How to determine margins for planning target volume (PTV): from 2D to 3D planning in radiotherapy for head and neck cancer? Portal imaging assessment for set-up errors

Baş-boyun kanseri radyoterapisinde iki boyuttan üç boyuta geçişte planlanan hedef hacim (PTV) sınırlarını nasıl belirleyelim?: Set-up hatalarının portal görüntülemeyle değerlendirilmesi

Evrim BAYMAN,[1,2] Özlem Uruk ATAMAN,[2,3] Münir KINAY,[2] Fadime AKMAN[2]

[1]*Samsun Mehmet Aydın Education and Investigation Hospital, Department of Radiation Oncology, Samsun, Turkey;*
[2]*Dokuz Eylül University, Department of Radiation Oncology (DEUDRO), Izmir, Turkey;*
[3]*AstraZeneca, Alderley Park, UK*

OBJECTIVES

To evaluate set-up errors using Electronic Portal Imaging (EPI) for Three Dimensional Conformal Radiotherapy (3D CRT) protocol for head and neck carcinoma in Dokuz Eylül University Department of Radiation Oncology (DEUDRO).

METHODS

Ten patients between July 2004 - September 2005 were included. Seven EPIs/5 weeks per patient were planned to evaluate by two independent observers. Differences between Digitally Reconstructed Radiography (DRR) images and EPIs measured in cranio-caudal (CC), anterior-posterior (AP) and medio-lateral (ML) directions. Random (σ) and the systematic ($\sum$) errors were calculated and used in van Herk margin formula ($2.5 \times \sum + 0.7 \times \sigma$) for PTV margin.

RESULTS

Ninety three EPIs with 186 [93 (50%) CC, 78 (42%) AP and 15 (8%) ML] measurements were evaluated. The σ were AP: 2.6 mm, CC: 2.9 mm, ML: 1 mm. The $\sum$ AP: 3.9 mm, CC: 1.8 mm, ML: 1.9 mm. PTV margins calculated were AP: 11.7 mm, CC: 6.6 mm, ML: 5.8 mm.

CONCLUSION

3DCRT protocol for head and neck cancer was amended using these PTV margins. These maybe wide especially for IMRT, and can reduce with better immobilization systems.

Key words: Portal imaging for head and neck radiotherapy; set-up errors.

AMAÇ

Baş boyun kanserinin üç boyutlu konformal radyoterapisinde (3D CRT) Elektronik Portal Görüntüleme (EPG) kullanılarak set-up hatalarının ve Dokuz Eylül Üniversitesi Radyasyon Onkolojisi (DEUDRO) klinik protokolünün değerlendirilmesi.

GEREÇ VE YÖNTEM

Temmuz 2004 - Eylül 2005 arasında radyoterapi uygulanan 10 hasta değerlendirildi. Her hastadan 5 hafta içinde 7'şer EPG'nin görüntülenmesi; dijital planlama görüntüleri ile EPG'ler arasındaki kranyokaudal (CC), anterior-posterior (AP) ve mediolateral (ML) farkların iki ayrı gözlemci tarafından ölçülmesi planlandı. Rastgele (σ) ile sistematik ($\sum$) hatalar hesaplandı, van Herk formülü ($2.5 \times \sum + 0.7 \times \sigma$) kullanılarak PTV sınırı belirlendi.

BULGULAR

Doksan üç EPG ve 186 [93 (%50) CC, 78 (%42) AP ve 15 (%8) ML] ölçüm değerlendirildi. Rastgele [AP: 2.6 mm, CC: 2.9 mm, ML: 1 mm] ve sistematik hatalar [AP: 3.9 mm, CC: 1.8 mm, ML: 1.9 mm], PTV sınırları [AP: 11.7 mm, CC: 6.6 mm, ML: 5.8 mm] hesaplandı.

SONUÇ

Bu çalışmada hesaplanan PTV sınırları değerlendirilerek baş boyun kanserinin 3D CRT kullanılan DEUDRO protokolü düzeltilmiştir. Bu sınırlar IMRT için geniş kabul edilip daha iyi immobilizasyon sistemleriyle azaltılabilir.

Anahtar sözcükler: Portal görüntüleme; baş boyun kanseri radyoterapisi; set-up hataları.

The goal of radiotherapy (RT) is to eradicate tumor cells in the target volume, while sparing surrounding organs at risk. Local or/and regional recurrence is correlated to overall survival in many tumor sites.[1,2] Although there is a relationship between tumor dose and tumor control probability, it's difficult to prescribe high doses because of especially late side effects of normal tissues. Organs at risk could be protected and target volume doses could be escalated with the improvement of patient stabilization systems and 3D CRT techniques. RT treatment delivery in head and neck tumors require highly accurate and reproducible treatment set-up due to many important organs at risk with confirmation by frequent portal imaging.[2] Organ motion in the head and neck region is generally unimportant and could be neglected except motions due to swallowing. However, set-up errors could make a significant difference for the doses planned to be delivered to the target volume and to organs at risk. These errors are classified as systematic and random which are contained in the Planning Target Volume (PTV) margins.

Nowadays margins to be added to have an adequate PTV is of major concern for departments where the 2D to 3D transition is taking place. With 3D conformation therapy, the volume of organs at risk being irradiated is reduced. Set-up errors can be measured using portal imaging by applying Electronic Portal Imaging (EPI) instead of megavoltage portal films taken during the RT. Over the last several years, EPIs have become available in a large number of institutions to measure the set-up errors.[2,3]

The aim of this study was to evaluate the set-up errors using EPI to form a basis for the 3D CRT protocol for the head and neck cancer treatment protocol to be used in DEUDRO.

MATERIALS AND METHODS

Patients: Between July 2004 - September 2005 10 patients who were planned to be treated with 3D CRT MLC for head and cancer and who had suitable bony landmarks in their EPI's were evaluated.

Radiotherapy Technique
Immobilisation: Thermoplastic casts with two point stabilisation of the head were used to immo-

bilise all patients in suitable anatomic positions. Proper neck supports were chosen by considering the primary tumor localization for the patient lying in supine position, but any shoulder immobilisation hasn't been used.

Computed Thomography (CT) simulation: The upper and lower limits of the anatomic field and slice interval were determined by the responsible physician, and was marked on the individual patient. Slice thickness was 3-5 mm. The mask of the patient was marked with radioopac labels with the help of laser beams.

Virtual simulation: The 3D conformal treatment plan was performed in consistency with ICRU (International Commitee of Radiation Units and measurements) 50 and ICRU 62 guidelines.[4-6] The findings on clinical examination and CT and/ or MRI before RT were used to constitute the GTV (Gross Tumor Volume), the CTV (Clinical Target Volume) and the PTV (Planning Target Volume). [4-6] Planning volumes were consulted with the radiology specialist in the complicated patients where the volumes were not very clear. GTV tumor delineation was done to include the primary tumor and GTV node consisted gross lymphatic metastasis. CTV (tumor and node) volumes were constructed by addingmargins to GTV volumes as to clinical protocols and experiences for probable microscopic extension of disease. PTV volumes were planned by adding 0.5 cm to the CTV, for possible set-up errors. Internal margin has been neglected in this study. The organ motion was insignificant because of tumor localization in our head and neck cancer patient in comparison with the other tumor sites.

Radiotherapy Dose and Energy: RT was given 1.8-2 Gy per fraction, 5 days a week, 25-35 fractions to a total dose of 60-70 Gy The patients were treated with high energy photons (6MVX). Spinal cord was protected after 44-46 Gy using with MLC at lateral fields. The dose planned for the posterior servical lymphatics is completed by 6-9 MeVé electron energies.

EPI Evaluation Protocol
The DRR (Digitally Reconstructed Radiographs) images of the treatment fields were used

as references. The DRR s were imported from the Treatment Planning to the treatment machine and were compared on the screen with the EPI protocol as mentioned below:

Frequency of the EPI: We aimed to evaluate 7 EPI images for each patient two during the first week and one on each of the following 5 weeks .

Reference bony landmarks for the comparison of the EPI: Lateral (L) image: base of the skull, body and spina of C2 vertebra and the other visible bony structures,

Anterioposterior (AP) image: nasal septum, maxillar sinus, base of posterior skull, vertebras.

Evaluation of the EPI: Evaluation protocol was an offline procedure. Images were evaluated by two observers at the same day independently. Siemens Primus Beamview TI® programme has been used for EPI evaluation. Reference Digitally Reconstructed Radiography (DRR) images were compared to the EPI and the differences between the EPI and the DRR using bony landmarks were measured in cranio-caudal (CC), anterior-posterior (AP) and medio-lateral (ML) directions. If the difference in the measurements between the two observers was smaller than 3 mm, the larger measurement was taken into account. However if the difference was larger than 3 mm than the mean of the two measurements was taken.[2]

EPI and Statistical analysis: Standard deviations were calculated using an easy excel programme prepared at Holland National Cancer Institute. This programme calculates the mean, median values and standard deviations. The random (σ) and the systematic (Σ) components of the errors were calculated using margin formula (2.5 x Σ + 0.7 x σ) proposed by Van Herk to find out the planning target volume (PTV) margin.[2,7] For each individual patient, the random displacement for a particular direction was assessed by the substraction of the systematic displacement from the daily displacement. For all patients, the distribution of random displacements was expressed by the standart deviation (SD) from all individual random values. Random, systematic and total standart deviations are related by the formula $S^2_{TD} = S^2_{SD} + S^2_{RD}$ where TD, SD and

Table 1
Patient characteristics

No.	Age	Gender	Tumor localization	Clinical stage
1	33	Female	Nasopharynx	T4N2M0
2	38	Male	Nasopharynx	Local recurrence
3	58	Male	Tonsil	TxN1M0
4	52	Female	Nasopharynx	T2bN0M0
5	67	Female	Nasopharynx	T2bN1M0
6	49	Male	Nasopharynx	T2bN1M0
7	76	Female	Nasopharynnx	T2aN0M0
8	67	Male	Unknown primary with neck nodes	TxN2M0
9	67	Male	Hypopharynx	T4N2cM0
10	58	Male	Unknown primary with neck nodes	TxN3M0

RD are total, systematic and random displacements, respectively.[8] From the displacements measured in each direction, 3- dimentional (3D) vector was calculated using the formula $d3D = \sqrt{d^2_{AP} + d^2_{CC} + d^2_{ML}}$ where d_{AP}, d_{CC} and d_{ML} are the deviations in AP, CC and ML directions, respectively.[8]

RESULTS

Patients: There were 6 (60%) male, and 4 (40%) female patients. The median age was 58 (33-76). Tumor localizations were as follows: 6 (60%) nasopharynx, 2 (20%) unknown primary with neck nodes, 1 (10%) hypopharynx and 1 (10%) tonsil. Patient characteristics are shown in Table 1.

Results of EPI evaluation: Ninety three EPI's from 30 fields have been evaluated and 186 measurements have been performed per observer. Total number of measurements were 372. Ninety three (50%) measurements were in CC, 78 (42%) were in AP and 15 (8%) were in ML directions. Ninety three EPI's were suitable for measurement in terms of bony landmarks and are evaluated in this study. Larger than 3 mm values between the observers have been determined in 28 (15%) measurements [median 3.75 (3.01-9.14) mm].

Random error (σ) was found to be 2.6 mm for AP, 2.9 mm for CC and 1 mm for, ML. System-

Table 2

Results of EPI evaluation

No. of patients	10 (100%)
No.of measurements per observer	186 (100%)
Anterior-posterior	78 (42%)
Cranio-caudal	93 (50%)
Medio-lateral	15 (8%)
Interobserver difference	186 (100%)
<3 mm	158 (85%)
≥3 mm	28 (15%)
Set-up errors	
Systematic error component (Σ)	
Anterior-posterior (mm)	3.9
Cranio-caudal (mm)	1.8
Medio-lateral (mm)	1.9
Random error component (σ)	
Anterior-posterior (mm)	2.6
Cranio-caudal (mm)	2.9
Medio-lateral (mm)	1
Margin for PTV	
(Margin= 2.5 x Σ + 0.7 x σ)	
Anterior-posterior (mm)	11.7
Cranio-caudal (mm)	6.6
Medio-lateral (mm)	5.8

Table 3

Total standart deviations for each direction and 3D vector

Direction	Total displacement (1 SD, mm)
STD_{AP}	4.69
STD_{CC}	3.41
STD_{ML}	2.15
d_{3D}	6.18

be added for PTV have been found to be AP: 11.7 mm, CC: 6.6 mm and ML: 5.8 mm. Results of EPI evaluation are shown in Table 2 and total standart deviations for each direction and calculated 3D vectors are shown in Table 3.

Distribution of the random displacements along the 3 directions (AP, CC, ML) at all measuments (Fig. 1), and scatter plot of the systematic set-up displacement along the two directions (AP-CC) (Fig. 2) are shown in figures.

DISCUSSION

RT of head and neck cancer has difficulties because of the organs at risk in vicinity of the tumor a high geometrical accuracy is required. Set-up uncertainties include not only the PTV, but also organ motions. Organ motions can be neglected for head and neck tumors.[2,8,9] Hence margins added for the PTV requires set-up reliability in particular for new users of 3D CRT. Consequently RT fields should be verified by means of portal imaging.
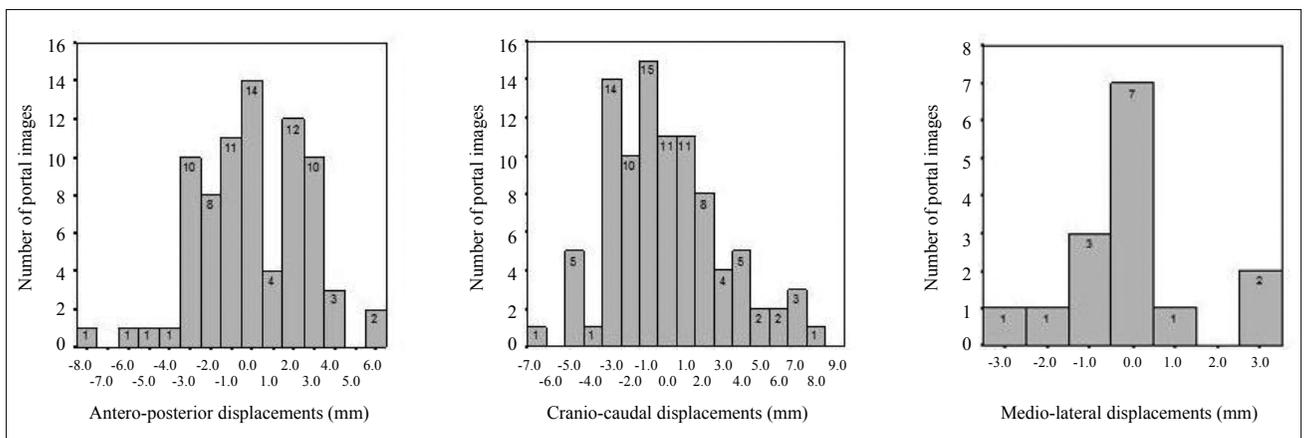
atic error (Σ) was found to be 3.9 mm for AP, 1.8 mm for CC and 1.9 mm for ML. These data have been used in the margin formula and margins to

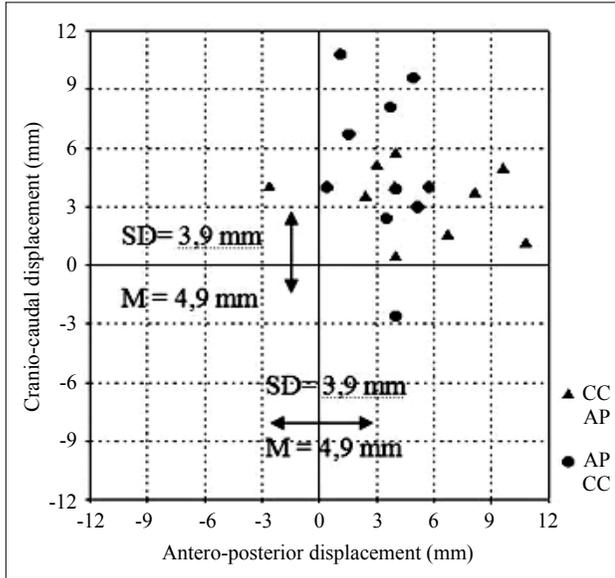**Fig. 1.** Distribution of the random displacements along the 3 directions.

Fig. 2. Scatter plot of the systematic set-up displacement along the two directions (AP-CC). Each dot represent the individual systematic displacement along the specified direction. The mean value (M) represents the average displacements for all patients.

The literature showed that, using portal imaging to evaluate the set-up errors is very important during the RT.[9-11] EPI is useful for easy repeated imaging, processing, and rapid assessment of set-up errors comparing with conventional portal images. [9,11] Correction protocols have been recommended for reduction of set-up deviations in many trials. [2,8,10-12]

In this study, we purposed to determine our margins for PTV for 3D RT and prepared an offline correcting protocol for set-up errors in head and neck cancer. Ten consecutive head neck cancer patients were evaluated. RT was given 1.8-2 Gy per fraction, 5 days a week, 25-35 fractions to a total dose of 60-70 Gy with 6MVX. Spinal cord was protected after 44-46 Gy using with MLC at lateral fields. The posterior servical lymphatic's dose was completed by 6-9 MeVé electron. Offline correction has been used in de Boer et al.'s and in many studies.[8-11,13]

Margins to be added to CTV to obtain PTV is 5-10 mm for RT of head and neck cancer in DEU-DRO - 3D CRT Protocol. It's similar with other studies[8,11] although there are differences between

tumor localization, organs at risk volume, RT indication (adjuvant/ radical) and immobilisation systems.[3,14] Especially immobilisation is a very important factor during the course of RT.[8,11,12,14] The patients' motions in the mask maybe increased due to the weight lose, the wearing mask during the RT. Many studies report on patient's immobilisation and describe different head and neck support system. In van Lin et al.'s study, two mask systems (standart versus customised head and neck support) have been compared. Set-up errors has been decreased with personalised equipment including neck support.[12] Willner et al. used dental bite block and non-customised neck support system for immobilisation.[13] Systematic errors are similar with our study. In Gilbeau et al.'s study, set-up errors in immobilisation from 3 fields were bigger than immobilisation from 4-5 fields.[8] Mitine et al. found larger systematic errors and much smaller random error values for head and neck patients immobilised in plastic masks.[15] They conclued that, set-up correction desicions based on a first-day image is an effective procedure, because the large systematic errors could be found with relatively high accuracy from such a single image. Not only set-up accuracy but also comfort level of patients, set-up time[16] and cost effectivity[17] are very important topics to decide choosing immobilisation system. Weltens et al. compared a plastic PVC cast and a thermoplastic cast and used a standart head and neck support.[18] They used EPI and magavoltage portal films and measured the set-up errors in craniocaudal (CC) and anterioposterior (AP) directions. Even systematic AP errors are similar, and CC measurements are better in our study. Thermoplastic head-and-shoulder mask system was compared with only head immobilisation mask in Rotondo et al's study. There were no significant differences between two systems about set-up accuracy.[16] Donato et al. assessed the cost of two different head and neck immobilization systems, and discussed that while displacements were slightly equal but one system of them was more expensive. [17] In our study orfit masks and personalised neck supports have been used.

In this study 210 EPI's have been planned to be measured, however only 93 have been evaluated.

Table 4
Set-up errors and accepted margins from different studies

	Systematic errors			Random errors		
	AP	CC	ML	AP	CC	ML
van Lin[12]*	2.3	2.3	2.2	1.6	1.6	1.4
	1	1	1.6	1.4	1.2	2
Mitine[15]	4.6	4.3	–	2	2.5	–
Willner[13]	2.7	2.5	3.1	–	–	–
Weltens[18]	3.6	3.4	–	2.1	2.1	–
DEUDRO	3.9	1.8	1.9	2.6	2.9	1

AP: Anterior-posterior; CC: Cranio-caudal; ML: Medio-lateral; *Two different mask systems have been compared.

The most frequent cause of this underachievement was high routine workload. The other causes were imaging and recording errors due to radiotherapy technicans Evaluation of the lower neck fields in the EPI's were very difficult because of the difficulty in finding reference bony landmarks. Seven EPI's for each field has been planned but only 3-7 EPI's were evaluated as in with some other studies.[9,13] Two observers have measured all EPI's in our study. Two observers have measured 186 points from 93 EPI's and interobserver variation were smaller than 3 mm in 85%. In Perera et al.'s trial this is smaller than 5 mm.[19] The variation between observers may decrease, if reference points are described very clearly.

Set-up errors (Table 2) and total standart deviations for each directions (Table 3) have been calculated. Systematic component of set-up error ($\sum$) in AP and STDAP was found larger than the other measurements. These influenced the "Margin" formula, and margin added to the PTV in AP direction. The distribution of the random displacements (Fig. 1) and scatter plot of systematic set-up displacement about AP-CC directions (Fig. 2) are shown that similar cumulative deviation as about 3 mm. So, in clinics which new user of the 3D CRT should be very careful while choosing the margin each directions. In Suzuki et al.'s study, the intrafractional organ motions and the interfractional set-up errors were analyzed for head and neck IMRT. The organ motions were determined as to

coordinates of the landmarks on the image. The set-up errors were defined as to bony landmarks on the portal imaging, and they adopted a PTV-margin of 5mm and a PRV-margin of 3mm for head and neck IMRT.[20]

Set-up errors and accepted margins from different studies are shown in Table 4.

CONCLUSIONS

Margins to be added for PTV have been found to be AP: 11.7 mm, CC: 6.6 mm ve ML: 5.8 mm in this study. Margins shoul not be equal in 3 directions. Set-up errors could be diminished with better immobilisation systems including the shoulders, education of the team, using spesific protocols and reporting the measurement data for different tumor localization. Conformal radiotherapy must be performed under optimal conditions and adequate experiences especially in new centers.

This study includes the head and neck cancer patients treated between July 2004-September 2005 in DEUDRO. These margins might be wide especially for IMRT, so nowadays PTV margins are efforted to reduce with better immobilization systems.

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