number of categories, including two-dimensional KV image, MV image and three-dimensional KV-CBCT image or MV-CBCT image. Image guided radiotherapy can be used to analyze the location of tumor, the size of target area, the changes of organs at risk and the changes of bladder. Therefore, image guided radiotherapy has been widely used in the radiotherapy of cervical cancer [20-21].

3.1 Body position and Body mass index affect the set-up error

Because of less rigid structure, more subcutaneous fat, soft and deformable abdominal wall, the effect of body position fixation is often inferior to that of head and neck tumor. As stated in Jian Xu et al.'s study, the volume of dangerous organs around cervical cancer, such as bladder and small intestine, changes with the filling degree and body position. Thus, how to improve the positioning accuracy through reasonable body position and fixation is particularly important [22]. According to Zhang et al.'s research, vacuum bag immobilization caused the least set-up errors compared with thermoplastic body model immobilization, while body model immobilization could reduce the position error compared with no immobilization ($P < 0.01$) [23]. In Ping Li et al.'s study, pre-and post-fraction CBCT scans were used for 18 cervical cancer patients. The moving distance of center point in tumor was (8. 890±7. 222) mm before CBCT, and after correction the distance was (1. 021±1. 075) mm, the result indicated that CBCT scans could significantly reduce setup errors after correction [24]. As stated in Liuetal's study, no significant difference was found between supine position and prone position if the body mass index (BMI) was not been taken into consideration. For the patients with BMI<24 kg/m^2, the setup errors of supine position were significantly more than those of prone position in Z direction, while for the patients with BMI>24 24 kg/m^2, the setup errors of supine position were significantly less than those of prone position in Z direction. Besides, no significant difference was observed between the two groups in X and Y direction [25]. Yi Liu et al.

also pointed out that the set-up errors of X-axis, Y-axis and Z-axis in the normal group was significant less than that in the obese group before correction. The result also indicated that CBCT can effectively corrected the positioning error and was not affected by the patient's BMI [26]. Cai et al. pointed out that the setup error of obese patients is larger. The application of CBCT image guided technology in setup error correction could reduce the impact of patient's body shape on MPTV value [27].

Obese patients lie down with skin traction on the surface. The thicker the subcutaneous fat layer, the more severe the skin pull, especially in patients with thick abdominal fat and loose skin. Therefore, the patients must avoid the left and right movement as much as possible to avoid local skin traction. The set-up errors might be related to the patients breathing, especially for the abdominal breathing. Since obese patients have a relatively thick body, and the amplitude of respiratory movement on the body surface will be larger than that of normal patients. It will be better for the patients to breathe steadily and adopt shallow breathing and chest breathing as much as possible.

3.2 Bladder filling state affects set-up error

Cervical cancer is a common malignant tumor of female reproductive system. With the progress of medicine and the prolongation of patients' survival time, the quality of life evaluation after treatment has become an important standard for quality methods [28]. IMRT (intensity modulated radiation therapy) can improve the accuracy of radiotherapy target area of cervical cancer, reduce radiation exposure to normal tissues and organs, reduce the incidence of complications, and improve the quality of life of patients, however, in the course of radiotherapy, with the tumor shrinking, the tumor volume and location may change dramatically. When the bladder is involved in the radiotherapy, the incidence of acute and chronic complications of the digestive system may occur [29].

The bladder is located in the center of the pelvic cavity. It is a kind of variable cystic organ. The volume, size and shape of bladder are determined by the filling degree. In general, the capacity of adult bladder is about 300-500 ml, and the maximum capacity is 800 ml. With the increase of bladder volume, the small intestine area can be pushed upward by the full bladder, and then the treatment irradiation area can be changed. When the bladder becomes smaller, the empty part is easily filled by the small intestine, and the treatment irradiation area will be changed as well. Reliability of bladder volume at the time of radiation treatment is low, regardless of bladder filling instructions, although an empty bladder reduces absolute variation in bladder volume. The filling degree of the bladder determines the change of the volume and position structure of the bladder, which may have a certain impact on the absorbed dose [30-32]. Besides, different doctors will also have different ways to sketch the bladder boundary, which may lead to the error of bladder volume [33]. Bladder filling can not only reduce the radiation dose of the bladder itself, but also the radiation dose of the small intestine [34]. Therefore, it's very important to ensure the fullness of bladder during the treatment.

4. Application of image guided radiotherapy in the analysis of cervical cancer target expansion

Before making the radiotherapy plan for cervical cancer, the tumor area and normal tissue should be sketched first. The tumor area (GTV) includes tumor focus and metastatic lymph nodes, while clinical target volume (CTV) includes tumor area, subclinical focus and possible invasion area. However, for the patients after the operation, CTV was needed to sketch [35, 36]. But at present, there is no uniform standard for CTV. Different units have different descriptions of target areas and organs.

The regression of CTV during radiotherapy will also affect the absorbed dose of bladder, while the larger CTV volume will obviously squeeze the bladder, resulting in the deformation of bladder volume and the displacement of geometric center, while the absorbed dose of large CTV target area to bladder will exceed 50% of V45 [37]. Therefore, it is necessary to closely monitor the patients with large CTV during radiotherapy, and modify the patient's plan and recalculate the evaluation dose in time [38].

For the normal tissues outlined, including rectum, bladder, small intestine and femoral head, some hospitals and units include bone marrow to reduce blood toxicity. It may cause the movement of the target area due to the movement of the organs in the pelvic tissue, deformation, regression and reduction of mass. How to avoid the impact of these factors, planning target volume (PTV) is conducted in this process [39, 40]. Uterus movements are large and extremely variable among patients. They carry uncertainties for the CTV coverage and justify consequent margins for the PTV, thus limiting the benefit of IMRT. According to the previous studies, a minimum of 10 mm around the centro-pelvic CTV (with 10 to 15 mm in anterior-posterior direction) and 7 to 10 mm around the nodal CTV seem to be a reasonable compromise for nonadaptive intensity-modulated pelvic radiotherapy [41].

5. Conclusion

In summary, the focus of high-risk cervical cancer on early stage is occult and easy to recur and metastasize. The clinical effect of surgery is poor, while postoperative adjuvant radiotherapy can eliminate the hidden focus of pelvic cavity and reduce the recurrence rate of pelvic cavity. Radiotherapy has been widely used after radical operation of cervical cancer. Image guided radiotherapy of cervical cancer can improve the accuracy of radiotherapy for cervical cancer patients. The development of image registration and fusion technology plays an increasingly important role in image-guided radiotherapy of tumor, which is crucial for the accuracy of target area and critical organ delineation. As the main treatment method of cervical cancer, there is no doubt that radiotherapy could improve the therapeutic effect of cervical cancer, but the complications caused by radiotherapy are still a problem that cannot be ignored in clinical.

6. Conflict

The authors declare no conflict of interest.

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