Comparison between irradiated lung volumes with two-dimensional and three-dimensional conformal radiotherapy techniques for locally advanced lung cancer*

Comparação entre os volumes pulmonares irradiados com técnica bidimensional e tridimensional conformada na radioterapia de pacientes com tumores de pulmão localmente avançados

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Abstract OBJECTIVE: To compare and quantify irradiated lung volumes using two-dimensional (2D) and three-dimensional (3D) conformal planning for radiotherapy in the treatment of lung cancer. MATERIALS AND METHODS: 2D and 3D conformal radiotherapy plannings were performed for 27 patients with lung cancer. Prescribed doses ranged from 45 to 66 Gy. The analysis covered the doses to planning target volume (PTV), gross tumor volume (GTV) and lungs (lung volume receiving 20 Gy or 30 Gy – V20 and V30, respectively, and mean dose). The doses to adjacent organs at risk (spinal cord, esophagus and heart) were maintained below the tolerance limits. RESULTS: GTV ranged from 10.5 to 1,290.0 cm^3 (mean, 189.65 cm^3). On average, a total of 59.33 fields were utilized in the 2D planning and 75.65 fields in the 3D planning. Lung volumes were significantly preserved ($P < 0.05$) with the 3D conformal planning in all the evaluated cases, with about 15% decrease in the irradiated lung volumes. Lungs without tumor were most benefited from this technique. CONCLUSION: 3D radiotherapy allowed a better sparing of the lungs, both in cases of early and advanced tumors. 3D radiotherapy should be used in the treatment of patients with lung cancer, even in cases of large tumors.
Keywords: Lung cancer; Radiotherapy; Conformal radiotherapy; Organs at risk; Lung volumes.

Resumo OBJETIVO: Comparar e quantificar os volumes pulmonares irradiados utilizando planejamentos bidimensional (2D) e tridimensional (3D) conformado na radioterapia de tumores de pulmão. MATERIAIS E MÉTODOS: Em 27 pacientes portadores de câncer de pulmão foi feito planejamento 3D e outro correspondente em 2D. As doses prescritas variaram de 45 a 66 Gy. Foram avaliadas as doses no volume alvo planejado (PTV), volume tumoral macroscópico (GTV) e pulmões (volume de pulmão que recebe 20 Gy ou 30 Gy – V20 e V30, respectivamente, e dose média). Os órgãos de risco adjacentes (medula espinhal, esôfago e coração) receberam doses abaixo dos limites de tolerância. RESULTADOS: O GTV variou de 10,5 a 1.290,0 cm^3 (média de 189,65 cm^3). Nos planejamentos 2D foi utilizado, em média, um total de 59,33 campos, e nos planejamentos 3D, 75,65 campos. Em todas as situações analisadas houve significante ($P < 0,05$) preservação dos volumes pulmonares com o planejamento 3D, com diminuição de cerca de 15% dos volumes irradiados. O pulmão sem tumor foi mais beneficiado. CONCLUSÃO: A radioterapia 3D permitiu maior preservação dos pulmões, tanto para tumores iniciais quanto avançados. A radioterapia 3D deve ser utilizada nos pacientes com tumores de pulmão, mesmo que volumosos.
Unitermos: Câncer de pulmão; Radioterapia; Radioterapia conformada; Órgãos em risco; Volumes pulmonares.

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INTRODUCTION

Lung cancer, besides being the first in incidence, is also accountable for most cancer-related deaths in the world[1,2].

In Brazil, estimates for 2008 indicate lung cancer as the second in incidence among men and fourth among women, with 17,810 expected new cases for men (incidence of 19 cases/100,000 men) and 9,460 for women (10 cases per 100,000 women)[3].

Lung cancer is mainly related to smoking, which may cause other pulmonary diseases such as chronic obstructive pulmonary disease and emphysema. Therefore, patients with lung cancer may in general present underlying lung function impairment. Besides allowing a safer dose escalation, three-dimensional conformal radiotherapy (3DCRT) allows an appropriate evaluation of treatment volumes and irradiated healthy tissue. In the treatment of lung tumors, this characteristic is particularly useful, mainly with respect to a greater sparing of the lungs, which are organs highly sensitive to radiation, and which may already be partially compromised in these cases.

In general, the incidence of locally advanced tumors (stage III) is high, and this group of patients is the one that has the main indication for radiotherapy, both as a curative as well as palliative treatment[4–6]. Additionally, the current standard treatment is associated with chemotherapy, which, in spite of better results, may also increase the treatment toxicity[4–6]. Due to the fact that such tumors are many times large pulmonary masses, the advantages of the three-dimensional (3D) over the conventional two-dimensional (2D) treatment may seem to be of little significance. Also, the large patient demand of the local public radiotherapy services in association with the larger workload and required planning time for 3DCRT, may lead to a lesser use of this tool in such cases.

Therefore, it is important to evaluate and quantify the benefits that 3DCRT brings comparatively with the 2D technique, with special regard to healthy tissues sparing.

The present study was performed to compare 2D and 3D radiotherapy in the treatment of lung tumors, quantifying the irradiated pulmonary volumes.

MATERIALS AND METHODS

Radiotherapy plannings of 27 patients with lung cancer submitted to conformal 3DCRT were evaluated. Volumes delineation was made on mediastinal and lung windows. Prescribed doses ranged from 45 to 66 Gy (1.8 to 2 Gy/day). For the same prescription and for each particular case, a conventional 2D planning was also simulated, based on computed tomography (CT) images.

The plannings were based on the recommendations from ICRU reports No. 50 and 62[7,8], considering at least 95% of the planned target volume (PTV) covered by 95% of the prescribed dose as appropriate. The 3D plannings were individualized and performed in two phases, with fields' reduction or new planning after 40 or 45 Gy, or in a single phase, depending upon clinical indication and dose received by the spinal cord. The 2D plannings were developed in two phases, the first one with two parallel and opposed fields, anteroposterior and posteroanterior (AP-PA) up to 40 or 45 Gy and following that, dose supplementation with protection of the spinal cord, in oblique parallel and opposed fields or two to three angled fields. Four patients received total dose of 45 Gy and were planned in a single phase. Doses to organs at risk — spinal cord, esophagus, heart and lungs — were kept below the tolerance limits, in accordance with Emami et al.[9] and Milano et al.[10] recommendations.

The following parameters were evaluated for comparison of the plannings in relation to the lungs: gross tumor volume (GTV), total number of fields, percentage of lung volume receiving 20 Gy (V20), percentage of lung volume receiving 30 Gy (V30) and mean dose (MD) to the lungs[11]. These parameters were calculated by means of dose-volume histograms for both lungs (total lung), and respectively, for the lung with tumor and for the lung without tumor ("healthy").

The 3D planning system Eclipse (Varian Medical Systems; Palo Alto, USA) was utilized for structures delineation and calculations.

The data were submitted to descriptive and frequency analysis. The data means were compared by means of the Student t test. In order to evaluate the interference of tumor volume in the planning quality, the patients were divided into two groups according to GTV: up to 125 cm³, and > 125 cm³. This value was chosen considering initial tumors, those presenting a maximum diameter of 5 cm, versus the remaining ones above 5cm in diameter, considered as locally advanced. The significance level was set at 5% ($P \leq 0.05$).

RESULTS

The GTV ranged from 10.5 to 1290.0 cm³ (mean, 189.65 cm³). Grouping the patients according to the GTV, 13 patients presented GTV $\leq$ 125 cm³ (mean, 62.94 cm³) and 14 patients presented GTV > 125 cm³ (mean, 307.36 cm³) ($P = 0.0001$).

On average, 59.33 fields (median, 60, ranging from 50 to 74 fields) were utilized in the 2D plannings; two fields/day, respectively in the first and second phases. In the 3D plannings, the average number of fields was 75.65, ranging from 50 to 112 (mean, 80) with a mean of 2.6 fields in the first phase and 2.9 in the second phase, respectively.

Tables 1 to 4 present the results from data regarding doses to lungs.

Both irradiated volumes and mean doses were significantly lower when 3DCRT was utilized, independently from the volume of the GTV (Tables 1 and 2). With the exception of V20 and the mean dose to the healthy lung for initial tumors, all the other evaluated parameters presented significant absolute benefit in favor of 3DCRT. The observed benefit was even greater for larger volume tumors when compared with the initial tumors (Tables 3 and 4).

Figures 1 and 2 present the comparative dose-volume histograms of the studied pulmonary volumes, respectively for a tumor considered as a small one, and a large one.

DISCUSSION

The advent of conformal 3DRT based on CT images, allowed both the tumor and

Table 1 Comparison between the 2D and 3D plannings. The mean values of each variable are presented analyzing both lungs as a single organ (total lung) or separated (lung with tumor and without tumor respectively).

	Parameter	2D planning	3D planning	P
Total lung	V20 (%)	26.22	23.09	0.0001
	V30 (%)	22.06	18.06	0.0001
	MD (cGy)	1652.78	1427.78	0.0001
Lung with tumor	V20 (%)	51.18	44.81	0.0001
	V30 (%)	45.76	38.19	0.0001
	MD (cGy)	2894.13	2440.86	0.0001
Healthy lung	V20 (%)	6.83	4.8	0.006
	V30 (%)	3.88	1.82	0.0001
	MD (cGy)	486.84	450.79	0.001

2D, conventional 2D radiotherapy; 3D, conformal 3D radiotherapy; V20, percentage of lung volume receiving 20 Gy; V30, percentage of lung volume receiving 30 Gy; MD, mean dose.

Table 2 Comparison between 2D and 3D plannings considering GTV.

	Parameter	GTV ≤ 125 cm³	P	GTV > 125 cm³	P
Total lung	V20 (%)				
	2D	24.99	0.006	27.06	0.0001
	3D	22.98		23.18	
	V30 (%)				
	2D	21.78	0.001	22.31	0.0001
	3D	17.73		18.37	
	MD (cGy)				
	2D	1486.78	0.003	1806.92	0.0001
	3D	1366.65		1484.53	
Lung with tumor	V20 (%)				
	2D	48.50	0.0001	53.67	0.0001
	3D	42.97		46.52	
	V30 (%)				
	2D	42.61	0.001	48.69	0.0001
	3D	35.75		40.46	
	MD (cGy)				
	2D	2613.38	0.0001	3154.83	0.0001
	3D	2248.84		2619.16	
Healthy lung	V20 (%)				
	2D	6.04	0.417	7.57	0.001
	3D	5.03		4.58	
	V30 (%)				
	2D	3.28	0.011	4.44	0.015
	3D	1.62		2.00	
	MD (cGy)				
	2D	365.18	0.410	599.81	0.002
	3D	457.41		444.65	

GTV, gross tumor volume; 2D, conventional 2D radiotherapy; 3D, conformal 3D radiotherapy; V20, percentage of lung receiving 20 Gy; V30, percentage of lung volume receiving 30 Gy; MD, mean dose.

Table 3 Mean values of the absolute benefit obtained with the conformal 3D technique in relation to irradiated pulmonary volumes (mean GTV = 189.65cm³) ($P < 0.05$).

Benefit with 3D	V20	V30	MD
Both lungs	11.94%	18.13%	13.61%
Lung with tumor	12.45%	16.54%	15.66%
Healthy lung	29.72%	53.09%	7.40%

3D, conformal 3D radiotherapy; V20, percentage of lung volume receiving 20 Gy; V30, percentage of lung volume receiving 30 Gy; MD, mean dose.

Table 4 Mean values of absolute benefit obtained with the conformal 3D technique in relation to irradiated pulmonary volumes according to GTV (≤ 125 cm^3 or > 125 cm^3).

Benefit with 3D	V20	V30	MD
Mean GTV = 62.94 cm^3			
Both lungs	8.04%	18.59%	8.08%
Lung with tumor	11.40%	16.10%	13.95%
Healthy lung	16.72%*	50.61%	−25.26%*
Mean GTV = 307.36 cm^3			
Both lungs	14.34%	17.66%	17.84%
Lung with tumor	13.32%	16.90%	16.98%
Healthy lung	39.50%	54.95%	25.87%

3D, conformal 3D radiotherapy; V20, percentage of lung receiving 20 Gy; V30, percentage of lung receiving 30 Gy; MD, mean dose.
* Non significant differences. In the case of mean dose in the normal lung, there was an increase of 25.26% between the means with 3D, however not significant.
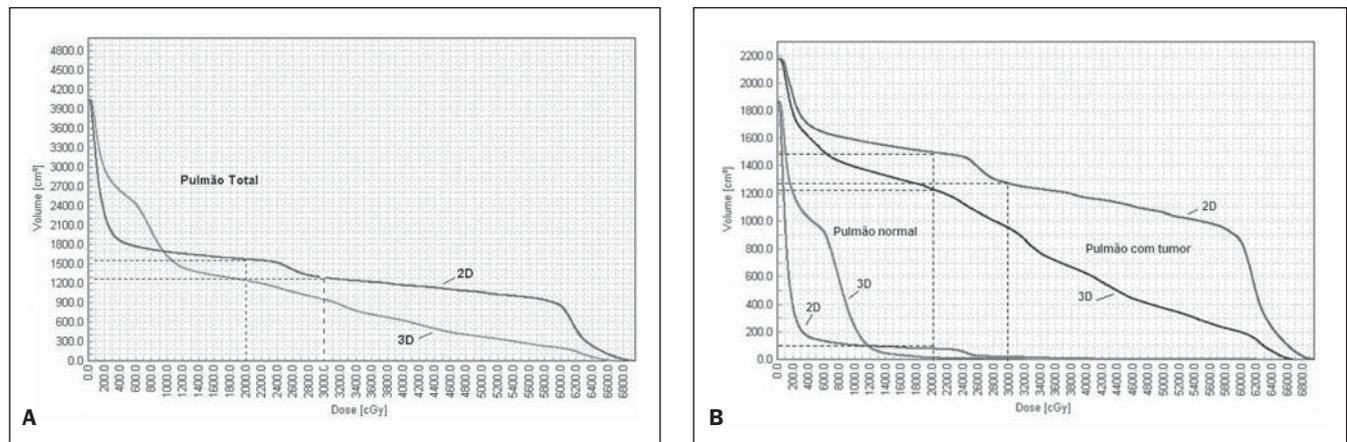
Figure 1. Dose-volume histogram of the lungs for a 49 cm^3 tumor, with the respective V20 and V30 marked. **A:** Total lung. **B:** Lung with tumor and healthy lung.
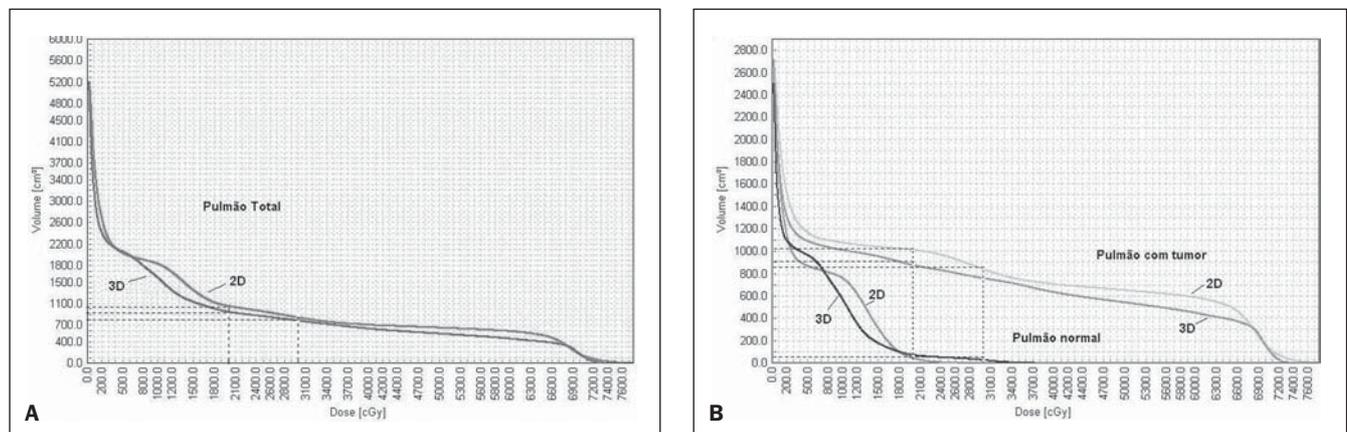
Figura 2. Dose-volume histogram of the lungs for a 183 cm^3 tumor, with the respective V20 and V30 marked. **A:** Total lung. **B:** Lung with tumor and healthy lung.

normal structures to be visualized and identified with higher accuracy in patients submitted to radiotherapy. The possibility of greater technical variations such as the use of several angled fields, non-coplanar fields and mainly the quantification of dose delivered to a given organ or tissue volume by means of the dose-volume histograms have consolidated the method that is currently widely used. In Brazil, this technology is already available in many centers, including the public health services. However, 3D planning is more time consuming for the radiation oncologist and the physicist, due to greater detailing in the delimitation of the target-lesion and structures at risk, and increased planning possibilities. In centers with a high demand, many times

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the benefit of a 3D planning may be questioned, particularly in the case of patients with advanced tumors, or those that should only receive a palliative treatment.

Furthermore, the actual benefit of 3DCRT in relation to survival of patients with lung cancer is not yet well established. Its' main advantage is the evaluation and possibility of decreasing or preventing the potential radiotherapy toxicity, on an individual basis[12]. For this reason, only from the advent of this technology innumerable studies on dose escalation[13–17] are being developed, in association or not with more advanced techniques such as image-guided radiotherapy (IGRT)[18], respiratory gating or breath-holding radiotherapy[19], hypofractionated radiotherapy[20] or still, the association with functional diagnosis methods such as positron emission tomography (PET), that allows a more accurate identification of the target volume[21].

The present study did not intend to discuss the lung tolerance doses, but to evaluate and quantify the benefit of 3DCRT for a group of patients with lung cancer undergoing treatment at the institution.

In spite of maintaining the same prescription doses utilized in the 2D plannings, 3DCRT provided a greater sparing of the lungs in practically all situations, specially the healthy lungs. Such benefit may be even greater, considering that the 2D planning was the best possible, as it was carried out in a 3D planning system, based on CT images, and not on plain simulation radiographs. However, even with a significant decrease of irradiated pulmonary volumes with 3DCRT (V20 and V30), the increase in the number of fields may lead to an increase of volumes receiving low doses, particularly for smaller tumors (Figure 1). Therefore, the evaluation of the mean dose is of great value in such situations, for analyzing each case individually.

The possibility of reduction of field margins by itself, besides the construction of individualized shielding blocks, increases the protection to healthy tissues, with appropriate target coverage in the 3D planning. When the PTV is subtracted from the pulmonary volume, the results in relation to the lungs sparing would be even better. Notwithstanding, the worst possible situation was analyzed, considering the

whole "useful" volume of the lung. In the simulations that were made, the field margins were equal, and we have chosen to compare patients regarding only the GTV, since it is better defined in a 2D planning than the PTV, and can be easily estimated on a diagnostic CT. With this type of analysis it was possible to observe an absolute reduction of irradiated lung volumes of about 15%, independently of the tumor size (Table 3). In patients for whom the dose escalation becomes more complex due to irradiation of large volumes of healthy tissue, the decrease in toxicity is a key issue. This fact may be of particular advantage in cases of patients with impaired pulmonary function, where chemotherapy may be associated.

The sparing of other organs at risk (esophagus, spinal cord and heart) was not evaluated in the present study, as it was possible to keep the doses for these organs below their tolerance limits, even on the 2D plannings. Additionally, both the esophagus and spinal cord are organs whose tolerance doses depend very little on the respective irradiated volumes and the dose in the heart may vary significantly according to the lesion location. The lungs, however, object of the present study, present tolerance doses much lower than those of the surrounding organs at risk[7,8].

Finally, specifically in Brazil, the number of fields that were utilized does not invalidate the technique regarding its use in the public health services, as most of the times it falls within the limits established by the Brazilian public health system ("Sistema Único de Saúde") (maximum of 90 fields)[22] for reimbursement of treatments.

CONCLUSIONS

3DCRT allowed the sparing of approximately 15% of the irradiated pulmonary volumes, both in the cases of initial and advanced tumors.

The benefit was greater for the lung without tumor, which can be better spared by the appropriateness of the irradiation technique.

The possibility of greater sparing of pulmonary volumes at the observed levels, supports the conclusion that 3DCRT

should be utilized in patients with lung tumors, regardless of size.

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