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EVALUATION TARGET VOLUME AND DISTRIBUTION ORGAN AT RISK IN NASOPHARYNX CANCER USING VOLUMETRIC MODULATED ARC THERAPY (VMAT)

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ABSTRACT

Background: Radiotherapy treatment for nasopharyngeal cancer can cause an increased risk of decreasing the dose to cancer tissue, increasing the dose to organs at risk (OAR), as well as increasing toxicity due to inappropriate dose distribution. Purpose: Analysis of results Dose Volume Histogram (DVH) on PTV and Organ At Risk (OAR) brainstem, spinal cord, optic nerves RT, optic nerves LT, parotid glands RT, parotid glands LT, eyes RT and eyes LT by comparing tolerance limits based on ICRU 62, as well planning Target Volume (PTV) in cases of nasopharyngeal cancer using the VMAT technique. Method: This research is descriptive and quantitative by making observations. The research period was from July to October 2023 at the This research was conducted at Department Radiotherapy in Jakarta area. The total data sample was 20 nasopharyngeal cancer patients. The total dose received by the patient was 70 Gray in 33 fractions with 6MV energy using the VMAT technique. The data analysis and decision-making were carried out using statistical tests with SPSS version 25. The statistical test uses one sample t-test to determine whether there is a difference between PTV and OAR with ICRU 62 recommendations with a p-value > 0.05. Results: PTV value and organ at risk which covers PTV 95%, PTV 100%, brainstem, spinal cord, optic nerves RT, optic nerves LT, parotid glands RT, parotid glands LT, eyes RT, eyes LT has a p-value below <0.05 indicating that PTV and OAR get a dose below the criteria set based on ICRU 62, the results of the study were adjusted to the policy of the radiotherapy department carried out in this study.

Keywords: Nasopharyngeal Cancer, Planning Target Volume (PTV), Organ At Risk (OAR), Volumetric Modulated Arc Therapy (VMAT).

I. INTRODUCTION

Radiotherapy is a non-surgical treatment that uses ionizing rays to kill cancer cells while still paying attention to healthy organs around the tumor so as not to receive excessive doses that can damage tissue [1]. Cancer is cell growth that cannot be controlled by the body, so it spreads and causes metastasis to other body tissues [2]. Epstein Barr is the name of a virus that is one of the causes of nasopharyngeal cancer. nasopharynx cancer is said to be a cancerous disease multifactorial because it is caused by factors of genetics, environment, and lifestyle [3]. Based on the latest report by World Cancer Research Fund Internasional There were 133,000 new cases of nasopharyngeal cancer with Indonesia ranking 3rd in the world. Indonesia's death rate from nasopharyngeal cancer is ranked 3rd in the world [4]. In Indonesia, the risk factor for nasopharynx cancer in men increases compared to American and European men, this is due to racial and geographical differences. The population proportion of nasopharyngeal cancer is 6.2/100,000, which is equivalent to around 13,000 new cases per day, but only a small proportion of these results have been documented [5].

Dose distribution in nasopharyngeal cancer must be covered by the area of gross tumor and cervical lymph nodes, the usual dose given is 66 Gray for stages T1 – T2, and a dose of 70 Gray is given for stages T3 – T4. The radiation dose must also cover the supraclavicular gland area with a dose of 50 Gray. Meanwhile for regions Planning Treatment Volume The planned (PTV) must be approximately 1 cm outside the Clinical Target Volume (CTV) area. The organs at risk found in cases of nasopharyngeal cancer consist of the temporal lobe, brainstem, spinal cord, optic nerve, chiasm, parotid gland, submandibular gland, and pituitary [5]. As technology becomes more sophisticated, radiotherapy techniques have developed, both equipment and imaging techniques—the development of this imaging technique results in better target volume accuracy. Volumetric Modulated Arc Therapy (VMAT) which is also known as rapid arc is a technique that has the advantage of being precise in achieving a very conformal dose distribution to better target volume coverage compared to other techniques and minimizing excess dose to healthy organs compared to conventional radiotherapy techniques with a faster radiation time than the IMRT technique [6]. To date, nasopharyngeal cancer is the biggest challenge in radiotherapy treatment, this is because the primary tumor is close to the OAR, so it is necessary to pay attention to the dose distribution that will be given. Several studies show that the use of VMAT in nasopharyngeal cancer has the advantage of reducing the late toxicity of radiotherapy related to the appropriate dose absorbed by the OAR, due to giving a high dose to the PTV but still paying attention to the lowest possible dose to the OAR [7]. However, Leung, 2019 & Fung, 2012 [8,9] explain a higher value of the maximum dose for the spinal cord, brain stem, spinal cord, and optic nerve for the VMAT plan. In line with Chen's research, 2018 [10] stated that the maximum dose increase in the VMAT plan was significantly higher, no matter in T1-2 patients or T3-4 patients ($p<0.05$). According to Hutcheson, 2012 & Mendez LC, 2012, there is a direct relationship between the distribution of radiotherapy doses and significant toxicity during and after treatment such as loss of saliva production or dysphagia [11,12].

In addition, Graff, 2013 & Kuo YC, 2006 [13,14] reported that changes in the contour of the neck and incorrect installation of the spinal cord in patients with nasopharyngeal carcinoma can cause a significant increase in dose to the spinal cord resulting in significant differences. between the administered and planned radiotherapy doses. This causes an increased risk of overdose exposure to organs at risk (OAR) [15]. This occurs because the mobility of the cervical spinal cord (SC), the geometric movement of the neck is more significant than the head, and the safety of the SC dose it self has also received attention [16].

Protect organ at risk in nasopharyngeal cancer it is very important to do this because the position of the primary tumor in this cancer is close to or coincides with critical organs including the temporal lobe, brainstem, spinal cord, optic nerve, chiasm, parotid gland, submandibular gland, pituitary This nerve plays a role in controlling important functions in the head and neck. Based on several studies above, it has been explained that there is an increased risk of tumor underdose, OAR overdose, and increased toxicity influenced by inappropriate dose distribution. Another study that is in line is research conducted by Greeshma, 2012 regarding compliance with the dose volume limits recommended by the QUANTEC guidelines for PTV and OAR in nasopharyngeal cancer, saying that only 35% of patients achieved a dose of less than or equal to 100% of the dose recommended by the guidelines. QUANTEC so that the incidence of brain radiation necrosis increases with doses exceeding 60 Gy. Gresshma suggested that more evaluation or attention should be paid to the parotid and temporal lobes during radiation treatment planning [17].

So it is very important to evaluate the dose distribution to the target volume and organs at risk using VMAT in nasopharyngeal cancer, this is to ensure the maximum radiation dose to the target volume including in areas that are difficult to reach, to minimize excess dose to the OAR and reduce the risk of side effects that will arise. Carrying out regular dose evaluations helps monitor confirm and identify any undesirable differences between the initial treatment plan and actual realization. Based on the background explanation above, researchers are interested in conducting research related to evaluating dose distribution on target volumes and organs at risk using the volumetric modulated arc therapy (VMAT) technique for nasopharyngeal cancer.

II. METHODS AND MATERIAL

Research design

This type of research is comparative evaluation research which is descriptive and quantitative. The data in this research is secondary data resulting from radiation planning in the form of dose Volume Histogram (DVH). This research was conducted at Department Radiotherapy in Jakarta area. The research was carried out by collecting supporting data from July to October 2023. This study used secondary data on nasopharyngeal cancer patients who underwent external radiation treatment with the VMAT technique. The data obtained was the result of planning at the TPS in the form of DVH, which contains the dose received by PTV and OAR. This data will be collected for evaluation and comparison, to see whether the planning results have been adjusted to previously established guidelines.

Data collection

Before collecting data at the hospital, the researcher asked for a permission letter from the campus to collect research data at the relevant hospital. Next, the researcher reduces the data, namely grouping the planning data into the Treatment Planning System (TPS) of each nasopharyngeal cancer patient based on gender, stage, and technique used (VMAT) which will be assessed through Dose-Volume Histogram (DVH) to determine the dose on PTV and OAR. After the data was collected, samples were calculated using the Slovin method. How to calculate the Slovin method [18]:

$$n = \frac{\mathrm{N}}{1 + N\,(e)^2} = \frac{20}{1 + 20\,(0{,}05)^2} = \frac{20}{1 + 20\,(0{,}0025)} = 19{,}047$$

Where the value of n is the sample to be studied, N is the population and e is the value of the margin of error (error magnitude value). The value set by this research is 5%. The variables that will be used in this research are patients with clinical nasopharyngeal cancer who have undergone radiotherapy using the VMAT technique by analyzing Volume Histogram (DVH) PTV and OAR.

Statistic analysis

The dose value for each PTV and OAR parameter is then compared with the ICRU 62 appropriate radiation criteria. Next, the processed data is presented in a narrative manner which will be equipped with pictures and charts that are by the research results. Evaluation and decision-making using statistical analysis using SPSS software. The data from this evaluation will then be compared with the specified tolerance limits, to evaluate the extent to which the data results from the VMAT technique conform to the established standards. The statistical test uses one sample t-test to determine whether there is a difference between PTV and OAR with ICRU 62 recommendations with a p-value > 0.05.

III.RESULTS AND DISCUSSION

The results of the research are in the form of planning data for nasopharyngeal cancer patients in the form of a Dose Volume Histogram (DVH) to show dose values for target volumes and organs at risk. As well as data from the isodose curve which describes the distribution of the dose received. Patient data is external radiation using the Volumetric Modulated ARC Therapy (VMAT) technique using 6MV photon energy. The patient was given a dose of 2.12 Gy per fraction, with 33 exposures, and a total dose of 70 Gy, radiation exposure using a LINAC. Data analysis was carried out in the form of a Dose Volume Histogram (DVH) on a computer Treatment Planning System (TPS). Dose Volume Histogram (DVH) shows the dose value received by the target volume (PTV). Based on ICRU Report 62, PTV must cover a minimum of 95% and must not exceed 107% of the total dose administered. normality test results on PTV70/33 D95≥95% are 0.684 and 0.070, then the conclusion is that the data normality is normally distributed, so it is continued with the SPSS test one sample t-test. In Table 1 the test results are known sample t-test PTV that the values obtained for PTV are 95% and 100%, p-value = 0.000, meaning there is a significant difference between the doses received at PTV 95% and 100% with ICRU report 62.

TABLE 1. Statistical One Sample T-Test on PTV

PTV	p-value
PTV 95%	.000
PTV 100%	.000

TABLE 2. Statistical One Sample T-Test on OAR

OAR	p-value
Brainstem	.044
Spinal Cord	.000
Optic Nerves RT	.000
Optic Nerves LT	.000
Parotid Glands RT	.003
Parotid Glands LT	.000
Eyes RT	.000
Eyes LT	.000

In this study, dose distribution analysis was also carried out in organs at risk (OAR). The data processed is DVH results from TPS. DVH can show the dose distribution value that will be received by healthy organs around the target. From the DVH results, it can be seen and assessed that the dose received is OAR brainstem, spinal cord, parotid glands, eyes dan optic nerves not allowed to exceed the tolerance limits of ICRU 62. Normality test values for organs brainstem p-value 0.050, spinal cord p-value 0.367, optic nerves RT p-value 0.748, optics nerves LT p-value 0.387, parotid glands RT p-value 0.050, parotid glands LT p-value 0.631, eyes RT p-value 0.245, eyes LT p-value 0.5, which means the significance value of the organ (p-value> 0.05) so that it is known that decision making from the normality test of normally distributed data.

Table 2 shows the statistical results of the testone sample t-test OAR brainstem has a significant value of 0.044, parotid glands RT the significance value is 0.003, and spinal cord, optic nerves RT, optic nerves LT, parotid glands LT, eyes RT, eyes LT each has a significance value of $p = 0.000$. Value the significance of all organ at risk is p value < 0.05, so the decision H0 is rejected, which means there is a difference between the distribution of the absorbed dose of Organ At Risk (OAR) received by the patient and the criteria limits set based on ICRU 62. Then in Table 3 shows the results of the Tolerated dose volume target and organ at risk for radiation in cases of nasopharyngeal cancer based on ICRU 62, PTV70/33 D95≥95% has a maximum value of 99.98%, this value is by the tolerance specified in the ICRU 95% to 100% dose.

The choice of technique for irradiating nasopharyngeal cancer also plays an important role in achieving optimal results. The technique used will affect the radiation dose exposure to the tumor and surrounding organs. Several studies say that the VMAT technique is a better technique for irradiating nasopharyngeal cancer because in nasopharyngeal cancer the tumor coincides with the organ at risk so precision is needed to follow the contour of the nasopharynx and good dose distribution organ at risk doesn't get an excess dose. In nasopharyngeal cancer planning, the VMAT technique provides good target coverage and dose suitability, VMAT also shows a significant increase in dose reduction to bone structures, reduction in the number of MUs and radiation time, dose distribution for OAR using VMAT is better than other techniques and homogeneity is good. better than IMRT. So several studies recommend the VMAT technique for nasopharyngeal cancer [19,20].

According to Henry C.K. Sze the total dose to the primary tumor is 70 Gy by administering 33-35 fractions to irradiate patients with nasopharyngeal cancer because using a dose of 70 Gy can improve the quality of treatment and reduce the prophylactic dose effect of the radiation dose to the primary tumor which has the potential to cause microscopic spread of the primary tumor to lymph node tissue. The prophylactic dose for nasopharyngeal irradiation for lymph node tissue is around 60 Gy and 50 Gy [21]. During the era of 2D radiotherapy, the total radiation dose given was 66 Gy. With an additional dose of 10 Gy if there is a large parapharyngeal spread [22]. Research according to Leung TW states that doses exceeding 66 Gy to the primary tumor are more beneficial even for nasopharyngeal cancer with T1-T2 [23]. In addition, other research states that prospective studies of NPC – 9901 and NPC – 9902 conducted by the nasopharyngeal cancer study group in Hong Kong showed that doses of less than 70 Gy were associated with worse control of local location and spread [24]. Thus the current standard is to deliver 70 Gy over 33 to 35 fractions to the primary tumor.

An organ at risk or OAR is an organ with high sensitivity to radiation, if the dose affected in the OAR is high it will cause significant effects if given beyond the tolerance dose limit. Another term is easily damaged if exposed to radiation [25]. Giving an accurate dose is very important in planning radiotherapy, this is to ensure that the dose received by the patient is effective in reaching the tumor while minimizing the risk of side effects on adjacent organs such as the brainstem, spinal cord, and optic nerves. According to ICRU 62, the tolerance limits for the brainstem are < 54 Gy, meaning that the dose received by the brainstem must not exceed 54 Gy, the spinal cord < 45 Gy, which means that the dose received by the spinal cord must not exceed 45 Gy, left optic nerve and the right have a tolerance limit of <50 Gy, so the dose received by both the left and right optic nerves each cannot exceed 50 Gy [26].

According to research conducted by White P, said that the VMAT technique in nasopharyngeal cancer produces values shown by Tumor Control Probability (TCP) and the value on Normal Tissue Complication

Probability (NTCP) showed better than IMRT. TCP and NTCP are two related concepts in radiotherapy that are used to predict and evaluate the results of radiation treatment. NTCP shows the value that normal tissue around the treatment target area will experience complications or adverse side effects due to radiation exposure. Each organ or tissue has a different tolerance to radiation, so NTCP is used to estimate the risk of complications in a particular organ. NTCP can be influenced by factors such as the radiation dose received by the organ, the volume of the affected organ, the organ's radiobiological sensitivity, and other patient risk factors. The primary goal in radiotherapy planning is to minimize NTCP as much as possible to protect healthy normal tissue [27].

Giving radiation to nasopharyngeal cancer patients or radiation patients to the head and neck area often affects changes in the morphology of the mucosa in the oral cavity which results in other complications such as the oral mucosa, salivary glands, teeth, and jaw bones. Apart from that, complications can be divided into several categories, including [28]. The next toxicity that often occurs in patients is xerostomia (reduced saliva production) Signs of xerostomia include a dry mouth, loss of oral function, excessive thirst, difficulty wearing a dental prosthesis, disturbed sense of taste, the mouth feeling like it is being burned, changes in the mucosal tissue in the mouth and caries on the teeth. Salivary dysfunction has been observed to correlate with an increase in the mean dose of parotid glands [29].

IV. CONCLUSION

The VMAT technique is recommended for the irradiation of nasopharyngeal cancer patients because it can maximize the dose to the PTV and minimize the dose to the OAR. The VMAT technique in nasopharyngeal cancer also shows significant improvements in terms of reducing the dose, reducing the number of MUs, or reducing the radiation time. In addition, using the VMAT technique provides far less late toxicity to patients than other techniques. PTV value and organ at risk which covers PTV 95%, PTV 100%, brainstem, spinal cord, optic nerves RT, optic nerves LT, parotid glands RT, parotid glands LT, eyes RT, eyes LT has a p-value below <0.05 indicating that PTV and OAR get a dose below the criteria set based on ICRU 62.

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