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International Journal of Radiology & Radiation Therapy

Research Article

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Determination of differences in dosimetry with and without intravenous contrast media for radiotherapy planning in the anatomical region of the head and neck

Abstract

In radiotherapy (RT), to determine the tumor volume (TV) and its morphology, computed tomography (CT) is used, acquiring images without and with intravenous iodinated contrast media (CM), where its influence has been poorly studied usually in artificial phantoms. Computerized dosimetries without and with CM from 10 CT of head and neck were analyzed using a before-after design. The same study group served as a control. Point doses and dose-area histogram (DAH) were evaluated, as well as a dose-volume histogram (DVH), using Student's t-test with 5% significance. Before and after administering CM, the average difference between point doses was –0.09% within the confidence interval (CI) 0.27% and –0.45%, with a standard deviation (SD) 0.52%. The average doses using DAH, resulted in a mean difference of 0.02%, within the 0.2% CI and -0.16%, with 0.27% SD. The standard volume within 100% of the dose utilizing DVH analysis resulted in an average of the differences of 0.1%, with CI 1.34% and –1.14% and SD 1.76%. The t-test of difference of means for paired designs, with α=0.05 found that there are no significant differences between the study and control groups for the different dose reading methods.

Keywords: dosimetry, radiotherapy, intravenous contrast, head, neck

Volume 8 Issue 4 - 2021

Pedro Hecht-López, Eduardo Parra-Villegas
Anatomy Laboratory, School of Medicine, Universidad de Tarapacá, Chile

Correspondence: Pedro Hecht-López, Anatomy Laboratory, School of Medicine, Universidad de Tarapacá, Arica, Av. 18 de Septiembre 2222, Arica, Chile, Tel +56582385777, Email pf.hecht@gmail.com

Received: October 26, 2021 | **Published:** November 17, 2021

Introduction

In radiotherapy (RT), the exact delimitation of the location and morphology of the tumor is critical when planning the treatment area, due to which the volume of tissues and organs to be irradiated is currently determined by computed tomography (CT) simulation. On the other hand, in diagnostic radiology, the use of intravenous iodinated contrast media (CM) in CT examinations has proven to be a good method to delineate the tumor volumen.[1]

Today, modern radiotherapy services take advantage of the CT using CM technique for radiation therapy planning. After which complex computer systems are used to process the images obtained by CT, and include in these the parameters of the treatment machines to predict the behavior of the radiation dose in the different tissues of the human body. In practice, it has been observed that in radiotherapy treatment plans for head and neck tumors, the delimitation of the irradiation zone is very critical, in the sense of irradiating only the pathological tissues to avoid toxicity in healthy tissues. Therefore, at present, tumor localization systems include the use of simulation by CT with CM, which differentiates tumor tissue better with respect to healthy tissue.[1] From these CT images, treatment planning is performed by a computer. The program (software) assigns a value of tissue density or electron density from the Hounsfield unit value (HU) in grayscale that is achieved through the CT study, to then simulate and evaluate the distribution of radiation when interacting with the different types of tissues and organs of the anatomical segment. The use of contrast medium results in a better delineation of the tumor volume, but with the problem of an artificial increase in the density of the tissue in which the drug is captured, which would produce a change in the dose distribution in the irradiated volume, distorting what actually occurs in radiation interactions in tissue with normal density. Although to date, the use of CM for treatment planning in radiotherapy has few studies that analyze its influence on the distribution of radiation doses, when performing clinical dosimetry, one must consider that, by concentrating this drug on the volume tumor by changing the density of the tissue, it is necessary to take into account a possible change in the distribution of the radiation dose.

In summary, it is necessary to state that in the local environment, it has been little studied if there are significant differences between the results delivered by treatment plans made with CM compared to plans made without CM. Therefore, the work protocol is to develop a treatment plan without CM to calculate the distribution of doses and monitor units (MU) and carry out a treatment plan with CM to delimit the tumor morphology and treatment volume. The present work seeks to contribute to the development of criteria for the use of CM in radiotherapy planning and obtain local information on the problem to optimize the planning procedure and the resources involved. The objective is to determine if there are significant differences between the dosimetry performed on tissue volume without CM and dosimetry performed on the same volume of tissue with CM in previously planned cases in the anatomical region of the head and neck. This is done through dosimetric analysis of point doses, dose-area histogram (DAH), and dose-volume histogram (DVH). As a working hypothesis, it was postulated that the use of CM allows a better visual delimitation of the anatomical structures and tumor morphology without significantly altering the distribution of the radiation dose in the RT treatment plan.

Materials and methods

Sample material

The sample corresponds to the CT images of 10 scan studies of the head and neck anatomical region performed without and with intravenous iodinated contrast medium. It was not discriminated

against according to the variables age and sex. The cases were rescued from a personal database consisting of dosimetry files for RT, planned between 1999 and 2001, from transverse anatomical sections by CT obtained in DICOM format and their volumetric reconstruction using a planning computer, configuring these data a previously unpublished national series, in addition to being original for the head and neck anatomical region.

Method

For each case studied by CT, the plans of the same anatomical region was rescued first without and then with CM, which were carried out by exactly reproducing the position of the anatomical segment in both series of tomographic sections, matching the locating lasers of a tomograph (Picker® pq 2000) with the reference alignment marks on the skin of the anatomical segment to be explored. The examinations were carried out at that time with the individual's informed consent. The CM used in the studies was Radiomiron® at a concentration of 300 mg/50 ml and a dose of 100 ml for a standard adult patient weighing approximately 70 kg. In the exploration protocol, the drug was administered by bolus injection with an automatic injector through a peripheral venous line in one of the patient's forearms. The delay in acquiring the images and the flow in the contrast injection was 2 to 3 ml/sec, selected in the automatic injector according to the type of examination to be performed and the morphological characteristics of the explored region, to achieve the best visualization of the vascularized anatomical structures or that capture CM. In each series, tomographic sections were made every 5 mm so that the entire field to be simulated as RT treatment was included, making sure that an area coincided with the entry mark of the radiation beam's central axis, considering it as the center of the TV. In addition, care was taken to program enough CT slices outside the treatment area so that the margins provided sufficient anatomical information and tissue densities for the subsequent volumetric dose calculation. Topograms (scout view) with the cutting lines in frontal and lateral projections were printed on the CT plates in order to check that the transverse (axial) sections coincided with the planned images. After each CT, the images were transferred through fiber optics, and later, using a Dicom 3.0 network, the information was retrieved at the Cadplan ® brand RT planner station. The program used was the treatment planning system (TPS) Cadplan-Dosetek® version 3.1.2 developed by the company Varian® Associates Inc., which can perform calculations of radiation dose distributions in three dimensions (3D), creating an electron density matrix. The mathematical calculation model used by the program was the "pencil beam convolution model or pencil beam kernel." The models used to correct inhomogeneities were "the generalized batho power-law model and the equivalent TAR model," depending on the type of X-radiation energy (XR) to be simulated. These factors correct the radiation dose distribution by considering the different electron densities of different tissues. The program's skin obliquity correction factor was calculated using the inverse squares law and the TAR/TMR ratio (Tissue air ratio/tissue maximum ratio). All cases were calculated with the highest possible sensitivity available in the software, using a "grid" (matrix or calculation mesh) of 1.25 mm wide between lines. Only studies of the head and neck anatomical region were rescued from the archive. The energies used to simulate the tissue's radiation interactions were X-rays of 6 MV (Mega Volt) and 20 MV.

After recovering the images using the Cadplan® software, in the "contouring" sub-program, the contours of the skin border of the scanned anatomical segments were digitized, by using the automatic option in both series of cuts, to Avoid operator-induced differences when attempting a manual drawing. To reconstruct a volume of tissue with known and reproducible characteristics to be used in the comparison of dosimetries, a standard quadrilateral was designed. In a simple planar image, this square had a known area (quadrilateral or pattern area) and susceptible to be studied in the irradiation field's central section, using a dose-area histogram (DAH). The same quadrilateral was designed in the cuts immediately superior and inferior to the image or central cut of the CT (in the planning called "central axis" or CAX), which later allowed to reconstruct in 3D and analyze a known and standard volume (volume or solid standard) by using a dose-volume histogram (DVH) after integrating the images through a volumetric calculation. It is worth mentioning that the third dimension given by the Z-axis in space corresponds in each scan to the value of the position in cm. of the CT slice when considering the position of the anatomical segment on the examination table of the scanner machine. All the cases simulated by the software were planned with the isocentric type treatment technique (maximum dose to the center of the TV), where the source isocenter distance was 100 cm ("Source to axis distance" SAD 100 cm). After locating the isocenter (spatial coordinates of the center of the TV), the treatment parameters to be simulated by computer were entered, such as radiation field limits, XR energy beam, etc.

In each case, first performed a dose calculation in the central section, normalized it by assigning 100% of the dose to the isocenter, which served as a parameter to contrast the dose value obtained at other points in the tissues. Once obtained the dose distribution in the central section, the entire explored anatomical segment's volumetric calculation was carried out. Took special care to verify that the integration of the calculation by the planning program was carried out in all the slices of each series in order to avoid loss of anatomical information from the peripheral tissue to the simulated irradiation field. To study the influence of CM on specific doses of the central section, the measurement was standardized in four peripheral control points to the isocenter, corresponding to the planar coordinates of the vertices of the standard quadrilateral. Once the positions of the control points were obtained, the dose value was recorded in each of them and they were printed together with the RT simulation parameters and dosimetry calculation. Subsequently, the average dose value of these points was used to make the comparison between the series without and with CM. Subsequently, the DAH of the standard quadrilateral was calculated in the central section of each scanned case to know the mean dose in its area. Then the values obtained in the dose statistics of the evaluated cut were recorded. The treatment plan was also printed in the central section, with graphs of dose distributions to tissues. For each case studied, the volumetric calculation allowed obtaining a DVH, where the value of the 3D solid volume was obtained within 100% of the radiation dose. To graph these results used the "cumulative" option. This graph was printed together with the volumetric dosimetry statistics, to compare the results between both series without and with CM. After reviewing the dose distribution impressions of all the cases, it was found that of an initial number of cases equal to twelve that had series without and with CM, two of them presented differences of 1 mm in the Z position value of the table (position in the longitudinal axis of the table or third dimension in the RT planner) between the series without and with contrast, at the time of acquiring the images. This motivated these cases to be eliminated from the study to avoid errors induced by the sampling. Due to the above, the number of cases in the study was reduced to n=10, which merited the use of the theory of small samples to perform the statistical analysis. After the recovery of the cases that make up the sample, the data obtained were tabulated and the results were analyzed.

Limitations

A limitation for the development of the study was the scarce and partly discrepant literature on the influence of the CM on RT planning during the years of implementation of the work protocol. On the other hand, a limitation for the development of this study was the time required to computationally process in the most sensitive and precise way possible the number of cases collected, since using the computer of that time for each of the series of images of each in this case, approximately 2 hours of mathematical calculation were allocated using the software.

Statistical analysis

This work is a retrospective analysis of a series of previously unpublished data from paired samples with a before-after design, where the same study group served as a control. As a hypothesis test, the Student's t distribution was used with a significance level of 5%. The mean difference test was used to determine statistically significant differences between the study group and the control group.

Results

The data obtained from the measurement of the dose readings, at different points peripheral to the isocenter in the central section, before and after the injection of CM, can be observed in Table I. These correspond to the average dose at standardized points in the plane of the central CT slice. The observed dose difference corresponds to the subtraction of the values after minus before the injection of CM.

Table I

Observing the absolute value of the differences shown in Table I, we can affirm that in 80% of the cases studied, the observed differences were less than or equal to 0.5%. It can also be observed that for the total number of cases, the differences between the study and control groups did not exceed 0.8% of the dose. Through the analysis of point doses in the central section, it was found that for the cases studied, the mean of the differences in the dose readings was –0.09% with a confidence interval of 0.27% and -0.45%, and a deviation standard (SD) of 0.52%.

Table 1 Evaluation of mean dose of points in the periphery of the isocenter in the standard quadrilateral, central section CAX

	Mean dose (%)		
Case	**Before (C-)**	**After (C+)**	**Diference***
1	71,50	71,20	-0,30
2	73,10	72,60	-0,50
3	77,10	77,60	0,50
4	87,70	88,40	0,70
5	80,00	79,50	-0,50
6	100,70	101,20	0,50
7	100,70	100,70	0,00
8	100,10	100,10	0,00
9	57,10	56,60	-0,50
10	50,70	49,90	-0,80
Mean	79,87	79,78	-0,09
SD	17,74	18,09	0,52

(C-; without contrast, C+; with contrast, *; after minus before, SD; standard deviation)

When performing the t test for difference of means in paired designs and obtaining t=-0.56 with α=0.05, no statistically significant differences were found between the study and control groups. To characterize the behavior of the dose in a standard area before and after the injection of CM, dose-area histograms were calculated in the central section of the treatment field in the series without and with CM. Table II shows the mean dose values in the standard area, obtained after the calculation in the central CAX section of the CT.

Table II

When analyzing the data presented in Table II and reviewing the absolute values of the differences, we can see that in 80% of the cases studied; the differences were less than or equal to 0.3% of doses. It can also see that in all the cases analyzed, the dose difference between both groups did not exceed 0.5%. Through the analysis with DAH, it was found that the mean of the dose differences was 0.02%, within the confidence interval of 0.2% and -0.16%, with a standard deviation of 0.27%. Employing the t-test for difference of means in paired designs, when obtaining the value t=0.25 with α=0.05, found no statistically significant differences between the study and control groups. After analyzing the influence of CM use in the central section, we proceeded to study the presence of this drug in a standard volume of known characteristics. Should remember that in current RT, the use of 3D volumetric calculations has gained importance, which allows a more precise relationship to the biological effect that the planned radiation doses will produce on the volumes that occupy organs or tissues of clinical interest.

The data on the behavior of the radiation dose in a standard volume are presented in Table III before and after the injection of intravenous iodinated CM.

Table 2 Evaluation of mean dose of the standard quadrilateral by DAH in the central CAX section

	Mean dose (%)		
Case	**Before (C-)**	**After (C+)**	**Diference***
1	99,40	99,50	0,10
2	99,60	99,60	0,00
3	100,50	100,60	0,10
4	100,30	100,30	0,00
5	100,20	100,20	0,00
6	100,70	101,00	0,30
7	100,50	100,30	-0,20
8	100,30	100,20	-0,10
9	99,90	99,40	-0,50
10	97,00	97,50	0,50
Mean	99,84	99,86	0,02
SD	1,08	0,97	0,27

(C-; without contrast, C+; with contrast, *; after minus before, SD; standard deviation)

Table III

The data presented in Table III show the behavior of the 100% radiation dose isodose and the volume it occupies within the standard solid before and after the injection of iodinated contrast medium.

Citation: Hecht-López P, Parra-Villegas E. Determination of differences in dosimetry with and without intravenous contrast media for radiotherapy planning in the anatomical region of the head and neck. *Int J Radiol Radiat Ther.* 2021;8(4):167–172. DOI: 10.15406/ijrrt.2021.08.00310

Table 3 Evaluation of percentage of the standard volume within 100% dose by DVH

	Standard volume within 100% (%)		
Case	**Before (C-)**	**After (C+)**	**Diference***
1	35,00	37,50	2,50
2	48,00	50,00	2,00
3	90,00	90,00	0,00
4	75,00	72,50	-2,50
5	80,00	80,00	0,00
6	53,50	55,50	2,00
7	90,00	89,50	-0,50
8	97,50	96,00	-1,50
9	50,00	48,00	-2,00
10	20,00	21,00	1,00
Mean	63,90	64,00	0,10
SD	26,23	25,29	1,76

(C-; without contrast, C+; with contrast, *; after minus before, SD; standard deviation)

After reviewing the table, it is observed that, considering the absolute values of the differences, for 50% of the cases studied, the dose difference is less than or equal to 1.5%.

It is important to note that in most cases studied (80% of the cases), the dose difference is less than or equal to 2%. We can also say that for all the cases studied by volumetric calculation, the difference in radiation dose before and after the contrast injection does not exceed 2.5% and that this difference was only registered in two of the cases studied.

When analyzing the sample by developing a DVH, it was determined that the mean of the differences between study and control groups was 0.1%, with a confidence interval of 1.34% and -1.14%, and with a standard deviation of 1.76 %.

When performing the t-test for difference of means in paired designs, after obtaining the value t=0.18 with α=0.05, no statistically significant differences were found between the study and control groups.

As an example of volumetric calculation for the same case before and after the injection of CM, the behavior of the radiation dose can be observed when comparing the DVH presented in Figure 1 and Figure 2, among which no important differences can be seen between both curves and 100% volume radiation dose integration.

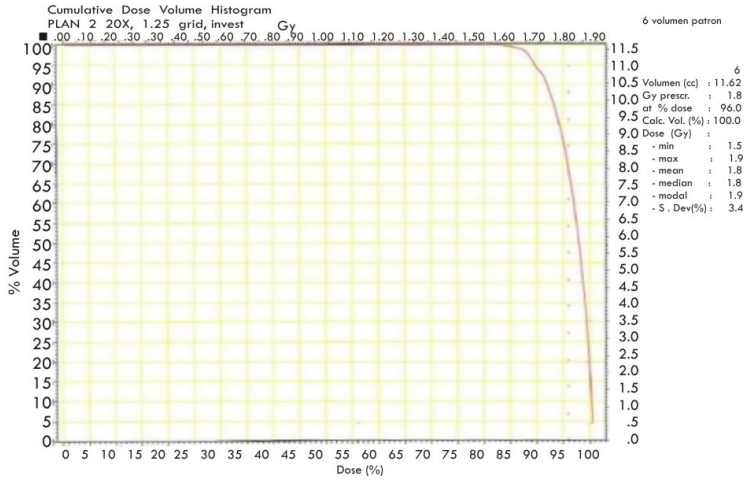

Figure 1 Example of DVH when performing dosimetry on a CT without CM for a case in the head and neck anatomical region.

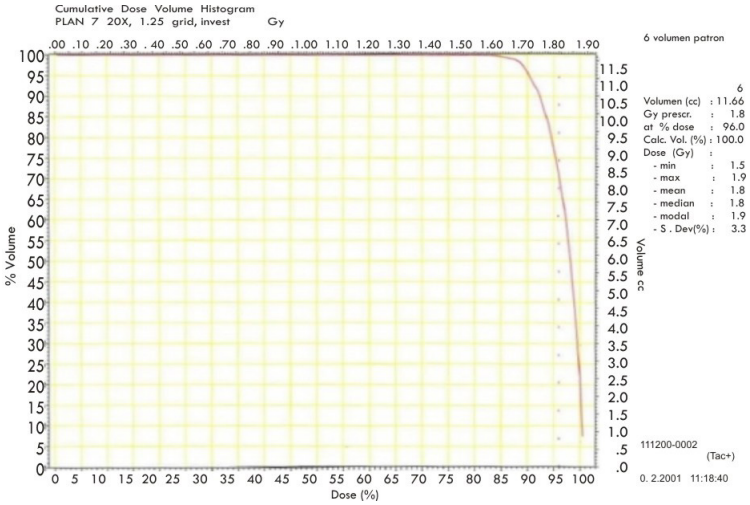

Figure 2 Example of DVH when performing dosimetry on a CT with CM for the same case of figure 1.

Citation: Hecht-López P, Parra-Villegas E. Determination of differences in dosimetry with and without intravenous contrast media for radiotherapy planning in the anatomical region of the head and neck. *Int J Radiol Radiat Ther.* 2021;8(4):167–172. DOI: 10.15406/ijrrt.2021.08.00310

Discussion

After analyzing the data obtained by registering the dose at points peripheral to the isocenter, DAH, and DVH, it is observed that the negative and positive differences are found at different frequencies when comparing the other radiation dose analysis techniques. Because found the reading points were far from inhomogeneity like air, we cannot say with certainty that the air present in anatomical structures of the head is the origin of the differences.

The same is valid in cases where the analysis was performed by DAH or DVH. The solid pattern was successfully integrated into all the images, either in the simple calculations in the CAX section or 3D volumetric calculations, so it is unlikely that the differences found to correspond to loss of volume or poorly integrated tissues in the calculation.

Minimal differences generated when entering the coordinates of the pattern solid in the CT slices cannot be ruled out, since, although these are the same in the coordinate axis system, it was observed that the location of a vertex of the pattern quadrilateral can coincide numerically with several pixels within one millimeter of the calculation grid (matrix or grid).

On the other hand, the dose, injection technique, and delay in the acquisition of images with CM were standardized by means of the protocols included in the software of the tomograph and automatic injector to perform specific examinations of the head and neck region by means of CT, for which it is It is unlikely that the differences found between the different cases derive from the imaging examination technique.

However, in some cases, the isocenter of the radiation beam was located near the skin surface, so it cannot be ruled out that the disturbances originating in the electron equilibrium region (buildup region) are the cause of the differences in readings dose, after applying the calculation model in the images obtained by CT before and after the injection of CM.

Likewise, differences caused by chance in the process of mathematical simulation of the electronic densities of tissues from the CT images cannot be ruled out, since the discrepancies registered were only consistent in the set of the three techniques of recording of dose in only one of the 10 cases analyzed.

To the above, we can add that the best correspondences regarding the behavior of the mean of the dose differences for each case were observed when comparing the results obtained by calculating DAH and DVH for the same anatomical segment explored.

The differences in radiation dose found in this study when comparing the data series without and with CM in each case did not exceed 2.5%. These results are consistent with the accuracy of the dosimetry for RT performed by the mathematical calculation algorithms used since the past decades.[2]

The results presented in this report oppose the 30% dose increase after CM injection, reported in a study carried out by CT study of brain tumors, in an experiment carried out in VX-2 rabbits.[3] Those discrepancies could be caused by the type and concentration of CM used in that research.

Another work has investigated the dose increase when irradiating brain tumors after injection of CM, by taking into account the generation of new photoelectrons, Auger electrons and XR in the tumor, product of the interaction of primary radiation with CM, using dose calculation through the Monte Carlo mathematical model.[4]

Consistent with the above, another article reports that using a CM bolus causes an overdose of 7.4% and 5.4% when using XR of 6 MV and 25 MV, respectively. However, since CM concentration and extent are somewhat low at the tissue level, the effect on dose calculation in treatment planning is negligible (1), which supports the results of our report.

On the other hand, a study that analyzes the effect of CM on the dosimetry of a 6 MV mega-voltage photon beam, when using a phantom found differences of the order of 7%, a value that differs from the increase in dose of 2.1% in the isocenter, reported in the same work when using the electron density data obtained by abdominal CT of 6 patients, considering it insignificant from the clinical point of view.[5]

This last dose value at isocenter is similar to that found in our results for dose readings. When considering the number of treatment fields to deliver the radiation dose before and after the addition of contrast medium to a phantom and then to a 5-patient CT series, an article describes that the dose difference is reduced as that the number of fields for treatment increases.[6] This supports the findings of the present work, where multiple treatment fields were used in most cases to form the dosimetry in the head and neck region.

A more recent article which used a design similar to the present work, including 11 cases of pelvic CT without and with contrast, showed that no statistically significant differences were found between the dosimetry plans before and after the CM, where the dose differences, relative mean dose and MU were less than 2% for any patient, when using photon energy of 20 MV.[7]

In summary, the differences found in the results of these studies may be due to factors such as the different CMs used, the administration technique and their particular concentrations in the different simulated tissues, either in animal models, CT of human patients, or in artificial phantoms that reproduce anatomical regions such as the thorax, abdomen or pelvis.

Due to the above, to clarify the current effect of the use of CM in the planning of dosimetry for RT, it is suggested that new investigations are necessary to verify the findings of the present work and its practical application to optimize clinical dosimetry and planning of RT in the anatomical region of the head and neck.

Conclusion

The use of CM allows a better visual delimitation of the anatomical structures without significantly altering the distribution of radiation doses in an RT plan when using computer simulation on images obtained by CT of the anatomical region of the head and neck. New investigations with modern computerized planning systems and updated mathematical calculation models are recommended to confirm the findings of this work in the anatomical region of the head and neck.

Acknowledgments

None

Conflicts of interest

There is no conflict of interest.

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