RESEARCH COMMUNICATION

Dosimetric Verification for Primary Focal Hypermetabolism of Nasopharyngeal Carcinoma Patients Treated with Dynamic Intensity-modulated Radiation Therapy

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Abstract

Objective: To make sure the feasibility with ^{18F}FDG PET/CT to guided dynamic intensity-modulated radiation therapy (IMRT) for nasopharyngeal carcinoma patients, by dosimetric verification before treatment. Methods: Chose 11 patients in III~IVA nasopharyngeal carcinoma treated with functional image-guided IMRT and absolute and relative dosimetric verification by Varian 23EX LA, ionization chamber, 2DICA of I'mRT Matrixx and IBA detachable phantom. Drawing outline and making treatment plan were by different imaging techniques (CT and ^{18F}FDG PET/CT). The dose distributions of the various regional were realized by SMART. Results: The absolute mean errors of interest area were 2.39%±0.66 using 0.6cc ice chamber. Results using DTA method, the average relative dose measurements within our protocol (3%, 3 mm) were 87.64% at 300 MU/min in all filed. Conclusions: Dosimetric verification before IMRT is obligatory and necessary. Ionization chamber and 2DICA of I'mRT Matrixx was the effective dosimetric verification tool for primary focal hyper metabolism in functional image-guided dynamic IMRT for nasopharyngeal carcinoma. Our preliminary evidence indicates that functional image-guided dynamic IMRT is feasible.

Keywords: NPC - functional image-guided dynamic IMRT - hyper metabolism - dosimetric verification

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Introduction

Nasopharyngeal carcinoma is a common malignant tumor in head and neck. The special structure parts and pathological types of nasopharyngeal carcinoma decided that the radiation is the first choice and the most effective treatment methods. It is clear that intensity-modulated radiation therapy (IMRT) has protective effects in parotid gland function, especially in early stages of nasopharyngeal carcinoma. It is also confirmed that .IMRT can protect the funcution of salivary glands in clinical treatment (Pow et al., 2006; Kam et al., 2007). But the follow-up after IMRT treatment, we found that the retention rate of nasopharyngeal carcinoma with local recurrence rate is as high as 30% (Sanguineti et al., 1997). It most occurred in the GTV, which exists a group of tumor cells that are highly resistant to radiation .The study also confirms that the cancer stem cells of nasopharyngeal carcinoma existed in this group of cells, which is the root cause of the relapse (Wang et al., 2007). In order to improve the overall survival rates of nasopharyngeal carcinoma, it is necessary to seek new diagnostic methods and technology to reduce the recurrence rate of local remains, In recent years, the function of imaging technology and the development of the application of the radiotherapy can precisely shows the tumor form at the same time and also show high metabolic area, which make highly appropriate target area of the biological characteristics in the dose distribution provided the necessary premise (Yu and Liu, 2009a) to make a creature target area (biology tumor volume, BTV) guides of the biological intensity-modulated (BIMRT) technology as possible, giving biological target area higher radiation dose radiation therapy can increase the curative effect (Yu and Liu, 2009b). However, IMRT is the output of each point in the wild dose rate adjusted to realize high doses in the three dimensional space of the agreement ,but target body outside of the dose fell rapidly, which realizes without any increase in normal tissue complications probability under the premise of improve tumor local illuminate dose and local control. The reverse calculation of the optimization algorithm in IMRT is still not mature in some ways, including some uncertain factors in radiotherapy, we should assure the dose learning verification treatment as a key step before treatment of high metabolism (Bortfeld et al., 1994; Tsai

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et al., 1998). At home and abroad, the verification methods of common dose contains absolute and relative doses verification (Li et al., 2002; Agazaryan et al., 2003). It is quite late to use the dose of IMRT verification in domestic. In the beginning, they use ionization chamber and film dosimeter for verification. Along with the development of dosimeter, stereo dosimeter can achieve the appearance of three-dimensional doses of verification. But because of its technology, cost and other reasons, routinely used in the individual patient plan won't happen in the dose of verification. Therefore, we use point and surface dosimeter to evaluate the dose distribution in the domestic to get similar effect in stereo dosimeter. On this basis, in order to achieve before treatment quality control.

We try to pass a point and the surface dose to verify the implementation of targeted radiotherapy dosimetry verification.

Materials and Methods

General information

Patients III~IVA period of nasopharyngeal carcinoma who treated ^{18F}FDG PET/CT were treated with dnamic intensity-modulated radiotherapy in XuZhou Medical College Affiliated Hospital Department of Radiation during 2010. 6 - 2011.6. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Department of Radiatiotherapy, Xuzhou Medical College Affiliated Hospital. Written informed consent was obtained from all participants.

Instrument equipment

23 EX Varian medical accelerator equipped with a Milleninm 80 leaf MLC, Eclipse DX 3D treatment planning system and the corresponding network system, 2DICA of I'mRT Matrixx and IBA detachable phantom, 0.6 cm^3 ionization chamber, GE16 scheduled to type CT, GE PET/CT, etc.

Verification phantom CT simulation positioning

Verification phantom is IBA company head mold which can tear open, its have ionization chamber insert jack. Place 0.6 cm^3 ionization chamber in depth for 6 cm body when CT scan, 3 mm thick layer. 2D ionization chamber matrix for the production of IBA company I 'mRT Matrixx two dimensional array, placed on 4.7 cm solid water (ionization chamber matrix effective measuring plane is in the matrix under surface about 3 mm place), and 3 cm solid water underneath, a thick layer of 3 mm scanning.

Treatment planning and verification plan generation

11 NPC patients' high metabolic area of tumors were outlined by two experienced doctors, Eclipse treatment planning system generates radiation treatment plans. Import body mold scan images into Eclipse treatment planning system. Recount to produce verification plan, to get the point and surface dose distribution.

Verification method

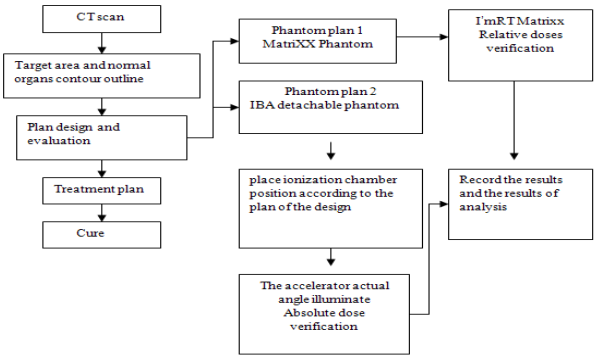

Figure 1. The Actual Verification General Process

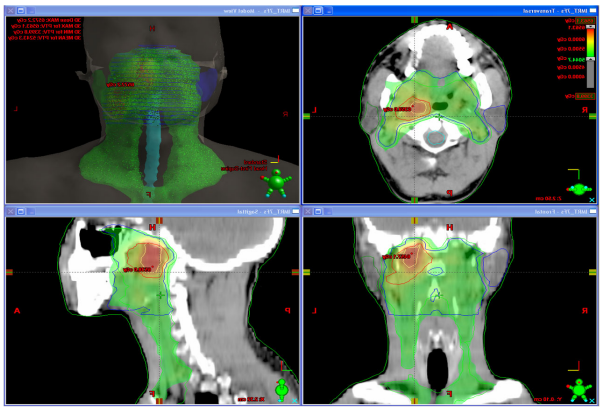

Figure 2. High Metabolic Nasopharyngeal Carcinoma Target of Outline

The actual verification general process is as follows in Figure 1.

Feasible experiment

Simulate actual treatment in the detachable phantom, including the clinical treatment volume (CTV), tumor treatment volume (GTV), high metabolic gross treatment volume (FGTV). Its size 10 × 7 cm, 4 × 4 cm, 2 × 2 cm respectively. The CTV put 0.3 cm into PTV. Treatment plans are designed according to PTV (nine fields), PTV is set to 1.80 Gy, GTV is set to 2.00 Gy, FGTV is set to 2.20 Gy.

Absolute dose verification

Transplant evaluated treatment plan to IBA detachable phantom, reassemble head phantom and find high metabolic area, as far as possible place ionization chamber in the designated area (Figure 2). Absolute dose measurement using the depth error measurement results, namely that point measurement compared TPS calculation Percentage relative error (%) = (measured values-calculated values) / × 100%. Relative doses verification: Regulate ionization chamber and I'mRT Matrixx before measurement. Put the I' mRT Matrixx on the accelerator bed, replace the bedplate for the measurement of the special flat, put solid water in the same location as simulation. The accelerator beam for 10 x 10 cm, SAD for 100 cm, SSD for 95 cm, the default 100 MU of accelerator for output calibration dose. With relative doses passing rate said, delivering 11 patients with 89 fields to the accelerator, the rack angle is zero, each field measurement results and TPS calculation are gamma analysised.

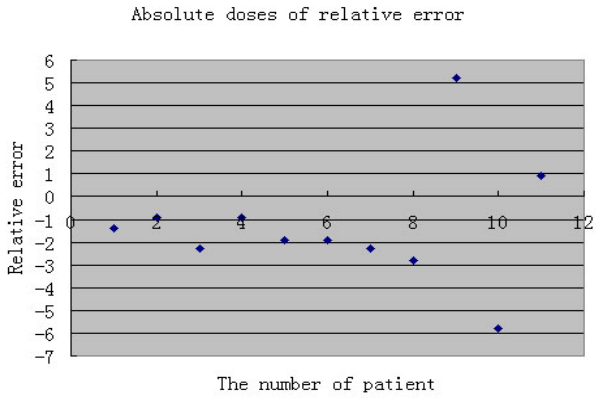

Figure 3. Absolutely Dose Error Distribution (relative error of 2.39% ± 0.66)

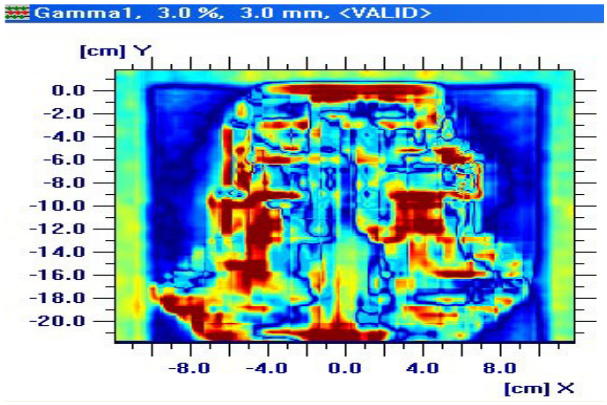

Figure 4. Gamma Results Passing Rate

Results

Absolute dose

In the feasible experiment, the FGTV is set to 2.20 Gy, FGTV measured result is 2.10 Gy, the result within 5%. So the experiment is feasible. The verification of 11 patients absolute error between -5.80% -5.23%, average error of plus or minus 2.39% ± 0.66, absolute doses of the maximum error is 5.80%, use 0.6 cm^3 3 times, each patient three times, and then to average. 9 in 11 times in error range (Figure 3).

Relative doses

Measured by 500 Mu/min and 300 Mu/min two dose rate way. 89 fields were used 500 Mu/min gamma value focused on 85% around. 89 fields used 300 MU/min, 11 fields didn't pass (Figure 4). Using the analysis method of the DTA, dosage is limited to 3%/3 mm standard conditions, of the total fields by the number of field 87.64 %in the 300 MU/min measurement.

Discussion

In the process of dynamic intensity-modulated radiotherapy, each beam machine hop decided the MLC movement speed, when the rate of movement of the MLC is limited, the accelerator will automatically reduce the field dose rate to adapt to the movement of MLC (Xiao et al., 2007). These characteristics of radiotherapy in treatment planning for targeted implementation of quality control and quality assurance make it as a big challenge, so it is an important step of radiation to verify the dose

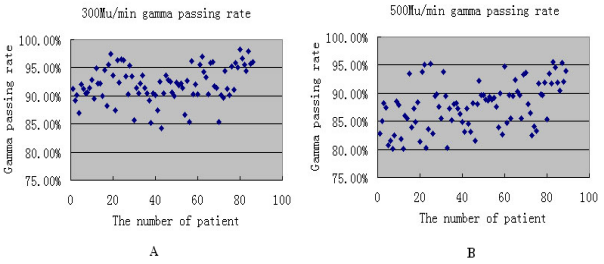

Figure 5. A) 500 Mu/min Gamma Passing; B) 6:300 Mu/min Gamma Passing. After t test, F = 8.778 p = 0.003 < 0.05, the variance not neat, use correction formula t test, t = 7.987 p = 0.000 < 0.01, there is a statistically significant

before treatment Absolute dosimetric verification and relative dosimetric verification is the course of treatment, which is also the reliable guarantee for quality assurance.

For absolute dosimetric verification, the dose distribution measurement of the basic dose meter is ionization chamber, although ionization chamber measurement efficiency is not high, but ionization chamber is accurate measurement of the main force of the absolute dosimetric verification (Intensity Modulated Radiation Therapy Collaborative Working Group, 2001). Absolute doses of measurement usually take to center position, but the tumor high metabolic area may not fall in central position, so we do not think that central measurement have too much significance. In addition, central position may be left in the center of large area, due to the size of the average ionization chamber sensitive effect, when the ambient dose not uniform points, measured and actual results may be significant differences. Therefore, measurements must be our push the quantity and the flat area dose. We use the ionization chamber is 0.6 cm^3, high metabolic area can use 0.15 cm^3 ionization chamber (Leybovich et al., 2003). In this lab, ionization chamber verification of 11 patients absolute error within -5.80% -5.23%, average error of plus or minus 2.39% ± 0.66, absolute doses of the maximum error is 5.80%, now at home and abroad, the standard is 5% (Hu, 1999), then part of the plan is not through the verification. But considering the ionization chamber itself faults, we think measurement error test result is satisfied. In this lab, most of measuring results calculated results by small to TPS. Through the analysis that: the center of ionization chamber is not down in doses relatively evenly region, dose change gradient is too big and lead to the result is unstable; Also, in IBA phantom CT scan, placed ionization chamber position with no equivalent material filled; And the system errors; In the course of treatment can also cause a dividing line between the result of the measurement error. The above experiments results we pass after adjustment, which proves that ours analysis is correct. In experiments also appeared TPS plan is bigger than the results, we observe TPS plan the measure point appears in the hot spots. In the process of measurement, a part of the ionization chamber of the metal rod into the area, and the resulting stem irradiation effect the measurement results. Through the analysis of the absolute doses of passing, we think that IMRT Matrixx in absolute dose not have advantages. I MRT Matrixx as plane dosimeter, can also measure the absolute dose, the key is how to find the IMRT Matrixx points ionization chamber, and ionization

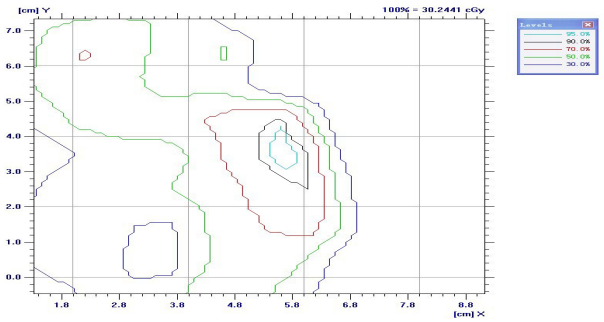

Figure 6. TPS Calculation Dose of Partial Enlargement Curve Effect

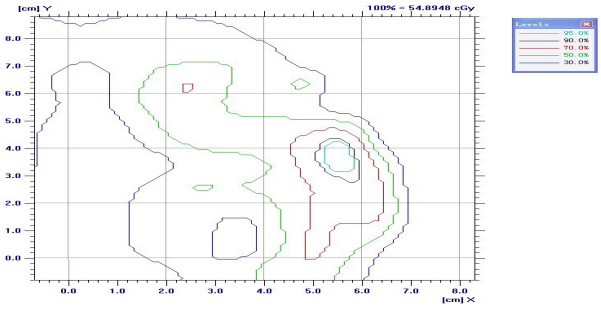

Figure 7. Measurement Results and Dose Curve of Partial Enlargement Effect

chamber will be correct coefficient (Zhang et al., 2007). Moreover, IMRT Matrixx is the average effect around the ionization chamber, a point doses of measurement, may involve ionization chamber around, which adds to the measurement error. Accordingly, the proposal in absolute verification doses choose ionization chamber more accurate. BaiPG etc (Bo et al., 2006; Zhou, 2008) using 0.6 cm^3 refers to the type of ionization chamber practical measurement in phantom are interested in point and TPS the dose of the point, it is concluded that the absolute error comparison between 0.06% and 3.38%, and the average error of 1.72% in that fit the largest clinical control error in 5% of the requirements.

For relative doses, 11 patients of nasopharyngeal carcinoma in the experimental use IMRT Matrixx to realize relatively dose verification. IMRT Matrixx can acquire large information in a short time, which can verifiy calculation value and TPS value accuracy, simple, and greatly simplify in the verification work. At home and abroad, it has gradually replaced ionization chamber and the combination of film verification method. Only IMRT Matrixx measurement results and TPS calculation results of the absolute difference and position the differences in allowed error range, the plan to get through and implement. Currently we use the gamma analysis standard (Low et al., 1998): dose deviation 3% or less or more than 3 mm distance bias. More than 90% of gamma passing, and absolutely dose in clinical validation error scope, the plan can be carried out. For gamma value less than 90%, the plan can't be carried out, we need to design plans until verification through treatment. 11 cases of nasopharyngeal carcinoma patients with 89 fields verification plan, in 500 MU/min measurement, most of the plan of the passing rate less than 90%, focus on 85% around, plans don't go through. In the use of 300 MU/min measurement, most plans pass through. Both after t test, $p = 0.000$, a statistical significance. Statistical results show that the use of 300 MU/min when measuring the passing rate obviously better than the use 500 MU/min of the measurement results (Figure 5). This suggests that the use of high dose rate in the dynamic IMRT can actually get the dose distribution of deviations from system calculation dose distribution (Litters et al., 2002; Li et al., 2010). In the use of 300 MU/min measurement, there are 11 fields of gamma analysis results of less than 90%, relative doses failed in verification, percent of passing is 87.64%. The main reason for the verification failed to pass is measurement error, and for a 7 or 9 fields intensity-modulated plan have one or two fields the dose distribution of more than 3% or 3 mm error is acceptable. For failed to pass verification plans, we need to redesign IMRT plans, we redesign verification error after drop to clinical allowed scope. From the analysis of the results, it is known that the plan has appeared in gradient large region, the average size of ionization chamber sensitive effects may be led to dose gradient change a large area after the reasons of the big verification error. If patients IMRT plans to target areas appear in the area more gradient dose, the passing rate is low, passing rate with target area doses of uniformity, there are certain relations. IMRT plans generally have different angle of several radiation fields, the accelerator in different angle of beam flatness, symmetry, and even dose rate, output dose may change. In the process, we put the accelerator angle to zero, it increases the source of the error humanly. So we should be as far as possible in the actual angle during measurements. According to the 11 patients passing rate analysis, whether that low dose rate or high dose rate, the passing rate is very high. We investigate its reason that: The patients' target area, no matter, GTV, FGTV, and CTV is smaller than other patients' , for small target of patients, we can use high dose rate for the treatment, but on the safe side, the optimal method is low dose rate treatment. In Figure 6 can see Eclipse plan system during dose carving, with the maximum dose point to a 100%, at 95% and 90% dose curve is very steep, it puts forward a lot of challenges to the measuring process measurement results, but we, from Figure 7, can get satisfactory results, 95% of the measurement results and 90% is steep curve in the dose distribution, this is what we really want to be. But there also have the insufficient place, 95% dose curve and 90% have some connecting area curve, the reason may be that IMRT Matrixx ionization chamber probe response consistency is not very good. Have reports in the literature:in the IMRT Matrixx illuminate immediately and after the 0.5 h after irradiation, there are 4% differences between measured (Zhang et al., 2009).

In a word, the experiments use ionization chamber and IMRT Matrixx to achieve functional image-guided dynamic IMRT absolute dosimetric verification and relative dosimetric verification. Use the IMRT Matrixx instead of the film, which greatly simplifies the verification of the workload. The result indicates that most patients targeted therapy programs can be implemented, the error is also within clinical acceptable limits, but there are still a few patients' plans could not be implemented, the errors beyond the permitted. This shows that dosimetric verification of the functional image-guided IMRT before the treatment is very necessary, which provides important

guarantee for precise execution plans. For the functional image-guided dynamic IMRT, we will combine ionization chamber of absolute dose measurement with IMRT Matrixx relative doses of measuring together, to better ensure accurate implementation of targeted radiotherapy.

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